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Rapid Fire 1-Basic Science

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Epac1-mediated RE/mitochondria interactions promotes mitochondrial Ca2+ overload and cell death during ischemia/reperfusion injury

L Fazal[1]; M Laudette[1]; S Paula-Gomes[1]; J Fauconnier[2]; J Mialet-Perez[1]; F Lezoualc'h[1]
[1]Institute of Cardiovascular and Metabolic Diseases, Toulouse, France; *[2]University of Montpellier, Montpellier, France*

Introduction: It is well accepted that ischemia/reperfusion (I/R) injury is accompanied by an increase in mitochondrial Ca2+ that triggers the opening of mitochondrial permeability transition pore (MPTP), the subsequent depolarization of the mitochondrial membrane potential ($\Delta\Psi m$), leading to cardiomyocyte death. However, the mechanisms that control mitochondrial Ca2+ entry in that context are far to be understood. Having shown that the cAMP binding protein Epac1 contributes to I/R injury, we therefore addressed whether Epac1 would play a role in such a process.
Purpose: To investigate the role of mitochondrial exchange protein directly activated by cAMP 1 (Epac1) in ischemia/reperfusion injury.
Methods: Isolated adult cardiomyocytes from Epac1 knock-out (KO) and wild-type (WT) littermates were exposed to hypoxia (HX) for 4h followed by a 2h of reoxygenation period (HX+R). Cell death was determined by Trypan blue staining and LDH release. MPTP opening was monitored by the calcein loading CoCl(2)-quenching technique. Mitochondrial Ca2+ uptake was measured with Rhod-2-AM fluorescent dye.
Results: Our data showed that HX+R induced a decrease in calcein fluorescence corresponding to MPTP opening in WT cardiomyocytes. Genetic deletion of Epac1 prevented MPTP opening in HX+R conditions. In addition we found that Epac1 was expressed in mitochondria and its activation induced a robust increase in mitochondrial Ca2+ accumulation in WT cardiomyocytes but not in those of Epac1-/- cardiomyocytes. Furthermore, treatment of Epac1-/- cardiomyocytes with 50 μM Ca2+ induced much less mitochondrial Ca2+ overload compared to WT suggesting that Epac1 regulates Ca2+ entry into the mitochondria. During ischemia, Epac1 favors Ca2+ exchange between the endoplasmic reticulum (ER) and the mitochondrion, by increasing interaction with VDAC1/GRP75/IP3R1 protein complex leading to mitochondrial Ca2+ overload and opening of the MPTP.
Conclusion: Epac1 regulates different aspects of mitochondrial function such as Ca2+ uptake and MPTP opening. Our findings suggest Epac1 as a promising target for the treatment of ischemia- induced myocardial damage.

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Intramyocardial delivery of mesenchymal stem cells transfected with minicircle-HIF-1a decreases LV adverse remodelling via release of cardioprotective miRNAs and pro-angiogenic factors

EG Edit Gara[1]; SG Ong[2]; J Winkler[3]; K Zlabinger[3]; D Lukovic[3]; A Jakab[3]; B Merkely[1]; JC Wu[2]; M Gyongyosi[3]; N Pavo[3]
[1]Semmelweis University, Heart Center, Budapest, Hungary; *[2]School of Medicine, Stanford Cardiovascular Institute, Stanford, United States of America*; *[3]Medical University of Vienna, Department of Cardiology, Vienna, Austria*

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Background: Intracoronary and intramyocardial autologous or allogeneic mesenchymal stem cell (MSC) therapy for treatment of acute and chronic ischemic heart disease has shown promising results in preclinical and early clinical trials mainly via the rich paracrine effects of MSCs, in spite of low cell retention rate. Hypoxia-inducible factor-1α (HIF1α) is one of the most powerful anti-ischemic factor, modulating over hundreds of angiogenic and regenerative substances.
Purpose: In order to enhance the paracrine anti-ischemic and anti-remodelling efficacy of the cell therapy, porcine allogeneic MSCs were transfected with virus-free minicircle plasmid driving HIF1α transgene (MSC-MiCi-HIF1α).
Methods: Domestic male pigs (n=16) underwent closed-chest reperfused acute myocardial infarction (MI) via balloon-occlusion of the mid-LAD for 90 minutes, followed by reperfusion. One month later (chronic ischemic left ventricular remodelling), the animals were randomized to receive either MSCs alone (n=6) or MSC-MiCi-HIF1α (n=10) (15 ± 3 x10^6 cells). Cells were injected into the border zone of infarction by using the 3D guided NOGA electro-anatomical mapping system (9 ± 1 locations). One animal at 3, 12, 24 hr, and 1 week of the MSC-MiCi-HIF1α group was harvested to prove the HIF1α expression and early angiogenesis in the heart. Magnetic resonance imaging with late enhancement was performed in the surviving 6 animals of each group. Angiogenesis proteome profiling were performed and RT-PCR quantified mRNA (Angiopoietin-2, VEGF-A, CD31) and miRNA (miR-1, miR-24, miR132) expressions. Immunohistology sections were stained with anti-caspase-3 antibody and apoptosis rate was quantified.
Results: Success of transfection procedure was confirmed by Western blots of the cell culture medium, showing HIF1α expression. Proteome profiling of the short-term follow-up hearts revealed upregulation of angiogenesis-related protein expressions (angiopoietin, endoglin, VEGF-A and TGF-alpha) up to 12 hr post-delivery, while the angiogenetic apelin expression increased after 12 hr. Anti-hypertrophic miR-1, pro-angiogenic miR-132, and anti-fibrotic miR-24 levels were increased in response to MSC-MiCi-HIF1α treatment (fold-changes vs control: 7.51 ± 0.61 miR1, 23.01 ± 4.87 miR132, and 6.50 ± 2.95 miR24) between 12 and 24 hr post-transfected cell injections. MSC-MiCi-HIF1α delivery resulted in moderate improvement of LV ejection fraction, and reduced infarct size and LV end-diastolic volume (111 ± 17 vs 133 ± 16 mL, $p<0.05$) at 1 month post treatment. Apoptosis in infarct border zone also decreased after MSC-MiCi-HIF1α delivery (fold-change vs control: 0.75 ± 0.07).
Conclusions: In a pre-clinical translational model of chronic post-infarction heart failure, therapy combining MSCs transfected with minicircle plasmid expressing HIF1α significantly decreases infarct size and improves adverse remodelling via modulation of angiogenic and antifibrotic processes of the heart.

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Prophylactic combined heart failure treatment attenuates the development of doxorubicin induced systolic and diastolic dysfunction in rats

M Lodi[1]; D Priksz[2]; GA Fulop[1]; J Kocsis[3]; I Edes[4]; I Czuriga[4]; Z Kisvarday[5]; B Juhasz[2]; A Toth[1]; Z Papp[1]; D Czuriga[4]
[1]University of Debrecen, Faculty of Medicine, Division of Clinical Physiology, Debrecen, Hungary; *[2]University of Debrecen, Faculty of Medicine, Institute of Pharmacology and Pharmacotherapy, Debrecen, Hungary*; *[3]University of Debrecen, Faculty of Medicine, Institute of Oncology, Debrecen, Hungary*; *[4]University of Debrecen Medical Center, Institute of Cardiology, Debrecen, Hungary*; *[5]University of Debrecen, Faculty of Medicine, Department of Anatomy, Histology and Embryology, Debrecen, Hungary*

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Background: Doxorubicin (DOX) is a widely used chemotheraputic agent with well recognised cardiotoxic side effects. High doses of DOX are frequently used to induce cardiomyopathy in experimental animal models of heart failure (HF). However, less data are available regarding the cardiotoxicity of therapeutic doses of DOX, analogous with human oncotherapy.
Purpose: Our aim was to establish a rodent model of cardiomyopathy demonstrating early myocardial injury induced by repeated iv. DOX injections, with concentrations (ccs) extrapolated from consecutive cycles of DOX chemotherapy applied in cancer patients. In addition, we tested prophylactic and delayed combined HF therapies in order to prevent DOX induced adverse myocardial changes.
Methods: We used 12-week-old male Wistar rats in our study and divided them into 4 subgroups. Blood pressures (BP) and heart rate (HR) were monitored during the

study by the tail-cuff method. DOX ccs were calculated from human doses of existing chemotherapy protocols and were corrected to the body surface of rats. Effective DOX doses were validated by in vitro electron microscopic measurements. Following baseline echocardiography, animals in the prophylactic group received a daily combination of oral bisoprolol (2.5 mg/kg), perindopril (2 mg/kg) and eplerenone (6.25 mg/kg) before (PRE), while those in the post-exposure group 1 month after DOX treatment (POST). Drugs were applied in a mucous vehicle by oral gavage. Positive controls received both DOX treatment and drug-free vehicle (D-CON), while negative controls received drug-free vehicle only (CON). DOX exposure was carried out by administering 1.5 mg/kg iv. DOX into the tail veins of the animals on 6 occasions. Follow-up echocardiography was carried out 1 and 2 months after the DOX treatment.

Results: Systolic and diastolic BP, as well as HR were significantly lower in the PRE group, compared to all other groups. Follow-up echocardiography revealed a gradually reducing ejection fraction (EF) in the D-CON and POST animals over the 2-month-period compared to CON (64.3 ± 3.5 and 67.4 ± 4.7% vs. 72.4 ± 3.2%, respectively, $p = 0.0001$), while the prophylactic treatment prevented any significant drop in the EF in the PRE group (79.2 ± 6.4%). At 2 months, a restrictive filling pattern was observed in the D-CON and POST groups but not in the CON and PRE animals. DOX induced a significant increase in the isovolumetric relaxation time, which could not be attenuated by either the PRE or POST treatment.

Conclusions: We successfully established a rodent model to examine the cardiotoxic side effects of DOX chemotherapy. Prophylactic, but not post-exposure supportive treatment was capable of attenuating the DOX induced systolic and diastolic dysfunction. This model seems eligible for future investigations to further elucidate cardiotoxic side effects of DOX, as well as for the development of early drug intervention protocols to eliminate myocardial injury induced by DOX chemotherapy.

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NPA7, an innovative multivalent designer natriuretic peptide: Co-therapy with Furosemide to mediate renoprotection in experimental ADHF

LMG Meems[1]; Y Chen[1]; GJ Harty[1]; GE Harders[1]; BK Huntley[1]; SR Iyer[1]; DM Heublein[1]; JC Burnett Jr[1]
[1]*Mayo Clinic, Cardiovascular Disease, Rochester, United States of America*

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Acute decompensated heart failure (ADHF) is a heart failure syndrome with high morbidity and mortality. Current initial therapy focuses on relief of signs and symptoms using diuretics, such as Furosemide (FURO). Diuretic therapy however may induce Cardiorenal Syndrome, which itself is a predictor of mortality and worse outcome. This warrants novel therapeutic strategies to protect the heart and kidney. We have previously reported the engineering of a highly novel multivalent cardiorenoprotective designer peptide that we call NPA7. In this study we test the renoprotective properties of NPA7 in a large animal model of ADHF compared with FURO. We furthermore investigate the actions of NPA7 and FURO co-therapy including the importance of NPA7 pre- or post-therapy, and hypothesized that the timing of NPA7 treatment is an important factor in obtaining maximal renoprotection. Ten male mongrel canines were paced at 240 beats per minute for 10 days. On day 11, canines randomly received 45 minutes infusion of NPA7 (8.66 pmol/L) or FURO (1mg/kg), followed by NPA7 + FURO or FURO + NPA7 co-therapy respectively. Hemodynamic parameters were monitored and continuous urines were collected. Results are presented as mean baseline changes ± standard deviation.

In canines with ADHF, NPA7 decreased systemic vascular resistance (SVR) (-9.6 ± 1 mmHg/L/min, $p < 0.001$) and reduced pulmonary capillary wedge pressure (-3.5 ± 0.1 mmHg, $p < 0.05$) while increasing renal blood flow (RBF) (+25 ± 3 mL/min, $p < 0.05$). Secondly, NPA7 increased urinary flow (UV) (+0.08 ± 0.02 mL/min, $p < 0.01$) and urinary sodium excretion (UNaV) (+24 ± 17 μEq/min, $p < 0.05$), albeit it to a lesser extent than FURO (NPA7 vs. FURO UV: +0.3 ± 0.2 vs +2.5 ± 0.8 mL/min,$p < 0.05$; UNaV: 26 ± 60 vs 246 ± 90 μEq/min, $p < 0.05$). In contrast to NPA7, FURO lacked vasodilatory actions (NPA7 vs. FURO SVR: -2.0 ± 1.0 vs. +2.0 ± 1.1 mmHg/L/min, $p < 0.05$), impaired kidney function (NPA7 vs. FURO estimated glomerular filtration rate (eGFR): 18 ± 5.0 vs. -2.1 ± 5.3 mL/min, $p < 0.05$) and activated the renin-angiotensin-aldosterone system (RAAS) (NPA7 vs FURO plasma Angiotensin II: -56 ± 22 vs. +85 ± 48, $p < 0.05$ pg/mL; plasma Aldosterone: -13 ± 3.4 vs 1.2 ± 3.6 ng/dL, $p < 0.05$). Importantly, NPA7 + FURO co-therapy had synergistic natriuretic and diuretic efficacy while preserving RBF and eGFR, which was not observed with FURO followed by NPA7 infusion.

In conclusion, in experimental ADHF, NPA7 is a vasodilatory therapeutic with cardiac unloading, diuretic and natriuretic actions. FURO is more diuretic, but is associated with significant renal impairment, vasoconstriction and RAAS-activation. In addition, pre-treatment with NPA7 enhances natriuresis and diuresis while preserving kidney function. Priming with NPA7 may therefore represent a novel renoprotective strategy for treatment of ADHF. Importantly, this study underscores the need for future studies assessing the impact of timing of diuretics on treatment effects of novel therapies in patients with ADHF.

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Eosinophils have an essential role in promoting a type 2 innate immune response and cardiac repair following myocardial infarction.

I S Iqbal Singh Toor[1]; D Ruckerl[2]; A Thomson[1]; A Rossi[1]; J Allen[2]; G Gray[2]
[1]*University of Edinburgh, Edinburgh, United Kingdom*; [2]*University of Manchester, Manchester, United Kingdom*

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Background: Eosinophils contain preformed IL-4 within their cytoplasmic granules, a cytokine which can mediate alternative activation of macrophages and promote tissue repair. Patients develop peripheral blood eosinopenia within 24 hours of the onset of myocardial infarction (MI) symptoms, but whether eosinophils are recruited to the infarct and have a role in regulating infarct repair is currently unknown.

Purpose: This study sought to investigate the role of eosinophils, a source of the Th2 cytokine IL-4, in infarct healing.

Methods: MI was induced by permanent coronary artery ligation in 12-15 week-old male wild-type (WT) BALB/c mice and ΔdblGATA mice that are deficient in eosinophils (BALB/c background). Cardiac function was assessed 7 days later by high-resolution ultrasound, and flow cytometry was performed on single cell digests of infarct zone tissue.

Results: Histochemical staining (Siglec F) and single cell digestion of infarcted WT BALB/c hearts revealed significant recruitment of (CD11b+ F4/80- SiglecF+) eosinophils to the infarcted heart. Genetic eosinophil deficiency in ΔdblGATA mice led to greater left ventricular dilatation relative to WT mice (End-Systolic Area: 29 ± 2 cm vs 22 ± 2 cm; $p = 0.02$) and worse cardiac function (Ejection Fraction: 22 ± 4% vs. 34 ± 4; $p = 0.04$) at Day 7 post-MI, despite comparable plasma troponin I (Infarcted BALB/c WT; 26 ± 4 ng/l vs. Infarcted ΔdblGATA; 25 ± 5 ng/l, $p = 0.74$), indicative of similar injury, at 24 hours after coronary artery ligation. Expression of CD206, a surface marker for pro-repair alternatively activated macrophages, was reduced on infarct zone CD11b+F4/80+Ly6G- macrophages from ΔdblGATA mice. Eosinophil replenishment of ΔdblGATA mice restored expression of CD206 on infarct zone macrophages after coronary artery ligation (Mean Fluorescence Intensity [MFI] for CD206: 2134 ± 536 a.u. in eosinophil replenished ΔdblGATA mice vs. 277 ± 134 a.u. in PBS treat ΔdblGATA mice; $p = 0.04$). Furthermore, treatment with IL-4 complexes was able to rescue the adverse cardiac remodelling of eosinophil deficient ΔdblGATA mice (ejection fraction: 32 ± 2% vs. 23 ± 2% in IL-4 complex and PBS treated ΔdblGATA mice, respectively, $p = 0.02$, $n = 8$-15 per group).

Conclusions: This study provides the first evidence for an essential role of eosinophils in modulating the inflammatory response and cardiac remodelling following MI, likely through provision of IL-4. Peripheral blood eosinopenia is a common feature of heart failure patients. Correcting a deficiency for eosinophils or specifically IL-4 therapy may offer a novel immune-modulatory intervention in the setting of heart failure.

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NADPH oxidase-4 promotes adaptive cardiac remodelling in the chronically stressed heart by driving protein O-GlcNAcylation and enhancing cardiac fatty acid oxidation

A A Adam Abner Nabeebaccus[1]; A Zoccarato[1]; A D Hafstad[2]; C X S Santos[1]; E Aasum[2]; A C Brewer[1]; M Zhang[1]; J West[3]; J Griffin[3]; T Eykyn[1]; M Mayr[1]; A M Shah[1]
[1]*King's College London, Cardiovascular Division, London, United Kingdom*; [2]*University of Tromso, Tromso, Norway*; [3]*University of Cambridge, Department of Biochemistry, Cambridge, United Kingdom*

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Background: Reactive oxygen species (ROS) production contributes to both adaptive and maladaptive remodelling pathways in the heart and is involved in the pathophysiology of cardiac hypertrophy and failure. NADPH oxidase-4 (Nox4), a specialised ROS-generating enzyme has beneficial effects by promoting adaptive remodelling during pressure-overload cardiac hypertrophy.

Purpose: To understand how Nox4, a ROS-generating enzyme promotes adaptive cardiac remodelling to achieve beneficial effects in the chronically stressed heart.

Methods and Results: An unbiased global overview of putative Nox4-mediated changes, from cardiac-specific Nox4 transgenic (TG) and wild-type (WT) mouse hearts was first characterised through a 2D-DIGE proteomics approach. The proteome of TG hearts demonstrated a significant over-representation of changes in protein levels of enzymes involved in glucose and fatty acid utilisation. Targeted LC-MS approaches identified a differential accumulation of glycolytic intermediates in the proximal part of glycolysis both in unstressed and pressure-overloaded TG hearts. To specifically quantify glucose uptake, glycolysis, glucose oxidation and fatty acid oxidation rates, ex vivo working heart studies were conducted. TG hearts had a marked increase cf. WT in palmitate oxidation rate in the unstressed

as well as pressure-overloaded heart (3.6 fold increase; n = 6/group; p = 0.01). Glucose uptake was unaltered but glycolysis and oxidation rates were decreased, suggesting diversion of glucose away from oxidation. Importantly, an increase in palmitate oxidation was not detrimental either for in vivo cardiac energetics (31P-NMR) or contractile function during pressure-overload hypertrophy. We found that activity of the hexosamine biosynthesis pathway (HBP), an alternative route for glucose metabolism, was increased in TG hearts as assessed by the O-GlcNAc post-translational modification of cardiac proteins by N-acetylglucosamine, the end-product of HBP. O-GlcNAc levels were 2.4 fold higher in TG cf. WT (n = 4/group; p = 0.02). In cultured cardiomyocytes, endogenous Nox4 induced similar changes in HBP and palmitate oxidation (extracellular flux analysis), and it was found that changes in O-GlcNAcylation regulated fatty acid oxidation. Mechanistically, the rate-limiting enzyme of HBP - Gfat1 was specifically upregulated by Nox4 and we could also demonstrate that the O-GlcNAcylation of Cd36 (the main fatty acid uptake protein in the heart) was dependent on Nox4, providing a potential reason for increased FAO.

Conclusion: These results show that Nox4 reprograms substrate utilisation in the heart by directing glucose towards the HBP and inducing a linked increase in fatty acid oxidation. These data identify a novel redox mechanism that drives beneficial metabolic reprogramming in the heart. In particular the results suggest that increasing fatty acid oxidation in the chronically stressed heart may be a beneficial therapeutic tratégy.

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Galectin-3 and dilated cardiomyopathy: distinct effect of pharmacological and genetic interventions

MN Nguyen[1]; H Kiriazis[1]; Z Thomas[1]; Y Su[1]; XM Gao[1]; JR Mcmullen[1]; J Sadoshima[2]; X-J Xiao-Jun Du[1]
[1]*Baker IDI Heart and Diabetes Institute, Experimental Cardiology, Melbourne, Australia*; [2]*New Jersey Medical School, Department of Cell Biology and Molecular Medicine Rutgers, New Jersey, United States of America*

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Background: Galectin-3 (Gal-3) is regarded as a potential biomarker of heart failure. Pre-clinical studies in models including hypertensive heart disease consistently reported 2˜5 fold increase in cardiac expression of Gal-3 and beneficial effects by treatment with Gal-3 inhibitors, such as modified citrus pectin (MCP). However, Gal-3 expression level and effects of anti-Gal-3 interventions in dilated cardiomyopathy (DCM) have not been investigated.
Purpose: Cardiac-restricted transgenic (TG) overexpression of mammalian sterile 20-like kinase 1 (Mst1) leads to typical DCM. We determined Gal-3 expression in TG hearts and studied effects of pharmacological (MCP) and genetic interventions on DCM phenotypes.
Methods: Mst1 TG and wild-type (NTG) littermates were used in MCP treatment study. MCP therapy was for a period of 4 months (2 to 6 months of age) at 200 mg/kg/day for 2 months and then 500 mg/kg/day for a further 2 months. Gal-3 gene deletion was achieved by cross-breeding TG mice with Gal-3 knockout (KO) mice and TG and TG/Gal3-KO mice as well as mice with relevant control genotypes. Echocardiography was performed using Vevo2100 system. RT-PCR was applied for gene expression and Gal-3 protein level was detected by ELISA kit. Collagen content was determined by hydroxyproline assay.
Results: Relative to NTG control (n = 13˜16/group), TG mice had atrial dilatation (by 3-fold), increase in weights of atria, lungs, liver and spleen duet to congestion, suppressed left ventricular (LV) ejection fraction (EF, 27% vs 55%) and cardiac output (CO, 10 vs 15 mL/min), higher myocardial collagen content (by 3-fold), and upregulated fibrotic genes (by 4-8 fold). These phenotypes were stable over 2-6 months of age. Gal-3 expression increased in TG than NTG hearts by 35-40-fold at mRNA and protein levels. Immunohistochemistry revealed lack of accumulation of neutrophils (CD45) or macrophages (CD68) in TG hearts, indicating that Gal-3 was derived from cardiac cells. A 4-month treatment with MCP failed to alleviate DCM phenotype nor to attenuate the level of collagen, Gal-3 or fibrotic genes. In contrast, Gal-3 depletion in Mst1-TG mice by cross-breeding lowered cardiac fibrosis (by 17%), suppressed expression of fibrotic genes (by 40-70%), and normalized pulmonary and left atrial weights. Echocardiography revealed reduced LV volume at end-diastole (51 ± 2 vs 70 ± 7 μL) and end-systole (32 ± 2 vs 51 ± 5 μL), and improved LV EF (37 ± 3 vs 27 ± 2%, all P < 0.01).
Conclusions: Gal-3 expression is markedly increased in Mst1 TG heart exhibiting overt DCM. Whereas MCP therapy showed no beneficial effect, partial or complete Gal-3 gene deletion effectively suppressed cardiac fibrosis and LV dilatation, and improved contractile function. Thus, suppression of Gal-3 expression forms a new therapeutic approach in DCM.

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Metformin prevents cardiac fibrosis by attenuating mitochondrial NADPH oxidase 4/PKC-alpha/Gal-3 signaling pathway in myocardial infarction

MC Asensio-Lopez[1]; AM Lax[1]; MJ Fernandez Del Palacio[2]; MC Sanchez-Perez[1]; Y Sassi[3]; R Hajjar[3]; DA Pascual-Figal[4]
[1]*Biosanitary Research Institute of Murcia (IMIB-Arrixaca)., Cardiology, Murcia, Spain*; [2]*Department of Animal Medicine and Surgery, Murcia, Spain*; [3]*Icahn School of Medicine at Mount Sinai, Cardiology, New York, United States of America*; [4]*University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain*

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Background: The antifibrotic mechanism of metformin (MET) is incompletely understood. We have determined the role of MET in cardiac fibrosis following myocardial infarction and characterized the molecular mechanism.
Methods: Eight-week-old male rats (Sprague-Dawley) were subjected to left ventricular systolic dysfunction by permanent ligation of the anterior coronary artery. Rats received MET (250 mg/kg/day) or normal saline for 4 weeks. An experimental model of biomechanical strain and a coculture, to allow cross talk between primary cultures of cardiomyocytes and cardiac fibroblasts (all obtained from C57BL6J mice using a Langendorff system), were established to characterize the underlying molecular mechanisms involved in the MET antifibrotic actions. The role of AMPK was determined via siRNA-mediated knockdown while those of the NADPH oxidase 4 (mitoNox) and PKCα were determined using the inhibitors GKT137831 and Chelerythrine, respectively. The mRNA and protein expression of different markers were measured by quantitative RT-PCR and Western blot, respectively. The enzymatic activities of mitoNox and PKCα were also assessed using spectrofluorimetry.
Results: MET treatment following MI, was associated with a reduction of myocardial fibrosis, Gal-3 mRNA and protein levels, as well as macrophages infiltration. MET also increased AMPK α1/α2 levels (p < 0.001) and blocked the mRNA expression of both mitoNox and PKCα as their enzymatic activities (p < 0.001, in all cases). Following MI, the increase in expression and activity of both enzymes was associated with an increase in the accumulation of the superoxide anion (p < 0.001) which positively correlated with mitoNox and PKCα activities (rs = 0.362, p = 0.018), as well as an increase in the lipid peroxidation (p < 0.001) and the activation of the apoptotic death program characterized by the activation of initiatory procaspase 9 (p < 0.001) and effectory procaspase 3 (p < 0.001). MET therapy was associated with lower superoxide accumulation (p < 0.001), lipid peroxidation (p < 0.001) and caspases activation (p < 0.001) after 4 weeks of treatment. These findings were replicated using a biomechanical strain model. The silencing of AMPK expression with siRNA blocked the ability of MET to protect adult cardiomyocytes from biomechanical strain, in terms of mitoNox and PKCα activities, Gal-3 levels, percentage of viability and proliferation and levels of reactive oxygen species (p < 0.001, in all cases). The use of the inhibitors GKT137831 or Chelerythrine supported that PKCα is downstream of mitoNox, and the activation of this pathway results in Gal-3 up-regulation. The Gal-3 secreted by cardiomyocytes has a paracrine effect on cardiac fibroblasts, inducing their activation.
Conclusions: MET-induced AMPK increase significantly improves cardiac remodeling post-MI, and this effect is related to the inhibition of mitoNox/ PKCα/Gal-3 pathway. Cardiomyocytes under biomechanical stress activate the fibroblasts in a paracrine manner.

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Effects of acute intravenous infusion of nitroxyl donor BMS-986231 on left ventricular function and cardiac rhythm in anaesthetised dogs with intracoronary microembolisation-induced heart failure

HN Sabbah[1]; JC Hartman[2]; J Reardon[3]
[1]*Henry Ford Hospital, Detroit, Michigan, United States of America*; [2]*Pharmaceutical R&D Consulting, LLC, Loveland, Colorado, United States of America*; [3]*HemoShear Therapeutics, LLC, Charlottesville, Virginia, United States of America*

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Background: BMS-986231 is a novel nitroxyl donor in development for the treatment of acute decompensated heart failure (HF).
Purpose: Assess the effects of BMS-986231 on left ventricular (LV) function and induction of arrhythmias in dogs with HF.
Methods: Chronic LV failure was produced in dogs via sequential embolisations until an LV ejection fraction of ˜30% was achieved. In Study A, seven isoflurane-anaesthetised animals each received continuous intravenous (IV) infusions of three different doses of BMS-986231 (0.7, 2 and 7 μg/kg/min) as well as vehicle for 4 hours; haemodynamic, angiographic and echocardiographic measurements were obtained. Animals were monitored for 1 hour post-infusion. In Study

B, another seven animals with induced HF received BMS-986231 (7 μg/kg/min) and vehicle over 2 hours, before undergoing programmed ventricular stimulation (PVS). PVS was terminated when it provoked ventricular fibrillation (VF) or a sustained monomorphic ventricular tachycardia (SVT) lasting >30 seconds. Threshold data for SVT or VF were quantified in which progressively increasing scores were indicative of higher magnitudes of required stimulation.
Results: With vehicle, all measured/calculated variables were stable from baseline through 4 hours. At 4 hours, BMS-986231 resulted in significant ($p < 0.05$) increases in early-to-late diastolic velocity-time integral ratio (mean Δ from baseline across doses: 1.6 to 2.7) and deceleration time of early mitral valve inflow velocity (Δ10.4 to 12.4 msec), and significant decreases in LV end-diastolic wall stress (Δ-9.3 to -13.4 gm/cm) versus baseline, all suggesting positive lusitropy. BMS-986231 also led to significant increases in LV ejection fraction (Δ5.6 to 8.8%), LV fractional area shortening (Δ6.1 to 11.3%), stroke volume (Δ3.7 to 5.9 ml) and cardiac output (Δ0.24 to 0.47 l/min), suggesting positive inotropy. Systemic vascular resistance was significantly decreased with all doses (Δ-457 to -704 dynes.sec.cm5), suggesting a vasodilatory effect. BMS-986231 had little effect on heart rate (Δ-0.6 to -1.6 bpm, p = NS) and no de novo arrhythmias were detected during infusion. Myocardial oxygen consumption was significantly reduced below baseline with the high dose (Δ-73.1 μmols/min). During PVS, BMS-986231 increased the mean threshold score for SVT or VF twofold versus vehicle (18.0 vs. 9.0) and had no impact on subsequent cardioversion to restore sinus rhythm.
Conclusions: BMS-986231 was associated with outcomes suggestive of inotropic, lusitropic and vasodilatory effects without an impact on heart rate, and with a reduction in myocardial oxygen consumption. BMS-986231 did not induce ventricular arrhythmias and significantly increased the threshold for triggering such episodes with PVS. Based on these findings, BMS-986231 may be a suitable candidate for further development in acute decompensated HF.

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Activation of the innate immune receptor toll-like receptor 4 (tlr4) by fibronectin fragments negatively regulates cardiac myofibroblast differentiation.

R J Richard Heads[1]; M Khan[1]; Y Chuluunbaatar[1]; V Budhram-Mahadeo[2]
[1]King's College London, Cardiovascular Division, London, United Kingdom; *[2]University College London, Medical Molecular Biology Unit, London, United Kingdom*

Activation of the innate immune system receptors such as Toll-like receptors (in particular TLR4) during post-MI myocardial remodelling and progression to heart failure is generally regarded as pro-inflammatory and pro-injury, leading to adverse remodelling, increased fibrosis and decreased cardiac function. However, these adverse effects are primarily driven by activation of TLR4 on professional innate immune cells such as monocytes and macrophages in the inflammatory infiltrate which secrete pro-inflammatory cytokines. Our work on isolated, cultured resident cardiac fibroblasts/endothelial cells has shown that activation of TLR4 actually inhibits myofibroblast differentiation, inhibits endothelial to mesenchymal transition (EndMT) in response to TGFb and reduces the expression of pro-fibrotic markers. Fibroblast TLR4 activation upregulates the expression of an anti-fibrotic, positive wound healing phenotype. This phenotypic switching is mediated by signal integration between the Ca2+ -dependent protein phosphatase calcineurin (CN) and protein kinase C epsilon (PKC) and controls the transcription of genes involved in cardioprotection and wound healing. This signalling occurs following activation of TLR4 by fragments of extra cellular matrix (ECM) proteins including specific type III repeats of fibronectin (FN), such as FN-EDA and FN-III1-c. This results in CN and PKC-dependent activation of the transcription factors (TFs) Nuclear Factor of Activated T-cells (NFAT) and Activator Protein-1 (AP-1) and synergistic induction of Cyclooxygenase-2 (COX-2), Lipocalin-2 (LCN2), interleukin-6 (IL-6) and Tissue Inhibitor of MetalloProteinase-1 (TIMP-1). At the same time TLR4 activation inhibits the expression of pro-fibrotic genes including Connective Tissue Growth Factor (CTGF), several collagen isoforms and fibronectin itself. Whereas the activation of CN alone is pro-fibrotic, the co-activation of PKCe converts this signal into an anti-fibrotic response. Interestingly, knockdown of PKCe using siRNA or ectopic expression of DN-PKCe causes a compensatory upregulation of PKCd which is pro-fibrotic. Furthermore, we have shown that the POU IV class POU domain TF POU4f1 (Brn3a) is expressed in cardiac fibroblasts and is upregulated in the border zone 24 hours after MI. Brn3a controls myofibroblast differentiation and regulates collagen expression via consensus TF binding sites in the Col1A1 promoter. TLR4 activation inhibits the expression and activity of Brn3a and downregulates collagen expression. Therefore, TLR4 activation by specific FN type III repeats leads to the switching of myofibroblast phenotype from a pro-fibrotic ECM secreting phenotype to a reparative wound healing phenotype and thus promotes beneficial myocardial remodelling.

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MicroRNA-21 attenuates post-ischemic inflammation triggered by DAMPs through targeting KBTBD7

Z Zhenzhen Zhan[1]; L Yang[1]; Z Liu[1]
[1]Shanghai East Hospital, Institute of Heart Failure, Shanghai, China People's Republic of

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Objective: MicroRNA-21 (miR-21) has been shown to inhibit apoptosis of cardiomyocytes and promote cardiac fibrosis. However, the role of miR-21 in post-ischemic inflammation remains obscure. Our aim is to determine whether miR-21 regulates DAMPs-triggered inflammation after MI in mice and investigate the underlying signal mechanism.
Methods: We engineered miR-21 knockout (KO) mice. For in vivo experiment, miR-21 KO mice or WT mice subjected with myocardial infarction which induced by left coronary ligation. The inflammatory cytokines in peri-infarct heart tissues were evaluated by Q-PCR, ELISA, IHC and double immunofluorescence staining. The LVEF, LVFS, LVESD and LVEDD were detected by echocardiography 14 days after MI induction and the myocardial infarct size was analyzed by Masson trichrome and TTC staining. The expression of inflammatory cytokines and the activation of MAPK and NF-B signal in macrophage triggered by DAMPs were determined, respectively. In mechanism, we analyzed the targeting gene using TargetScan7.1and verify the interaction between miR-21 and targeting gene with luciferase reporter assay. With silence of target gene by specific siRNA in mouse macrophagesQ-PCR and Western blot analysis were respectively use to detect the DAMPs-induced production of inflammatory cytokines and the activation of MAPK and NF-B signal.
Results: In peri-infarct heart tissues of miR-21 KO mice, the expression of IL-1β, IL-6 and TNF-α were higher than that in WT mice. LVEF and LVFS were significantly decreased, and LVESD, LVEDD and myocardial infarct size were apparently increased in miR-21 KO mice compared with WT mice. Macrophages from miR-21 KO mice have an increased production of IL-1β, IL-6 and TNF-α stimulated with rmHSP60 and rmHMGB1. The phosphorylated levels of P38, IKK-α/β and P65 were significantly increased in stimulated macrophages from miR-21 KO mice. Furthermore, we found that miR-21 mimic markedly decreased the luciferase activity of wild type KBTBD7 luciferase (KBTBD7-Luc) and the expression of KBTBD7 was found to be increased in miR-21 KO mice macrophage. Moreover, the production of IL-1β, IL-6 and TNF-α and the phosphorylated levels of P38, IKK-α/β and P65 were significantly reduced in siRNA silence of KBTBD7 macrophages stimulated with rmHSP60 and rmHMGB1 compared to that with control siRNA. In addition, KBTBD7 could interact with MKK3 and MKK6 which were the upstream regulator of P38 and NF-B in mouse macrophages.
Conclusions: These data show that miR-21 down-regulates inflammatory response after MI by alleviating the activation of P38 and NF-B signalling pathway. MiR-21 inhibits the protein and mRNA expression levels of the KBTBD7 in mouse macrophages, these data indicate that miR-21 attenuate MI-induced inflammatory response by regulating the target gene KBTBD7.

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Hypoxia induces gene-specific epigenetic modifications in human cardiac fibroblasts which are associated with the development of myocardial fibrosis and aberrant post-ischemic cardiac remodelling

N Glezeva[1]; S Das[1]; B Moran[1]; M Ledwidge[2]; K Mcdonald[2]; C Watson[3]
[1]University College Dublin, Conway Institute of Biomolecular and Biomedical Research, Dublin, Ireland; *[2]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*; *[3]Queen's University of Belfast, Wellcome-Wolfson Institute for Experimental Medicine, Belfast, United Kingdom*

Introduction: Ischemia caused by coronary artery disease and myocardial infarction leads to aberrant ventricular remodelling and cardiac fibrosis. This occurs partly through accumulation of gene expression changes in resident fibroblasts, resulting in an overactive fibrotic phenotype. Long-term adaptation to a hypoxic insult is likely to require significant modification of chromatin structure. We have recently shown that human myocardial tissue hypoxia is associated with an enhanced pro-fibrotic gene profile in the tissue and, more significantly, that hypoxia-induced pro-fibrotic changes in cardiac fibroblasts are associated with global DNA hypermethylation. Based on this epigenetics data, we have conducted a gene-specific methylation study to investigate methylation changes that occur in hypoxic fibroblasts and to gain novel insights into pathways and mechanisms that may contribute to post-ischemic cardiac remodelling.
Methods: Human ventricular cardiac fibroblasts were exposed to 1% oxygen for up to 8 days. Global methylation changes were assessed using anti-5-methylcytosine (5MeC) staining, flow cytometry, QPCR, and western blot. Gene-specific methylation changes associated with hypoxia and an increased fibrotic state were determined by 5MeC immunoprecipitation and GeneChip human promoter arrays (Affymetrix),

and validated by bisulphite genomic sequencing (BGS). Gene functional classification and pathway analysis were performed (DAVID, FUNRICH).
Results: Hypoxia-induced pro-fibrotic changes in cardiac fibroblasts included increased cell proliferation and increased alpha smooth muscle actin (αSMA), collagen 1, DNA methyltransferase 1 (DNMT1) and DNMT3B expression which associated with global DNA hypermethylation. In specific, 32 gene-specific hypermethylation changes and 101 hypomethylation changes occurred in hypoxia. Fifteen pathophysiologically relevant genes (5 hypermethylated, 10 hypomethylated) were identified by functional classification and pathway analysis to have a role in cardiac fibrosis, extracellular matrix remodelling, transforming growth factor beta (TGF) signalling, cell proliferation and fate, wound repair, ischemia, hypertension, hypertrophy, and heart failure. These were validated using BGS.
Conclusion: Epigenetic modifications and changes in the epigenetic machinery identified in cardiac fibroblasts during prolonged hypoxia may contribute to the pro-fibrotic nature of the ischemic milieu in the heart during disease. The potential use of epigenetic modifiers, such as DNA methylation modifiers, as a treatment option for cardiac pathologies associated with fibrosis, ischemia, and hypertrophy may provide therapeutic benefit.

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Studying beta-adrenergic signalling in a patient-specific induced pluripotent stem cell model for Takotsubo syndrome

D Huebscher[1]; T Borchert[1]; D Lam[1]; Cl Guessoum[1]; C Templin[2]; G Hasenfuss[1]; K Katrin Streckfuss-Boemeke[1]
[1]Heartcenter, Dept. of Cardiology und Pneumology, Georg-August-University of Gttingen, Gttingen, Germany; *[2]University Heart Center, Clinic for Cardiology, Zurich, Switzerland*

Funding Acknowledgements: DZHK, Heidenreich von Siebold, IRTG1816, SFB1002

Purpose and Aim: Takotsubo syndrome (TTS) is characterized by acute transient left ventricular dysfunction in the absence of responsible obstructive coronary lesions. The pathogenic mechanism leading to TTS is still unknown. However an adrenergic overstimulation seems to play an important role in TTS. The aims of the study were to use an in vitro induced pluripotent stem cell (iPSC)-TTS model to prove the hypothesis of an altered β-adrenergic signaling under high catecholamine stress in patient specific TTS iPSC-cardiomycytes (ps-iPSC-CMs), and to gain a comprehensive understanding into the pathophysiology of TTS.
Methods and Results: Human somatic TTS cells and controls were reprogrammed to ps-iPSCs and high-quality iPSC clones were directly differentiated into pure functional cardiomyocytes (CMs). 3-month-old iPSC-CMs were treated with catecholamines to mimick a TTS-specific phenotype and analyzed regarding β-adrenergic signaling and cardiac function. To study cAMP dynamics in these cells, we transduced iPSC-CMs with an adenoviral construct expressing a Frster Resonance Energy Transfer (FRET)-based cAMP sensor Epac1-camps. TTS-iPSC-CMs show a higher cAMP response to increasing β-adrenergic receptor (β-AR) agonist Iso levels, which was shown by a significant increase of the FRET ratio at high Iso (1mmol/L) concentration. In comparison, control iPSC-CMs reacted to low Iso concentration (100nM) with a clear cAMP response but without any further increase at higher Iso.
We analyzed the -adrenergic signalling on a molecular level and found an increase of 1-AR expression in TTS and control iPSC-CMs after Iso stimulation, whereas 2-AR-expression was decreased under the same conditions. In accordance to an increased -AR signaling, the Iso-dependent activation of the PKA and specific hyperphosphorylation of its cellular targets including RYR2-S2808 and phospholamban-S16 is enhanced in TTS-iPSC-CMs.To analyze the different beta-AR classes, we pretreated the iPSC-CMs with selective β1- and β2-AR inhibitors before Iso stimulation. Control-iPSC-CMs show a Iso- and β2-dependent response. In contrast, we found a similar subtype-specific signaling of β2-AR and β1-AR in TTS-iPSC-CMs. In addition, in TTS-iPSC-CMs β1-AR and β2-AR cAMP responses are significantly inducible by increasing Iso concentrations of 1μmol/L, which was not found in control cells.
Conclusion: Our data show an induction of stressful events and an altered functionality in response to Iso in iPSC-CMs of TTC patients including the -adrenergic signaling. The FRET measurements pointed to an increasable cAMP response by rising catecholamine levels and argue for higher receptor sensitivity towards high catecholamines under intensive stress conditions in TTS patients. Our study highlights that iPSC-CMs can be used to study the disease mechanism of TTC to provide a versatile tool for evaluating new treatment options for TTC.

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Crosstalk between FGF23 and angiotensin II-mediated calcium handling in cardiac hypertrophy.

K Mhatre[1]; P Wakula[1]; S Menzel[1]; E Bisping[2]; B Pieske[1]; F Heinzel[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Experimental Cardiology, Berlin, Germany; *[2]Medical University of Graz, Cardiology, Graz, Austria*

The hormone fibroblast growth factor 23 (FGF23) is strongly linked to heart failure-related cardiovascular mortality. It is a mediator of left ventricular hypertrophy which may involve calcium-regulated transcriptional pathways. High circulating levels of FGF23 are associated with an altered systemic renin-angiotensinaldosterone system (RAAS) response. Our aim was to compare and study FGF23 and angiotensin II (ATII)-mediated calcium-dependent signaling in ventricular cardiomyocytes.
Neonatal rat ventricular cardiomyocytes (NRVMs) were isolated and cultured for 5 days. ATII (1μM) or FGF23 (25ng/ml) were used as hypertrophy stimuli. Cell surface area was studied by immunostaining with NRVM specific desmin antibody. Time-dependent changes in gene expression (1-24h) were accessed by qPCR. Calcium transient (CaT) amplitude (F/F0peak at 1Hz; Fluo-4 AM) and integral were quantified in cytosol and nucleus. Phospholipase C (PLC-) phosphorylation levels were detected by Western blot.
Both FGF23 and ATII treatment induced hypertrophy in NRVM as reflected by cell area and pro-hypertrophic gene expression. Cell area was increased by 46.8% with ATII and by 37.4% with FGF23 after 48h ($p < 0.001$). ATII showed peak increase at 1h in ACTA-1 (1.98fold $p = 0.08$) and RCAN-1 (1.91fold $p < 0.05$) gene expression. For FGF23, peak increase was observed at 6h for ACTA-1 (5.2fold) and RCAN-1 (2.4fold) ($p < 0.05$).
NRVMs treated (15 mins-1h) with ATII or FGF23 showed similar early changes in CaT. Both the treatment elicited increase in F/F0peak (1.5fold) and integral (2-2.8fold) in cytosol ($p < 0.01$). However, there was more pronounced rise in integral for ATII (2.9fold) and FGF23 (3.7fold) in the nucleus ($p < 0.001$) than in cytosol, suggesting augmented calcium release into the nucleus with both thehormones. Further, this effect of ATII and FGF-23 on nuclear CaT integral was decreased with inositol trisphosphate receptor (InsP3R) inhibitor 2-APB (5-10μM), implyinginvolvement of InsP3R in the nuclear calcium release.
Further, we used ATII receptor antagonist, losartan (1μM) on the FGF23 treated NRVMs to decipher the overlap between FGF23 and ATII signaling. Losartan inhibited FGF23-induced increase in cell surface area after 48h ($p < 0.001$) and completely attenuated the FGF23-mediated alterations in CaT. These outcomes indicate an involvement of intracellular ATII in FGF23-mediated signaling. On the other hand, FGFR4-PLC--Calcineurin pathway is known to mediate FGF23 induced cardiomyocyte hypertrophy.Losartan inhibited PLC- phosphorylation in presence of FGF23 ($p < 0.005$) suggesting a possible mechanism by which it obstructs the effects of FGF23 treatment.
In conclusion, the response of cardiomyocytes to FGF23 and ATII were comparable at multiple levels (cell hypertrophy, increased cellular and nuclear CaT integral, effect of InsP3R inhibitor). Overall, our results suggest a crosstalk between FGF23 and ATII mediated calcium-dependent hypertrophic signaling in cardiomyocytes.

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Cardiotrophin-1 is associated with perivascular fibrosis, increased collagen cross-linking and diastolic dysfunction in Dahl salt-sensitive hypertensive rats with heart failure with preserved ejection

A Gonzalez Miqueo[1]; C Brugnolaro[1]; B Lopez Salazar[1]; S Ravassa Albeniz[1]; MU Moreno Zulategui[1]; J Beaumont Ezcurra[1]; G San Jose Eneriz[1]; J Diez Martinez[1]
[1]CIMA, University of Navarra, Program of Cardiovascular Diseases, Pamplona, Spain

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Background: Myocardial interstitial fibrosis, characterized by increased deposition and stiffness (i.e. collagen cross-linking or CCL) of collagen fibres, is a common feature in patients with heart failure with preserved ejection fraction (HFPEF). On the other hand, cardiotrophin-1 (CT-1) has been shown to be associated with myocardial fibrosis in experimental models but its role has been poorly analysed in HFPEF.
Purpose: This study was designed to analyse the expression of CT-1 in a rodent model of hypertension and HFPEF and to evaluate its association with myocardial fibrosis and left ventricular (LV) morphology and function.
Methods: Dahl salt-sensitive male rats started receiving a high salt diet at 7 weeks of age (HSD; n = 18) until sacrifice (at 23 weeks). A control group (n = 8) was fed with a normal diet all along the study. Blood pressure was evaluated in a subgroup of animals (n = 3 per group) by telemetry. LV mass, morphology, systolic and diastolic

function were evaluated by echocardiography. Total, interstitial and perivascular myocardial fibrosis was measured in picrosirius red- stained sections using an image analysis software (Cell^D). CCL was evaluated by colorimetric and enzymatic techniques. CT-1 mRNA and protein levels were analysed by real time RT-PCR and western blotting, respectively. Lysyl oxidase (LOX) protein levels were analysed by western blotting.

Results: Compared to control rats, HSD animals showed increased ($P < 0.05$) mean arterial pressure, LV hypertrophy (increased left ventricular mass [$P < 0.001$] and relative wall thickness [$P < 0.05$]), and diastolic dysfunction (decreased E/A [$P < 0.05$] and increased isovolumetric relaxation time [$P < 0.05$]) with similar ejection fraction. These rats presented higher LV fibrosis ($P < 0.01$) with an increase both in interstitial ($P < 0.05$) and perivascular ($P < 0.001$) fibrosis. They also showed increased CCL ($P < 0.01$) and increased expression of LOX ($P < 0.05$), the main enzyme responsible for CCL. The myocardial expression of CT-1 was higher in HSD rats than in control rats both at mRNA ($P < 0.05$) and protein ($P < 0.05$) level. CT-1 protein was directly correlated with total ($r = 0.438$; $P < 0.05$) and perivascular ($r = 0.481$; $P < 0.05$) LV fibrosis, with CCL ($r = 0.493$; $P < 0.05$) and with LOX ($r = 0.721$; $P < 0.001$) in all animals. Moreover, it was inversely correlated with the E/A ratio ($r = -0.457$; $P < 0.05$) in all rats.

Conclusions: CT-1 is increased in the myocardium of hypertensive HSD rats with HFPEF and is associated with LV perivascular fibrosis and increased CCL, as well as with diastolic dysfunction. These results suggest that CT-1 facilitates the development of myocardial fibrosis and stiffening which may contribute to the development of LV diastolic dysfunction and the progression to HFPEF in this experimental model.

MODERATED POSTER SESSION 1 - PROGNOSIS

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Daytime periodic breathing patterns and risk of appropriate cardioveter defibrillator therapies in heart failure patients

M T La Rovere[1]; R Maestri[2]; E Robbi[1]; M Lovagnini[1]; D Rossi[1]; E Traversi[1]; GD Pinna[2]
[1]Istituti Clinici Scientifici Maugeri, IRCCS Montescano, Department of Cardiology, Montescano (Pavia), Italy; *[2]Istituti Clinici Scientifici Maugeri, IRCCS Montescano, Department of Biomedical Engineering, Montescano (Pavia), Italy*

Background: Although Central Sleep Apnea (CSA) is a recognized risk factor for life-threatening arrhythmias (T Bitter and coll, Eur Heart J 2011), the occurrence of arrhythmic events does not show an increased nighttime frequency (T Bitter and coll, Int J Cardiol 2014). Abnormal breathing patterns in the form of periodic breathing (PB) - are frequently observed during daytime in patients with heart failure (HF) but their contribution to an increased malignant arrhythmia susceptibility is not known.
Methods: We analysed data from 378 patients with clinically stable, optimally treated moderate-to-severe HF (age 59 ± 9 years, NYHA class 2.7 ± 0.5, LVEF 31 ± 9%) who had a cardioverter defibrillator implanted according to current guidelines. All patients were submitted to a 10-minute daytime supine respiratory recording. PB was defined as an oscillation of 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. Cox regression models were used to assess the association between PB and appropriate ICD discharge.
Results: PB was observed in 158/378 (42%) patients. Patients with PB were older (60 ± 9 vs 57 ± 9 years, p = 0.002), with a lower ejection fraction (29 ± 8 vs 31 ± 9%, p = 0.04) and a higher NT-proBNP (2611 ± 3747 vs 1988 ± 2390, p = 0.008) and creatinine value (1.5 ± 0.6 vs 1.4 ± 0.5, p = 0.03). During a median of 33.5 months, 71 patients had an appropriate ICD discharge. No significant differences were observed in clinical predictors between patients who did or did not receive appropriate ICD discharge. At univariate analysis PB was a significant predictor of ICD discharge (Relative Risk 1.72, 95% CI 1.08-2.77, p = 0.02). The presence of PB remained significant (p = 0.033) in a multivariable model including LVEF, creatinine, NT-ProBNP, serum potassium level, NYHA cl, and six-minute walking test.
Conclusions: The presence of PB has a relevant impact on the occurrence of malignant ventricular arrhythmias requiring ICD discharge in patients with heart failure.

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Global longitudinal strain (GLS) by speckle-tracking echocardiography (STE) predicts appropriate defibrillator therapy in patients with dilated cardiomyopathy (DCM)

H Hazem Omran[1]; D Hering[1]; N Bogunovic[1]; D Horstkotte[1]; L Faber[1]
[1]Herz- und Diabeteszentrum NRW, Ruhr-Universitt Bochum, Clinic for Cardiology, Bad Oeynhausen, Germany

Background: Patients (pat) with DCM have an increased risk for sudden cardiac death (SCD) which may be prevented by an implantable cardioverter-defibrillator (ICD). Current guidelines link the indication to implant an ICD in DCM pat to a left ventricular ejection fraction (LV-EF) of 35%. LV GLS as assessed by STE, directly measuring myocardial deformation in the longitudinal dimension, is a new method to characterize global LV function.
Aim: The aim of this study was to assess whether GLS measurements predict the rate of appropriate ICD therapies in DCM-pat.
Methods: Pat with DCM who underwent primary prophylactic ICD implantation from 2011-2016, who had baseline echocardiographies adequate for STE analysis, and a follow-up duration of >6 months were included. ICD interrogation data were retrieved from our electronic records. Pat with secondary preventive ICD indication were excluded.
Results: 115 pat were included (26% females, age: 61.3 ± 12.4 years, LV-EF 27.9 ± 5.4%, NYHA functional class 2.7 ± 0,5). During a follow-up time of 35.2 ± 12.3 months 30 pat had at least one appropriate ICD therapy (25 pat had anti-tachycardia pacing (ATP), 8 pat had ICD-shocks). Mean GLS in pat with ICD therapy was significantly worse than in those without ICD therapy (-6.4% vs. -7.8%, p = 0.018). Multivariate logistic regression analysis showed that GLS (odds ratio 1.31, 95% confidence interval: 1.07-1.60, p = 0.01) and FU duration (OR 1.05, 95% CI 1.02-1.07, p = 0.001) but not LV-EF (OR 0.001, p = 0.17) were the only independent predictors of appropriate ICD therapy.
Conclusion: Our findings indicate that LV GLS is a useful marker to risk stratify pat with DCM, outperforming the current standard LV-EF.

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Remote ischemic conditioning in ST elevation myocardial infarction as adjuvant to primary angioplasty: one-year results of a randomized clinical trial

A Gaspar[1]; A Lourenco[1]; P Azevedo[2]; M Pereira[2]; J Marques[2]; A Leite-Moreira[1]
[1]Faculty of Medicine University of Porto, Department of Physiology and Cardiothoracic Surgery, Cardiovascular R&D Unit, Porto, Portugal; *[2]Hospital de Braga, Cardiology, Braga, Portugal*

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Background: Despite a significant improvement in STEMI care, mortality and morbidity remain high. One of the possible reasons is that reperfusion itself may paradoxically cause additional myocardial injury, through the so-called ischemia-reperfusion injury (IRI). Remote cardiac ischemic conditioning (RCIC) has shown encouraging results in reducing IRI.
Purpose: To evaluate the clinical impact of RCIC as an adjuvant to primary angioplasty in STEMI.
Methods: We conducted a randomized clinical trial to evaluate RCIC versus no intervention in patients with STEMI with < 12 h of symptom evolution (exclusion criteria: shock, post-cardiorespiratory arrest status or indication for surgical revascularization rather than angioplasty). RCIC consisted of intermitent left thigh ischemia through three cycles of 5-min inflation followed by 5-min deflation of a blood-pressure cuff. The primary endpoint was a combined endpoint of cardiac death or hospitalization for heart failure (including device implantation: implantable cardioverter defibrillator, cardiac resynchronization, or left ventricular assist device). We report an interim evaluation at one-year follow-up.
Results: 516 patients were randomized, of which 448 were retained for analysis (231 in the RCIC group and 217 in the no-intervention group). There were no differences in baseline characteristics between the 2 groups. Patients without RCIC evolved more frequently with heart failure during the initial hospitalization (24.4% vs. 16.9%, p = 0,06). There were also more in-hospital deaths of cardiac cause among patients not submitted to RCIC (1.8% vs. 0%, p = 0.05). At follow-up, patients not submitted to RCIC had more frequently an EF < 40% (18.8% vs. 10.1%, p = 0.03). At one-year follow-up, the combined endpoint was more frequent in nonconditioned patients (8.2% vs. 2.3%, p = 0.007).
Conclusion: In this randomized study, RCIC as an adjuvant to primary angioplasty was associated with a better prognosis.

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Importance of structural heart disease and diastolic dysfunction in heart failure with preserved ejection fraction assessed according to the ESC guidelines

D Matan[1]; H Persson[1]; E Donal[2]; L H Lund[3]; E Oger[2]; C Hage[3]; J-C Daubert[2]; C Linde[3]
[1]Danderyd University Hospital, Cardiology, Stockholm, Sweden; *[2]University Hospital of Rennes, Cardiology, Rennes, France*; *[3]Karolinska University Hospital, Cardiology, Stockholm, Sweden*

On behalf of: To be presented by Dmitri Matan on behalf of KaRen Investigator group

Background/Introduction: Forty to 50% of the patients with heart failure (HF) have preserved left ventricular (LV) ejection fraction (EF), named HFpEF. Both morbidity and mortality in HFpEF are similar to those in HF with reduced LVEF, but there is no established treatment.
Purpose: To study prevalence and prognostic importance of presence and severity of diastolic or structural dysfunction in patients with suspected HFpEF in the prospective KaRen registry.
Methods: Following an acute HF-presentation, using Framingham criteria, BNP >100 ng/L or NT-pro-BNP >300 ng/L, and LVEF >45%, echocardiography was repeated after 4-8 weeks and analysed at a core laboratory. Eight diagnostic

echocardiographic criteria for HFpEF were used according to the 2016 ESC HF guidelines. A total of 539 patients were included, complete echocardiography and ECG at 4-8 weeks were available in 356 patients. The primary study endpoint was time to death from all causes or first hospitalisation for HF.

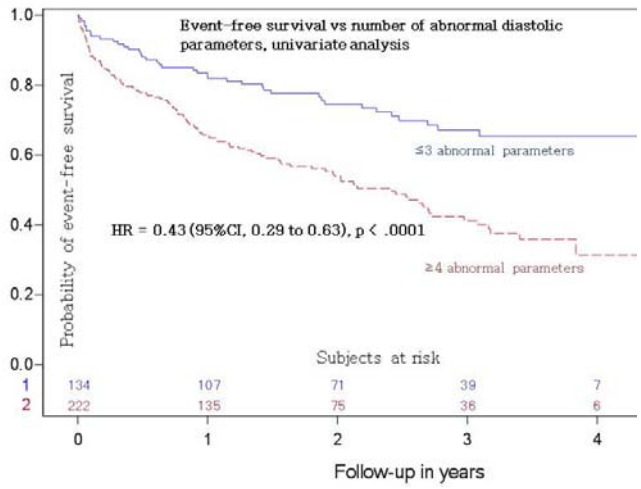
Results: Signs of structural dysfunction (LAVI ≥ 34 ml/m2 or LVMI ≥ 95/115 g/m2) were found in 92% (n = 328) and diastolic dysfunction (DD) (E/e ≥ 13, or < 9 cm/s, or TR ≥ 2.8 m/s) in 82% (n = 290). At least one criterion for HFpEF was found in 98% (n = 351) and 94% (n = 333) had ≥2 criteria. Grading was possible in 352 (99%): 107 patients (30%) had mild DD, 97 patients (27%) had moderate DD and 124 patients (35%) had severe DD. Normal diastolic LV function was found in 24 patients (7%) and 4 (1%) were non-classifiable. After multivariate analyses with adjustment for age, gender, LVEF and natriuretic peptides we found two independent predictors of worse prognosis for event-free survival: moderate to severe diastolic dysfunction (p = 0.0037) or a high number (≥4) of abnormal echocardiographic parameters (p = 0.0033).

Conclusion(s): A vast majority of patients presenting with acute suspect HFpEF met objective echocardiographic criteria for HFpEF according to ESC guidelines. Our findings support the use of ESC guidelines for diagnosis and risk prediction in HFpEF.

Table

Number of pathological diastolic parameters	Hazard ratio	95% CI L	95% CI Up	
4-8 vs 1-3 pathological parameters	0.51	0.32	0.79	0.0033
-	-	-	-	-
Grade of diastolic dysfunction (DD)				
Moderate/severe DD vs none/mild DD	0.56	0.37	0.83	0.0037

Multivariate analysis of 1) the nr of diastolic parameters and 2) grade of diastolic dysfunction, with adjustment for age, gender, EF and BNP/NTpro-BNP. CI L / CI U = lower/ upper control limit of 95% confidence interval.



Survival vs nr of abn. diast. parameters

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Heart failure with a preserved ejection fraction in asia

J Tromp[1]; THK Teng[1]; WT Tay[1]; CL Hung[2]; C Narasimhan[3]; W Shimizu Sw Park[4]; HB Liew[5]; T Ngarmukos Eb Reyes[6]; BB Siswanto Cm Yu[7]; S Zhang J Yap[8]; M Macdonald[9]; AM Richards[10]; MR Zile[11]; IS Anand[12]; CS Lam[13]

[1]National Heart Centre Singapore, Cardiology, Singapore, Singapore; *[2]Mackay Memorial Hospital, Taipei, Taiwan ROC*; *[3]CARE Hospitals, Hyderabad, India*; *[4]National Cardiovascular Centre, Tokyo, Japan; Korea University Hospital, Seoul, Korea Republic of*; *[5]Jeffrey Cheah School Of Medicine And Health Sciences, Monash University Malaysia , Kuala Lumpur, Malaysia*; *[6]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, Manila Doctors Hospital, Manila, Philippines*; *[7]National Cardiovascular Center Universitas Indonesia, Jakarta, Indonesia, Heart Centre, Hong Kong Baptist Hospital, Hong Kong, Hong Kong SAR People's Republic of China*; *[8]Fuwai Hospital, Beijing, The People's Republic of China, National Heart Centre Singapore, Singapore, Singapore*; *[9]Changi General Hospital, Singapore, Singapore*; *[10]National University Heart Centre, Singapore, Singapore*; *[11]Medical University of South Carolina, Ralph H. Johnson Department of Veterans Affairs Medical Center, Charleston, United States of America*; *[12]Veterans Affairs Medical Center, Minneapolis, United States of America*; *[13]National Heart Centre Singapore; National University Heart Centre; Duke-NUS Medical School, Singapore, Singapore*

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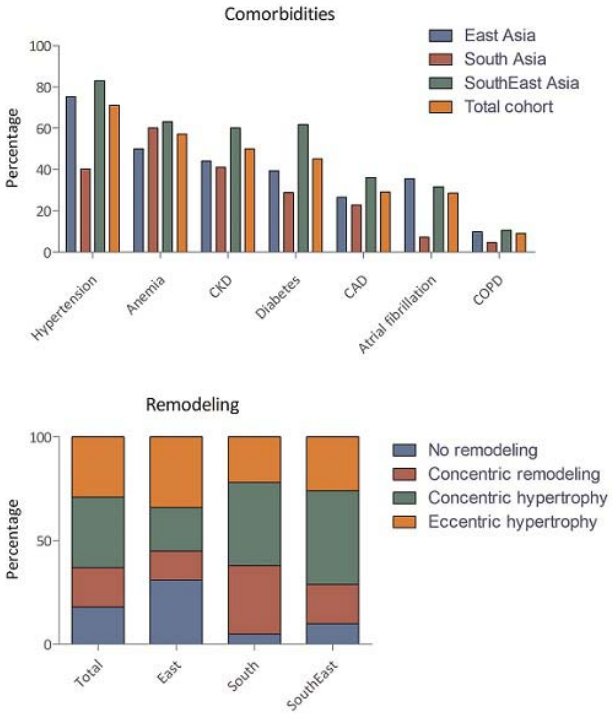
Background: Asia has the largest proportion of the worlds population, and has the highest global burden of hypertension and diabetes, both known risk factors for heart failure with preserved ejection fraction (HFpEF). However, little is known about the clinical characteristics of HFpEF across different parts of Asia.

Purpose: To compare the clinical characteristics and outcomes of HFpEF across Asia

Methods: The baseline clinical characteristics and outcomes of 1203 patients with HFpEF (LVEF ≥ 50%) from 11 Asian countries, grouped as East Asia (Hong Kong, Taiwan, China, Japan and Korea, n = 543); South Asia (India, n = 252); and Southeast Asia (Malaysia, Thailand, Singapore, Indonesia, Philippines, n = 408) were analyzed. Outcomes were independently adjudicated.

Results: The mean age was 68 ± 12 years (37% were < 65 y), 50% were women, body mass index was 27 ± 6 kg/m2 and 80% were in NYHA Class II/III. South Asian patients (63 ± 13 years) were the youngest, and East Asians the oldest (72 ± 12 years). Comorbidities were highly prevalent albeit varying by region (Figure): 70% of patients had 2 or more comorbidities, with hypertension (71%) being the most common, followed by anemia (57%), chronic kidney disease (50%), diabetes (45%), coronary artery disease (29%), atrial fibrillation (AF; 29% by history; 24% by ECG) and chronic lung disease (9%). Notably, Southeast Asian patients had the highest prevalence of all comorbidities except AF. South Asians had the lowest prevalence of all comorbidities except anemia. These regional differences in the burden of comorbidity were associated with differences in echocardiographic characteristics and outcomes. Concentric remodeling and hypertrophy were most prominent among South and Southeast Asians respectively, whereas East Asians had the most eccentric remodeling (Figure; p < 0.001). Among 883 patients who completed 6 months follow-up, 69 (7.8%) patients died or were hospitalized for HF, with the highest number of events in Southeast Asians (14.1%).

Conclusion: These first prospective multinational data from Asia show that Asian patients with HFpEF carry a high burden of co-morbidities despite relative youth, with approximately a third of patients being under the age of 65 years. There is striking diversity of HFpEF in Asia, with the highest rates of comorbidities, concentric hypertrophy and adverse outcomes observed in Southeast Asia. These findings have important implications for public health measures and global HFpEF trials.



figure

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Do patients with acute heart failure and preserved ejection fraction have heart failure at follow-up, impact of framingham criteria

C Camilla Hage[1]; U Lofstrom[1]; E Donal[2]; E Oger[3]; J-C Daubert[2]; C Linde[1]; LH Lund[1]
[1]*Karolinska Institutet, Department of Medicine, Cardiology unit, Stockholm, Sweden*; [2]*Dpartement de Cardiologie & CIC-IT U 804, Centre Hospitalier Universitaire de Rennes, , Rennes, France*; [3]*Clinical Investigation Centre of Rennes, INSERM CIC-1414, CHU, Rennes, France*

On behalf of: KaRen group

Purpose: Heart failure with preserved ejection fraction (HFpEF) is heterogeneous and poorly defined. We assessed prevalence and consistency of Framingham signs and symptoms in acute vs. stable HFpEF.
Methods: In the multi-center Karolinska-Rennes HFpEF study, patients with acute HF according to Framingham criteria, EF ≥45% and elevated brain natriuretic peptides (NPs; NT-proBNP >300 ng/L; BNP >100 ng/L) were assessed again in stable condition 4-8 weeks after hospitalization. Logistic regression was used to assess association between baseline characteristics and types and number of Framingham criteria in acute HFpEF, and the presence of HF at follow-up defined according to four models based on Framingham, the ESC and the PARAGON trial echo criteria (TABLE 1).
Results: In 398 patients, all met Framingham criteria for HF in acute HFpEF and the number of Framingham "points" (2 for major criterion; 1 for minor) were in median 8 (Interquartile range 6-10) in acute HFpEF and 2 (1-4) at stable follow-up ($p < 0.01$). The most common criteria in acute HFpEF were dyspnoea at exertion (90%) and pulmonary rales (71%), which were present in 70% and 13% respectively at follow-up. At follow-up HF was present according to the four models in 27%, 22%, 22% and 22% respectively. Associations between acute characteristics and presence of HF at follow-up are shown in TABLE.
Conclusions: Among patients with acute HFpEF, only a quarter meet the HF definition at stable follow-up according to different contemporary criteria. Characteristics of acute HFpEF that predict persistent HF at stable follow-up were higher age and JVD but not severity of HF. Pleural effusion and tachycardia may yield "false positive" HFpEF diagnoses. This has implications for HFpEF trial design and patient screening.

Table 1

Variable at baseline	Framingham criteria only	Framingham criteria + NP criteria	Framingham criteria + NP criteria + ESC ECHO HFpEF criteria	Framingham criteria + NP + Paragon ECHO structural heart disease criteria
	n=107 (27%)	n=82 (22%)	n=61(22%)	n=69 (22%)
Age per year	1.02	1.04*	1.05*	1.04*
NYHA I + II vs. III + IV	0.76	0.80	1.10	1.03
NT-proBNP per log	1.30	1.23	1.29	1.29
BNP per log	1.09	1.40	1.34	1.37
Framingham per point	1.06	1.09	1.09	1.10*
Jugular venous distension	1.80*	2.56	2.89*	2.58*
Pleural effusion	0.45*	0.41*	0.34*	0.35*
Tachycardia (>100 bpm)	0.87	0.61	0.51	0.52*

Odds ratios for presence of HFpEF *$p < 0.05$

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Capnography in spontaneously breathing chronic heart failure patients: resting partial pressure of end-tidal carbon dioxide a new non-invasive factor on heart failure.

ACGB Alexandra Lima[1]; FMF Silva[1]; FMT Teixeira[1]; ML Silva[1]; AA Missias[1]; R Furtado[1]; SHR Ramalho[1]; F Staufer[1]; G Cipriano[1]
[1]*University of Brasilia, Health Sciences and Technologies, Brasilia, Brazil*

Introduction: Given the elevated risk of adverse events in patients with heart failure (HF), identifying clinical variables with prognostic value that are also easily obtainable and cost-efficient is a high priority. The partial pressure of end-tidal CO2 (PetCO2) measured by cardiopulmonary exercise testing (CPX) at rest and during exercise has been shown to accurately reflect disease severity and cardiac function in HF patients. The partial pressure of end-tidal CO2 (PetCO2) measured by capnography was introduced by Fletcher during the early 1980s and most clinical applications concerning intubated and ventilated patients. The use of capnography in spontaneously breathing patients resulted however in additional technical and clinical challenges.
Purpose: The purpose of the current study was to evaluate the pattern of behavior of resting PetCO2 measured by LifeSense Tabletop Capnography in spontaneously breathing HF patients, compare to PetCO2 measured in resting and exercise by CPX (rest PetCO2CPX and peak PetCO2CPX) and evaluate the correlation with important prognostic parameters in HF (peak Oxygen consumption peak VO2 and the minute ventilation–carbon dioxide production relationship VE/VCO2 Slope).
Methods: A total of 155 patients with reduced left ventricle ejection fraction (LVEF < 50%) in current standard medical therapy were included in this analysis. All patients collected the resting PetCO2CAP after one, two and three minutes of rest, followed by a symptom limited CPX in bicycle for the measured of resting PETCO2CPX, peak PETCO2CPX, peak VO2 and VE/VCO2 slope). The data were analyzed in SPSS 21 and significance was considered as $p < 0.05$. The strength of reproducibility between three measures of resting PETCO2Cap was evaluated by the intra-class coefficient (ICC) of correlation. The association between PetCO2CAP, PetCO2CPX and VE/VCO2 slope was made by the Pearson correlation test.
Results: One hundred fifty-five HF patients (gender = 60.0% male; age = 56.3 ± 12.9 years; 35.5% isquemic HF, 39.4% NYHA class III, peak VO2 = 13.6 ± 5.5 ml.kg-1.min-1, VE/VCO2 Slope = 35.9 ± 12.5, LVEF = 38.0 ± 5.1%) were evaluated. The ICC between the three measures of resting PetCO2CAP demonstrate concordance among observations (ICC = 0.983 (0.978-0.987), $p < 0.001$). There was positive correlation between mean resting PETCO2CAP and peak VO2 ($r = 0.352$, $p < 0.001$), resting PETCO2CPX ($r = 0.373$, $p < 0.001$) and peak PETCO2CPX ($r = 0.431$, $p < 0.001$) and inverse correlation between resting PETCO2CAP and VE/VCO2 Slope ($r = -0.481$, $p < 0.001$).
Conclusion: Data supporting the potential clinical utility of capnography in spontaneously breathing chronic HF patients. The results of our study support the correlation between resting PETCO2 by capnography and measured during CPX and the VE/VCO2 slope). We are describing a new non-invise parameter that could be a useful prognostic marker in HF patients resting PETCO2 by capnography.

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The left ventricular noncompaction syndrome in fifty adults: clinical variants, follow-up and outcomes

O V Blagova[1]; AV Nedostup[1]; EV Pavlenko[1]; VP Sedov[1]; NV Varionchik[1]; NV Gagarina[1]; EA Mershina[2]; VE Sinitsyn[2]; VA Sulimov[1]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*; [2]*Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*

Purpose: to study clinical variants, follow-up and outcomes of the left ventricular noncompaction (LVN) syndrome in adult patients.
Methods: The diagnosis of LVN was established in 50 adults (22 females, 18-76 years, on the average 42.8 ± 14.9) on the basis of visual criteria, in 12 patients using three methods (Echo-CG, MRI, CT), in 32 patients using any two methods. Were also performed myocardial biopsy and autopsy (n = 10/4) with viral DNA detection (real-time PCR), anti-heart antibody measurement. The mean follow-up was 12 [5.5; 25.5] months.
Results: there was a high frequency of the association of LVN syndrome and other heart disease by adults: 7 patients (14%) had congenital heart disease (atrial and ventricular septal defects, pulmonary artery stenosis, bicuspid aortic valve, vascular malformations), 3 (6%) hypertrophic cardiomyopathy, 2 (4%) arrhythmogenic right ventricular dysplasia, 1 (2%) systemic myodystrophy, 1 (2%) restrictive cardiomyopathy, 1 (2%) Danon disease. Only one patient with LVN syndrome had no symptoms, but signs of dilated cardiomyopathy (DCM). In 9 patients (18%) LVN had "idiopathic" arrhythmias mask, in 15 patients (30%) mask of DCM, in 7 patients (14%) LVN was first identified at the same time with acute myocarditis. In 6 cases (12%) LVN was associated with coronary atherosclerosis, but in 2 patients (4%) the initial diagnosis "ischemic heart disease" was false. The associated myocarditis was in 29 patients (58%) detected, incl. 12 patients by morphologic study of myocardium and one patient with sarcoidosis. The virus was found in 6 patients in the myocardium (parvovirus B19 in 5, human herpes virus type 6 in 2, herpes simplex virus type 1, 2 in 1 and Epstein-Barr virus in 1) and in 12 patients in the blood.
Heart failure was in 86% of patients and angina pectoris in 32% diagnosed; 7 patients had a typical signs of the myocardium infarction. The incidence of atrial fibrillation was 30%, stable and unstable ventricular tachycardia 78%. The average LV diastolic size was 6.1 ± 0.8 cm, LV ejection fraction 34.6 ± 14.0%. Eleven patients (22%) without anticoagulants had intracardiac thrombi; 10 of them had LV ejection fraction less than 40%. Six patients (12%) had embolism (renal,

pulmonary, myocardium infarct, stroke). The devices were in 23 patients (46%) implanted: CRT/D in 1/4, ICD in 14, pacemakers in 4 patients. In three patients was cardiac transplantation performed. The mortality was 10.0% (5 patients) due to myocardial infarction, arrhythmias, heart failure. Conclusions. LVN syndrome in adults is vary polymorphic and often associated with other cardiomyopathy (18%) and myocarditis (58%). The frequency of complications (incl. stable ventricular tachycardia, embolism) is high, that requires development of differential approaches to the treatment.

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Causes and consequences of longitudinal left atrial dysfunction assessed by 2d-strain echocardiography in patients with cardiac amyloidosis

D Diane Bodez[1]; A Guellich[1]; U Vergeylen[1]; E Alonso[1]; S Guendouz[1]; A Galat[1]; AS Cottereau[2]; V Plante-Bordeneuve[3]; JL Dubois-Rande[1]; L Hittinger[1]; JF Deux[4]; D Mohty[5]; T Damy[1]

[1]*University Hospital Henri Mondor, Department of Cardiology, Creteil, France*; [2]*University Hospital Henri Mondor, Department of Nuclear Medicine , Creteil, France*; [3]*University Hospital Henri Mondor, Department of Neurology, Creteil, France*; [4]*University Hospital Henri Mondor, Department of Radiology, Creteil, France*; [5]*University Hospital of Limoges, AL Amyloidosis referral center, Limoges, France*

Background: In cardiac amyloidosis (CA), left atria (LA) enlargement, dysfunction (LASD) and intra atria thrombi have been described mostly in systemic light chain CA (AL). The prevalence and physiopathological causes and consequences of these alterations are unclear.

Purpose: Demonstrate that LA 2D strain echocardiography (2D-SE), a new tool, is useful to anlayse LA systolic dysfunction and to explore its causes, consequences and association with thromboembolic events in different types of CA.

Methods: CA patients in sinus rhythm were included. At baseline, history of thromboembolic event, clinical and biological characteristics and echocardiography were recorded. Global and regional LA longitudinal strain (LS) by 2D speckle-tracking echocardiography (2D-SE) were measured. Patients were followed-up to identify independent predictors of mortality.

Results: Seventy-six CA, of whom 21 had AL, 42 hereditary transthyretin (m-TTR) and 13 wild-type (wt-TTR) were included. Peak atrial longitudinal strain (PALS-4C) was negatively correlated to NT-proBNP ($r = -0.6$, $p < 0.0001$) and to LA end-diastolic volume ($r = -0.48$, $p = ou < ? 0.0001$). LA volume was higher and PALS-4C more altered in wt-TTR compared to the AL and m-TTR. The 19 patients who presented a history of thromboembolic event at baseline, had a significantly lower PALS-4C compared to those without ($p = 0.003$). No association of PALS-4C and LA infiltration estimate by Cardiac MRI and by bone scintigraphy was observed. Multivariate analysis identified PALS-4C as the only left atrial echocardiographic independent factor of mortality with an optimal cutoff value of 9.5% (AUC 0.75, IC95% 0.60-0.89). Therefore including all the variables, only NTproBNP was an independent marker of prognosis.

Conclusions: Atrial function estimated by strain is useful to identify patients at risk of death and might be helpful to select patients that may benefit from preventive anticoagulant treatment.

Clinical Case Corner 1 - HoT heart: inflammation and infections in heart failure

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Eosinophilic myocarditis due to vasculitis

P Prithwish Banerjee[1]; V Dhakshinamurthy[1]
[1]*University Hospital, Coventry, United Kingdom*

Acute heart failure with eosinophilia is not a common presentation but may signal an underlying reversible myocarditic process if recognised early. Making a diagnosis of the aetiology of the heart failure in this situation involves investigating the several causes of eosinophilia. We present such a patient who presented many learning points to the heart failure team looking after him.

A 65 year old lady with a previous history of asthma and skin rashes presented with a clinical picture of a respiratory tract infection with marked oesinophilia of 9.06 x 109 /L but no pneumonia. She later developed signs of acute heart failure with a higher eosinophil count of 22.94 x 109 /L and a large Troponin T rise of 3153 ng/L with a normal ECG and severe left ventricular systolic dysfunction on echocardiography. Myocarditis was suspected and confirmed on cardiac MRI which showed patchy late gadolinium enhancement with myocardial oedema and a LVEF of 28%. Coronary angiography was normal and the vasculitis screen showed an indeterminate pattern anti-neutrophil cytoplasmic antibodies (ANCA) and raised IgE. Other causes of eosinophilia such as parasitic and other infections, haematological malignancies (including bone marrow biopsy, trefine and cytogenetic studies) and drugs were excluded but peripheral neuropathy was diagnosed on neurophysiology investigations. The differential diagnosis at this point was between hyperoesinophilic syndome and Eosinophilic Granulomatosis with Polyangitis (EGPA). An endomyocardial biopsy was undertaken which showed eosinophilic myocarditis. Finally, EGPA was felt to be the most likely diagnosis.

She was successfully treated with high dose steroids and azathioprine along with standard heart failure medications resulting in significant improvement in LV systolic function. Eosinophilic myocarditis should be strongly considered in patients with acute heart failure and peripheral oesinophilia.

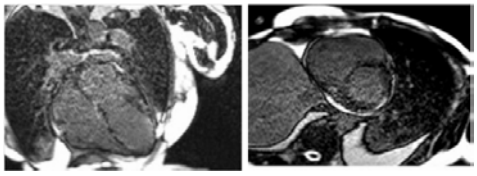

Figure 1. Delayed enhancement on MRI

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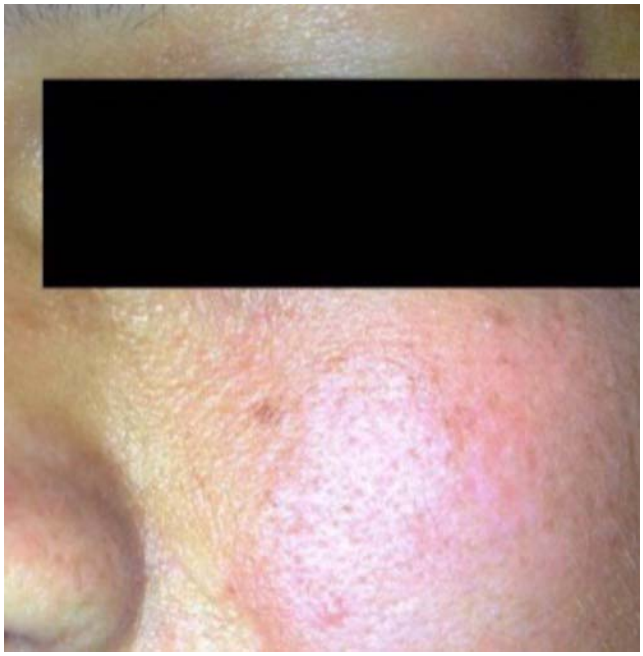
Acute reactivation of chagas disease in post cardiac transplant patient under immunosuppression with cutaneous lesions manifestation

SL Sarah Leandro Da Silva Souza[1]; FS Fabricio Da Silva[1]; RSC Rafael Silva Cortes[1]; MB Marcelo Botelho Ulhoa Junior[1]; VSB Vitor Salvatore Barzilai[1]; FAA Fernando Antibas Atik[1]; RBC Renato Bueno Chaves[1]
[1]*Instituto de Cardiologia do Distrito Federal, Brasilia, Brazil*

Introduction: Chagas disease is a parasitary infection caused by Trypanosoma cruzi, transmitted by a triatomine insect, popularly known as "barbeiro" or "kissing bug". Epidemiologically, this disease was already diagnosed in the whole American continent, since the south of United States of America till Argentina. The patient, once infected, presents both forms acute and chronic, and, in some occasions, the reactivated chronic form. This one, at first, occurring in immunosuppressed patients, whether by hematological diseases, HIV or post transplant patients in use of immunosuppressant drugs aiming to inhibit the graft rejection. In the presence of the acute chronic form, its necessary the early diagnostic with the intention to stop the damages to the organism and, when it comes to a post transplant patient, to the graft. The goal, in this case, is to attempt to the clinical signs of reactivation like fever, acute myocarditis signs and cutaneous lesions for the treatment to be soon implemented.

Case report: S.O.A, female, 39 years old, with chagasic myocardiopathy and cardiac transplant in October 2013. The patient was under immunosuppresion with tacrolimus, mycophenolate mofetil and predinisone, undergoing outpatient follow-up. Routine ecocardiography, in July 2015, showed significant loss of left ventricule with ejection fraction of 25%. In despite of no symptomes, the patient was hospitalized for investigation. During hospitalization, the patient presented characteristic face, upper and lower limbs cutaneous rash, soon interpreted as Chagas disease reactivation. With this evidence, the patient was submitted to oral treatment with benznidazole for eight weeks. After thirty days of the treatment beggining, it was noticed an increase of the left ventricule function, with a left ventricule ejection fraction of 40% and full remission of the cutaneous lesions. After the end of the treatment, there was a ventricular function recovery. The patient was discharged asymptomatic and, till the send date of this case, there werent new episodes of the disease reactivation and the graft function remains preserved.

Conclusion: The patient with Chagas disease, after cardiac transplant, must me submitted to immunosuppressant therapy aiming to avoid the graft rejection. Therefore, he becomes susceptible to the disease reactivation. The focus, in this case, is the early diagnosis, once further damages must be avoided, between them, the loss of cardiac function. Thus, a classical sign as the presence of cutaneous lesions, easily seen to the ectoscopy, cant become unnoticed, for the treatment to be soon begun and the reactivation reversed.



Lesion

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Acute myocarditis and myositis after immune checkpoint inhibition

D Witham[1]; S Knauss[1]; A Marek[1]; H Dreger[1]; L Harms[1]; K Joehrens[1]; W Stenzel[1]; G Baldenhofer[1]; V Stangl[1]; K Stangl[1]
[1]*Charite - Campus Mitte (CCM), Berlin, Germany*

A 74 year old man with metastatic malignant melanoma presented to the emergency department with exertional dyspnea, fever, diplopic images, and muscle weakness nineteen days after intravenous infusion of nivolumab and ipilimumab. There were no abnormalities in the examination of heart and lung. Edema and signs of a deep venous thrombosis were absent. Neurological examination revealed bulbar deviation and ptosis on the left side. An ECG showed sinus rhythm tachycardia (110/minute), new atrioventricular block I, complete right bundle branch block, and left anterior hemiblock. The blood work revealed ten-fold elevated troponin T and creatinkinase levels. Initial transthoracic echocardiography showed septal dyskinesia. Suspected non-ST-segment elevation myocardial infarction was immediately ruled out by invasive coronary angiography. As D-dimers were not elevated, pulmonary embolism was unlikely. Neurological symptoms gave rise to perform a cerebral MRI scan, which did not show any abnormalities. Further analyses revealed strongly elevated anti-myolemmal, anti-sarcolemmal, anti-titin, and anti-voltage gated calcium-channel-(VGCC, N-Type) antibodies. Cardiovascular MRI showed a slight, but insignificant myocardial gadolinium uptake. The findings led us to suspect autoimmune related adverse events after administration of nivolumab and ipilimumab. Thus, oral glucocorticoid therapy was initiated. Septal dyskinesia, atrioventricular, and right bundle branch block disappeared. During short term follow up, the patient reported amelioration of dyspnea, but still suffered from diplopic pictures. An intravenous immunoglobuline therapy was performed over five days, but the patient still was compromised and creatinkinase and troponin levels did not decrease. Finally, skeletal and endomyocardial biopsy were performed.
The diagnosis of myositis and myocarditis was confirmed and most likely attributed to the past therapy with nivolumab and ipilimumab. PCR for typical cardiotropic viruses was negative. Both, the myocardium and skeletal muscle showed interstitial fibrosis and inflammatory cell infiltration dominated by lymphocytes. Immunohistochemical staining revealed that about 80% of the cells were CD3+ T-lymphocytes and accounted in equal parts to the CD4+ and CD8+ subgroup. Myophagocytosis was seen in areas where CD68+ macrophages were infiltrating skeletal muscle and myocardium. Interestingly, there was a significant membranous expression of Programmed Cell Death Protein 1 (PD1) ligand on cardiomyocytes and myocytes whereas about 50% of the infiltrating lymphocytes were positive for PD1 receptor.
Nivolumab blocks the PD1 receptor on T-lymphocytes, thereby inhibiting immunosuppressive signaling throughout cancer cells overexpressing PD1 ligand in order to evade the hosts immune system. Accordingly, PD1 receptor blockade on lymphocytes with nivolumab might not only have lead to an intensified immune attack against cancer cells, but also to an intensified autoimmune attack against the patients self tissues including striated muscle cells with the result of a cytotoxic and humoral immune reaction.
Immune checkpoint inhibitors actually belong to the most promising therapy options for patients with end stage melanoma and probably many other cancer entities. Accordingly, the absolute number of irAE might increase in the future challenging inpatient and outpatient physicians.

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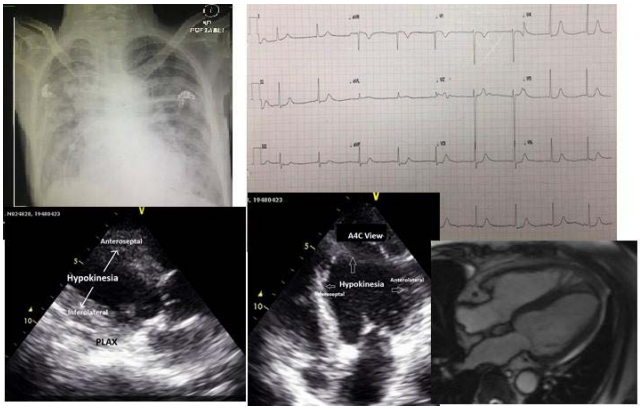
Managing acute heart failure (AHF) in severe dengue-leptospirosis co-infection - Walking a tightrope

TIAU Wei Jyung Patrick[1]; SG Shatishkumar Govindaraju[1]; TS Tan[2]; SHAWAL Mohd Shawal Faizal Mohamad[1]; CK Choor[1]; HH Hamat Hamdi Che Hassan[1]; OM Oteh Maskon[1]
[1]*University Kebangsaan Malaysia (UKM), Cardiology, Kuala Lumpur, Malaysia*;
[2]*University Kebangsaan Malaysia (UKM), Kuala Lumpur, Malaysia*

Introduction: Acute myocarditis often caused by a viral infection, and less commonly non-viral pathogens. It is usually mild and self-limiting, but may rarely manifests as a severe fulminant form, resulting in cardiogenic shock with a high mortality.
Case: We present a 68 year-old man complaining of fever and lethargy for 5 days. He was febrile, dehydrated and hypotensive. Fluid resuscitation was given but he developed acute pulmonary oedema shortly after. ECG showed diffuse ST depressions over leads V3-V6. An echo showed global LV hypokinesia EF 35%, elevated LV filling pressure (elevated E/e 15, ePWCP of 17mmHg). Cardiac troponins were markedly raised. He denied chest pain and there were no symptoms of heart failure prior to this. Investigations showed severe thrombocytopaenia and lactate acidosis. He was reviewed by cardiologist and ID team, and was diagnosed with fulminant myocarditis secondary to severe dengue-leptospirosis co-infection, based on positive serology for the two disease.
His condition remained critical, required BiPAP respiratory support. Antibiotic was started. He was in the critical phase of an acute dengue infection with potential plasma leakage, hence, the use of diuretic would risk of further depleting the intravascular volume and causing distributary shock. Cardiac output was maintained with inotrope infusion (noradrenaline,dobutamine) and continuous hemodynamic (CO,CI,SVRI,SVR) monitoring were used to guide fluids/diuretic therapy during the critical phase.
His condition started to improve after 48 hours. Serial echo showed good LV function recovery (EF 52%). He did not agree for angiogram and was discharged after one week. CMR which was done 3 weeks later showed no LGE in the myocardium.
Discussion: In this patient who presented with acute febrile illness and thrombocytopaenia; dengue hemorrhagic virus and zoonotic-leptospirosis infection need to be considered as it is highly prevalent in the South East Asia, and acute myocarditis has been reported in both conditions, resulting in AHF. Differentiate acute myocarditis from an acute myocardial infarction(MI) can be challenging, and to perform a diagnostic procedure such as endomyocardial biopsy or angiogram here would certainly carry a high risk of bleeding and complications. Therefore, diagnosis of fulminant myocarditis here could only be made clinically, and the absence of chest pain would make the diagnosis of Type 1 spontaneous MI less likely.
Dengue shock syndrome has a high mortality and it is often due to plasma leakage during the critical phase, causing hypovolaemic shock which would require fluids resuscitation. However, in this patient who also complicated with severe LV dysfunction and cardiogenic shock, excessive fluids had resulted in acute pulmonary oedema. Therefore, managing this patient was extremely challenging, as on one hand it was essential to maintain adequate cardiac output and perfusion, but on the other hand, overzealous fluid replacement could lead to worsening pulmonary congestion. The use of continuous hemodynamic assessment (CO,CI,SVRI) here has become invaluable in determining the inotropic/fluids/diuretic therapy.
Fulminant myocarditis is associated with a higher mortality, but following the acute phase, LV function usually recover. Mechanical circulatory support with VAD as a bridge to recovery has been successfully used in intractable HF.
Conclusion: In summary, identifying the underlying aetiology of AHF is crucial, in order to tailor the individualise treatment for AHF. In this case, a multidisciplinary care is important, and resulted in a favourable clinical outcome.



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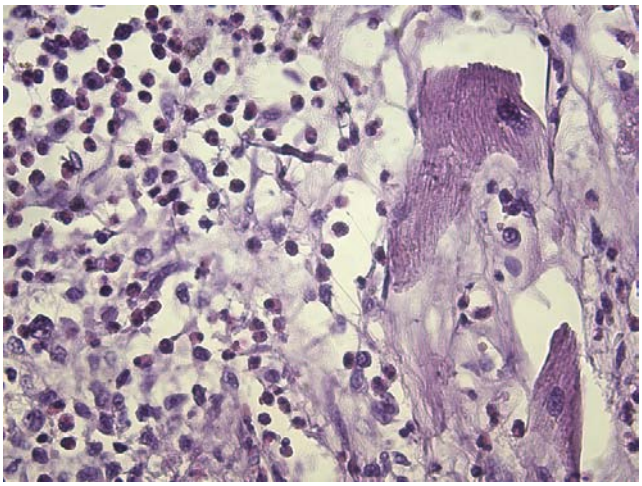
Endomyocarditis as a rare complication of toxocariasis

M KH Lepshokova[1]; NV Kijvatova[1]; OM Mesheryakova[1]; O N Ponkina[1]; HD Kosmachova[1]; IA Shelestova[1]; A M Namitokov[1]
[1]*Krasnodar Regional Clinical Hospital No1, Krasnodar, Russian Federation*

We present a case of a patient with rare and life-threatening cardiac complication of toxocariasis.
A 53-year-old man was admitted to neurological department of hospital for recent motor weakness, ataxia, pruritus and increased body temperature to 37.5. He had a previous history of asthma, but did not take any medications. The vital signs were blood pressure 110/70 mmHg, heart rate 110/min, respiratory rate 19/min, body temperature 37.5. Initial laboratory investigations showed leukocytosis (29,800/μL) with hypereosinophilia (8.84/μL), elevated CK-MB (55.2/μL); troponin I was 29.73 ng/μL. Serum total IgE level was 401 IU/mL, C-reactive protein was 158.59 mg/L. Chest x-rays was unremarkable. An electrocardiogram showed sinus tachycardia and nonspecific T wave and ST depsession on inferior and posterolateral leads. Computer tomography of the brain did not revealed pathology and computer tomography of the chest and abdomen showed a splenomegaly and an increased number of normal-sized mediastinal and retroperitoneal lymph nodes. Echocardiogram revealed increased left ventricule (LV) wall thickness (12

mm) with decreased LV systolic function (EF 48%) and a mass 14 mm in diameter from lateral wall of LV, that reduced mobility of mitral valve posterior leaflet. Peripheral blood eosinophilia, elevated level of cardiac enzymes, previous history of asthma, LV wall thickness, decreased LV systolic function are the important clues for early suspicion of eosinophilic myocarditis. While all this symptoms may be a parts of paraneoplastic syndrome of heart malignancy, our aim was to differential diagnosis between this diseases. We performed screening for helminthiasis using an in-house enzyme-linked immunosorbent assay. The next step we planned to performe endomyocardial biopsy, but about 6 hours after arrival patient had ventricular fibrillation and unsuccessful resuscitation. Screening for helminthiasis revealed a positive titer for Toxocara spp of 6.2 optical density ([OD] normal, <0.5 OD). Autopsy and histological examination showed myocardial disarray, interstitial oedema with diffuse eosinophilic inflammatory infiltrate and myocardial necrosis, nonbacterial thrombotic endocarditis with in mitral valve.
Thus, patient had Toxocariasis-associated endomyocarditis. Eosinophilic myocarditis is one of the most fatal and rare complications of hypereosinophilia. One of the reasons of hypereosinophilia is parasite infection. In case of heart injury accompanied by fever and eosinophilia with allergic skin rashes, tissue infestation by parasites should be considered.



Endomyocardial biopsy

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A case of myopericarditis in a patient with crohn's disease who responded promptly to selenium supplementation

H Altay[1]; F Ozkalayci[1]; B Yasar[2]
[1]Baskent University Istanbul Hospital , Cardiology, Istanbul, Turkey; *[2]Baskent University Istanbul Hospital , gastroenterology, Istanbul, Turkey*

Introduction and case report description: A 44-year-old woman was evaluated for progressive, severe dyspnea and tachycardia while she had been hospitalized for crohns disease with multiple intestinal fistules and perianal abscess in the gastroenterology department. Physical examination revealed an under-nourished cachectic and ortopneic woman. She had a blood pressure of 100/60 mmHg and a persistent sinus tachycardia at a rate of 140 beats per minute, repiratory rate of 23 breaths per minute and an oxygen saturation of 90% despite continuous oxygen therapy given at a rate of 4 liter per minute. She had an elevated jugular venous pressure and third heart sound heard at apex but no pericardial friction rub. Fine crackles and decreased breath sounds were heard at bilateral bases of her lungs, left greater than right. Laboratory studies revealed a hematocrit level of 32,4%, a white blood cell count of 11,3 X 103 and a normal platelet count. Her high-sensitivity troponin and NT- proBNP levels were elevated, at 78,1 ng/ml (normal range $<$ 15 ng/ml) and 35,000 pg/ml,respectively. The eritrocyte sedimentation rate was 22 mm/h, C-reactive protein concentration 192 mg/L and the albumin level 2,8 g/dL. Serum selenium level was 3,62 microgram per liter (normal range 46-143). The electrocardiogram showed sinus tachycardia with non specific ST-T wave changes. A chest radiograph revealed interstitial pulmonary edema and left-sided pleural effusion. Transthoracic echocardiography (TTE) revealed global hypokinesis of left ventricular (LV) walls, severe LV systolic dysfunction with an ejection fraction of 30% and a mild- to moderate-sized pericardial effusion without evidence of tamponade physiology (Figure 1). Angiography showed normal coronary arteries. Description of the problem This patient had decompensated heart failure most probable due to subacute myopericarditis. She also had selenium deficiency due to malnourishment. Answers and discussion: Myocarditis in this patient could be related to enhanced systemic inflammatory immune response which is a well known condition in crohns disease. Myocarditis and cardiomyopathy could also be due to selenium deficiency which is usually described in crohns disease. She was treated with ramipril, karvedilol, spirinalactone and furosemide. After that, dyspnea diminished and she was discharged with selenium supplementation. After one month of discharge, she was seen in the outpatient clinic. Echocardiographic measurements were within the normal limits as well as the serum selenium level Conclusions and Implication for clinical practice: The case was unique in the way she responded to treatment with selenium supplementation for subacute myopericarditis and selenium deficiency in crohns disease with a rapid recovery of cardiac function in a matter of weeks. The possibility of selenium deficiency should be considered in all malnourished patients with myocarditis and crohns disease.

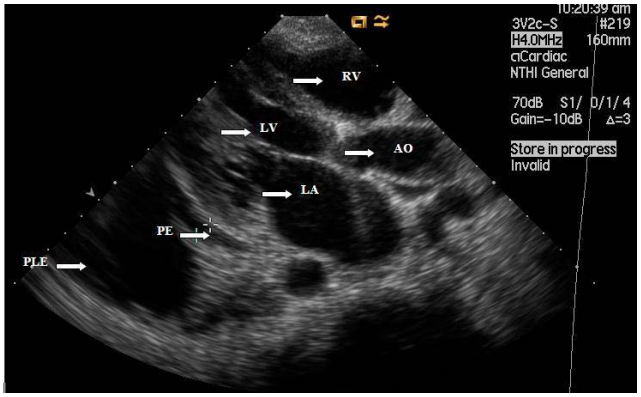

Figure 1.echocardiography, Parasternal view

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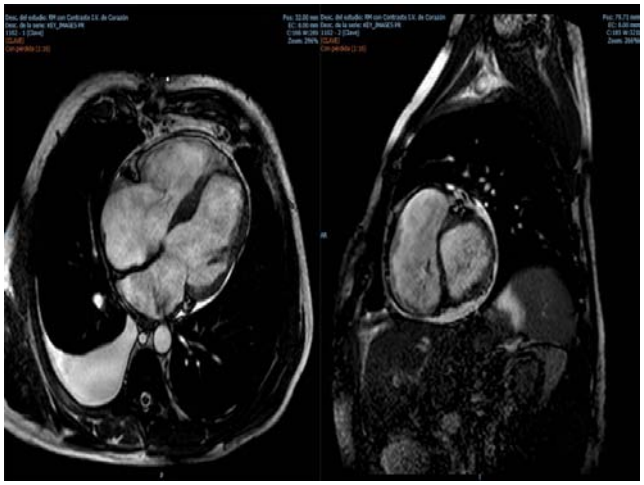
Autoinmune acute myocarditis induced by pembrolizumab

C Anaya-Quesada[1]; D Rangel Sousa[1]; A Campos-Pareja[1]; E Jimenez-Baena[1]; MP Gotarredona-Serrano[2]; MP Villa Gil-Ortega[3]; JM Sobrino-Marquez[1]; E Lage-Galle[1]
[1]University Hospital of Virgen del Rocio, Heart Failure and Heart Transplantation Unit. Service of Cardiology, Seville, Spain; *[2]University Hospital of Virgen del Rocio, Cardiothoracic Image Unit, Seville, Spain*; *[3]University Hospital of Virgen del Rocio, Haemodynamic and Interventional Cardiology Unit, Seville, Spain*

Introduction: Immune checkpoint inhibitors (ICI) have improved clinical outcomes associated with numerous cancers, but high-grade, immune-related adverse events can occur, particularly with combination immunotherapy. Pembrolizmab (PEM) is an ICI, an antiprogrammed death-1 (PD-1) antibody that have individually improved survival in patients with melanoma. Case-report:53 years old caucasian man with personal history of arterial hypertension, light alcohol comsumption up to 2014 and no previous heart disease known. Diagnosed of advanced melanoma (debut in 2007 with right foot skin lesion) stage IV BRAF wild-type enrolled in a clinical trial reciving PEM 200 mg iv QW3 plus Epacadostat 300 mg BID for the two previous months. Admitted to Emergency Room complaining sudden paroxysmal nocturnal dyspnea and oedema in lower limbs wihout chest pain. No flu-like symptoms the previous days. A 3-millimeter ST elevation was detected throughout the precordial series in ECG with evidence of myocardical necrosis (Troponin T us 5341 ng/L, CPK 981 mU/mle) and myocardial wall stress (NT-ProBNP 8452 pg/ml) biomarkers elevation. Red and white blood cells count and platelets were normal. Urgent coronary angiography was performed without evidence of epicardial coronary artery obstructive lesions neither vasospasm. A transthoracic echocardiogram was carried out showing a dilated left ventricle with global hypokinesis and severely depressed LVEF(29%) with mild functional central mitral regurgitation, and dilated right ventricle with severe systolic dysfunction along with severe tricuspid insufficiency due to tricuspid ring dilatation. Acute pulmonary tromboembolism (APE) was ruled out with angio-CT. Cardiac magnetic resonance showed biventricular enlargement with systolic disfunction (22% RVEF and 30% LVEF) with signs of acute inflammation (edema) and necrosis (pathological late gadolinium enhancement -LGE-) with a patchy non-coronary intra myocardium LGE pattern) with main RV involvement compatible with toxic myocarditis by drug (Fig.1). Evolution with medical treatment including steroids was adequate and the patient could be discharged. Discussion: Acute myocarditis diagnosis is sometimes a challenge. Acute coronary syndromes, APE, stress cardiomyopathy, e.g. should be ruled out. Clinical data along with image techniques as CMR improves accuracy of diagnosis. A toxic aetiology of myocarditis always should be considered as the patient is enrolled in a clinical trial. Conclusion: The development of myocarditis from ICI does have biologic plausibility. In studies in mice, PD-1 plays a role in myocardial

immune responses and protects against inflammation and myocyte damage in models of T-cellmediated myocarditis. Genetic deletion of PD-1 in mice leads to cardiomyopathy that is caused by autoantibodies against cardiac troponin I. As nivolumab, another antiprogrammed death-1 (PD-1) antibody, PEM can be related to toxic myocarditis due an autoinmune mechanism.



CardioMR

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A new phenotype of immune related cardiac adverse events induced by immune checkpoint inhibitors

Y Yuki Fujii[1]; M Takei[1]; R Onoguchi[1]; A Endo[1]; N Hirata[1]; K Suzuki[1]; T Hasegawa[1]; T Takahashi[1]; S Nakagawa[1]
[1]*Saiseikai Central Hospital, Cardiology, Tokyo, Japan*

Introduction: Anti PD-1 antibody, nivolumab, is a new anti-cancer drug which works as an immune checkpoint inhibitor. Despite the impressive benefits of this drug, its use can cause serious immune related adverse events (irAEs), characterized by abnormal invasion of immune cells into normal tissues. Some cases of myocarditis with infiltration of CD8+ immune cells into cardiac tissue have already been reported as the cardiac manifestation of irAEs. We report cases of two patients who developed cardiomyopathies during treatment with nivolumab. Interestingly, clinical courses and histopathological analyses of hearts were different from those of previously reported. Case reports: Patient 1; A 56-year-old woman with lung adenocarcinoma was admitted to our hospital due to acute decompensated heart failure two months after the initiation of the treatment with nivolumab. Her chest X-ray showed bilateral pleural effusions and cardiac dilatation. The plasma BNP level increased to 1600 pg/ml, and the echocardiogram revealed diffuse left ventricular hypokinesis with an ejection fraction of 32%. CT coronary angiogram showed no stenosis in her coronary arteries. Biopsy samples from her heart showed mild myocardial hypertrophy without any evidence of inflammation nor fibrosis. Cardiac MRI showed no apparent late gadolinium enhancement and T2 high spots. Cardiomyopathy caused by nivolumab was suspected, thus the interruption of the drug and the initiation of βblocker and ACE inhibitor were undertaken. 2 months later, her left ventricular systolic function improved to normal range. Patient 2; A 71-year-old man with lung adenocarcinoma was admitted to our hospital with anorexia after receiving the treatment with nivolumab for a month. His ECG showed ST segment elevation in leads V2-V6. The high sensitive troponin I level increased to 400 pg/ml, and the echocardiograms showed preserved left ventricular systolic function. No significant stenosis was found with coronary angiography. Biopsy samples from his heart revealed myocardial hypertrophy and subtle replacement of myocardium with fibrotic tissue. He was treated with hydrocortisone for 5 days and his symptom was gradually improved. ST segment elevation was resolved and he was discharged to home after two weeks of hospital stay. Discussion: Some cases of myocarditis during treatment with immune checkpoint inhibitors were already reported. Most of them resulted in death in spite of treatment with high-dose steroid. Furthermore, in those cases, histopathological analyses of hearts demonstrated lymphocytic infiltration with a predominance of CD8+ T cells. In our two cases, however, the patients were recovered and histopathological analyses of their hearts did not show lymphocytic infiltration. These two cases suggest the existence of new phenotypes of cardiac adverse events induced by immune checkpoint inhibitors, distinguished from previously reported lymphocytic myocarditis with histopathological findings.

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A case of reversible dilated cardiomyopathy caused by Takayasu arteritis

S-H Sung-Hee Shin[1]; JH Jang[1]; SW Kwon[1]; SD Park[1]; SI Woo[1]; DH Kim[1]; J Kwan[1]
[1]*Inha University Hospital, Incheon, Korea Republic of*

27-year-old female was consulted to the cardiology because of cardiomegaly on chest X ray. She had been treated with a suspicion of bronchial asthma at local clinics. She had no history of hypertension or diabetes and suffered from exertional dyspnea from 6 months ago. Transthoracic echocardiography showed dilated left atrium and left ventricle (LV) with severely depressed LV systolic function. The aortic valve was mildly thickened with moderate regurgitation. On subcostal view, abdominal aorta was diffusely narrowed. Abdomen CT was done and it revealed diffuse wall thickening of lower thoracic and abdominal aorta with segmental narrowing from celiac axis to inferior portion of renal vein, which was compatible with aortits. Coronary angiography showed no significant stenosis of coronary artery. Brain MRA demonstrated severe stenosis of bilateral common carotid artery and proximal subclavian artery. Cardiac MRI showed delayed hyperenhancement at the mid wall of mid to basal antero- and infero- lateral wall. Takayasus arteritis was finally diagnosed. Immunosuppressive treatment was started with traditional heart failure management. After 3 months, follow-up echocardiography showed that LV function markedly improved with decreased LV size.

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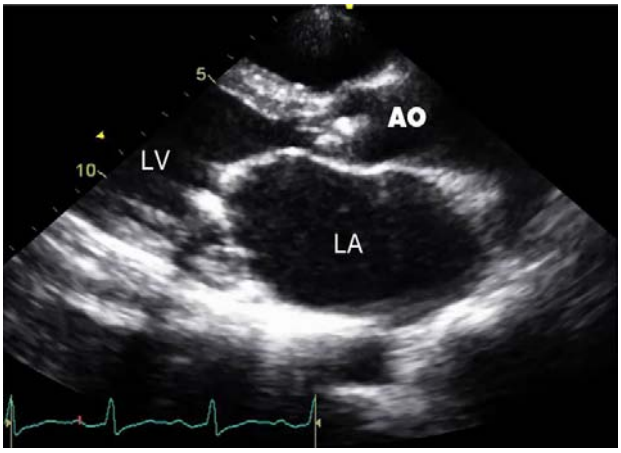
Acute heart failure in patient with zoonotic endocarditis

O Pachirat[1]; D Kaewkes[1]; K Anutarapongpan[1]
[1]*Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Introduction: Infective endocarditis (IE) is a life-threatening disease. Zoonotic pathogen can cause blood-culture negative endocarditis(BCNE). The study aimed to diagnose IE caused by zoonotic agents, Bartonella spp., Coxiella burnetii in BCNE by non-culture assays to enhance the standard diagnostic evaluation.
Case: A 45 year-old male with underlying rheumatic heart disease who was referred to our center because of shortness of breath, orthopnea and weight loss for 3 months. On admission he had clinical evidence of congestive heart failure, heart murmur consistent with severe aortic regurgitation, mitral stenosis and regurgitation. A transthoracic echocardiogram showed mobile vegetations on the aortic with perforation of right coronary cusp with severe aortic regurgitation and on the mitral valve (Figure 1). Intravenous ampicillin and gentamicin were begun on admission. The patient underwent urgent aortic and mitral valve replacement due to intractable heart failure. Histopathological examination of the heart valve tissue showed subacute, active endocarditis. Three sets of routine blood cultures were negative but B. henselae was demonstrated in the excised heart valve tissue by serology, PCR and immunohistochemical staining. The patient' s overall clinical condition improved soon after surgery and was discharged from the hospital within three weeks. One year follow-up, the patient remained clinically stable. Discussion: Bartonella is a zoonotic, fastidius, gram-negative pathogen that causes a wide spectrum of clinical infections from asymptomatic to IE. Zoonotic pathogens are important cause of BCNE and should be included in the differential diagnosis. Increase awareness of this agent in patient who has previous valvular heart disease with BCNE should be consider. Conclusion and implication: The targeted therapy and prompt surgical intervention are important to treat Bartonella endocarditis with good outcome.



RAPID FIRE 3 - ACUTE HEART FAILURE - FROM DIAGNOSIS TO PROGNOSIS

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Impact of Iron Deficiency on exercise capacity and outcome in heart failure with reduced, mid-range and preserved ejection fraction.

P Pieter Martens[1]; P Nijst[1]; FH Verbrugge[1]; J Duponselle[1]; K Smeets[1]; M Dupont[1]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*

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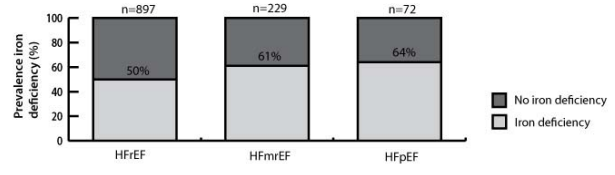
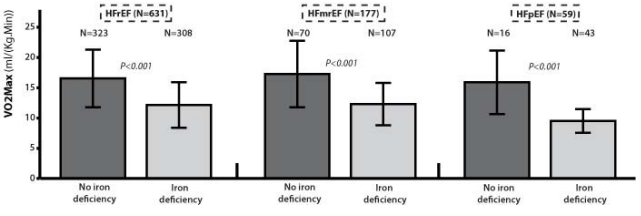
Background: Both iron deficiency and anemia are prevalent in heart failure with reduced ejection fraction (HFrEF) and affect clinical outcome. Little information is available about the prevalence, impact on excercise capacity and outcome of iron deficiency in Heart failure with mid-range (HFmrEF) and preserved (HFpEF) ejection fraction in comparison to HFrEF. Furthermore, no data is available about the progression of iron deficiency in patients without baseline anemia.
Methods: We evaluated baseline iron and hemoglobin (Hb) status in a single center, prospective heart failure database. Baseline functional status including New York Heart Association (NYHA) class, VO2max, echocardiography data and clinical outcome defined as all-cause mortality and heart failure admission were evaluated. Iron deficiency was defined according to established criteria (a ferritin below 100 μg/L or a ferritin between 100 - 300 μg/L with a transferrin saturation below 20%). Anemia was defined according to WHO-criteria (Hb < 12g/dl in females and Hb < 13 g/dl in males). LVEF was used to categorize patients in HFrEF (< 40%), HFmrEF (40-50%) and HFpEF(>50%).
Results:A total of 1197 patients (71% male) were evaluated (HFrEF;n = 897, HFmrEF;n = 229, HFpEF;n = 72). The overall prevalence of iron deficiency was 53% (panel A depicts prevalence for HFrEF, HFmrEF and HFpEF) and 36% for anemia. Iron deficiency was associated with a lower VO2max in patients with HFrEF, HFmrEF and HFpEF (panel B). Iron status more closely related to a poor VO2max than anemia status (p < 0.001). Furthermore, poor clinical-outcome was more strongly associated with iron status than anemia status. Iron deficiency without anemia associates with an adjusted HR = 3.24 (2.31-4.56;p < 0.001) and iron deficiency with anemia associates with an adjusted HR = 4.93 (3.47-7.00;p < 0.001) for heart failure admission and all-cause mortality. While patients with anemia in the absence of iron deficiency had an adjusted HR = 1.74 (1.09-2.78;p = 0.020) for the same combined endpoint. Exposing 8 patients without anemia to iron deficiency for 39 months resulted in one patient developing new-onset anemia (defined as progression of iron deficiency). Patients with progression of iron deficiency exhibited a significant higher risk of heart failure hospitalization and all-cause mortality (HR = 1.4; CI = 1.01-1.94; p = 0.046) than patients without progression.
Conclusions: Iron deficiency is common in patients with HFrEF, HFmrEF, and HFpEF and negatively affects VO2max and clinical-outcome. Progression of iron deficiency parallels an increased risk for worsening of heart failure.

Panel A: prevalence of iron deficiency in HFrEF, HFmrEF and HFpEF.



Panel B: impact of iron deficiency on excercise capacity.



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Phase 2 open-label extension (OLE) study of patisiran for the treatment of hereditary ATTR (hATTR) amyloidosis: 24-month safety and efficacy in subgroup of patients with cardiac involvement

D Adams[1]; T Coelho[2]; I Conceicao[3]; M Waddington Cruz[4]; H Schmidt[5]; J Buades[6]; J Campistol[7]; J Pouget[8]; JL Berk[9]; N Ziyadeh[10]; AM Partisano[10]; M Sweetser[10]; J Chen[10]; J Gollob[10]; OB Suhr[11]
[1]*National Reference Center for FAP (NNERF)/ APHP, Le Kremlin-Bictre, France*; [2]*Hospital de Santo Antnio, Centro Hospitalar do Porto, Porto, Portugal*; [3]*Centro Hospitalar Lisboa Norte-Hospital de Santa Maria, Lisbon, Portugal*; [4]*Federal University of Rio de Janeiro, Rio de Janeiro, Brazil*; [5]*Universittsklinikum Mnster, Munster, Germany*; [6]*Hospital Son Llatzer, Palma de Mallorca, Spain*; [7]*University of Barcelona, Barcelona, Spain*; [8]*Hospital La Timone of Marseille, Marseille, France*; [9]*Boston University, Boston, United States of America*; [10]*Alnylam Pharmaceuticals, Cambridge, United States of America*; [11]*Umea University, Umea, Sweden*

Funding Acknowledgements: Study supported by Alnylam Pharmaceuticals

Intro: Hereditary ATTR (hATTR) amyloidosis is a rapidly progressive, life-threatening disease caused by a mutation in the transthyretin (TTR) gene, resulting in misfolded TTR proteins accumulating as amyloid fibrils in multiple organs, including the nerves, heart, and gastrointestinal tract. hATTR is a heterogeneous disease and includes sensory, motor/autonomic neuropathies, and cardiac dysfunction. Patisiran, an investigational RNAi therapeutic, targets mutant and wild-type TTR. Data from the patisiran Phase 2 OLE study showed a >80% sustained mean reduction of serum TTR, that it was generally well tolerated in patients (pts) with hATTR and resulted in stabilization or improvement of neuropathy.
Purpose: To highlight the 24 month (mos) safety/efficacy data in the cardiac subgroup from the patisiran Ph 2 OLE study in hATTR.
Methods: In this study (NCT01961921), pts with hATTR received patisiran (0.3mg/kg IV) q3W x 24 mos and a corticosteroid-containing premedication prior to each dose. Primary objective: safety/tolerability of patisiran; secondary objectives: change in mNIS + 7 (composite measure of neurologic impairment).A subgroup of pts with cardiac involvement (cardiac subgroup) included pts with LV wall thickness of ≥13 mm on baseline echocardiogram (echo) and no history of uncontrolled hypertension or aortic valve disease. Patients in this subgroup had additional assessments, including serial quantification of cardiac biomarkers. Results: 27 pts were enrolled, 11 of whom met criteria for the cardiac subgroup. In this subgroup, baseline characteristics included: median age 69 yrs (range: 58-75); V30M TTR mutation 73%; FAP stage 1 82%; mean mNIS + 7: 66.2 (range: 30-122.4); NYHA Class I 45%, Class II 55%; mean LV wall thickness 16mm (range: 13-19); mean NT-proBNP 809.8 ng/L (range: 105-2070); mean Troponin 0.14 ng/mL (range: 0.03-0.69); mean ejection fraction (EF) 62% (range: 41-76); and mean 10-meter walk test (10MWT) speed: 0.95 m/s (range: 0.4-1.5). Safety profile of patisiran in the cardiac subgroup was consistent with that observed in the overall study population. 3 pts in cardiac subgroup had SAEs unrelated to study drug (including one death [MI]); AEs reported in ≥20% of pts included flushing (36%); cataract, infusion site extravasation, pyrexia, UTI, wound, and insomnia (27% each); 1 pt (9%) had a mild infusion related reaction. Following 24 mos of patisiran, pts in the cardiac subgroup had a mean 10.0-point decrease (improvement) in mNIS + 7 (range: -34.6-3.9); echo (including LV wall thickness, EF), circulating cardiac biomarkers (NT-proBNP, troponin) and 10MWT were stable. Additional clinical activity and cardiac parameters data to be presented. Conclusions: Following 24 mos of dosing, patisiran was generally well-tolerated in pts with cardiac involvement. The decrease in mNIS + 7 and stability of cardiac measures among these pts suggest that patisiran can potentially reduce progression of disease in this heterogeneous condition.

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Heart failure and inflammation-related biomarkers as predictors of new onset diabetes in the general population

N Suthahar[1]; W C Meijers[1]; F P Brouwers[1]; H J Lambers Heerspink[1]; R T Gansevoort[1]; S J L Bakker[1]; R A De Boer[1]
[1]*University Medical Center Groningen, Cardiology, Groningen, Netherlands*

Funding Acknowledgements: CVON-DOSIS, grant 2014-40, to Dr. de Boer (Netherlands Heart Foundation); NWO VIDI, grant 917.13.350 to Dr. de Boer (IRIS program of NOSR)

Background : There is a strong reciprocal relationship between Heart Failure (HF) and Diabetes Mellitus (DM). Shared pathophysiological mechanisms might be a possible explanation. Therefore, we hypothesized that biomarkers that have been linked to new onset HF might also predict new onset DM in the general population.
Methods: The study cohort consisted of 6087 participants of the Prevention of Vascular and Renal End-stage Disease (PREVEND) study that were free of DM and HF at baseline. To study the relationship between HF and DM, we evaluated the incidence of new onset DM in subjects who developed new onset HF and vice-versa. Multiple HF-related, inflammation-related and renal function-related biomarkers were evaluated regarding their predictive value for new onset DM. These biomarkers included: N-terminal-pro B-type natriuretic peptide (NT-proBNP), MR-pro-atrial natriuretic peptide (MR-proANP), Mid-regional pro-Adrenomedullin (MR-proADM), c-terminal pro Endothelin-1 (CT-pro-ET-1), Plasminogen activator inhibitor-1 (PAI-1), high sensitivity Troponin-T (hs-TnT), Galectin-3, Copeptin, Procalcitonin (PCT), hs-C-Reactive Protein (hs-CRP), Cystatin-C, Urinary Albumin Excretion (UAE), Renin and Aldosterone.
Results : The study populations mean age was 48 (SD 12) years and 54% were female. 318 (5.2%) were diagnosed with new-onset DM and 207 (3.4%) were diagnosed with new-onset HF over a mean follow up of 11 (±3) years. Total incidence over time of DM in patients who first developed HF was 11.6% versus 5.0% in those who had not developed HF ($p < 0.001$). Incidence of HF in patients who first developed DM was 7.5% versus 3.2% in those who had not developed DM ($p < 0.001$). Out of the 14 biomarkers that we examined, the classical HF biomarkers NT-proBNP and hs-TnT were not associated with increased risk for new onset DM. However, the inflammatory biomarkers hs-CRP [HR 1.12 (95% 1.04-1.21 CI)], procalcitonin [HR 1.20 (95% 1.00-1.44 CI)] and PAI-1 [HR 1.46 (95% 1.32-1.61 CI)] were predictive for new onset DM. This association remained significant after multivariable adjustment of established predictors of DM (age, sex, smoking, hypertension, waist circumference and family history of DM).
Conclusions : We validate the intimate relation between HF andDM. Further, we observed that several biomarkers of inflammation were associated with new onset DM. Although HF and DM have been described to have a very strong correlation with each other, systemic biomarkers that predict new onset HF do not predict new onset DM, suggesting that other, indirect, pathophysiological mechanisms may explain their strong relation.

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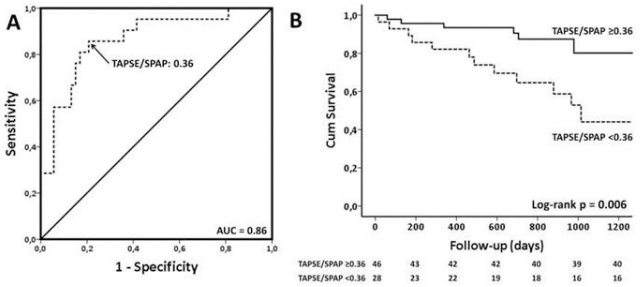
Right ventricular-vascular coupling in heart failure with preserved ejection fraction and pre- versus post-capillary pulmonary hypertension.

T M Thomas Gorter[1]; DJ Van Veldhuisen[1]; AA Voors[1]; YM Hummel[1]; CSP Lam[2]; RMF Berger[3]; JP Van Melle[1]; ES Hoendermis[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands; *[2]National Heart Centre Singapore, Cardiology, Singapore, Singapore*; *[3]University Medical Center Groningen, Paediatric Cardiology, Groningen, Netherlands*

Background: Many patients with heart failure with preserved ejection fraction (HFpEF) develop post-capillary pulmonary hypertension (PH) due to increased left-sided filling pressures. However, a subset of patients develops combined post- and pre-capillary PH.
Purpose: We studied the characteristics and non-invasive identification of pre- versus post-capillary PH in HFpEF, using invasive hemodynamics as gold standard.
Methods: Consecutive HFpEF patients with simultaneous right heart catheterization and echocardiography were identified. Patients were divided into: no PH, isolated post-capillary PH and post-/pre-capillary PH based on right heart catheterization. Systolic pulmonary arterial pressure (SPAP), tricuspid valve annular plane systolic excursion (TAPSE) and right ventricular-vascular coupling (TAPSE/SPAP) were measured on echocardiography. VO2-max was assessed as well. The primary endpoint was defined as all-cause mortality.
Results: A total of 97 patients were included: 22% no PH, 47% isolated post-capillary PH and 31% post-/pre-capillary PH. Patients with post-/pre-capillary PH had more often diabetes mellitus (47 vs. 24%, $p = 0.04$), had more heart failure hospitalizations (57 vs. 26%, $p = 0.007$) and lower VO2-max (10 vs. 13 ml/min/kg, $p = 0.008$), compared to those with isolated post-capillary PH. Patients with post-/pre-capillary PH also had more reduced TAPSE (17 vs. 21 mm, $p = 0.001$) and TAPSE/SPAP ratio (0.3 vs. 0.5, $p < 0.001$). TAPSE/SPAP ratio <0.36 had a good accuracy of identifying patients with additional pre-capillary PH (C-statistic 0.86, sensitivity 86% and specificity 79%). TAPSE/SPAP ratio was independently associated with increased mortality (HR 2.16 [95% CI 1.16-4.01], $p = 0.02$).
Conclusion: Abnormal right ventricular-vascular coupling (i.e. low TAPSE/SPAP ratio) reliably identifies patients with additional pre-capillary PH and predicts poor outcome in HFpEF.



TAPSE/SPAP ratio in HFpEF

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Definition of iron deficiency based on the gold standard of bone marrow iron staining and treatment effect of ferric carboxymaltose in heart failure patients

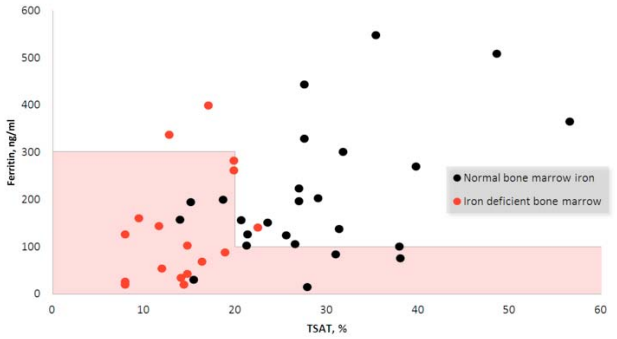
N Niels Grote Beverborg[1]; P Van Der Meer[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands

On behalf of: the DEFINE-HF study group

Background: The most commonly used definition of iron deficiency (ID) (ferritin < 100ng/ml or ferritin 100-300ng/ml and transferrin saturation [TSAT] < 20%) has not been validated in patients with heart failure (HF).
Purpose: We aimed to validate and possibly optimize the biomarker-based definition of ID in HF, using bone marrow iron staining as the gold standard. Second, we aimed to apply this optimized definition to the treatment response to ferric carboxymaltose in patients with HF.
Methods: Bone marrow aspiration with iron staining was performed in 42 patients with HF and a reduced ejection fraction (LVEF45%) undergoing median sternotomy for coronary artery bypass grafting. Subsequently, an individual patient data meta-analysis of clinical trials (N=837) on the effects of intravenous ferric carboxymaltose in patients with HF was used to test if the optimal definition of ID identified treatment responders from non-responders on cardiovascular morbidity and mortality.
Results: Patients in the bone marrow study were mostly male (76%), mean age was 68±10 years, median NTproBNP 914ng/L [IQR:454-1755]. Bone marrow ID was found in 17 (40%) of the HF patients. The most commonly used definition of ID (ferritin < 100ng/ml or ferritin 100-300ng/ml and TSAT < 20%), had a sensitivity of 82% and a specificity of 72%. A definition solely based on TSAT (optimal cut-off 19.8%) had a sensitivity and specificity of 94% and 84% ($p < 0.05$ compared to the former definition). In the meta-analysis, TSAT19.8%, and not ferritin, distinguished responders from non-responders to intravenous ferric carboxymaltose (interaction $p = 0.009$; rate ratio for cardiovascular morbidity and mortality [RR] (95%CI): 0.45 (0.290.71) for patients with TSAT19.8% and RR (95% CI): 1.55 (0.693.47) for patients with TSAT>19.8%).
Conclusions: The conventional definition of ID performs reasonably in diagnosing ID. However, a single value (TSAT19.8%) alone performs at least as good in selecting patients with true ID and identifies responders to ferric carboxymaltose.

Diagnostic characteristics for ID		
	Ferritin < 100ng/ml or ferritin 100-300ng/ml and TSAT < 20%	TSAT≤19.8%
Sensitivity, %	82.4	94.1
Specificity, %	72.0	84.0
ROC-AUC	0.772	0.891
Positive Predictive Value, %	66.7	80.0
Negative Predictive Value, %	85.7	95.5

The diagnostic characteristics for the diagnosis of iron deficiency of the conventional definition and TSAT19.8% ID=iron deficiency; TSAT=transferrin saturation; ROC=receiver operating characteristics; AUC=area under the curve.



Legend. Each dot represents one patient with the black dots reflecting normal bone marrow iron status and the red dots iron deficient patients. The red coloured area represents the most commonly used definition (ferritin <100 ng/ml or ferritin 100-300 ng/ml with a TSAT <20%). TSAT=transferrin saturation.

Biomarkers vs. bone marrow iron status

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Circulating miRNAs as biomarkers for familial dilated cardiomyopathy

D De Gonzalo Calvo[1]; S Blasco-Turrion[2]; FJ Morales[2]; P Gonzalez[2]; A Lopez Granados[3]; J Segura[3]; D Mesa-Rubio[3]; J Fernandez-Armenta[4]; L Cano Calabria[4]; F Rosa Longobardo[5]; I Izquierdo[6]; A Garcia[6]; A Mangas[5]; V Llorente-Cortes[1]; R Toro[5]

[1]Biomedical Research Institute Sant Pau (IIB Sant Pau), Lipids and Cardiovascular Pathology Group, Barcelona, Spain; *[2]Puerto Real University Hospital, Cardiology Department, Cdiz, Spain*; *[3]University Hospital Reina Sofia, Cardiology Department, Cordoba, Spain*; *[4]University Hospital Puerta del Mar, Cardiology Department, Cadiz, Spain*; *[5]University of Cadiz, Medicine Department, Cadiz, Spain*; *[6]Instituto de Investigacin Sanitaria de Santiago, Platelet Proteomic Group, Santiago de Compostela, Spain*

On behalf of:
Funding Acknowledgements: Fundacin Pblica Andaluza Progreso y Salud (PI-0011/2014), Sociedad Espaola de Cardiologa (005-2014), Instituto de Salud Carlos III (CD14/00109)

Background: LMNA-related familial dilated cardiomyopathy (fDCM) is caused by mutation in the LMNA gene and is characterized by left ventricular enlargement and reduced systolic function. LMNA-related DCM is an aggressive disease often leading to heart transplantation and sudden cardiac death. Currently, there are not circulating biomarkers that could be used to monitor cardiac abnormalities in LMNA-related DCM. Circulating microRNAs (miRNAs) are mediators of intercellular communication with great potential as cardiovascular biomarkers. However, no previous study has evaluated the clinical association between fDCM and circulating miRNAs.
Purpose: We aimed to identify novel diagnostic biomarkers of LMNA-related fDCM.
Methods: An initial screening study was performed in 8 patients with fDCM carrying the mutation in the LMNA gene and 8 age-matched healthy subjects without the LMNA mutation. Validation study was performed in three study groups: i) 20 fDCM patients with a LMNA pathogenic variant; ii) 20 idiopathic DCM (iDCM) patients without LMNA pathogenic variant; iii) 20 age-matched healthy subjects. Detailed clinical and echocardiographic information was obtained from each subject. The plasma miRNA signature was analysed using RT-qPCR as previously described by our group. Bioinformatic analysis was performed to explore the potential molecular pathways related to the miRNA profile observed in plasma.
Results: From the panel of 179 miRNAs evaluated in the screening study, a total of 111 miRNAs were specifically deregulated in patients with fDCM compared to healthy controls, even after adjusting for multiple comparisons. The expression level of 20-candidate miRNAs was then assessed in the validation study. Following post-hoc analysis, thirteen miRNAs were significantly upregulated in both DCM groups, fDCM and iDCM, compared with healthy group. Five miRNAs were significantly increased in fDCM group compared to healthy and iDCM control groups (let-7a-5p, miR-125a-5p, miR-142-3p, miR-145-5p and miR-454-3p). Two miRNAs (miR-191-5p and miR-222-3p) were different expressed between all study groups. Differences remain statistically significant even after adjusting for potential confounders. These miRNAs signatures were associated with molecular pathways potentially implicated in the disease pathology. The levels of the established clinical parameter NT-proBNP differed between healthy and DCM groups; however, similar levels were observed between fDCM and iDCM groups.
Conclusions: We have identified, for the first time, a specific circulating miRNA profile which is differentially expressed in patients with fDCM. Interestingly, the miRNA signature of fDCM was different from that observed in a similar clinical entity such as iDCM. This circulating miRNA signature could serve as novel non-invasive biomarker for risk stratification in this challenging population and provide clinical information about the physiopathology of LMNA-related DCM.

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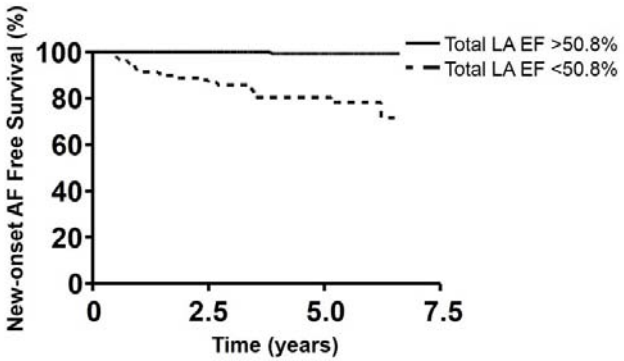
Total left atrial emptying fraction determined by real time 3-dimensional echocardiography is an independent predictor of new-onset atrial fibrillation in patients with Chagas disease

CAS Nascimento[1]; NP Pacheco[2]; GF Alves[2]; FS Madeira[2]; AR Costa[2]; AS Sousa[2]; MT Holanda[2]; LHC Sangenis[2]; FSNS Mendes[2]; HH Veloso[2]; GMS Silva[2]; MF Mediano[2]; SS Xavier[2]; RM Saraiva[2]

[1]National Institute of Cardiology, Rio de Janeiro, Brazil; *[2]Oswaldo Cruz Foundation, Evandro Chagas National Institute of Infectious Disease, Rio de Janeiro, Brazil*

Background: Changes in LA function are common in heart failure and Chagas disease. LA function parameters predict risk of atrial fibrillation (AF) in several conditions. Therefore, LA function analysis can yield new prognostic indicators in Chagas disease.
Purpose: Evaluate if LA function indexes derived from new echocardiographic techniques, including real time three-dimensional echocardiography (RT3DE) and strain () analysis, can predict new-onset AF in patients with Chagas disease.
Methods: This is a prospective longitudinal study including adult patients with indeterminate and cardiac forms of Chagas disease. All patients underwent echocardiographic evaluation including 2-dimensional echocardiography, evaluation of left ventricular (LV) diastolic function (mitral inflow, pulmonary vein flow, color M-mode echocardiography, and tissue Doppler analysis), and LA function by RT3DE and strain analysis. New echocardiographic indexes studied included LA maximal, minimal and pre-A volumes, total, passive and active LA emptying fractions, and LA total, positive and negative . A multivariate Cox proportional-hazards regression analysis was performed to identify independent predictors of new-onset AF. ROC (receiver operating characteristic) curves were generated to determine the optimal cut-offs, with corresponding sensitivities and specificities, to preview new-onset AF. Cumulative survival curves were constructed using the KaplanMeier method in combination with log rank test. P values of 0.05 or less were considered significant.
Results: A total of 391 patients with Chagas disease (age 53 ± 11 years old; 40% male) were included and followed prospectively for the occurrence of new-onset AF during 3.9 ± 1.9 years. From those, 145 patients presented the indeterminate form and 246 presented the cardiac form of Chagas disease. A total of 24 events occurred during the study period. Cox proportional-hazards regression revealed that total LA emptying fraction (HR 0.93, 95% CI 0.91 to 0.96, P < 0.0001) and age (HR 1.06, 95% CI 1.00 to 1.12, P=0.03) were independent predictors of new-onset AF. The optimal cut-off value of total LA emptying fraction to predict new-onset AF prediction was 50.8% according to ROC curve analysis (area under curve 0.83, sensitivity 95.4%, specificity 69.2%, P < 0.0001). According to Kaplan-Meier analysis of survival, patients with total LA emptying fraction under 50.8% had a worse prognosis (HR=49.8, 95% CI 8.9 to 52.7, P < 0.0001).
Conclusions: In this series of patients with Chagas disease, a low total LA emptying fraction, determined by RT3DE, was an independent predictor of new-onset AF. This new echocardiographic index may add prognostic power to traditional parameters to predict new-onset AF in Chagas disease.



Survival curve free of new-onset AF

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High prevalence of subclinical right ventricle cardiomyopathy among patients infected with human immunodeficiency virus on highly active antiretroviral therapy

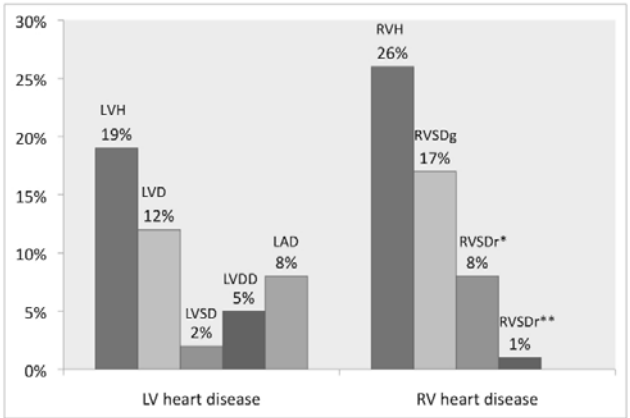
MN Montoro Lopez[1]; CI Soto[2]; R Florez Gomez[1]; A Alonso Ladreda[1]; I Ponz De Antonio[1]; E Refoyo Salicio[1]; M Moreno[1]; JI Bernardino[2]; JJ Rios Blanco[2]; G Guzman Martinez[3]
[1]University Hospital La Paz, Department of Cardiology, Madrid, Spain; *[2]University Hospital La Paz, Internal Medicine, Madrid, Spain*; *[3]National Centre for Cardiovascular Research (CNIC), Madrid, Spain*

Background. The development of highly active antiretroviral therapy (HAART) has entailed a significant decrease in AIDS-related complications and mortality. However, cardiovascular disease has become the main cause of mortality among HIV + patients on HAART. Most of the published has been focus on LV pathology but there is scarce data about the existence of right ventricle (RV) abnormalities. Because of its known relation to pulmonary hypertension (PH) and hepatitis virus co-infection (HCV) hypothesized that there might be a significant prevalence of subclinical RV abnormalities in ambulatory HIV patients.
Methods: We conducted an analytic, observational, cross-sectional study in a tertiary hospital (Spain). We included HIV infected patients under routine follow-up in the specialized Internal Medicine clinic of our institution. All of them provided written informed consent. and underwent a comprehensive transthoracic echocardiogram at the Imaging Unit of the Cardiology department.
Results: A total of 100 HIV infected patients were included. Sixty-two showed some cardiac abnormality. RV heart disease was more frequent than LV disease (48 vs. 30 patients). Biventricular abnormalities were found in 15 patients. The most common abnormal finding was RV hypertrophy (RVH, 26 patients), although only 3 patients showed signs of PH. Abnormal RV fractional area change was observed in 17% while only 2% showed impaired LV ejection fraction(figure). Patients with RVH, were more prevalent among those with positive viral load, history of intravenous drug use and HCV co-infection(table).
Conclusion: In HIV-infected patients on HAART, subclinical RV abnormalities were common and even more prevalent than LV disease. RVH seems to be related not only to the presence of PH but also to positive viral load, history of IDU or HCV co-infection.

Factors linked to RVH

	RVH (total n=26)			RVH (without PH n=23)		
Variables	OR	95% CI	p	OR	95% CI	p
VL	4.14	1.14-14.99	0.02	3.61	0.94-13.86	0.05
IDU	3.78	1.47-9.72	0.006	3.75	1.39-10.13	0.007
HCV	2.79	1.08-7.23	0.03	2.71	1.00-7.42	0.05

RVH: right ventricle hypertrophy, VL: viral load, IDU: intravenous drug user, HCV: hepatitis C virus. PH: pulmonary hypertension Figure legend. LVH: left ventricle hypertrophy, LVD: LV dilation, LVSD: LV systolic dysfunction measured by Simpson biplane, LVDD: LV diastolic dysfunction, LAD: Left atrial dilation, RVH: right ventricle hypertrophy, RVSDg: RV systolic dysfunction measured by RV fractional area change, RVSDr*: RVSD measured by Pulsed Doppler S wave, RVSDr**: RVSD measured by TAPSE



Prevalence of cardiac abnormalities

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Safety of metformin use in hospitalized acute heart failure patients with diabetes mellitus

J J Jin Joo Park[1]; JH Ohn[1]; CH Yoon[1]; DG Park[2]; IH Chae[1]; DJ Choi[1]
[1]Seoul National University Bundang Hospital, Division of Cardiology,, Seongnam, Korea Republic of; *[2]Hangang Sacred Hospital, Division of Cardiology, Seoul, Korea Republic of*

Funding Acknowledgements: This work was supported by Research of Korea Centers for Disease Control and Prevention [2010-E63003-00, 2011-E63002-00, 2012-E63005-00, 2013-E63003-0

Background: Diabetes mellitus is a common comorbidity in heart failure patients. Metformin is the drug of choice in diabetic patients; however, in contrast to chronic stable heart failure patients, there exists concern about lactic acidosis associated with metformin use in acute heart failure requiring hospital admission.
Methods: In Korea acute heart failure registry, a total of 5,620 patients with confirmed diagnosis of acute heart failure patients were consecutively enrolled at 10 university hospitals. In this analysis we included only patients with diabetes mellitus. The primary outcome was the composite of in-hospital all-cause mortality or heart transplantation. Secondary outcomes included admission to intensive care unit, the use of mechanical circulatory support, mechanical ventilation, and renal replacement therapy.
Results: Overall, 1,998 patients (35.5%) had diabetes mellitus. At hospital admission the prescription rate of anti-diabetic medication was 46.4%, 35.3%, 35.2%, 1.8%, 8.3%, and 11.9% for insulin, sulfonylurea, metformin, thiazolidinedione, acarbose, and DPP-4 inhibitor, respectively.
Patients with metformin use had lower all cause in-hospital death or urgent heart transplantation than those without metformin use (2.1% vs. 7.4%, $P < 0.001$). The rate of ICU admission, cardiopulmonary resuscitation, intravenous inotropes and vasopressor use did not differ between the patients with and without metformin use. Interestingly, the use of mechanical ventilation and renal replacement therapy, a potential outcome variable for lactic acidosis, was lower in patients with metformin use. After adjustment for significant covariates, metformin use was associated with reduced risk for in-hospital death and heart transplantation (OR, 0.37; 95% CI, 0.17-0.82).
Conclusions: Metformin use at admission for acute heart failure was not associated with an excess risk of in-hospital death or heart transplantation, suggesting that its use may be safe in heart failure patients.

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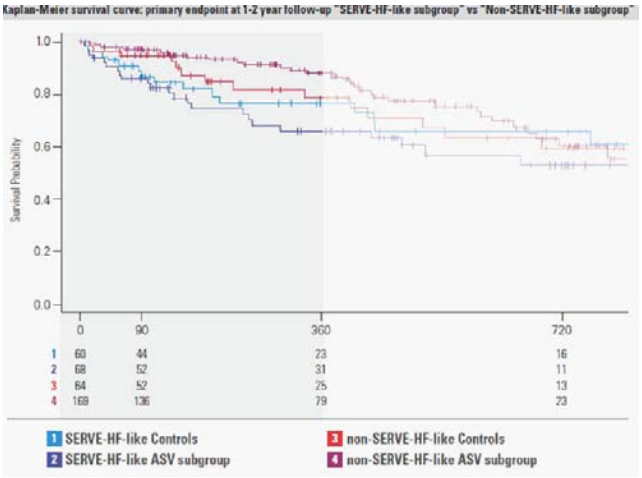
Morbidity and mortality of chronic heart failure (CHF) patients with central sleep apnoea (CSA) treated by adaptive servoventilation (ASV): Interim results of FACE cohort study

T Damy[1]; R Tamisier[2]; JL Pepin[2]; P Levy[2]; L Morin[3]; MP D'ortho[4]; JM Davy[5]
[1]University Hospital Henri Mondor, Heart Failure and Amyloidosis , Creteil, France; *[2]University Hospital of Grenoble, Physiology, sleep and Exercise, Grenoble, France*; *[3]ResMed Science Center, Martinsried, Germany*; *[4]University Hospital Bichat-Claude Bernard, Physiology and Functional Explorations, Paris, France*; *[5]University Hospital Arnaud de Villeneuve, Cardiology, Montpellier, France*

On behalf of: FACE Investigators
Funding Acknowledgements: ResMed

Background: Central Sleep Apnea (CSA) is associated with a worse prognosis of CHF. However SERVE-HF randomized control trial showed an increase of mortality risk in CHF with Reduced (CHF-REF) Left Ventricular Ejection Fraction (LVEF) with predominant CSA treated with ASV therapy.
Purpose: The multicentre cohort study FACE is collecting long-term real world clinical data of CHF-REF or CHF with Preserved LVEF (CHF-PEF) with CSA and eligible for ASV therapy.
Methods: Morbidity and mortality, changes in cardiac function, respiratory/sleep data, quality of life (using Minnesota Living with Heart Failure questionnaire) are assessed over a period of 2 years. The control group included patients who refused or was not compliant with ASV therapy. Combined primary outcome is time for all-cause death or unplanned hospitalization for worsening HF. Secondary outcomes are time for all-cause or cardiovascular-related death, all-cause unplanned hospitalization or unplanned hospitalization for worsening HF. Event-free survival will be estimated by Kaplan-Meier method and compared using log-rank test. Interim 1-2 year follow-up (FU) data are presented here.
Results: 361 CHF pts with CSA were included in the ITT analysis. Median FU for analysis was 11 months. Baseline characteristics were: age 70.7 ± 11.0 y, 88% male, body mass index 28.1 ± 5.1 kg/m2. LVEF was reduced or preserved in 65% and 35% of patients, respectively. 71% had predominantly CSA, and 29% had coexisting CSA and obstructive apnoea (CSA-OSA). Mean apnoea-hypopnoea index (AHI) was 43 ± 18/h and 76% of pts had severe sleep apnoea (AHI >30/h). ESS



score was 7.6 ± 5.2 (75% had no excessive sleepiness). Major comorbidities were arterial hypertension (72%), dyslipidemia (60%), moderate to severe Chronic Kidney Disease (54%), atrial fibrillation (42%), diabetes (37%), obesity (34%), cerebrovascular event (25%) or Chronic Obstructive Pulmonary disease (12%). Drug treatment included -blockers (77%), ACE inhibitors or angiotensin II receptor blockers (81%), diuretics (72%), and aldosterone antagonists (28%); non-drug therapy was a cardiac resynchronization device (12%) or implantable cardioverter defibrillator (17%). 66% of patients were compliant to ASV therapy (≥3h/night). Globally, adjusted multivariate analysis did not confirm any benefit or deleterious effect of ASV. However, CHF-REF with predominant CSA seemed to have poorer prognosis under ASV therapy compared to untreated patients. Conversely, other CHF populations (CHF-PEF or CHF with CSA-OSA) treated with ASV may have better survival.

Conclusion: CHF patients eligible for ASV therapy have severe CSA and multiple cardiac and metabolic comorbidities. These results are consistent with those of SERVE-HF trial. Furthermore, the FACE cohort study may be a useful tool to better understand the impact of ASV therapy in other CHF populations with CSA, especially in CHF-PEF or CHF with CSA-OSA. Long-term FU is expected for additional analysis of the FACE study.

HOT INSIGHTS IN METABOLIC INTERVENTIONS

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Nicotinamide riboside preserves cardiac functions in a mouse model of dilated cardiomyopathy

N Diguet[1]; S Trammel[2]; C Tannous[3]; J Piquereau[3]; N Mougenot[1]; R Deloux[3]; M Gressette[3]; M Breton[3]; J Decaux[1]; G Lavery[4]; I Baczko[5]; J Zoll[6]; C Brenner[2]; Z Li[1]; M Mericskay[3]
[1]University Pierre & Marie Curie Paris VI, Paris, France; *[2]University of Iowa, Iowa City, United States of America*; *[3]University of Paris-Sud 11, INSERM Signalling and cardiovascular Pathophysiology , Chatenay-Malabry, France*; *[4]University of Birmingham, Birmingham, United Kingdom*; *[5]University of Szeged, Szeged, Hungary*; *[6]University Hospital of Strasbourg, Strasbourg, France*

Funding Acknowledgements: AFM

Background Myocardial metabolic impairment is a major feature in chronic heart failure (HF). The major drugs used in the clinic to treat HF do not directly address this problem. As a major coenzyme in fuel oxidation and oxidative phosphorylation metabolism and a co-substrate molecule for enzymes signaling energy stress and oxidative stress response (e.g. SIRT1, PARP1), NAD+ is emerging as a metabolic target in a number of diseases including HF. However, little is known on mechanisms regulating homeostasis of NAD+ in the failing heart and the interest of stimulating NAD+ biosynthetic pathways for HF therapy.
Methods: To explore possible alterations of NAD+ homeostasis in the failing heart, we quantified the myocardial levels of NAD+ and the expression of NAD+ signaling and biosynthetic enzymes in the heart of a mouse model of dilated cardiomyopathy and in human failing heart and studied the impact of NAD+ precursor supplementation on cardiac functions.
Results: We observed a 30% loss in levels of NAD+ in the murine failing heart that was accompanied by a shift in the expression level of enzymes involved in NAD+ synthesis. The expression of the NAMPT enzyme that recycles the nicotinamide (NAM) precursor is depressed whereas the NMRK2 kinase that phosphorylates the nicotinamide riboside (NR) precursor is strongly increased. This shift was also observed in human failing heart biopsies compared to non-failing controls. We show that the Nmrk2 gene is an AMPK and PPARalpha responsive gene that is activated by energy stress and NAD+ depletion and that NR efficiently contributes to NAD+ synthesis in isolated neonate and adult rat cardiomyocytes. Accordingly, NR supplementation in food stabilizes myocardial NAD+ levels in the murine failing heart while raising the levels of methyl-NAM and N1-Methyl-4-pyridone-5-carboxamide, which are terminal products of NAD+ metabolism inducing NRF2 antioxidant responses. NR supplementation also preserves citrate synthase activity and raises the acetylation level of FoxO1 transcription factor. Conclusions The data show that nicotinamide riboside could be useful for treatment of HF notably in the context of dilated cardiomyopathy, a disease with few therapeutic options.

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Anti-remodeling effects xanthohumol-fortified beer in experimental pulmonary arterial hypertension

A F Silva[1]; G Faria-Costa[1]; MF Santos[1]; F Sousa-Nunes[1]; MJ Ferreira-Pinto[1]; D Moreira-Goncalves[1]; R Negrao[2]; T Henriques-Coelho[3]
[1]Faculty of Medicine University of Porto, Department of Surgery and Physiology, Porto, Portugal; *[2]Faculty of Medicine University of Porto, Department of Biomedicine - Biochemistry Unit, Porto, Portugal*; *[3]Faculty of Medicine University of Porto, Department of Gynecology, Obstetrics and Pediatrics, Porto, Portugal*

Funding Acknowledgements: Fundao para a Cincia e Tecnologia (PEst-OE/SAU/UI0038/2014; UID/BIM/04293/2013), The European Foundation for Alcohol Research (EA 14 23)

Introduction: Recent evidence demonstrates that polyphenol-enriched alcoholic beverages can be beneficial for several chronic diseases. The purpose of this study was to investigate if consumption of a polyphenol-enriched beer could modulate the pathophysiology of pulmonary arterial hypertension (PAH).
Methods: Male Wistar rats (180-200g) were divided in two groups: Monocrotaline (MCT, sc, 60 mg/kg) and Control (sc, 0.9% saline solution). Animals were randomly divided accordingly to beverage intake: 5% ethanol (Control + ETOH, MCT + ETOH) and xanthohumol (XN)-fortified beer (Control + XN, MCT + XN). After 25 days of MCT, animals were submitted to cardiac stress test. At the end of the protocol (D28) the animals were submitted to hemodynamic evaluation, followed by sample collection of cardiac and pulmonary samples for histology and molecular biology.
Results: After 4 weeks of MCT, MCT + ETOH group presented a significant increase in the pulmonary arteries medial thickness (38%, $p < 0.0001$ vs. Control + ETOH). This remodelling was prevented in the MCT + XN groups through a decrease in the expression of proteins responsible for proliferation such as ERK1/2 (-50%, $p < 0.01$ vs. MCT + ETOH) and for cell viability such as AKT (-58%, $p < 0.05$ vs. MCT + ETOH). Additionally, the intake of XN-fortified beer resulted in the inhibition of the anti-apoptotic protein BCL-XL (-64%, $p < 0.05$ vs. MCT + ETOH). At cardiac level, MCT + ETOH rats presented an elevation of RV systolic pressure (128%, $p < 0.01$ vs. Control + ETOH). This increase was correlated with a rise in RV mass ($r = 0.71$, $p < 0.05$), fibrosis ($r = 0.87$, $p < 0.05$) and cardiomyocyte cross sectional area ($r = 0.24$, $p < 0.05$). Moreover, the cardiac remodelling observed in the MCT + ETOH animals was also associated with an increase in the VEGF-R2 expression (147%, $p < 0.05$ vs. MCT + ETOH). The ingestion of XN-fortified beer resulted in a significant attenuation of all these alterations in the MCT + XN group ($p < 0.05$ vs. MCT + ETOH). Lastly, the cardiopulmonary improvements observed in the MCT + XN animals contributed to the increase in the VO2max (30%, $p < 0.05$ vs. MCT + ETOH), exercise tolerance (73%, $p < 0.05$ vs. MCT + ETOH) and survival rate (40%, $p < 0.05$ vs. MCT + ETOH) of these.
Conclusion: This study demonstrates that regular consumption of polyphenol-enriched beer can interfere with proliferation and apoptosis signalling pathways associated with PAH, contributing to ameliorate some features in experimental PAH.

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The role of endothelin-1 in mediating myocardial steatosis in diabetes cardiomyopathy

B Bambang Widyantoro[1]; N Hersunarti[1]; AU Rahajoe[1]; M Kasim[1]; N Emoto[2]; AM Soesanto[1]
[1]Dept of Cardiology and Vascular Medicine, Universitas Indonesia-NCVC Harapan Kita Hospital, Jakarta, Indonesia; *[2]Kobe University, Cardiovascular Medicine, Kobe, Japan*

Diabetes may cause endothelial dysfunction and remodelling of cardiac structure and function, independent to atherosclerosis and hypertension. Considering the increased risk of heart failure in diabetic cardiomyopathy, investigation of etiology and mechanism is important. Pre-clinical studies have shown association of endothelin-1 (ET-1) with cardiac fibrosis, and we have reported the involvement of endothelial cells-derived ET-1 in mediating cardiac fibrosis through endothelial-to-mesenchymal transition (EndMT). However, litle is known about mechanism of cardiac accumulation of triglycerides (cardiac steatosis/fatty heart). This present study combined experimental and clinical works to investigate the role of ET-1 in development of fatty heart in diabetes animal model and patients.
For animal study, we used mice with conditional knockout of ET-1 in vascular endothelial cells (VEETKO mice) and develop streptozotocin-induced diabetes model. VEETKO mice have less accumulation of triglycerides (TG) in myocardium as compared to its wild-type littermates, as shown by quantification of lipid droplets from electron microscopy and myocardial TG content by radioimmunoassay. The mechanism is under investigation, with oxidative stress and glucose transporter enzyme regulation being focused.
In addition, 41 diabetes and non diabetes subject with no history of myocardial infarct were recruited. PlasmaET-1 level were measured with radioimmunoassay, diastolic function by doppler echocardiography and myocardial TG content by MRI spectroscopy.
Plasma ET-1 level is higher in diabetes group (1.48 + 0.50 vs. 1.08 + 0.22 pg/ml, $p < 0.05$). All diabetes subjects develop diastolic dysfunction with higher grade as compared to non diabetes. Subject with severe diastolic dysfunction has higher ET-1 as compare to normal one (1.78 + 0.50 vs. 1.09 + 0.19 pg/ml). Diabetes subject with high plasma ET-1 level had higher myocardial TG content reflecting cardiac steatosis (0.77 + 0.04 vs. 0.60 + 0.03).
In conclusion, our animal study revealed prevention of cardiac steatosis in mice with lack of ET-1 and higher plasma ET-1 level is associated with accumulation of TG in diabetic human.

CLINICAL CASE AWARDS

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An intriguing case of cardiogenic shock: 2 pathologies and 2 modes of mechanical support

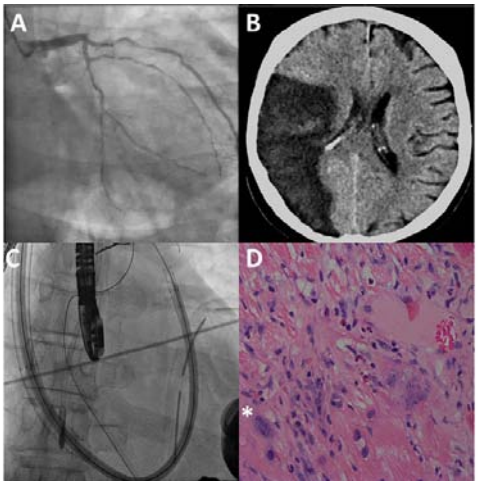
T A Tarique Al Musa[1]; D Neil[1]; H S Lim[1]
[1]*University Hospital Birmingham NHS Foundation Trust, Transplant Cardiology, Birmingham, United Kingdom*

A fit and well 54-year-old man presented acutely with an anterior ST elevation myocardial infarction. Primary percutaneous coronary intervention to the culprit LAD was attempted (Figure A) but revascularisation was unsuccessful. Cardiac MRI revealed an EF of 10%, transmural infarction with 12 non-viable segments, and anterior wall and septal microvascular obstruction. Catheter study showed RA pressure 4mmHg, PA systolic/diastolic/mean pressure 34/15/23, PA wedge pressure 20, cardiac index 1.7 L/min/m2 dependent upon on Intra-Aortic Balloon Pump. High sensitivity troponin remained persistently >10,000 over one week into admission. He underwent LVAD implantation with successful LV unloading and good RV systolic function. Post-operatively there was notable left-sided weakness and CT confirmed extensive infarction within the right MCA territory (Figure B). Stroke team evaluation deemed he was likely to be wheel-chair bound with preservation of right sided function and speech. On day 6, he developed recurrent episodes of haemodynamically significant VT and VF despite amiodarone, lignocaine and beta-blocker, requiring in excess of 60 external defibrillations. This precipitated a significant deterioration in RV function. We proceeded with temporary percutaneous RVAD support after extensive discussions with the family, in accordance with the patients perceived wishes for full treatment. A percutaneous dual lumen cannula was positioned in the PA via the right internal jugular vein (Figure C) and connected to a centrifugal pump. With biventricular support, he was treated with intravenous flecainide, which resulted in cessation of ventricular arrhythmias. By day 12, he developed profound hypoxemia despite oxygenator support with radiographic changes consistent with ARDS. Treatment was withdrawn on the basis of his large stroke, worsening ARDS and multi-organ dysfunction following discussions with his family. Examination of the ventricular core from LVAD implant revealed extensive necrosis, infiltrates and multinucleate giant cells diagnostic of Giant Cell Myocarditis (GCM) (Figure D, *).

Problems: 1) The survival benefit of an LVAD is balanced by the recognised potential for stroke and prognostication in this context is challenging 2). Malignant arrhythmias can compromise RV function and requires both anti-arrhythmic therapy and RV support. 3) GCM is a rare cause of malignant arrhythmias.

Discussion: 1). Stroke following LVAD mandates a multidisciplinary approach to decision making 2). Persistently high troponins and ventricular arrhythmias may well have been manifestations of an unexpected coexistent GCM. 3). The use of a percutaneous RVAD avoided re-sternotomy and facilitated control of ventricular arrhythmias.

Conclusions: Stroke, ventricular arrhythmias and RV failure post LVAD are clinically challenging. The histology of the ventricular core from LVAD implant should be examined routinely.



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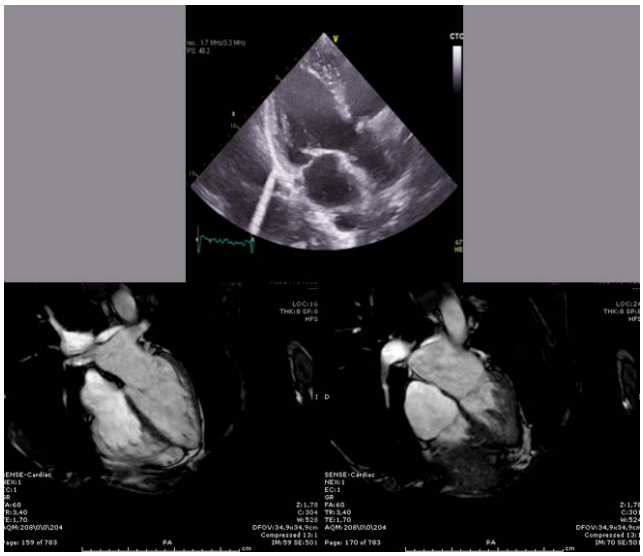
The starving myocardium

P Pastor[1]; F Dronda[2]; D Del Val[1]; GL Alonso[1]; M Valverde[1]; A Marco Del Castillo[1]; S Fernandez-Santos[1]; M Castillo[1]; E Gonzalez-Ferrer[1]; JL Zamorano[1]
[1]*University Hospital Ramon y Cajal de Madrid, Cardiology, Madrid, Spain*; [2]*University Hospital Ramon y Cajal de Madrid, Infectious Disease Unit, Madrid, Spain*

Case description: A 51 year old man with previous diagnosis of HIV infection and heroin consumption presented in the emergency room because of breathlessness and orthopnea. He had a previously normal functional capacity and no heart disease was known. During the 5 weeks prior to admission, he had suffered progressive dyspnea with orthopnea and bilateral ankle swelling. He denied chest pain, syncope and palpitations. Besides, he had suffered severe dysphagia during the last three months due to oesophageal candidiasis. Physical exam at admission revealed cachectic appearence (body mass index: 16), audible third heart sound, bilateral pulmonary crackles, elevated yugular pressure and bilateral leg oedema. Arterial pressure was 121/68 and heart rate 102 bpm. Arterial oxygen saturation was 89% and respiratory rate was 19 breaths per minute. Chest x-ray showed an enlarged cardiac silhouette and bilateral pulmonary rales. ECG was unremarkable and BNP was elevated (2670 pg/mL). He was admitted with the diagnosis of normotensive acute heart failure and managed with intravenous diuretic therapy. A transthoracic echocardiography showed an enlarged left ventricle with global hypokinesis and moderately depressed systolic function (LVEF 38% by Simpson-biplane mode), as well as moderate functional mitral regurgitation secondary to annular dilation. Diastolic function showed a pseudonormal pattern and pulmonary artery pressure was mildly elevated. Right ventricle had a normal size function. Coronary angiography showed normal coronary arteries and elevated left ventricular telediastolic pressure. Because of the HIV-infection, subacute dysphagia and physical appearance, a complete nutritional evaluation was performed.



Pre-post nutritional supportive therapy

Possible differential diagnosis: In this scenario (HIV patient with poor nutritional status) two main possibilities need to be differentiated: HIV-related cardiomyopathy and malnutrition cardiomyopathy. The first nutrition-focused blood analysis showed low levels of total proteins (5.6 g/dL, normal values 6.4-8.3), serum albumin concentration (3.0 g/dL, normal values 3.5-5 g/dL), phosphorus (1.3 mg/dL, normal values 2.7-4.5 mg/dL), cholesterol (HDL 31 mg/dL, LDL 60 mg/dL), retinol binding protein (2.58 mg/dL, normal values 3.0-6.0 mg/dL), pre-albumin (10.9 mg/dL, normal values 20-40 mg/dL), vitamine A (22.2 ug/dL, normal values 30-60ug/dL) and L-carnitine (6uM/l, normal values 33-50 uM/l). Hemoglobin and platelet levels were within normal limits. Severe lymphopenia was present (470/μL), with 9.8% CD4 cells.

Oral nutritional supplements were initiated following current malnutrition guidelines. Diuretic intravenous treatment was continued for 4 days, and after congestive symptoms decreased oral enalapril and bisoprolol were initiated. The patients clinical situation improved quickly and he was discharged 16 days after admission in a good nutritional status, with all previously reported parameters within normal limits and a body mass index of 21. A cardiac magnetic resonance was performed in his last day of hospitalization, showing a normal-sized left ventricle without alterations in contractility and an LVEF of 52%, mild functional mitral regurgitation and no late-gadolinium enhancement. At discharge, he was included in an occupational integration programme and followed by social services, and his clinical situation one year later is good, without signs and symptoms of heart failure and controlled HIV status.

Conclusion: This case illustrates an infrecuent and reversible cause of heart failure (malnutrition-related cardiomyopathy) that might be underdiagnosed in clinical practice (especially in patients with chronic comorbidities) and emphasizes the importance of a multidisciplinary management of heart failure.

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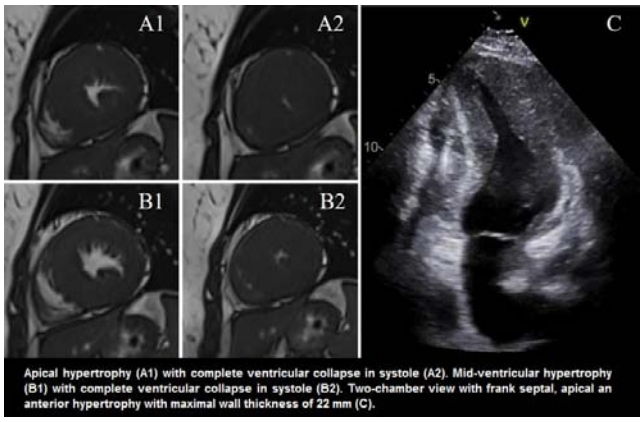
Recurrence of hypertrophic cardiomyopathy in a 25-year-old woman post heart transplant

J Jacinthe Boulet[1]; E Carelli[1]; N Giannetti[1]
[1]*McGill University Health Centre, Internal Medicine, Montreal, Canada*

This is a 25-year-old woman who was diagnosed at the age of 13 with autosomal dominant hypertrophic cardiomyopathy (HCM). She underwent an uncomplicated heart transplant 10 years ago. No genetic testing was done at the time of diagnosis but she had a strongly positive family history. The pathology of her native heart showed marked myocardial hypertrophy with focal interstitial fibrosis and no significant disarray or inflammation. The initial transthoracic echocardiogram (TTE) post transplant revealed an unremarkable heart. One year later, there was evidence of hyperdynamic left ventricular (LV) function. Four years post transplant, the cardiac apex appeared to be hypertrophied with obliteration of the distal LV cavity. A cardiac magnetic resonance imaging (CMR) showed LV apical hypertrophy suggestive of apical HCM. Significant progression of disease was observed on CMR 4 years later (July 2016) with maximum wall thickness of 22 mm at the apex, marked increase in LV mass (201g and LV mass index 112g/m2), and large areas of patchy subendocardial and mid wall scarring affecting the hypertrophied segments of the mid ventricle and apex (representing approximately 38% of the myocardial mass).

The differential diagnosis for apical HCM includes cardiac variant of Fabry disease, transthyretin-related hereditary amyloidosis, iatrogenic causes such as Tacrolimus-induced hypertrophy, and coronary artery disease. Undiagnosed pathologies in the donor heart include apical variant of HCM, isolated ventricular non-compaction, and neoplasm. At that time, Tacrolimus was stopped and changed for Cyclosporine. A Holter, requested in the context of palpitations, was remarkable only for intraventricular conduction delay. The patient underwent a PM/ICD insertion in November 2016 given her family history of sudden cardiac death. In December, she was treated for acute cellular rejection with Alemtuzumab and Prednisone. Repeat biopsies showed no evidence of rejection.



Apical hypertrophy (A1) with complete ventricular collapse in systole (A2). Mid-ventricular hypertrophy (B1) with complete ventricular collapse in systole (B2). Two-chamber view with frank septal, apical an anterior hypertrophy with maximal wall thickness of 22 mm (C).

Apical hypertrophy of transplanted heart

In January 2017, genetic analysis demonstrated that the allograft was heterozygous in the TTN gene for a sequence variant that has not previously been described in the primary literature. All biopsies and imaging to date have been inconclusive for the differential diagnoses elaborated upon above. Tacrolimus-induced apical variant of HCM remains a diagnosis of exclusion. At this time, the transplant team has decided to proceed with retransplantation.

Despite the significant advances of genetic testing for HCM, this case illustrates the limitations of detection of disease-causing mutations in patients with a phenotype of HCM. This may be relevant given the presence of HCM mimickers, such as Fabry disease which could have different implications for prognosis and management. On the other hand, management of true HCM is not influenced by the substantial heterogeneity described in pathogenic gene mutations.

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Familial amyloidotic polyneuropathy and chylous ascites: The heart of the problem

M Maria Trepa[1]; I Silveira[1]; R Baggen Santos[1]; MF Oliveira[1]; L Caiado[1]; VA Dias[1]; S Torres[1]
[1]*Hospital Center of Porto, Cardiology, Porto, Portugal*

Hereditary transthyretin amyloidosis (ATTR) is the most frequent form of familial systemic amyloidosis. It remains a challenging diagnosis due to great phenotypic variability ranging between the most common and well known neurological involvement to strictly cardiac presentation.

We report the case of a 70 years old patient with late-onset familiar amyloid polyneuropathy (diagnosed late at 60yo with V30M mutation). We was the index case in his family and presented with peripheral polyneuropathy. His previous history was also remarkable for pacemaker implantation in 2010 due to 2 degree AV block and syncope, stage 2 (by MDRD) chronic kidney disease and class II NYHA heart failure with no previous decompensations.

He was transferred from his local hospital to our cardiology ward due to decompensated heart failure and acute on chronic kidney injury. In the two months preceding hospital admission, he developed generalized edema unresponsive to up-titration of oral diuretics, rapidly worsening dyspnea and orthopnea, and multiple episodes of symptomatic orthostatic hypotension. At hospital admission he was in anasarca with tension ascites and need for diagnostic and therapeutic paracentesis. Breath sounds were abolished at the base of both lungs and X-Ray had severe pulmonary congestion and pleural effusion with heart silhouette enlargement. There was no respiratory insufficiency. EKG was in ventricular pacemaker rhythm. The analysis of the peritoneal liquid showed an unsual high value for triglycerides (444 mg/dL) meeting criteria for chylous ascites. Transthoracic echocardiogram revealed severe biventricular hypertrophy (LV mass index 244g/m2) with moderate impairment of left ventricular ejection fraction. Right heart function was compromised with signs of pulmonary hypertension (PSAP 50 mmHg) and dilated inferior vena cava. There was diastolic dysfunction (E/e': 22) and pericadial thickening with small effusion.

Given the discrepancy between the relatively acute onset of HF symptoms andthe grade of myocardial hypertrophy combined with a surprising finding of chylous ascites we sought to rule out any other contributing causes for the clinical picture. Serum immunoelectrophoresis revealed a polyclonal band corresponding to a immunoglobulin G of uncertain significance. Tc-DPD scintigraphyshowed significantly enhanced DPD uptake (visual score 3) in the myocardium, compatible with transthyretin amyloid deposition. Extensive laboratory work up and a thoracic-abdominal-pelvic computed tomography ruled out neoplasic, obstructive or lymphatic causes for chylous ascites. After reviewing the literature for similar cases, we assumed the diagnosis of chylous ascites due to right heart failure and associated portal hypertension.

The patient slowly improved clinically and was discharged after 3 weeks although fluid management was challenging. Due to the preferential depletion of intravascular volume by loop diuretics, moderate increases in their dose lead to various episodes of symptomatic hypotension. Balance was achieved by careful dosing of furosemide, metolazone and spironolactone combined with scheduled paracentesis combined and fluid intake restrictions.

This case is remarkable because of three distinct important messages:

The late onset and the exuberant cardiac infiltration is quiteuncommon for patients with Portuguese type V30M mutation who usually have mainly a neurological phenothype.

Heart failure is a rare cause of chylous ascites and its usually an exclusion diagnosis. Severely impaired cardiac compliance creates challenges to achieve optimal diuretic dosing that permits sufficient removal of third space fluid without major intravascular depletion.

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An 85-year-old man with progressive dyspnea after eating fish

H Park[1]; J Y Jae Yeong Cho[1]; KH Kim[1]; HJ Yoon[1]; JC Park[1]; DY Hyun[1]; JM Won[1]
[1]*Chonnam National University Hospital, Cardiology, Gwangju, Korea Republic of*

An 85-year-old male patient presented to emergency room with a complaint of progressive dyspnea started 2 days ago. He complained of al little bit of abdominal

discomfort also. On chest auscultation, inspiratory crackles were noted on both lung field suggesting pulmonary edema. His electrocardiogram showed mild left ventricular hypertrophy and widespread T-wave inversions in precordial leads. His chest x-ray revealed a haziness in both lung field suggesting pulmonary congestion. In the laboratory findings, leukocytosis (11,100 /mm3), mildly elevated liver function tests, elevated serum creatinine (1.4 mg/dL) and hyperkalemia (6.0 mEq/L) were noted. However, cardiac troponin was not elevated on admission.

His echocardiography showed decreased basal wall motion and relatively preserved mid to apical contraction with a left ventricular ejection fraction of 28%. A coronary angiogram was performed to rule out acute coronary syndrome and showed patency on the left and the right coronary arteries. A ventriculogram also displayed good mid to apical left ventricular wall motion with an akinesia in the basal wall.

The management of heart failure was performed with diuretics and an angiotensin-converting enzyme inhibitor. The peak cardiac troponin- I level was increased up to 10.8 ng/ml.

By the way, we looked at the chest x-ray again and discovered some kind of inverted-J-shaped material in the midline within the trachea. It was obviously silhouette of a fish hook. The fish that he ate 2 days ago must have been caught with the hook by a fisherman. The final diagnosis was made as a stress-induced cardiomyopathy associated with a foreign body in the esophagus and a surgical removal of a 2cm-sized fish hook from his esophagus was performed to prevent mediastinitis with rupture. The procedure was successful and the cardiac troponin-I level started to decrease after the surgery. On hospital day 14 just before discharge, his ECG showed normal sinus rhythm and T-wave inversion in multiple precordial leads has been resolved. Follow-up echocardiography showed no regional wall motion abnormality and the ejection fraction of 68%. He was discharged without any further problem.

Stress-induced cardiomyopathy is usually caused by emotional or physical stress. However, the actual causes are unknown in up to 30% of cases. In the present case, we discovered a fish hook a little bit late because the old man strangely did not complain of throat or chest pain at first. Physicians should not overlook chest X-ray and food history in acute heart failure without any coronary lesion.

A fish hook from the patient's esophagus

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Making the case for complex cardiogenic shock: from profile to recovery

A Hernandez-Montfort[1]; E Lau[1]; M Slawsky[1]; A Islam[1]; G Valania[1]; J Chou[1]
[1]*Baystate Medical Center, Heart and Vascular Center, Springfield, United States of America*

Introduction: Cardiogenic shock remains a complex and heterogeneous clinical disorder associated with high mortality challenging cardiovascular programs across the world. We present a profiled case of cardiogenic shock in which staged interventional and pharmacological therapies to treat complex coronary and stenotic aortic disease where performed with the aid of two separate temporary mechanical circulatory support devices.pgtaghb**Description:** 71 year old gentleman (BMI 26) with hypertension, dyslipidemia, CAD s/p CABG 2006 (LIMA-LAD, SVG-OM1 and SVG-R PDA), severe calcific aortic stenosis, HFrEF NYHA II ACC D due to ischemic cardiomyopathy presented with de novo ACS related acute heart failure syndrome with pulmonary edema clinical profile associated with new onset atrial fibrillation with rapid ventricular response/aberrant conduction which required mechanical ventilation followed by PAC insertion which showed: RA 20 mmHg, PA 80/50 mmHG, PCWP 30 w/V waves 40 mmHg and CI by Fick 2.0. ECHO estimated AVA 0.8 cm2, LVEF 20% akinesis of anterolateral/apical/inferior wall with moderate functional MR and reduced right heart function. Intra-aortic balloon pump was placed with angiography revealing patent LIMA-LAD and SVG-R PDA but 100% occluded SVG-OM1 graft with severe LM disease (80%) and mid LAD (80%) and critical osteal LCX (90%) this latter vessel supplying territory of the previously occluded vein graft to OM1. The IABP + dobutamine under PAC guided therapy was then transitioned to Impella CP in which BAV and PCI with balloon angioplasty of LAD and rotational atherectomy with DES of LCX. The patient had a favorable clinical response and Impella CP was weaned and removed following our standard daily echo/hemodynamic protocol in 72 hrs and was extubated off inotropes 3 days after. He was discharged on low dose diuretics with no residual end organ function damage. Patient returned from home 6 weeks after and underwent succesful TAVR with #26 Edward-Sapiens bioprosthesis and has remained 1-2 months after with adequate functional capacity and quality of life, while tolerating neurohormonal therapy with a low range proBNP.pgtaghb**Question:** Does adequate profiling in complex CS treated with early temporary MCS allows the possibility of treating potentially reversible rhythm, valvular and coronary abnormalities with the aim of transition to myocardial recovery?

Conclusion: Further research studies in CS are needed and should focus on profiling with adequate clinical, echocardiographic and hemodynamic data in addition to best practices in transitions from acute MCS to durable solutions that are focused on myocardial recovery rather than LVAD or HTx.

THE VERY BEST FROM CLINICAL CASES - 1

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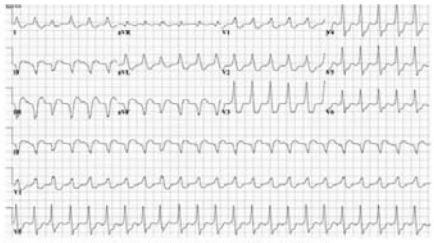
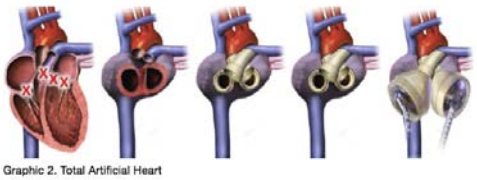
Acute heart failure exacerbation of idiopathic cardiomyopathy in the setting of electrical storm secondary to ventricular tachycardia: Total artificial heart or left ventricle assist device?

J S Juan Rico Mesa[1]; C Hoyos[1]; R Correa[2]; M Prasad[3]; S Kapa[3]
[1]University CES, Antioquia, Medellin, Colombia; *[2]Cardiovascular Clinic Santa Maria, Medellin, Colombia*; *[3]Mayo Clinic, Rochester, United States of America*

Introduction and Background: Acute Heart Failure (AHF) may have multiple etiologies. Ventricular Tachycardia (VT) electrical storm is a life threatening-condition that can cause AHF., In patients with VT electrical storm and reduced Left Ventricular Ejection Fraction (LVEF), who are refractory to medical management, salvage therapies with mechanical heart assist devices as a bridge to Orthotopic Heart Transplantation (OHT) may be useful.
Case report description: A 64-year-old male presented with AHF secondary to VT electrical storm. He had a history of idiopathic dilated cardiomyopathy with reduced LVEF (16%) and had a dual-chamber Intracardiac Defibrillator (ICD) for secondary prevention of sudden cardiac death. After admission, he failed medical management with Amiodarone, Lidocaine and Sotalol, requiring multiple electrical cardioversions despite dose optimization. Subsequently, endocardial and epicardial VT ablations were attempted followed by stellate ganglion block, without rhythm control. Unfortunately, he had worsening LVEF, evident signs of low cardiac output despite inotropes and multiple cardiac arrests in the context of recurrent episodes of sustained VT.



Graphic 1. Electrical storm secondary to ventricular tahycardia



Graphic 2. Total Artificial Heart

VT electrical storm and TAH

Description of the problem, procedures and clinical decision-making: A discussion involving the Heart Failure (HF) team and Electrophysiology (EP) staff suggested that his cardiovascular condition would benefit from OHT in the long-term. To achieve this, bridge therapy was considered for AHF compensation. Veno-arterial Extra Corporeal Membrane Oxygenation (ECMO) was utilized in the acute setting for hemodynamic stabilization, but given that its use was only possible for a limited period of time, long-term therapies were the main objective. Thus, further artificial therapies with a Left Ventricle Assist Device (LVAD) or Total Artificial Heart (TAH) were considered as a bridge to transplant. LVAD would have provided left ventricular support but given the severe right ventricular dysfunction and recurrent arrhtymias, this was not thought to be a good option. Total Artificial Transplant instead, guaranteed superior hemodynamic stability and eliminated the need for medical right ventricular support or rhythm control. Acute heart failure compensation was achieved after he successfully responded to TAH implantation. Long-term support with TAH was continued and he is currently on a waiting list for OHT with ventricular biopsy results pending.

Conclusions and implications for clinical practice: This case exemplifies the importance of a multidisciplinary heart team decision on AHF management. Clinicians should carefully evaluate the benefits of TAH over LVAD as an alternative therapy for those patients with biventricular AHF in the setting of refractory VT and end-stage heart failure. These patients often present with right ventricular dysfunction, making TAH a suitable option. Further studies are needed to define specific indications for TAH implantation on clinical practice.

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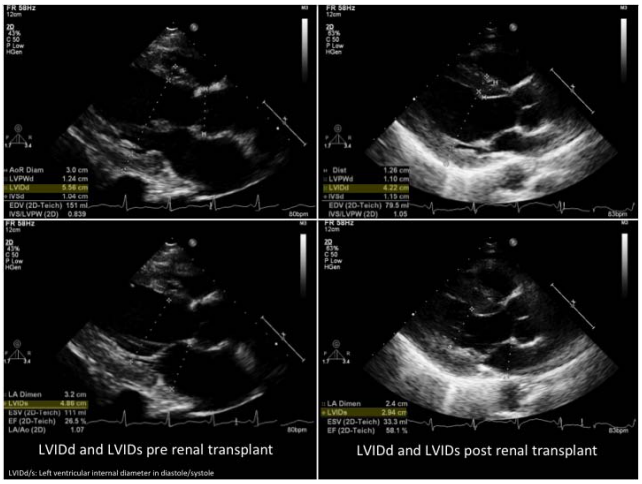
Two for the price of one: improvement in left ventricular systolic function in a patient with end stage renal disease following successful kidney transplantation.

M Webber[1]; P Dupont[2]; P Jeetley[1]
[1]Royal Free Hospital , Cardiology, London, United Kingdom; *[2]Royal Free Hospital , Acute Kidney Unit, London, United Kingdom*

Introduction: Left ventricular systolic dysfunction (LVSD) is prevalent amongst patients with end stage renal disease (ESRD) on dialysis and can disadvantage patients considered for renal transplantation. The best treatment strategies for these patients remain unclear and poorly understood.



LV dimensions pre and post transplant

Case: A 37-year-old female with a background of ESRD on haemodialysis secondary to renovascular disease presented to our department for routine assessment prior to renal transplantation. A transthoracic echocardiogram (TTE) revealed a dilated left ventricular (LV) cavity size with LV internal dimensions of 5.56cm in diastole and 4.86cm in systole. Her ejection fraction (EF) by Simpsons method was 25-30% indicating severe LV dysfunction. Following discussion in the cardio-renal MDT, she underwent exercise stress echocardiography to assess her LV response to exercise and to exclude underlying ischaemia. She had a reasonable effort tolerance achieving stage 3 of the Bruce protocol. Post stress echocardiography demonstrated contractile reserve with an improvement in LV function and no ischaemia. Coronary angiography confirmed the absence of significant coronary artery disease. She subsequently underwent an uncomplicated live donor related renal transplant. Two months later she reported an improvement in her exercise tolerance to NYHA class I. Her post-transplant TTE showed normalisation of her LVSD with an estimated EF of 55% and an improvement in her LV cavity dimensions to 4.22cm in diastole and 2.84cm in systole.pgtaghb**Problems:** Improvement in LVSD in ESRD patients post renal transplant has been described but the reason for this phenomenon is not

well understood. The optimal management for these patients is unclear, in particular whether recommendations for conventional treatment for LVSD can be extrapolated from the general population. These patients may be turned down for transplant on the basis of increased perioperative morbidity and mortality.
Discussion: It is thought that a prolonged exposure to uremic toxins, particularly "middle molecules", in dialysis patients may lead directly to cardiac myocyte dysfunction and LV impairment. Dialysis induced variations in blood volume and haemodynamics can also significantly affect systolic function. We have seen an improvement in EF in the post-transplant period in a number of our patients with non-ischaemic cardiomyopathy. We therefore postulate that in addition to conventional medical therapy for LV dysfunction, treatment regimes should also include optimising fluid management and early consideration for renal transplantation.
Conclusions: We have successfully demonstrated that renal transplantation can be safely performed in selected patients with LVSD and results in the improvement of EF, LV systolic dimensions and symptoms of heart failure. These patients, traditionally considered high risk for surgery, may benefit from early renal transplantation and demonstrate reversibility of their LV dysfunction.

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A patient with human immunodeficiency virus infection and acute decompensated heart failure; never forget the pericardium

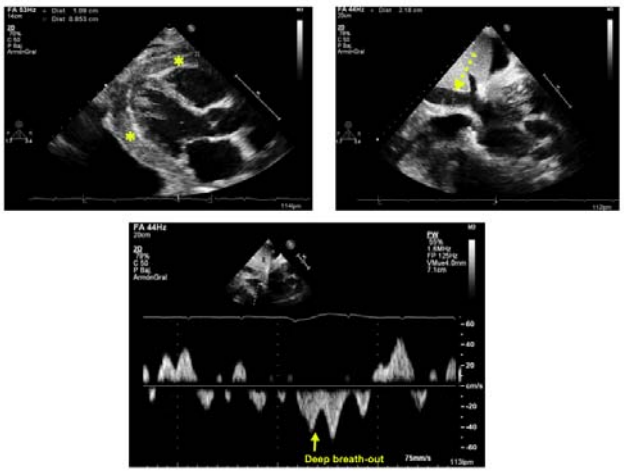
AF Miranda-Arboleda[1]; JP Florez-Munoz[2]; JA Gandara-Ricardo[2]; E Arevalo-Guerrero[2]; E Munoz-Ortiz[2]
[1]Universidad de Antioquia, Cardiologa , Medellin, Colombia; [2]Hospital Universitario San Vicente Fundacin, Servicio de Cardiologa, Medellin, Colombia

A 35-year-old male patient with past medical history of Human Immunodeficiency Virus (HIV) infection non-compliant to antiretroviral therapy (ARV) presented complaining of 2 moths of dyspnoea on exertion, fever, night chills and weight loss. M. tuberculosis was found from cultures and genome detection through protein chain reaction (PCR) in bronchial samples, pericardial fluid and pericardium samples obtained from a pericardial window. Disseminated tuberculosis infection was diagnosed and therapy was started.
He was readmitted due to dyspnoea, ortopnea, paroxysmal nocturnal dyspnoea, abdominal pain and anasarca. Exploration revealed bilateral jugular vein dissension, hepatojugular reflux, reduced breath sounds reduced, hepatomegaly, ascites and bilateral lower leg pitting edema. Electrocardiogram showed generalized low voltage, echocardiography proved pericardial thickening up to 13 mm, mild pericardial effusion, restrictive diastolic dysfunction, bilateral atrium enlargement, interventricular interdependence with inspiration, inversion of the flow diastolic in suprahepatic veins in exhalation, reduction of left ventricular inflow (E wave) >25% with inspiration and IVC dilation. Left and right ventricle systolic function were preserved.

Microbiological test.	
Adenosine deaminase in pericardial fluid	86 U/L (Reference: 0 to 10)
M. tuberculosis culture in pericardium biopsy	Positive
M. tuberculosis culture in pericardial fluid	Positive
M. tuberculosisprotein chain reaction in pericardial fluid	Positive
Pericardium biopsy	Granuloma formation with multinucleate cells and caveating necrosis.
M. tuberculosis culture in bronchoalveolar lavage	Positive
M. tuberculosis protein chain reaction in bronchoalveolar lavage	Positive
CD4 positive lymphocytes	294/ul
HIV Viral load	6595 copies/ml

HIV: human immunodeficiency virus

Questions, problems or possible differential diagnosis: What is the most probable diagnosis of this patient? What would be the acute initial management? What would be the best option for the long-term management?
Answers and discussion: Final diagnosis was tuberculous constrictive pericarditis in an HIV positive patient. Tuberculosis is the main cause of pericarditis and pericardial effusion in patients living in endemic countries and in patients with HIV infection it responds for more than 90% of cases. The mortality after pericardial tuberculosis can be as high a 40% six months after diagnosis.
Acute management was based on support intervention and symptomatic relief. Long-term management of this patient was made by the cardiovascular staff. The patient had poor prognosis predictors such as cachexia and limitation to give treatment for the primary diagnosis due to patient persistent refusal to take ARV medications. Taking this into account and the high mortality and morbidity associated with pericardiectomy, the patient was discharged with follow-up
Conclusions and implications for clinical practice: Tuberculosis and HIV infection are still a dangerous combination affecting patients living in developing countries. Pericardial involvement during M. tuberculosis infection can be disastrous during acute episodes generating the necessity of invasive procedures or extensive work-up increasing risk of complications. The decision-making process is not easy and must be individualized to each patient because medical therapy and surgical interventions also have the potential risks.



Echocardiographic findings

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First report of heart failure due to zika myocarditis

I Mendoza[1]; K Karina Gonzalez Carta[2]; I Mendoza Britto[3]; I Morr[1]; T Allison[2]; F Misticchio[1]; Y Meza[1]; V Finizola[4]
[1]Central University of Venezuela (UCV), Instituto de Medicina Tropical, Caracas, Venezuela; [2]Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America; [3]Jackson Memorial Hospital, Cardiac Electrophysiology, Miami, United States of America; [4]Lisandro Alvarado University , ASCARDIO, Barquisimeto, Venezuela

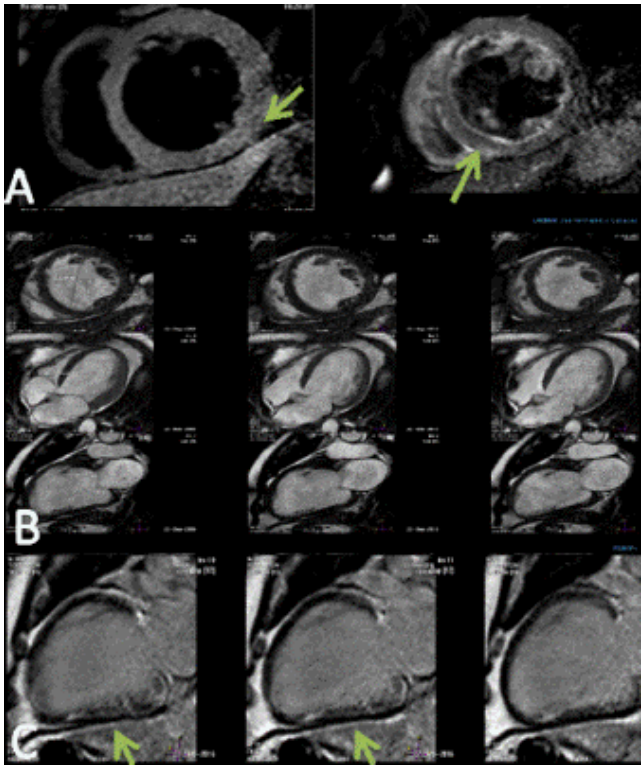
Introduction. Zika virus infection (ZIKV), is a mosquito-borne disease that has become a global health hazard. There are no reports of cardiovascular manifestations, heart failure (HF) or arrhythmias associated with ZIKV disease. Case report: A 51 year-old man from Venezuela, previously asymptomatic and with a history of well-controlled arterial hypertension and type 2 diabetes mellitus that in a recent medical evaluation had a normal electrocardiogram (ECG) and echocardiogram (TTE) with a left ventricular ejection fraction (EF) of 68 %. On May 2016, he developed low-grade fever, polyarthralgia, widespread pruritic maculopapular rash, conjunctivitis and myalgia. These clinical manifestations were resolved in 2 days. Five days after the onset of this acute episode, however, he was admitted to the hospital with rapid progressive dyspnea, rated according to the New York Heart Association (NYHA) as class IV. The ECG, five days after onset, showed a new left-bundle branch block and on the TTE a severely reduced EF of 16%. A coronary angiogram was performed which was normal. A holter recording showed frequent atrial and ventricular premature beats. A cardiac MRI (cMRI) exhibited severe impaired left ventricular systolic function (EF 16%), hiperintensive inferior wall signal on T2-weighted and lateral subepicardial enhancement in late gadolinium sequence. ZIKV-induced myocarditis was diagnosed based on the following criteria: i) ZIKV RNA was detected in serum with the use of reverse-transcriptase polymerase chain reaction (RT-PCR) and Zika virus-specific IgM antibody; ii) Potential simultaneous infection including Dengue, Chikungunya, HIV, and other virus or parasitic infections such as Chagas were ruled out; iii) Clinical, TTE, ECG and cMRI evidence of myocarditis was detected; iv) Normal coronary arteries on angiogram. The patient was initially treated with intravenous furosemide and oral digoxin for a period of one month, along with enalapril, carvedilol and eplerenone and his condition improved to NYHA Class II-III and then, after discontinuing enalapril and administering sacubutril/valsartan titrated

up to 200 mg twice daily, improved further to NYHA Class I. Discussion. Zika virus infection is usually mild with non-specific symptoms. Cardiovascular complications might be underdiagnosed in clinical practice. Therefore the importance of cardiovascular screening in suspected cases. Further research is needed to determine the pathophysiology of Zika myocarditis and would help to develop a pharmacological target and treatments for countering progression of the disease.
Conclusion: This is the first report of cardiac involvement with congestive heart failure in a patient with Zika. This case is unique since the patient developed rapidly progressive left ventricular dysfunction and new ECG changes, previously known to have normal cardiac function. Future research is needed to determine the incidence of cardiovascular involvement of Zika virus infection.

Zika myocarditis

	NYHA	EF (%)	ECG	Treatment
Pre_Zika	I	68	Normal	ACEI, BB
Onset	IV	16	LBBB	ACEI, BB, MRA, D
Follow-up	I	25	LBBB	ARNI, BB, MRA, D

ACEI: Angiotensin-converting enzyme inhibitor. BB: beta blocker. MRA: mineral corticoid/aldosterone. D: diuretics. ARNI: angiotensin receptor neprilysin inhibitor



Cardiac MRI patient wit Zika myocarditis

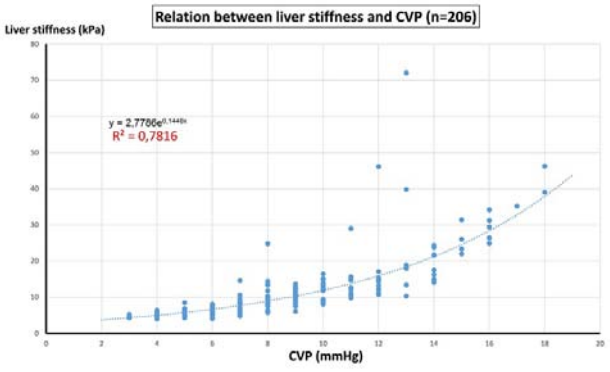
POSTER SESSION 1

ACUTE HEART FAILURE

P213
Towards non-invasive assessment of central venous pressure variations using real time and quantitative liver stiffness estimation

O Villemain[1]; F Sitefane[1]; M Pernot[2]; S Malekzadeh-Milani[1]; M Tanter[2]; D Bonnet[1]; Y Boudjemline[1]
[1]M3C Necker, Pediatric and Congenital Cardiology, Paris, France; *[2]Waves and Acoustics Laboratory Institute Langevin, Paris, France*

Objectives: The main purpose of this study was to assess the correlation between the liver stiffness (LS) estimated by shear wave elastography (SWE) and the central venous pressure (CVP) during hemodynamic variations in a cohort of children with heart disease.
Background: SWE has been shown and used as a non-invasive, quantitative and reproducible approach to assess LS. LS has been reported to be associated with fibrosis but there is also a potential dependence of LS with the CVP.
Methods: 103 children (6.8 ± 5.5 years) referred to our institution for diagnostic or interventional right heart catheterization (RHC) were prospectively enrolled. CVP and LS were measured simultaneously at baseline and after 15 ml/kg of volume loading. Inferior vena cava (IVC) diameter and pulsed-Doppler profile of hepatic veins were also evaluated. Plasma level of NT-pro-BNP was assayed during the RHC.
Results: At baseline RHC, the mean CVP was 7.4 ± 2.9 mm Hg [range 3–16] and the mean LS was 9.0 ± 5.8 kPa [4–46.1]. After volume loading, the mean CVP increased significantly to 10 ± 3.3 mm Hg [3-18] ($p < 10\text{-}4$) and the mean LS increased significantly to 14.4 ± 9.1 kPa [4.3-72] ($p < 10\text{-}4$). LS strongly correlated with CVP, pre-loading ($r=0.86$, $p < 10\text{-}4$) and post-loading ($r=0.87$, $p < 10\text{-}4$)]. Optimal cut-off value of LS for detection of CVP > 10 mmHg was 10.8 kPa (Se=89.3%, Sp = 86.0%), with an area under the curve of 0.946 (95% CI 0.920 to 0.971; $p = 0.01$). Beyond this correlation, LS is sufficient to provide an indirect and reliable measurement of quantitative CVP variations ($p < 10\text{-}4$, multivariate model). IVC diameter, pulsed-Doppler profile of hepatic veins and NT-pro-BNP were less robust than LS to estimate CVP.
Conclusions: Here, we show that LS measurement using SWE is a reliable surrogate of quantitative estimation of the CVP. It can also be used to measure CVP changes in real time. LS could potentially be a useful non-invasive tool for evaluation and follow-up of acute and chronic right heart failure.



Relation between liver stiffness and CVP

P214
Heart failure with mid-range ejection fraction: who are these patients?

L Reis[1]; A Fernandes[1]; C Lourenco[1]; R Teixeira[1]; M Marta[1]; P Dinis[1]; J Ribeiro[1]; L Puga[1]; I Almeida[1]; J Nascimento[1]; L Goncalves[1]
[1]University Hospitals of Coimbra, Coimbra, Portugal

Introduction: Classification in heart failure (HF) is based on the left ventricular ejection fraction (LVEF). The most recent European guidelines created a new group of patients with a LVEF - 40-49% (mid-range LVEF). However, few data are available regarding these patients (P).
Objectives: To evaluate P with HF with mid-range LVEF in demographic, clinical, treatment and prognostic terms.
Methods: Retrospective and single-center study involving 263 P consecutively admitted into a cardiac intensive care unit during 6 years. Three groups were created according to the LVEF: reduced LVEF (G1: LVEF < 40%, N=182), mid-range LVEF (G2: LVEF 40-49%, N=34) and preserved LVEF G3: FEVE≥50%, N=47). Demographic, laboratory, echocardiographic, therapeutic and prognostic data were compared. Clinical follow-up (5 years) was performed targeting for readmission with AHF and mortality.
Results: The population mean age was 70 ± 13 years old with a majority of male patients (78%). Readmission for HF occurred in 40% of the cases. In-hospital mortality was 15% and during the follow-up 42%.
During admission the groups presented similar clinical and analytical characteristics: congestive HF (G1 100% vs G2 91% vs G3 100%), NT-proBNP values (G1 17590 ± 23014 pg/nL vs G2 29137 ± 57308 pg/nL vs G3 13895 ± 16897 pg/nL) and creatinine (G1 151 ± 81 ug/dL vs G2 168 ± 137 μg/dL vs G3 157 ± 148 ug/dL). The etiology was ischemic in 28% of the P in G1, 4.1% in G2 and 22% in G3. Regarding treatment, no statistically significant differences were found in terms of intravenous diuretics were given in the majority (G1 72% vs G2 62% vs G3 63%); noradrenaline/dobutamine (G1 24% vs G2 14% vs G3 16%) and noninvasive ventilation (G1 52% vs G2 41% vs G3 56%).
When comparing the P of G1 and G2 we found that they had similar in-hospital mortality (93% vs 7.4%, $p = 0.204$) however P of G1 had higher mortality during follow-up (92% vs 8.0%, $p = 0.009$) and a higher rate of readmisson for HF (88% vs 12%, $p = 0.002$).
When comparing the P of G2 and G3, we found that P with mid-range LVEF had higher in-hospital mortality (85% vs 15%, $p = 0.034$) and during follow-up (77% vs 23%, $p = 0.009$), however, readmission rates for HF were similar (52% vs 48%, $P = 0.502$).
At discharge, there were no statistically significant differences among groups in terms of angiotensin-converting enzyme inhibitors, beta-blockers and diuretics treatment.
Conclusions: In our population, we concluded that P with mid-range LVEF presented a similar clinical profile to P with reduced and preserved LVEF. However, they present a higher in-hospital mortality and during follow-up as compared to P with preserved FEVE and similar in-hospital mortality as compared to P with reduced FEVE.

P215
HFmrEF in elderly patients: the pathogenetic role of ischemia. Real world data from the ATHENA registry.

F Orso[1]; A Pratesi[1]; S Parlapiano[1]; A Herbst[1]; F Bacci[2]; G Ciuti[2]; A Berni[2]; AC Baroncini[1]; G Baglioni[1]; N Marchionni[3]; L Gabbani[1]; L Poggesi[2]; A Moggi Pignone[2]; C Nozzoli[2]; S Baldasseroni[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA study group

Background: Heart failure (HF) classification based on the presence of preserved or reduced left ventricular systolic function, which identifies two main categories of patients, those with HFpEF and those with HFrEF, has become important from an epidemiological, clinical, therapeutical and prognostic point of view. Recently, the European Society of Cardiology has recognized the presence of a "gray area" of patients with ejection fraction (EF) between 40 and 49% defined as "mid-range" (HFmrEF). Purpose: to better characterize patients with HFmrEF from an etiopathogenetic point of view in a real world setting of elderly patients hospitalised for acute HF.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of AHF (worsening or de novo) to the Emergency department (ED) of a tertiary University teaching-hospital in the period 01.12.2014-01.12.2015. The present analysis included patients with complete echocardiographic data.
Results: 246 patients were included in the present study: patients with HFmrEF were 19.5%, 30.5% had HFrEF and 50.0% had HFpEF. Patients with HFmrEF and HFpEF shared similar demographic characteristics: higher mean age 83.8, 84.5 and 79.9 years, $p < 0.001$; higher prevalence of females 41.7%, 67.5% and 32.0% for HFmrEF, HFpEF and HFrEF respectively, $p < 0.001$. Ischemia seemed to be a common denominator for HFmrEF and HFrEF patients. History of coronary artery disease (CAD), was more frequent in patients with HFmrEF (41.7%) and HFrEF (36.0%) than patients with HFpEF (19.5%), $p = 0.004$, as well as the prevalence of previous percutaneous coronary intervention that was 27.1%, 25.3% and 11.5% for HFmrEF, HFrEF and HFpEF respectively, $p = 0.014$. Furthermore, ischemic aetiology of HF was typically present in patients with HFmrEF (47.9%) and HFrEF (40.0%), differently from those with HFpEF in which it was present only in the 28.5% of cases, $p = 0.038$. To further support the importance of ischemia, acute coronary syndromes represented, in patients with HFmrEF, the most frequent precipitating cause of acute HF (11.6%) and coronary angiography was the procedure most frequently performed during hospitalisation in elderly with HFmrEF (12.5%) and in those with HFrEF (22.7%) with percentage values higher than those reported for patients with HFpEF (6.5%), $p = 0.004$.
Conclusions: These data suggest that ischemia plays an important role in the pathogenesis of HFmrEF. We could therefore hypothesize that patients with HFmrEF are a heterogeneous group consisting of a subgroup of patients with HFpEF that, following an acute event, could have experienced a reduction of ejection fraction (EF) and of a subgroup of patients with HFrEF that, due to the positive effect of therapeutic strategies, could have improved at least part of the left ventricle EF: this group has also been recently been classified as HFrecEF (Heart Failure with Recovered Ejection Fraction).

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HFmrEF in elderly patients hospitalised for acute heart failure: data from the ATHENA registry.

S Parlapiano[1]; S Baldasseroni[1]; A Herbst[1]; A Pratesi[1]; F Bacci[2]; C Tozzetti[2]; C Ghiara[1]; G Ciuti[2]; G Baglioni[1]; L Poggesi[2]; C Nozzoli[2]; A Moggi Pignone[2]; L Gabbani[1]; N Marchionni[3]; F Orso[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA study group

Background: Heart failure (HF) is a pathological condition that involves 65 million of people worldwide and has a high prevalence in the elderly. Recently, the European Society of Cardiology (ESC) has recognized the presence of a "gray area" of patients with ejection fraction (EF) between 40 and 49% defined "mid-range" (HFmrEF) and has redefined the specific cut off values for HF with preserved EF (> 50%, HFpEF) and HF with Reduced EF(< 40%, HFrEF).
Purpose: to better characterize patients with HFmrEF and compare them to those with HFpEF and HFrEF in a real world setting of elderly patients hospitalised for acute HF.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of AHF (worsening or de novo) to the Emergency department (ED) of a tertiary University teaching-hospital and transferred to cardiology, internal medicine and geriatric wards in the period 01.12.2014-01.12.2015.
Results: 246 patients with complete echocardiographic data composed the study population: patients with HFmrEF were 19.5%, 30.5% had HFrEF and 50.0% had HFpEF. HFmrEF and HFpEF had similar demographic characteristics, compared to patients with HFrEF: mean age of three group of patients was respectively 83.8, 84.5 and 79.9 years, $p < 0.001$; the prevalence of females was 41.7%, 67.5% and 32.0% for HFmrEF, HFpEF and HFrEF respectively, $p < 0.001$. With regard to cardiovascular risk factors: hypertension was more frequent in patients with HFmrEF (82.2%) than patients with HFrEF (79.5%) and diabetes was more frequent in patients with HFmrEF (41.3%) than patients with HFrEF (39.2%) and HFpEF (35.0 %). Furthermore with HFmrEF many of the most important comorbidities, such as chronic obstructive pulmonary disease, chronic kidney disease, atrial fibrillation, cognitive impairment or depression, were present with values more similar to those of patients with HFpEF. No significant differences were found in the setting of care for HFmrEF patients who were equally distributed among cardiology, internal medicine and geriatric wards ($p = 0.2$). In-hospital mortality was not significantly different in the three groups of HF patients ($p = 0.977$): HFmrEF (6.3%), HFpEF (5.7%) and HFpEF (5.3%). Patients with HFmrEF, however, had an increased, even if not statistically significant, hospital length of stay: 11.7 days, 9.4 days and 10.1 days for HFmrEF, HFpEF and HFrEF respectively ($p = 0.18$).
Conclusions: Our study shows that patients with HFmrEF represent a significant portion of patients with HF. These patients appear to have clinical and demographic characteristics similar to patients with HFpEF. Hospital length of stay and in-hospital mortality of patients with HFmrEF do not differ significantly to those with HFpEF and HFrEF. Studies are needed to confirm whether patients with HFmrEF can get the same benefits from the treatments that have proved to be effective for patients with HFrEF.

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Modified shock index at admission as predictor of in-hospital adverse events in patients with myocardial infarction

RA Rui Azevedo Guerreiro[1]; J Pais[1]; D Bras[1]; K Congo[1]; J Carvalho[1]; M Carrington[1]; D Neves[1]; AR Santos[1]; B Picarra[1]; A Caeiro[1]; J Aguiar[1]
[1]Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal

Introduction: Myocardial infarction (MI) presents even today a considerable in-hospital morbimortality. There are several risk scores to stratify patients with MI – TIMI, GRACE – but its sophisticated calculus does not help its utilization on a daily basis. Modified shock index (MSI), defined by the ratio of cardiac frequency / mean blood pressure at admission, due to its easy calculation, can be an advantage in the risk stratification of patients with MI.
Purpose: Authors pretend to validate MSI as predictor of in-hospital adverse events in patients with myocardial infarction and to calculate the best cut-off point that maximizes sensibility and specificity.
Methods: Observational retrospective study, with a sample of consecutive patients admitted for MI. MSI at admission was calculated for all patients. As in-hospital adverse events were considered death by any cause, aborted sudden cardiac death, cardiogenic shock, acute pulmonary oedema and re-infarction during hospitalization. The value with the highest Youden-index of ROC curve was defined as the cut-off point and its sensibility and specificity was calculated. MSI with values above the cut-off point were considered positive. Uni and multivariate analysis were performed to access the association between positive MSI and in-hospital adverse events.
Results: 692 patients were included, with mean age 67.56 ± 13.79 years, 503 (72.69%) men, of which 135 (19.51%) patients had an in-hospital adverse event. Patients with positive MSI were older (69.33 vs 66.78 years, $p = 0.025$), less men (65.6% vs 75.8%, $p = 0.005$), with higher prevalence of diabetes (42.7% vs 31.7%, $p = 0.005$), less prevalence of smoking (21.1% vs 30.3%, $p = 0.013$) and without statistically significant difference in the prevalence of arterial hypertension (78.7% vs 76.3%, p = NS), hyperlipidaemia (57.5% vs 54.7%, p = NS) and family history of coronary artery disease (7% vs 6.7%, p = NS). Patients with positive MSI had similar distribution of types of MI ($p = 0.057$; with ST-segment elevation: 43.4% vs 42.7%), similar severity of coronary artery disease ($p = 0.115$) but with more frequent occlusion of left anterior descending coronary artery (25.7% vs 18.7%, $p = 0.018$) and less frequent reperfusion therapy (73.3% vs 86.1%, $p = 0.009$). Area under the curve ROC for MSI as predictor of in-hospital adverse events in patients was 0.664 and the best cut-off point was 0.9, with 51% sensibility and 77% specificity. In univariate analysis, positive MSI was predictor of in-hospital adverse events (OR 3.03, 95% CI 2.05 – 4.46, $p < 0.001$). In multivariate analysis, controlling for age, sex, diabetes and smoking, positive MSI was still predictor of in-hospital adverse events (OR 2.69, 95% CI 1.77 – 4.09, $p < 0.001$).
Conclusion: MSI at admission was predictor of in-hospital adverse events in patients with myocardial infarction. Patients with MSI above 0.9 have 169% more risk of having in-hospital adverse events, with 51% sensibility and 77% specificity.

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CHA2DS2VASc score an useful tool to predict heart failure in patients admitted with STEMI

G Abreu[1]; P Azevedo[1]; C Rodrigues[1]; I Campos[1]; C Braga[1]; J Martins[1]; C Arantes[1]; S Rocha[1]; A Gaspar[1]; M Alvares Pereira[1]; J Marques[1]
[1]Hospital de Braga, Cardiology, Braga, Portugal

Background: The CHA2DS2VASc score is used clinically for stroke risk stratification in atrial fibrillation (AF). Many of the individual risk factors included in this score are also risk factors for heart failure.
Aim: To examine the CHA2DS2-VASc score performance in predicting acute heart failure in subjects admitted with ST segment elevation myocardial infarction.

Methods: We analysed 851 patients admitted consecutively in our coronary care unit with a diagnosis of ST segment elevation myocardial infarction in a five-year period. Patients with previous atrial fibrillation (n = 36) or in cardiogenic shock (n = 30) were excluded. CHA2DS2-VASc score was calculated for each patient. The cohort was divided in three groups according to the value obtained: CHA2DS2VASc 0-1 (n = 243, 31%); CHA2DS2VASc 2-3 (n = 334, 42.5%); and CHA2DS2VASc ≥4 (n = 208, 20.5%). For each group we compared clinical and laboratory features, treatment and adverse events. Primary endpoint was the occurrence of acute heart failure after a STEMI.
Results: Patients from CHA2DS2VASc ≥4 group were older (76 ± 9 vs 64 ± 11 vs 55 ± 9 years; $p < 0.001$). Conventional risk factors were more represented in the higher CHA2DS2VASc score groups: diabetes (51.0% vs 31.1% vs 7.4%; $p < 0.001$), hypertension (90.9% vs 75.7% vs 37.9%; $p < 0.001$) and dyslipidaemia (59.6% vs 59.9% vs 42.6%; $p < 0.001$); except for smoking (8.2% vs 33.2% vs 56.8%; $p < 0.001$). On admission patients with CHA2DS2VASc ≥4 had more often anaemia (40.1% vs 20.1% vs 12.3%; $p < 0.001$), renal insufficiency (eGFR < 60 ml/min) (54.6% vs 19.5% vs 3.7%; $p < 0.001$) and three vessels disease (21.2% vs 17.5% vs 9.1%; $p = 0.005$). Left systolic ventricular dysfunction was more prevalent (59.1% vs 39.8% vs 34.6%; $p < 0.001$) in that group. During hospital-stay, patients with CHA2DS2VASc ≥4 developed more frequently heart failure (52.4% vs 24.9% vs 16.9%; $p < 0.001$), new-onset atrial fibrillation (19.2% vs 11.1% vs 4.1%; $p < 0.001$); ischemic stroke (2.9% vs 0% vs 0.4%; $p = 0.002$) and respiratory tract infection (11.1% vs 3.0 vs 5.3%; $p < 0.001$). In-hospital (8.7% vs 2.4% vs 0.4%; $p < 0.001$) and 6-month overall mortality (16.7% vs 6.4% vs 2.5%; $p < 0.001$) were higher in patients with higher CHA2DS2VASc score. In multivariate analysis and after adjusting for different baseline characteristic CHA2DS2VASc score revealed to be an independent predictor of development of heart failure (0.041). Patients with CHA2DS2VASc ≥4 were associated with higher risk of development heart failure [OR 2.88, 95% CI (1.27 - 6.54), $p = 0.012$] compared to those with CHA2DS2VASc 0-1.
Conclusion: CHA2DS2VASc score revealed to be a strong predictor of acute heart failure among STEMI patients.

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Endocan - Novel biomarker in patients with acute heart failure?

I Potocnjak[1]; M Trbusic[2]; S Dokoza Teresak[1]; G Pregartner[3]; S Frank[4]; V Degoricija[2]
[1]University Hospital Centre Sisters of Charity, Zagreb, Croatia; *[2]University of Zagreb School of Medicine, Zagreb, Croatia*; *[3]Medical University of Graz, Institute for Medical Informatics, Statistics und Documentation, Graz, Austria*; *[4]Medical University of Graz, Institute of Molecular Biology and Biochemistry, Center of Molecular Medicine, Graz, Austria*

On behalf of: AHF study group

Background: Endocan is known as an endothelial cell-specific molecule 1 (ESM-1), exhibiting anti-inflammatory properties. It is a proteoglycan with a chondroitin/dermatan sulfate chain. Its elevated level is connected with endothelial activation, inflammation and carcinogenesis. According to the manufacturer, the normal range is 0.3-3ng/mL. To our knowledge, endocan has not been previously investigated in Acute heart failure (AHF) patients (pts).
Purpose: The aim of this study was to investigate the impact of sex, age, ejection fraction (EF), NYHA classification, CRP and blood pressure (BP) on endocan values in AHF pts.
Methods: The study was performed as a prospective, non-interventional, single-center observational study from November 2013 to February 2015 in the University hospital centre, Croatia. There were 80 pts with AHF included. Complete analysis was performed for 75 pts since five of them had high endocan values (≥20ng/ml), which were considered unmeasurable. For analysis, ELISA kit was used to detect and quantify human Endocan/ESM-1 in serum. Pts were grouped according to demographic and laboratory parameters, with cut-off values of 5mg/L for CRP, ≤40%, 41-49%, and ≥50 for EF, and 140/90mmHg for BP. Pts were classified and treated according to ESC guidelines. The study was conform to the principles of the Declaration of Helsinki of the World Medical Association. Differences between the groups were determined by the non-parametric Mann-Whitney U or Kruskal-Wallis test. Results will be shown as median and minimum and maximum. The analyses were conducted using R version 3.3.1.
Results: The median endocan concentration was 4.8ng/ml (1.3-15.2). Endocan was not significantly different between the sexes [4.8ng/ml (1.3-15.2) for men, 4.4ng/ml (1.5-14.7) for women; $p = 0.848$]. Pts ≤75 years of age had a median value of 3.2ng/ml (1.6-14.7) and pts >75 had 5.2ng/ml (1.3-15.2) ($p = 0.054$). The median endocan value in NYHA classification groups 2 or 3 was 4.8ng/ml (1.3-15.2) and 4.6ng/ml (1.5-14.7) in group 4 ($p = 0.630$). In pts with normal CRP (≤5), median endocan was 4.3ng/ml (1.6-14.7) and with elevated CRP (>5) was 5.2 ng/ml (1.3-15.2) ($p = 0.610$). According to EF, the median endocan value for pts with decreased EF ≤40% was 5.0ng/ml (1.5-14.7), with an EF 41-49% was 4.8ng/ml (1.3-14.3) and with EF ≥50 was 4.4ng/ml (1.6-15.2) ($p = 0.625$). Pts with a systolic BP of < 140mmHg had a median endocan value of 5.5ng/ml (1.3-15.2) whereas with ≥140mmHg had 4.2ng/ml (1.6-14.7) ($p = 0.148$). For diastolic BP, pts with < 90mmHg had a median endocan value of 4.8ng/ml (1.3-15.2) whereas with ≥90mmHg had 4.4ng/ml (1.6-14.7) ($p = 0.595$).
Conclusion: To our knowledge this was the first research of endocan in AHF pts. According to the results of this study on 75 pts, endocan was higher in our AHF pts compared to previously measured values in healthy volunteer, but did not differ significantly between groups according to sex, age, EF, NYHA classification, CRP and BP.

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Impact of an advanced heart failure program on the characteristics and care of patients admitted with worsening heart failure in a developing country

F Bader[1]; M Al-Sarie[2]; G Gabra[1]; M Soliman[1]; B Bassam Atallah[3]; M Khalil[1]
[1]Cleveland Clinic Abu Dhabi, Cardiovascular Medicine, Abu Dhabi, United Arab Emirates; *[2]University of Toledo Medical Center, Toledo, United States of America*; *[3]Cleveland Clinic Abu Dhabi, Pharmacy Services, Abnu Dhabi, United Arab Emirates*

Background: Heart failure (HF) is a leading cause of global morbidity and mortality. Management of HF patients requires comprehensive multidisciplinary clinical care, best provided through the establishment of advanced HF programs. Such programs have become increasingly important in developing countries, where healthcare systems face educational and socioeconomic challenges. Our aim is to highlight the impact of advanced HF program establishment on the characteristics and care of acutely decompensated heart failure (ADHF) patients.
Methods: We conducted a retrospective chart review to identify patients admitted with ADHF before and after the establishment of an advanced HF program. One-hundred and forty ADHF admissions within the 24 months period prior to the establishment of the program (Group 1) were compared with 54 ADHF admissions that took place 6 months after program establishment (Group 2). Demographic, clinical, hemodynamic, and laboratory characteristics were evaluated at the time of admission and hospital discharge.
Results: At hospital admission, patients in group 1 tended to be more symptomatic, had higher mean arterial pressure (MAP) and higher heart rate (HR) than patients in group 2 (Figure, 1 panel A). At discharge, patients in group 2 had lost more weight and had lower MAP. Duration of hospital admission was not significantly different between the two groups (Figure, panel B). HF medications were used more in group 2, both at hospital admission and at discharge (Figure 1, panels A and B).
Conclusion: After the establishment of an advanced HF program, patients admitted with ADHF were more optimally managed before and during their admission, with more evidence- based therapies and better hemodynamics. Although the duration of hospital stay was the same, more effective diuresis took place when patients were followed by the HF program. Longer follow up is needed to assess differences in readmission rate.

A

	Group 1 (n=140)	Group 2 (n=54)	P Value
Chest pain	66 (47.1)	14 (25.9)	0.007
Dyspnea	140 (100)	52 (96.3)	0.022
Crackles	140 (100)	39 (73.6)	< 0.001
MAP, mmHg	102.9 ± 14	82.3 ± 22.4	< 0.001
HR, bpm	98.1 ± 20.7	85.1 ± 16.9	< 0.001
Medications			
B Blocker	27 (19)	30 (56)	< 0.001
ACEi/ARB	45 (32)	29 (54)	0.006
Aldosterone antagonist	28 (20)	27 (50)	< 0.001
Diuretic	60 (43)	42 (78)	< 0.001
Digoxin	42 (30)	12 (22)	NS

Patient characteristics at admission. MAP: mean arterial pressure, HR: heart rate, B Blocker: beta blocker, ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker. Values expressed as mean ± SD or n (%)

B

	Group 1 (n=140)	Group 2 (n=54)	P Value
Duration of admission, days	6.4 ± 0.48	6.1 ± 0.53	NS
Weight loss during admission, kg	1.4 ± 0.11	3.8 ± 1.3	0.0046
MAP, mmHg	87.3 ± 0.78	81.4 ± 1.1	0.0001
HR, bpm	75.8 ± 1.0	78 ± 1.3	NS
Medications			
B Blocker	48 (34)	39 (72)	< 0.001
ACEi/ARB	90 (64)	34 (63)	NS
Aldosterone antagonist	70 (50)	46 (85)	< 0.001
Diuretic	129 (92)	51 (94)	NS
Digoxin	77 (50)	15 (28)	0.001

Patient characteristics at discharge. MAP: mean arterial pressure, HR: heart rate, B Blocker: beta blocker, ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker. Values expressed as mean ± SEM or n (%)

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The PARASAIL study Patient reported outcomes from the Canadian real world experience use of sacubitril/valsartan in patients with heart failure and reduced ejection fraction

H Haddad[1]; S Bergeron[2]; A Ignaszewski[3]; G Searles[4]; N Bastien[5]
[1]University of Saskatchewan, Saskatoon, Canada; *[2]Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, Canada*; *[3]University of British Columbia, Vancouver, Canada*; *[4]Saint John Regional Hospital, Saint John, Canada*; *[5]Novartis Pharmaceuticals Canada Inc, Dorval, Canada*

Background/Introduction: Following the completion of the PARADIGM-HF trial, there is an opportunity to further explore the drug knowledge in a broader patient population through real world experience. PARASAIL, a Canadian prospective, multicenter, open-label, study aims at characterizing the effectiveness and safety of Sacubitril/Valsartan (Sac/Val) in 300 Canadian patients with heart failure with reduced ejection fraction (HFrEF) followed for 12 months.
Methods: The exploratory objectives from this study focus on validated quality of life questionnaires recorded by patients (Minnesota living with HF questionnaire (MLHFQ), EQ-5D questionnaire and patient global assessment (PGA)who have been converted to Sac/Val at 4, 12 and 24 weeks. Participants who were considered to be eligible were adult HFrEF outpatients with an ejection fraction of < 40%, NYHA class II or III and on stable doses of ACEI or ARB recruited in 32 centers across Canada. The suggested starting dose of Sac/Val was 24 mg/26 mg bid replacing ACEI or ARB. Up-titration to 49 mg/51 mg bid then to 97 mg/103 mg bid can occur every 2-4 weeks as per clinical judgement. Symptomatic hypotension and/or SBP below 100 mmHg, estimated GFR below 30mL/min/1.73m2, angioedema or necessity to use ACEI or ARB concomitantly, were amongst the exclusion criteria. The results presented here are those from the initial 54 patients who completed 24 weeks of treatment.
Results: Mean patient age was 66 years old, 82% male, 89% Caucasian, and BMI of 31.3 kg/m2, mostly NYHA Class II (91%), with baseline blood pressure of 123/73 mmHg. Baseline standard HF therapy was commonly used in most patients: 63% on ACEI or 26% ARB before Sac/Val initiation, 89% on beta-blockers, 46 % on MRA and 52% on diuretics. Drug initiation and titration started at the 24/26 mg dose of Sac/Val for most patients (87%) and up-titration to maximum dose of Sac/Val was achieved for the majority (70%) at 12 weeks. For both PGA and MLHFQ, there were improvement in the QoL: 45% of patients experienced an improvement of their scores (slightly, moderately and markedly) with PGA at week 4 and 56% at week 12, and there was a significant improvement in the MLHFQ at both weeks 4 and 12 with 18% and 26% decrease in the score compared to baseline respectively (P= 0.0096 and P= 0.0020 respectively). For the EQ-5D questionnaire, there were no changes in the VAS score at week 4 and week 12, and no changes in the 5 individual domains either. The treatment was safe and well tolerated and no patient discontinued it within the initial 12 weeks of follow-up.
Conclusion: The PARASAIL trial is designed to evaluate real-life effectiveness and safety of Sac/Val in HFrEF patients. Initial results of QoL questionnaires detected early signs of improvement in 2 of the 3 validated questionnaires. While placebo effect cannot be ruled out, further analysis of the total cohort of the patients will provide more insights about this possibility.

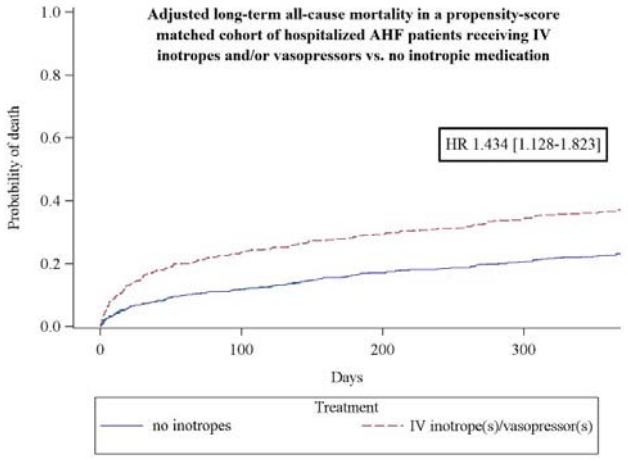
P222

Long term safety of inotropes and/or vasopressors in acute heart failure: results from ESC-HF-LT registry

A Mebazaa[1]; J Motiejunaite[2]; E Gayat[1]; E Akiyama[2]; MG Crespo-Leiro[3]; LH Lund[4]; AP Maggioni[5]; O Chioncel[6]; F Ruschitzka[7]; G Filippatos[8]
[1]Hospital Lariboisiere, Department of Anesthesiology and Critical Care, Paris, France; *[2]Inserm UMR-S 942, Paris, France*; *[3]Complexo Hospitalario Universitario A Coruna, CHUAC, Unidad de Insuficiencia Cardiaca Avanzada y Trasplante Cardiaco, La Coruna, Spain*; *[4]Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden*; *[5]ANMCO Foundation For Your Heart, Florence, Italy*; *[6]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; *[7]University Heart Center, Department of Cardiology, Heart Failure Clinic and Transplantation, Zurich, Switzerland*; *[8]Attikon University Hospital, Athens, Greece*

On behalf of: on behalf of ESC-HF-LT registry investigators

Introduction: Increasing short term safety concerns have been reported concerning the use of inotropes and/or vasopressors in the initial management of acute heart failure (AHF). However, data on long-term safety of these agents is scarce. We therefore sought to assess safety, especially long term mortality, of intravenous inotropes and/or vasopressors in AHF by a post-hoc analysis of a large AHF registry.
Methods: The European Society of Cardiology Heart Failure Long – Term Registry (ESC-HF-LT) was a multicenter prospective observational registry conducted in 21 countries between 2011 and 2013. Median follow-up duration was 381 [363; 457] days. For present analysis we selected patients (pts) with unscheduled hospitalizations for AHF, for whom intravenous (IV) therapy was needed (n = 6900), including 833 (12%) pts who received one or more inotropes and/or vasopressors. A further analysis of 1212 pts was derived using propensity score matching (606 pts in each treatment group) in which 35 baseline variables were balanced as assessed by standardized mean differences. Primary endpoint was long-term all-cause mortality. Secondary endpoints were in-hospital mortality, all-cause post-discharge mortality and post-discharge rehospitalization.
Results: Long-term all-cause mortality was greater in pts receiving IV inotrope and/or vasopressor compared to those who did not, both in the whole (43.7 % vs. 23.2 %) and the matched cohorts (39.8 % vs. 29.4 %). Adjusted hazard ratio (HR) for the association between the use of IV inotrope and/or vasopressor and long-term all-cause mortality was 1.720 [1.498 – 1.975] in the whole cohort and 1.434 [1.128-1.823] in the matched cohort. Adjusted HR for associations between the use of IV inotrope and/or vasopressor and in-hospital mortality were 3.138 [2.432-4.048] in the whole and 1.873 [1.151 – 3.048) in the matched cohorts. Adjusted HR for long-term all-cause mortality in patients discharged alive were 1.249 [1.059-1.474] in the whole and 1.078 [0.769-1.512] in the matched cohorts. No association was found between the use of IV inotropeand/or vasopressor and post-discharge rehospitalization, neither in the whole nor in the matched cohorts (HR 1.101 [0.924-1.311] and 1.117 [0.788-1.582] respectively).
Conclusions: The use of inotropes and/ or vasopressors in AHF was associated with increased long-term risk of all-cause death.



P223

The bleeding risk in thrombolysed patients with intermediary-high risk pulmonary embolism

A Alexandru Ion[1]; C Andrei[1]; M Raducan[2]; C Sinescu[1]
[1]University of Bucharest Carol Davila, Bagdasar Arseni Emergency Hospital, Cardiology Department, Bucharest, Romania; *[2]Bagdasar-Arseni Emergency Hospital, Cardiology, Bucharest, Romania*

Background: The intermediary-high risk pulmonary embolism (PE) is associated with an early mortality risk which shows the need for upgrading medical therapy. The main purpose in using thrombolytics in patients with intermediary-high risk PE is to obtain an improvement in the clinical status and the mortality risk, without increasing the bleeding risk
Purpose: The purpose of this study is to assess the bleeding risk in patients with intermediary-high risk PE thrombolysed with t-PA compared to patients treated with unfractionated heparin (UFH). The main purpose is to identify the group of patients which has the lowest bleeding risk with thrombolytic therapy, in order to reduce the main side effect.
Material and methods: We included 65 patients with intermediary-high risk PE. The inclusion criteria were: 1. First symptomatic acute PE (in the last 2 weeks). The exclusion criteria were: 1. Age > 80 y.o.; 2. Severe anemic syndrome (Hb < 8 g/dl); 3. Pre-existing pulmonary hypertension; 4. Dilative cardiomyopathy with severe LV dysfunction (EF < 30%); 5. Aortic or mitral valvulopathies which may produce pulmonary hypertension. The subjects were divided in two groups : 1. study group - received t-PA (10mg bolus and 90 mg in 2 hours) and UFH -; 2. control group was treated with UFH alone, with therapeutic aPTT. In the control group were included patients with contraindications for thrombolysis, with BMI > 30

or BMI < 18.5, or with end stage renal failure, as these factors were associated with an increased thrombolytic bleeding risk. The patients were assessed regarding the bleeding risk by major and minor bleeding events and the severity of the bleeding event was calculated by the Hb decrease compared to inclusion status. There were no differences regarding the sex distribution in the two groups but there was a significant difference between the medium age (68.48 +/- 12.3 y.o. in control group vs 63.32 +/- 17.4 y.o. in study group (p 0.05)). This difference can be explained by the inclusion and exclusion criterias.
Results : Regarding the major bleedings there was only one major bleeding in the study group (intracerebral hematoma) and no major bleedings in the control group. Meanwhile the minor bleeding rate was 1:7 in the study group vs 1: 9.25 (p 0.075). The medium Hb value on admision in the study group was 13.32 +/- 1.1 g/dl vs 12.91 +/- 1.24 g/dl in the control group, with no statistical difference. Comparing the Hb value between the two groups in the fifth day we noticed a decrease of 6.08% in the study group vs 3.87% in control group(p 0.04).
Conclusion: These data prove the safety use of thrombolytics in selected patients with intermediary-high risk PE, these leading to an optimal risk/benefit ratio which may identify the best patient profile for receiving this therapy.

P224

Clinical profile of heart failure admissions in a tertiary hospital. Implications for multidisciplinary management

L Vicent[1]; A Ayesta[1]; MT Vidan[1]; JM De Miguel-Yanes[1]; J Garcia[1]; V Gomez-Carrillo[1]; S Veliz[1]; M Tamargo[1]; H Gonzalez-Saldivar[1]; F Fernandez-Aviles[1]; M Martinez-Selles[1]
[1]*University Hospital Gregorio Maranon, Cardiology, Madrid, Spain*

Introduction. Population aging has produced notable changes in heart failure admissions.
Purpose: Our aim was to analyse the characteristics, comorbidity, management, and outcomes of these patients in three departments.
Methods: Prospective registry during 45 days. All patients admitted for heart failure in Internal Medicine, Cardiology and Geriatrics were included.
Results: From 235 patients, 124 patients (52.7%) were admitted in Internal Medicine, 83 (35.3%) in Cardiology, and 28 (11.9%) in Geriatrics. Mean age was 77.0 ± 20.2 years (Cardiology 71.5 ± 13.5; Internal Medicine 79.2 ± 21.1; Geriatrics 89.9 ± 5.1; p < 0.001). Preserved ejection fraction was found in 121 patients (51.5%) and this rate was higher in Internal Medicine (62.5%) and Geriatrics (70.0%) than in Cardiology (31.3%), p < 0.001. Comorbidity was frequent, especially atrial fibrillation (126; 53.6%) renal disease (89; 37.8%), and chronic obstructive pulmonary disease (65; 27.6%). Infections were the most common decompensating trigger in Internal Medicine (56; 45.2%) and frequently there was no trigger in Cardiology (45; 54.2%) and Geriatrics (14; 50.0%), p < 0.0001. Treatment administered is resumed in the table. During 45 days follow-up 23 patients (9.9%) were readmitted, this was more frequent in Internal Medicine than in Cardiology (odds ratio 3.0 [95% confidence interval: 1.1 - 8.6], p = 0.03), without other significant comparisons.
Conclusions: Patients admitted for decompensated heart failure are elderly and present frequent comorbidity. There are major differences between services with respect to age and clinical profile.

Treatment in patients with LVEF<40%

	Total (n = 70, 31.5%)	Cardiology (n = 44, 53.0%)	Internal Medicine (n = 23, 18.5%)	p
Pre admission				
Renin-angiotensin system inhibitors	45 (64.3%)	30 (68.2%)	14 (60.9%)	0.32
Betablockers	42 (60.0%)	24 (54.5%)	16 (69.6%)	0.07
Spironolactone	29 (41.4%)	24 (54.5%)	4 (17.3%)	0.001
At discharge				
Renin-angiotensin system inhibitors	52 (74.3%)	35 (79.5%)	13 (56.5%)	0.001
Betablockers	45 (64.3%)	29 (65.9%)	12 (52.1%)	0.003
Spironolactone	46 (65.7%)	39 (88.6%)	6 (26.1%)	< 0.0001

Treatment in patients with left ventricular ejection fraction <40% according to the department of admission. Geriatrics data are not presented since only 3 patients of this department had ventricular dysfunction, and at discharge all were treated with beta-blockers and ACE inhibitors (angiotensin converting enzyme inhibitors/angiotensin-2 receptor blockers).

P225

Current use and impact on 30-day mortality of pulmonary artery catheter in cardiogenic shock patients: results from the CardShock Study.

M Rivas Lasarte[1]; J Sans-Rosello[1]; M Vila[1]; H Tolppanen[2]; J Lassus[2]; M Lindholm[3]; A Mebazaa[4]; V-P Harjola[2]; A Sionis[1]
[1]*Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain*; [2]*Helsinki University Central Hospital, Cardiology department, Helsinki, Finland*; [3]*Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*; [4]*Inserm UMR-S 942, Paris, France*

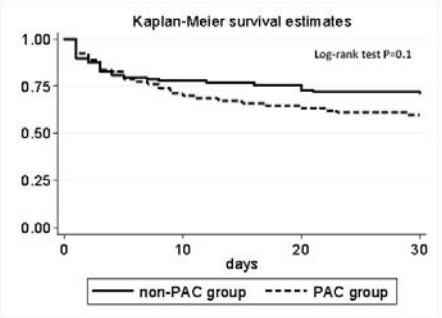
On behalf of: CardShock Investigators

Background: Cardiogenic Shock (CS) is the most life-threatening manifestation of heart failure (HF). Its complexity and high mortality, would justify the need for invasive monitoring with a pulmonary artery catheter (PAC) that may allow the clinician to establish an accurate diagnosis at all times and to guide treatment. Randomized clinical trials have failed to demonstrate clinical benefit of PAC use in critically ill patients, but CS patients were grossly underrepresented.
Purpose: This study aims to describe the real-world use of PAC in a contemporary cohort of patients with CS and to evaluate its prognostic impact on 30-day mortality.
Methods: This is a sub-study of the previous published CardShock study an observational, prospective, multicenter cohort of patients with CS. The use of PAC was within the discretion of the physician in charge.
Results: The CardShock study included 219 patients; PAC was used in 82 patients (37.4%). The management was more aggressive in those with PAC (table). Overall 30-day mortality was 38.6%, with no differences between PAC and non-PAC patients (figure).PAC use did not affect mortality [OR: 1.24 (95% CI 0.60-2.56) p = 0.56], in a multivariate analysis adjusted by a propensity score (including the history of prior myocardial infarction, inotropic use at admission, etiology of shock, mechanical ventilation, and assist device use).
Conclusions: This study revealed that PAC is used in 1/3 of CS patients. They are characterized by a prior poorer prognosis and by more aggressive management. PAC use was not associated with 30-day mortality.

Characteristics of the study population

	PAC group (82 patients, 37.4%)	Non-PAC group (137 patients, 62.6%)	P value
SBP at admission, mean (SD)	79.61 (1.75)	76.47 (1.05)	0.10
Inotrope use at admission*, n (%)	41 (50.00)	36 (26.28)	0.000
Confusion at admission, n (%)	63 (77.78)	85 (62.96)	0.02
Baseline LVEF, mean (SD)	31.43 (1.73)	33.94 (1.20)	0.22
IABP, n (%)	56 (76.71)	57 (46.34)	0.000
ECMO and LVAD, n (%)	6 (7.41)	5 (3.73)	0.23
Mechanical ventilation, n (%)	73 (89.02)	64(47.06)	0.000
30-day mortality, n (%)	35 (42.68)	49 (35.77)	0.31

PAC: pulmonary artery catheter; SD: standard deviation; SBP: systolic blood pressure; HR: heart rate; ACS: acute coronary syndrome, LVEF: left ventricular ejection fraction, IABP: intra-aortic balloon pump; ECMO: extracorporeal membrane oxygenation; LVAD: left ventricular assist device, CRR: continuous renal replacement. *Inotrope use refers to dobutamine, adrenaline, levosimendan or milrinone use.



Kaplan-Meier curves for 30-day survival

P226

Intravenous beta-blocker therapy in st-segment elevation myocardial infarction

E Elmir Omerovic[1]; O Angeras[1]; I Haraldsson[1]; C Dworeck[1]; J Odenstedt[1]; D Ioanes[1]; P Petursson[1]; S Volz[1]; P Albertsson[1]; B Redfors[1]
[1]*Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: Beta-blockade is recommend in all stable patients with ST-elevation myocardial infarction (STEMI) within 24 hours. However, the role of intravenous (IV) beta-blockade is less clear in the modern era of reperfusion therapy.
Aims: To investigate the impact of intravenous (IV) beta-blockade therapy on short-term mortality and risk of development of cardiogenic shock in patients with STEMI.
Methods: We used data from the nationwide Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry for patients in Västra Götaland County. All patients with STEMI undergoing PCI between 2006 and 2014 were included. The primary endpoint was mortality within 30 days and the secondary endpoints was in-hospital cardiogenic shock. We used multilevel modeling based on complete-case mixed-effects logistic regression to adjust for clustering of observations in a hierarchical database and for differences in patient characteristics.
Results: In total, 5,869 patients were included in the study of which 1,131 (19.3%) were treated with IV beta-blockade. At 30 days, there were 688 (11.7%) deaths and 426 (7.3%) cases of cardiogenic shock. IV beta-blockade was not associated with higher risk of death (OR 1.01, 95% CI 0.80-0.1.28, P=0.91) nor with higher risk of in hospital cardiogenic shock (OR: 1.18, 95% CI 0.90-1.54).
Conclusion: In our study, the use of IV beta-blockade in patients with STEMI was not associated with higher risk of short-term mortality and in-hospital cardiogenic shock.

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Relationship between improvements in long term outcomes and baseline systolic blood pressure in acute heart failure patients treated with TRV027: an exploratory subgroup analysis of BLAST-AHF

G Gadi Cotter[1]; PP Pang[2]
[1]*Momentum Research Inc., Durham, United States of America*; [2]*Indiana University School of Medicine & Regenstrief Institute , Indianapolis, United States of America*

On behalf of: BLAST-AHF Executive Committee and Investigators

TRV027 is a novel 'biased' ligand of the angiotensin II type 1 receptor (AT1R). In a large phase 2b acute heart failure (AHF) trial (BLAST-AHF), TRV027 did not affect a composite clinical outcome at 30 days.
Methods: Post-hoc analyses from BLAST-AHF (n = 618) were performed to examine the effects of TRV027 according to baseline systolic blood pressure (SBP) on changes in: post-baseline SBP, renal function, and 180-day outcomes. Patients were treated with one of four TRV027 dosing regimens, 1, 5 or 25 mg/hr, or matching placebo for up to 96 hours. Interactions between baseline SBP and the selected endpoints were identified using subpopulation treatment effect pattern plots (STEPP) analysis, grouping patients by SBP tertile: < 127 mmHg, ≥ 127 mmHg and < 140 mmHg, and ≥ 140 mmHg
Results: TRV027 did not affect SBP in patients with lower baseline SBP but was associated with a trend towards SBP increase in patients in the highest two SBP tertiles. TRV027 induced a trend towards increased creatinine over the first 3 days in patients with lower baseline SBP. In patients in the higher two SBP tertiles, TRV027, specifically the 1 mg/hr dose, tended to reduce creatinine at days 5 and 30. Beneficial effects on 180-day outcomes, especially all-cause mortality and cardiovascular (CV) death or readmission, were observed in patients with higher baseline SBP (≥ 127 mmHg) in the TRV027 1mg/hr dose group (all-cause mortality HR 0.39, 95% CI 0.14 - 1.06, p = 0.056; CV death or HF/RF rehospitalization HR 0.53, p = 0.049), while more adverse outcomes were observed in patients with baseline SBP in the lower tertile.
Conclusions: In this post-hoc analysis from the BLAST-AHF trial, patients with baseline SBP ≥ 127 mmHg treated with TRV027 experienced improved 180-day outcomes.

P228

feasibility of integrating multiple remote monitoring technologies as a single heart failure decision support tool

E Berry[1]; A Silvera[1]; W Downer[1]; D Agar[1]; S Beske Radford[1]; N Chiromeras[1]; M Bogart[1]; N Bonnet[1]
[1]*Morristown Medical Center, The Heart Success Program, Morristown, United States of America*

Funding Acknowledgements: Verizon

Background: Acute heart failure (AHF) is the leading cause of hospitalizations in patients aged 65 and older, and one of the leading diagnoses associated with 30-day readmissions. Preventing hospital admissions and reducing short-term readmissions is a critically important unmet need for patients, caregivers, and hospitals due to its high morbidity and cost. Non-invasive remote monitoring provides capabilities that enable patient self-care management, thereby leading to a greater patient engagement, empowerment, satisfaction and efficiencies.
Purpose: The purpose was to evaluate the feasibility of merging two disparate remote monitoring and management systems into an enhanced singular decision support tool that enabled timely and impactful interventions by a mature heart failure (HF) disease management program. The rate of hospital readmissions or ED visits 30 days post discharge was evaluated.
Methods: This is a prospective, interventional, nonrandomized study of AHF patients. Patients hospitalized for AHF were identified. Patients discharged to home were supplied with cutaneous wearable sensors and connected to a telehealth system. Patients discharged to a skilled nursing facility were given cutaneous wearable sensors and connected to a separate mobile monitoring application. Patients were monitored by these technologies for 30 days post discharge. Clinicians were alerted using variables from the remote monitoring systems to evaluate and guide further assessment and intervention.
Results: A total of 31 patients were enrolled during the 13 month study period. The mean age of participants was 78.5 years, 58% being 80 years old or older. 42% percent were male and 58% female. Of the participants, seven withdrew within 30 days. The readmission rate of patients that did not withdraw from the program was 20.8%. Thirteen patients had atrial fibrillation detected remotely.
Conclusion: The combination of these two disparate systems were successfully integrated within an established HF management program to provide decision support for HF interventions. The readmission rate of 20.8% suggests improved outcomes; however requires further investigation.

P229

Tolvaptan reduces readmission rates in acute heart failure patients with hypervolemic hyponatremia

L Lynne Wagoner[1]; CE Walton[2]; EK Walton[3]; R Cassidy[1]; DL Dietrich[1]
[1]*Mercy Fairfield Hospital, Mercy Heart Institute, Cincinnati, United States of America*; [2]*Summit Country Day School, Cincinnati, United States of America*; [3]*Wake Forest University, Winston Salem, United States of America*

Background: A significant portion of health care dollars is spent in the hospitalization and management of acute heart failure (AHF) patients (pts). Tolvaptan, an oral vasopressin receptor antagonist, is approved for treatment of pts with AHF and hypervolemic hyponatremia. In the EVEREST trial, no difference was observed in mortality or readmissions in pts admitted with AHF (not necessarily with hyponatremia) treated with tolvaptan vs placebo. We used tolvaptan to assist in the management of pts admitted with AHF with hyponatremia (defined as sodium < 135 mmol/L).
Methods: We reviewed charts of admitted pts at 5 community hospitals owned by Mercy Health in Cincinnati, Ohio between 2012 and 2016. Charts of our treatment group were reviewed for pts who had received tolvaptan for treatment of hyponatremia and AHF. A control group included pts with AHF and hyponatremia that did not receive tolvaptan. Charts were reviewed at admission and discharge for sodium (Na) levels, BUN, creatinine, weight loss, length of stay, cost per case, number of readmissions within 6 mos., and death.
Results: Our pertinent findings are listed in the table below. For the calculated cost per pt: # of readmits is multiplied by Cost/admission.
Conclusion: In clinical practice, pts with hypervolemic hyponatremia and AHF treated with tolvaptan demonstrated a greater improvement of sodium levels and a reduction in the number of readmissions in the next 6 mos. Furthermore, the 6 month calculated cost per patient is significantly lower for the patients treated with tolvaptan. Although the LOS and cost/case did not reach statistical signficance in the pts treated with tolvaptan, the cost of readmissions alone is important in reducing health care costs. Thus, tolvaptan can be a cost effective therapy when used in the management of hyponatremic AHF pts.

Tolvaptan vs Control

	Tolvaptan (n = 172)	Control (n = 71)	p value
Change in Sodium (mmol/L)	+ 7.9 ± 0.4	+ 4.8 ± 0.7	< 0.0001
# of Readmits in 6 months	1.01 ± 0.10	1.48 ± 0.2	0.038
Length of Stay (days)	8.7 ± 0.5	9.2 ± 0.7	NS
Cost/Admission (U.S. dollars)	16,525 ± 1,576	18,202 ± 2,533	NS
Calculated cost per pt in 6 months (U.S. dollars)	22,145 ± 6,565	35,125 ± 2,118	0.032

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Clinical experience with eplerenone in patients with heart failure nyha iii-iv functional class and midrange ejection fraction

T Tatqna Chakalova- Yancheva[1]; K Gospodinov[1]; Y Mladenova[1]; N Stancheva[1]; P Tonchev[1]; S Tisheva[1]
[1]*Medical University Pleven, Pleven, Bulgaria*

Objective: Clinical evaluation of the effect and safety of the addition of eplerenone to standard diuretic therapy in patients with heart failure III-IV NYHA functional class compared with that of the spironolactone.
Material and methods: A total of 78 patients with symptoms of decompensated heart failure III-IV functional class NYHA, where treated in University Hospital "G. Stransky"- Pleven, Bulgaria, between 1.01.2015-31.06.2015. The patients included were with left ventricular ejection fraction (LVEF) 40 to 49% - 'HF with midrange EF" in the absence of renal failure with creatinine clearance < 30 mL/min 1.73/ m2.The treatment was initiated with high-dose loop diuretic furosemide 120 mg per 24 hours. Co-medication with spironolactone was used in 42 patients (Group1) and with eplerenone in 36 (Group 2). The included patients were treated and closely monitored in the intensive care unit of the clinic of cardiology.
The treatment effect was assessed by clinical improvement of the patient expressed in mastering the congestion, reduction of subjective complaints, weight and diuretic response. The potassium levels were monitored during hospitalization in both groups.
Statistical methods: Chi-square test, Student test, IBM SPSS 21 were used for statistical analysis.
Results: The groups did not differ significantly by gender, age and severity of HF by NYHA. Diuretic response> 3000m / 24h. Was considered as good. Good diuretic response was demonstrated in 24 patients (78%) from the eplerenone group vs. 23(55%) in the spironolactone group (Chi Squared = 4.537, p = 0,03317 < 0,05)
Hypokalemia (K < 3,5) was observed in 29 patients (69%) treated with spironolactone vs. 11 patients (31%), treated with eplerenone. (Chi Squared = 11,496, p = 0,000697 < 0.05,).
Conclusion: The efficiency regarding additive diuretic effect of eplerenone to standard therapy with a loop diuretic in the study group is greater than that of spironolactone in patients with decompensated heart failure III-IV NYHA class and moderately reduced ejection fraction. Greater safety of eplerenone use is demonstrated in reduction the risk of potentially dangerous hypokalemia.

P231

Short course oral digoxin treatment in acute heart failure: a case control study

I Imen Trabelsi-Bchir[1]; TN Tounsi[1]; BK Beltaief[1]; MMA Msolli[1]; EM Echeikh[1]; SA Sekma[1]; BN Bziouich[1]; FN Fredj[1]; ZZ Zina[1]; GMH Grissa[1]; BH Boubaker[1]; BR Boukef[1]; BW Bouida[1]; NS Nouira[1]
[1]*university of Monastir, monastir, Tunisia*

Heart failure (HF) is a major worldwide health problem and one of the most important causes of hospitalization and readmission in older adults. Digoxin is one of the oldest and least expensive modulator for the management of HF. We conducted a matched case control study including 42 patients consulting the emergency department (ED) for acute HF (AHF), treated with short course digoxin, and 162 control patientsadmitted to the ED for AHF during the same period and did not receive digoxin. In these patients, hospital death and 30-day readmission rates were considered as main outcome. Secondary outcome was the effect of digoxin on left ventricular ejection fraction (LVEF), cardiac output (CO), and systolic time intervals including pre-ejection periode (PEP) and left ventricular ejection time (LVET) 72 hours after ED admission. Results showed that digoxin treatment was associated with reduction in mortality (12.3% vs 7.1%, p = 0.027) and all cause hospital readmission (16.05% vs 9.5%,p = 0.012). Compared to control group, LVEF and cardiac output increased in digoxin group (p = 0.003, p = 0.155,respectively). Simultaneously, digoxin decreased PEP (p = 0.018) and increased LVET (p = 0.013). NT proBNP decreased but not significantly in digoxin group (p = 0.06). We conclude that digoxin has a beneficial clinical and physiological effect in patients admitted to the ED for AHF.

P232

HFrEF, HFmrEF and HFpEF: which is the treatment of choice at discharge? Real world data from the ATHENA registry.

A Pratesi[1]; S Baldasseroni[1]; A Herbst[1]; S Parlapiano[1]; A Berni[2]; F Bacci[2]; G Ciuti[2]; C Tozzetti[2]; A Cortese[2]; C Nozzoli[2]; L Gabbani[1]; L Poggesi[2]; A Moggi Pignone[2]; N Marchionni[3]; F Orso[1]
[1]*Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy*; [2]*Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; [3]*Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA study group

Background: Heart failure (HF) is a highly prevalent condition particularly in the elderly. Prognosis has improved in HFrEF due to the availability of evidence based treatments. Currently, no treatments have proven efficacy in HFpEF patients and also in HFmrEF, the new category of HF, recently introduced by the Heart Failure Association of the European Society of Cardiology.
Purpose: to evaluate treatments at discharge in a real world setting of elderly patients after an episode of acute HF in the three different groups of HF: HFpEF, HFrEF and HFmrEF.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of AHF to a tertiary University teaching-hospital in the period 01.12.2014-01.12.2015.
Results: study population was composed by 246 patients: 19.5% with HFmrEF, 30.5% with HFrEF and 50.0% with HFpEF. Mean age of three group of patients was respectively 83.8, 84.5 and 79.9 years, p < 0.001. Pharmacological treatments at discharge in the three HF groups are shown in the attached table. BBs and MRAs were the only two classes of drugs that had a statistically different prescription rate across the three HF groups: patients with HFmrEF received BBs in similar percentage to patients with HFrEF. MRAs prescription rate in HFmrEF was intermediate compared to the other two groups. Furthermore, the average number of drugs taken by patients at the time of discharge was 11.8 with no differences across the groups.
Conclusion: at present, in the absence of specifical evidences from randomised clinical trials, patients with HFmrEF are treated similarly to those with HFrEF. Also, a high percentage of patients with HFpEF receive treatments that only have been to improve prognosis in HFrEF patients. Randomised clinical trials evidences are needed to appropriately treat HFmrEF patients.

Treatments	Tot n=246	HFrEF n=75	HFmrEF n=48	HFpEF n=123	P Value
ACE-I s	36.1	40.0	40.9	31.9	0.41
ARBs	19.1	22.9	15.9	18.1	0.61
BBs	6 8.3	84.3	79.5	54.3	0.001
MRAs	38.3	52.9	36.4	30.2	0.008
IVABRADINE	4.3	7.1	4.5	2.6	0.34
DIURETICS	90.0	94.3	90.9	87.1	0.28
DIGOXIN	13.9	15.7	13.6	12.9	0.87
TOT. DRUGS	11.8±3.7	11.2±3.4	11.6±3.8	12.1±3.8	0.30

ACE-I= Angiotensin Converting Enzyme Inhibitor. ARBs= Angiotensin Receptor Blockers. MRAs= Mineralcorticoid Receptor Antagonists. BBs= Beta-blockers.

P233

Frequency and prognostic impact of heart failure type following an episode of cardiac decompensation

S Brenner[1]; M Breunig[1]; C Morbach[1]; G Ertl[1]; CE Angermann[1]; S Stork[1]; G Guder[1]
[1]*University of Würzburg, Department of Internal Medicine I / Comprehensive Heart Failure Center , Würzburg, Germany*

On behalf of: INH-study group

Aim: The current European Society of Cardiology heart failure (HF) guidelines define three stages of left ventricular ejection fraction (LVEF): HF with reduced LVEF (< 40%, HFrEF), HF with mid-range LVEF (40-49%, HFmrEF) and HF with preserved LVEF (≥50%, HFpEF). We evaluated the progressive change of LVEF and its subsequent effect on LVEF staging and prognosis in patients initially presenting with HFrEF.
Methods: We studied patients from the Randomized INH Trial leaving the hospital with a LV ejection fraction ≤40% after an episode of decompensated HF. Six months after discharge, LVEF was re-evaluated by echocardiography and patients were grouped as defined above into HFrEF, HFmrEF, HFpEF. Events on cause-specific death and re-hospitalisation were subsequently collected for another follow-up period of 12 months.
Results: We report on 679 patients, 75% male, mean age 66 ± 12years, i.e. about 70% of the original cohort (n = 1032) surviving at least 6 months after discharge from index hospitalisation and providing echocardiography data. Six months after discharge, HFrEF, HFmrEF and HFpEF was found in 267 (39%), 225 (33%) and 187 (28%) of all patients, respectively. During the subsequent 12 month follow-up period, 52 patients (7.7%) died, 32 of those (5.0%) from cardiac causes. Further, 270 patients (39.8%) experienced re-hospitalization, of which 154 (22.7%) happened for cardiac reasons. In univariable Cox regression, HFrEF but not HFmrEF was associated with an increased risk of all-cause and cardiac death in comparison to the referent stage HFpEF (hazard ratio with 95% confidence interval); for all-cause death: 3.9 (1.6-9.4; p = 0.002) vs 2.0 (0.8-5.1; p = 0.164); for cardiac death: 3.1 (1.2-8.2; p = 0.023) vs 1.0 (0.3-3.3; p = 0.98), respectively. However, both, HFrEF

and HFmrEF were associated with increased risk for all-cause rehospitalisation and re-hospitalisation for cardiac reasons; for all-cause rehosp: 1.9 (1.4-2.6; p < 0.001) and 1.4 (1.0-2.0; p = 0.030); for cardiac reshosp: 4.4 (2.6-7.4; p < 0.001) and 2.5 (1.4-4.3; p = 0.001), respectively.
Conclusions: In patients leaving the hospital after an episode of cardiac decompensation with the phenotype of HFrEF, LVEF remains very dynamic. Six months later, prevalence of HFmrEF and HFpEF is about 30% each in survivors. LVEF recovery is a very important feature in these patients as both HFrEF and HFmrEF indicate worse prognosis compared to HFpEF.

P234

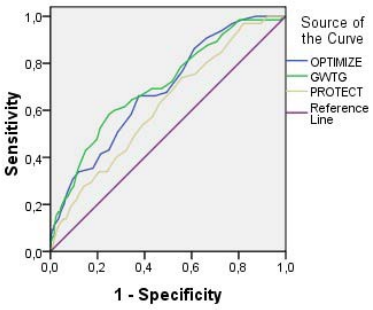
Prediction of in-hospital mortality in acute heart failure: comparing risk scores

J G Julio Gil Goncalves Pereira[1]; H Antunes[1]; L Abreu[1]; L Goncalves[1]; B Marmelo[1]; I Pires[1]; I Cunha[1]; R Silverio[2]; LF Santos[1]; J Costa Cabral[1]
[1]Hospital Sao Teotonio, Cardiology, Viseu, Portugal; *[2]Hospital Sao Teotonio, Internal Medicine, Viseu, Portugal*

Introduction: Risk stratification of patients with Heart Failure (HF) could improve clinical outcome and allocation of resources. Multiple risks scores (RS) have been created for the prediction of in-hospital mortality, such as OPTIMIZE-HF (1) by Abraham, the Peterson et al study GWTG-HF (2) and the work formulated by O´Connor. PROTECT (3).
Purposes and Methods: A retrospective study was performed on patients admitted for HF. Clinical, analytical, and echocardiographic parameters were evaluated. Calculation of the OPTIMIZE-HF, GWTG-HF and PROTECT RS were determined and compared. The risk score better at predicting in-hospital mortality was determined.
Results: A total sample of 952 patients were evaluated, 50.8% male, with a mean age of 77 ± 10 years old. Regarding in-hospital mortality, the ROC curve detailed in the image was ascertained.
The following table shows the mean values of each RS in alive vs deceased patients and the AUC of the ROC curve and the corresponding statistical significance.
Conclusion: In this population, only the GWTG-HF RS performed moderately well at predicting in-hospital mortality. Both the PROTECT and OPTIMIZE-HF RS underperformed, although the latter RS achieved better predictive power. Since HF represents such a heterogeneous group, creating risk scores is especially difficult in this population.
1. Abraham WT Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). J Am Coll Cardiol 2008; 52: 347-356
2. Peterson PN. A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association get with the guidelines program. Circ Cardiovasc Qual Outcomes 2010; 3: 25-32
3. O'Connor CM. The PROTECT in-hospital risk model: 7-day outcome in patients hospitalized with acute heart failure and renal dysfunction. Eur J Heart Fail 2012; 14: 605-612.

		PROTECT	GWTG-HF	OPTIMIZE-HF
In-hospital mortality		46 ± 9 vs 49±8	45±9 vs 48±9	33±6 vs 36±6
	p = 0.001	p = 0.001	p < 0.001	
AUC	0.619	0.704	0.685	
p	p = 0.001	p < 0.001	p < 0.001	

Risks Scores and In-Hospital Mortality



P235

Towards a multimarker prognostic strategy in acute heart failure. A role for GDF-15

P Bettencourt[1]; MJ Pinto[2]; P Rodrigues[2]; P Marques[2]; H Moreira[2]; JT Guimaraes[3]; P Lourenco[2]
[1]Hospital CUF, Internal Medicine, Porto, Portugal; *[2]Sao Joao Hospital, Internal Medicine, Porto, Portugal*; *[3]Faculty of Medicine University of Porto, Pathology, Porto, Portugal*

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Background: Growth differentiation factor (GDF) -15 mirrors inflammation and oxidative stress in cardiovascular diseases. Brain Natriuretic peptide (BNP) is associated with cardiomyocyte stretch in heart failure (HF). We aimed to evaluate the correlation between these biomarkers and to study the it´s prognostic impact acute HF.
Methods: We studied a group of patients prospectively recruited as part of an acute HF registry. Patients admitted with the diagnosis of acute HF were elegible. Patients were treated at the discretion of the attending physician. A venous blood sample was drawn at discharge. Patients were followed up to 2 years and the endpoint was all-cause mortality. A spearman correlation coefficient was used to study correlation between GDF 15 and BNP, age, creatinine, C-reactive protein (CRP) and hemoglobin. Patients with discharge GDF 15 below and above the median value were compared. Cox-regression multivariate models were built to study the association of GDF 15 (continuous and dichotomized according to the mean) and mortality. Patients were further cross-classified according to discharge GDF 15 (mean) and discharge BNP (mean) and independent association with mortality was studied. RESULTS: We studied 158 patients. Seventy (50%) male, mean age 75 years, 87 (55.1) had left ventricular ejection fraction <40%; mean discharge BNP was 1000.2pg/mL and mean discharge GDF 15 was 3013.3ng/mL. During the 2-year follow-up 71 patients (44.9%) died. Patients with higher GDF 15 (≥3000ng/mL) were significantly older and had higher BNP, higher creatinine and CRP and lower hemoglobin. No differences were observed concerning sex, etiology of HF and left ventricular function. GDF 15 correlated positively with age (Rho=0.27), BNP (Rho=0.36), creatinine (Rho=0.51) and CRP (Rho=0.28) and negatively with hemoglobin (Rho=-0.305). BNP and GDF 15 (analyzed as continuous or as categorical variables) associated with 2-year mortality. Patients with discharge BNP≥1000pg/mL had an age-, gender-, creatinine-, CRP-, hemoglobin- and GDF 15-) independent risk of 2-year mortality of 2.10 (95% CI: 1.22-3.61) and the age-, gender-, creatinine, CRP-, hemoglobin- and BNP- adjusted risk for GDF15≥ 3000ng/mL was 1.70 (95% CI:1.01-2.87). Patients discharged with both BNP and GDF 15 above the mean had a multivariate adjusted HR of 2-year death of 3.64 (1.80-7.34) p < 0.001 when compared with the reference category (both BNP and GDF 15 below the mean). Patients with only one of the variables above the mean had an HR of 2-year mortality of 1.66 (0.94-2.92), p = 0.08 CONCLUSIONS: Higher GDF15 associated with worse prognosis in acute HF independently of BNP. When both biomarkers GDF 15 and BNP were elevated at discharge, the 2-year mortality risk increased over 3-fold. Biomarkers related to different pathophisyologic pathways can provide incremental prognostic information in acute HF. We reinforce the concept of a multimarker approach in the prognostic assessment of acute HF

P236

Risk scoring system for prediction of clinical outcomes in Korean patients with acute decompensated heart failure: KorAHF score

J Y Jae Yeong Cho[1]; KH Kim[1]; HY Lee[2]; ES Jeon[3]; MS Kim[4]; JJ Kim[4]; KK Hwang[5]; SC Chae[6]; SH Baek[7]; SM Kang[8]; DJ Choi[9]; BS Yoo[10]; HY Park[11]; MC Cho[5]; BH Oh[2]
[1]Chonnam National University Hospital, Cardiology, Gwangju, Korea Republic of; *[2]Seoul National University Hospital, Seoul, Korea Republic of*; *[3]Samsung Medical Center, Seoul, Korea Republic of*; *[4]Asan Medical Center, Seoul, Korea Republic of*; *[5]Chungbuk National University Hospital, Cheongju, Korea Republic of*; *[6]Kyungpook National University Hospital, Daegu, Korea Republic of*; *[7]Seoul St. Mary's Hospital, Seoul, Korea Republic of*; *[8]Severance Hospital, Seoul, Korea Republic of*; *[9]Seoul National University Bundang Hospital, Seongnam, Korea Republic of*; *[10]Wonju Christian Hospital, Wonju, Korea Republic of*; *[11]National Institute of Health, Osong, Korea Republic of*

On behalf of: KorAHF registry
Funding Acknowledgements: Korea Centers for Disease Control and Prevention

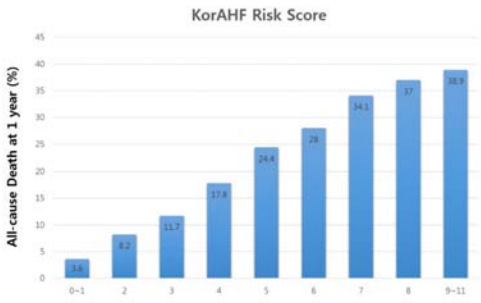
Background: Assessment of risk at time of admission could be a useful tool for guiding management of acute decompensated heart failure (ADHF). The aim of this study was to develop a novel and simple assessment tools for better hospital discharge risk stratification.
Methods: A total of 5,625 cohort patients enrolled in Korean acute heart failure registry (KorAHF). Clinically relevant variables were collected in all the patients (Table 1).

The entire study population had complete 1-year follow-up data. Multivariate analysis by step-wise Cox regression models tested variables that were significant at a p value < 0.2 in univariate analysis.
Results: During 1-year follow-up, all-cause death occurred in 970 out of 5,625 patients (17.2%) in the development cohorts. By multivariate Cox regression analysis, the 11 independent factors that increased the risk of 1-year mortality were described in Table 1. The score was calculated by sum of one point for each variable. A new risk score (KorAHF score) for ADHF showed a strong graded relation to 1-year mortality (2.4% to 53.2%; Figure 1).
Conclusion: The KorAHF score for Korean patients with ADHF is a simple and relevant risk scoring system in prediction of 1-year all-cause mortality. Validation of the risk scoring system in a larger cohort would be needed.

Variables in the risk score system

	BetaCoefficient	P value	Multivariate Hazard Ratio(95% CI)
Age >75 years	0.642	< 0.0001	1.90 (1.66-2.17)
NYHA Fc IV	0.183	0.006	1.20 (1.06-1.37)
SBP < 100 mmHg	0.397	< 0.0001	1.49 (1.26-1.75)
GFR < 60 ml/min	0.350	< 0.0001	1.42 (1.23-1.63)
LVEF < 30%	0.185	0.008	1.20 (1.05-1.38)
Na+ < 135 mEq/L	0.386	< 0.0001	1.47 (1.29-1.68)
Hemoglobin < 10 g/dL	0.373	< 0.0001	1.45 (1.25-1.69)
Nutritional risk index < 89	0.539	< 0.0001	1.71 (1.50-1.97)
Uric acid >7.5 mg/dL	0.138	0.048	1.15 (1.00-1.32)
BNP>1000 pg/ml or NT-proBNP >5000 pg/ml	0.398	< 0.0001	1.49 (1.30-1.71)
No use of RAAS or Beta-blocker	0.328	< 0.0001	1.39 (1.21-1.59)

NYHA Fc = New York Heart Association functional class; SBP = systolic blood pressure; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; BNP = brain natriuretic peptide; NT-proBNP = N-terminal pro B type natriuretic peptide; RAAS = renin-angiotensin-aldosterone system; NRI = (1.519 x serum albumin[g/dl]) + (41.7 x weight [kg]/ideal body weight [kg])



P237
Precipitating factors leading to hospitalization and subsequent clinical outcomes in acute decompensated heart failure

J-H Ju-Hee Lee[1]; DH Bae[1]; KK Hwang[1]; MC Cho[1]
[1]*Chungbuk National University Hospital, Cardiology, Cheongju, Korea Republic of*

On behalf of: KorAHF investigators

Background: There are few data examining the factors identified as contributing to heart failure (HF) hospitalization. We evaluated the frequency of clinical factors leading to admission for heart failure and the association between precipitating factors and subsequent outcomes.
Method: We evaluated acute decompensated HF patients hospitalized in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to February 2014. Precipitating factors were identified at admission and included acute coronary syndrome/ischemia, severe hypertension, atrial or ventricular tachyarrhythmia, bradyarrhythmia, infection, pulmonary embolism, renal failure, anemia or bleeding, medications which can aggravate HF, noncompliance, excessive alcohol or illicit drug use, endocrine abnormalities, recent addition of negative inotropic drugs. In-hospital mortality and 1-year mortality were assessed.
Results: Mean age was 68.5 ± 14.5 and 2,993 patients (53.2%) were male. Among the 5,625 patients who were registered at KorAHF Registry, 4,874 patients (86.7%) had 1 or more precipitating factors identified, with acute coronary syndrome/ischemia (26.3%), atrial or ventricular tachyarrhythmia (20.5%), and infection (19.6%) being most frequent. Acute coronary syndrome/ischemia was most common precipitating factor in HFrEF whereas atrial or ventricular tachyarrhythmia was most common in HFpEF. Acute coronary syndrome/ischemia (8.2% vs 3.5%, P < 0.001) and renal failure (7.6% vs 4.6%, P=0.018) were associated with higher in-hospital mortality, and infection (19.4% vs 11.8%, P=0.038), renal failure (29.5% vs 16.6%, P < 0.001) and anemia or bleeding (26.8% vs 17.0%, P < 0.001) were associated with higher 1-year mortality. But in multivariate analysis adjustment for 14 risk variables, only acute coronary syndrome/ischemia was independently associated with higher in-hospital mortality (odds ratio 2.00, 95% CI 1.44-2.78, P < 0.001) and anemia or bleeding was independently associated with higher 1-year mortality independently (hazard ratio 1.45, 95% CI 1.04-2.03, P=0.031) in all HF patients. In HFrEF patients, acute coronary syndrome/ischemia was also associated with higher in-hospital mortality (odds ratio 1.81, 95% CI 1.26-2.58, P=0.001), whereas renal failure and medications which can aggravate HF were associated with higher 1year mortality (hazard ratio 1.38, 95% CI 1.04-2.03, P=0.046; hazard ratio 1.62, 95% CI 1.04-2.03, P=0.012). In HFpEF patients, infection is associated with higher in-hospital mortality (odds ratio 2.11, 95% CI 1.03-4.33, P=0.041) whereas no precipitating factor can predict 1-year mortality.
Conclusion: Precipitating factors are frequently identified in patients hospitalized for HF and are associated with clinical outcomes independent of other predictive variables. Increased attention to these factors, many of which are avoidable, is important in optimizing the management of HF.

P238
Prognostic role of severe renal impairment in patients with HFrEF or HFpEF hospitalised for acute heart failure: data from the IN-HF Outcome Italian Registry

F Orso[1]; A P Aldo Pietro Maggioni[2]; G Fabbri[2]; L Gonzini[2]; M Bernardinangeli[3]; G Celona[4]; M Gori[5]; F Venturi[6]; L Tavazzi[7]
[1]*AOU Careggi, Department of Geriatrics, Section of Geriatric Medicine and Cardiology, Florence, Italy*; [2]*ANMCO Research Center, Florence, Italy*; [3]*Azienda USL Umbria 2, Cardiology Department, Terni, Italy*; [4]*AOR Villa Sofia-Cervello P.O. Cervello, Cardiology Department, Palermo, Italy*; [5]*Ospedale Papa Giovanni XXIII, Cardiology Dept. 1 Heart Failure and Transplant, Bergamo, Italy*; [6]*Ospedale San Giuseppe, Cardiology Department, Empoli, Italy*; [7]*Maria Cecilia Hospital, GVM Care & Research - E.S. Health Science Foundation, Cotignola, Italy*

On behalf of: IN-HF Outcome Investigators
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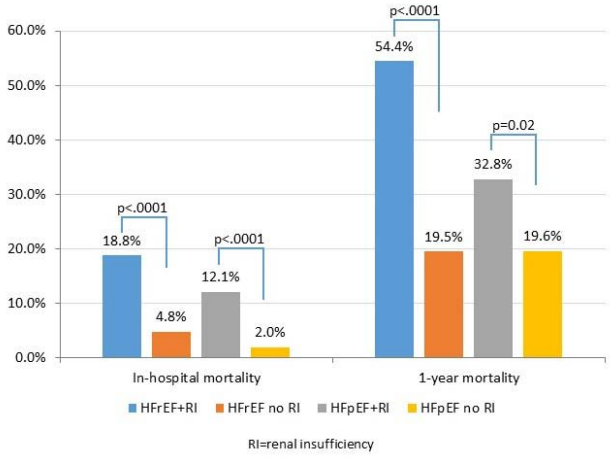
Background: Renal insufficiency (RI) frequently coexists with heart failure (HF) and worsens outcomes by adding a negative prognostic effect per se and by limiting the use of HFrEF life-saving treatments such as ACE-Inhibitors (ACE-I) and mineralcorticoid receptor antagonists (MRAs). Prognostic impact of RI in patients with HFpEF is less defined.
Aims: To evaluate the prognostic role of RI in patients with HFrEF or HFpEF hospitalised for HF.
Methods: We analysed patients hospitalised for acute heart failure (AHF) included in the IN-HF Outcome Italian registry with available data regarding left ventricular ejection fraction (LVEF) and estimated glomerular filtration rate (eGFR) data on admission. We than compared the prognostic role of severe RI (< 30 ml/min/1.73m2) in patients with HFrEF (LVEF < 45%) and in patients with HFpEF (LVEF≥45%).
Results: The study population was composed by 1643 patients: 1131 patients had HFrEF and among these patients the prevalence of severe RI was 13.2%. Compared to those with more preserved renal function, HFrEF patients with severe RI were older (75 ± 10 vs 70 ± 12 years, p < 0.0001), with a higher prevalence of females (40.9% vs 30.4%, p = 0.010) and had a higher prevalence of ischemic aetiology of HF (62.4% vs 47.2%, p < 0.001). Analysing treatments in the week prior to admission, HFrEF patients with severe RI received a lower prescription rate of ACE-I or angiotensin receptor blockers (46.3% vs 59.2%, p = 0.003) and of digoxin (7.4% vs 15.4%, p = 0.009), while prescription rates of betablockers and MRAs were similar. HFrEF patients with severe RI had higher in-hospital and one-year all-cause mortality (see Figure). Patients with HFpEF were 512 and 11.2% of these had severe RI. Compared to those with more preserved RI, HFpEF patients with

severe RI had a similar percentage of females (55.2% vs 56.67%, p = 0.84) and similar age (77 ± 9 vs 74 ± 10 years, p = 0.07) and a higher prevalence of ischemic aetiology of HF (39.7% vs 29.2%, p = 0.03). The in-hospital and 1-year mortality rates of HFpEF patients with or without severe RI are reported in Figure.
CONCLUSIONS. In patients with AHF, severe RI is significantly associated with a worse in-hospital and one-year all-cause mortality not only in patients with HFrEF but also in those with HFpEF.



P239

Clinical characteristics and outcome of acute heart failure patients with mid-range ejection fraction

E Edoardo Sciatti[1]; V Carubelli[1]; A Ravera[1]; D Tomasoni[1]; E Vizzardi[1]; I Bonadei[1]; CM Lombardi[1]; M Metra[1]
[1]University of Brescia, Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Brescia, Italy

Background: Heart failure (HF) with mid-range ejection fraction (HFmrEF) is a new entity defined by the recent ESC heart failure guidelines.
Purpose: To investigate the medium-term prognosis of HFmrEF after hospitalization for acute heart failure (AHF).
Methods: In a retrospective, single center study we included patients hospitalized for AHF at our Institute. Left ventricular ejection fraction (LVEF) was assessed with echocardiography during the hospitalization in all patients. For the purposes of this analysis patients were divided according LVEF in HFrEF (LVEF < 40%), HFmrEF (LVEF 40-49%), and HFpEF (LVEF ≥ 50%). Primary outcomes were cardiovascular (CV) death and CV death and HF hospitalization at day 180.
Results: A total of 948 patients were included in this analysis, 625 (65.9%) HFrEF, 117 (12.4%) HFmrEF, and 206 (21.7%) HFpEF. HFmrEF patients showed intermediate characteristics between HFrEF and HFpEF as regards age, sex, cardiac and extracardiac comorbidities. At baseline systolic blood pressure differed significantly in the three groups (HFrEF 125 ± 27 vs HFmrEF 138 ± 32 vs HFpEF 138 ± 31 mmHg; p < 0.001) as well as values of Nt-proBNP (6665 [IQR 4369-13753] ng/mL vs 4826 [IQR 2847-6915] ng/mL vs 3264 [IQR 1976-4766] ng/mL; p < 0.001). Treatment with ACEi/ARBs and beta blockers was highly implemented in both HFrEF and HFmrEF patients at discharge (HFrEF 69.8% baseline to 77.6% discharge vs HFmrEF 67.5% baseline to 74.4% discharge for ACEi/ARB; HFrEF 65.1% baseline to 83.5% discharge vs HFmrEF 62.4% baseline to 82.1% discharge, for beta blockers). At Cox regression analysis, the risk of CV mortality to day 180 did not differ across groups (HFrEF HR 1.576, 95% CI 0.983-2.527; p = 0.059 vs HFmrEF HR 0.580, 95% CI 0.268-1.254; p = 0.166 vs HFpEF HR 0.746, 95% CI 0.435-1.279; p = 0.286). Similarly the risk of CV death and HF hospitalization was comparable between groups (HFrEF HR 1.180, 95% CI 0.919-1.515; p = 0.195 vs HFmrEF HR 0.956, 95% CI 0.669-1.368; p = 0.807 vs HFpEF HR 0.824, 95% CI 0.614-1.106, p = 0.198) (Figure 1a and b).
Conclusion: AHF patients with mid-range LVEF seem to show intermediate clinical characteristics and similar outcomes of patients with HFrEF and HFpEF. This study confirms the limited prognostic power of LVEF in predicting post discharge events in AHF setting.

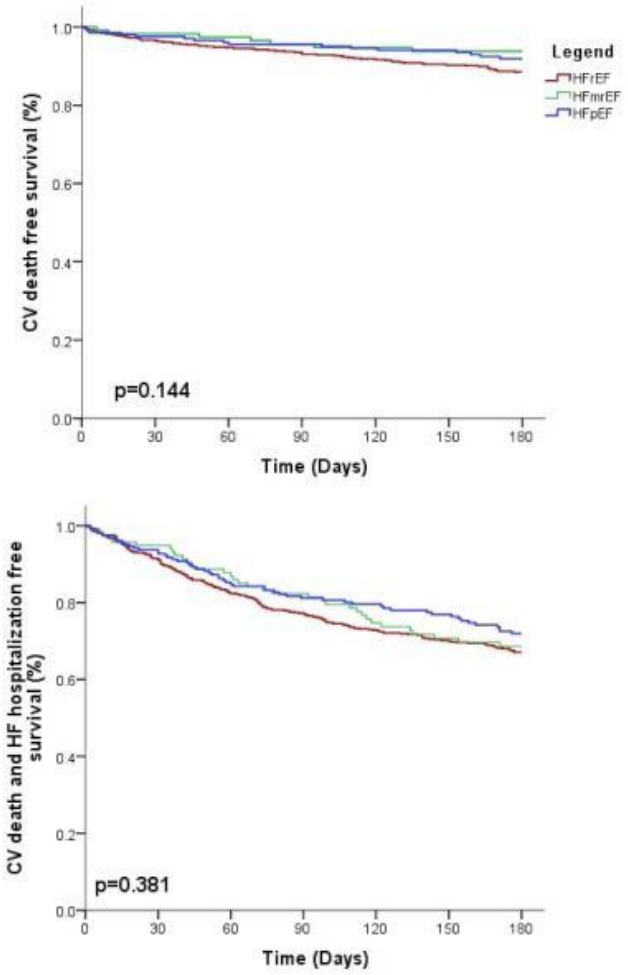


Figure 1

P240

Contemporary assessment of lung ultrasound, bnp and echocardiography predicts outcome in patients with acute heart failure independently to systolic dysfunction

A Palazzuoli[1]; G Ruocco[1]; M Beltrami[1]; R Nuti[1]; JG Cleland[2]
[1]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy; *[2]Imperial College London, National Heart & Lung Institute and National Institute of Health Research Cardiovascular Biomedical , London, United Kingdom*

Background: Pulmonary and systemic congestion at hospital discharge predict an adverse prognosis in patients with heart failure. Lung ultrasound (LUS) may be a simple, accurate, fast and economic tool to assess pulmonary congestion by imaging 'comets' or B-lines.
Purpose: 1) To investigate the relationships of B-lines to B-type natriuretic peptide (BNP), left ventricular ejection fraction (LVEF) and LV filling pressure at admission. 2) To evaluate their relationship to prognosis at six months and the added value of repeat measurements before discharge. 3) To explore potential differences in patients with HFpEF and HFrEF.
Methods: Patients admitted for worsening heart failure were assessed within 12h of admission. B-lines and BNP values were also evaluated at discharge. The primary composite outcome was re-hospitalization for heart failure or death at 6 months. Continuous variables are shown as median and inter-quartile range (IQR). Categorical variables are shown in percentage (%) or count.
Results: Of 162 patients enrolled, 95 had HFrEF and 67 had HFpEF; median age was 80 [77-85] years and 85 (52%) were women. The median number of B-lines at admission was 31 [27-36] and median plasma BNP was 1007 [768-1540]ng/L. Patients with HFrEF were slightly older, more likely to be men and less likely to have a history of hypertension. At admission, B-lines correlated with BNP (r=0,43;p < 0,001), clinical congestion (r=0,25; p = 0,001) and PAP (r=0,42; p < 0,001). Failure to reduce

B-lines during hospitalization was strongly associated with worse outcome (AUC 0,91 [0,85-0,96]; p < 0,001); a B-line reduction of <40% from admission to discharge had a sensitivity 90%, specificity 70% and correctly predicted outcome at 180 days in 76% of cases (p < 0,001). In univariate Cox regression analysis, the number of B-lines at discharge (HR 1.12 [1.09-1.16]; p < 0,001) and change in B-lines during admission (HR 0.95 [0.94-0.96]; p < 0,001) were related to poor outcome. Multivariable analysis confirmed the association with change in B-lines.
Conclusions: LUS appears a useful method to assess the severity and monitor the resolution of lung congestion. Measurement of lung congestion at discharge provides prognostic information for patients with either HFpEF or HFrEF.

P241
Genetic determinants of heart failure prognosis

RM Agra[1]; M Gago-Dominguez[2]; B Paradela-Dobarro[3]; M Torres[4]; L Alvarez[5]; A Fernandez-Trasancos[3]; A Varela-Roman[5]; S Eiras[3]; E Ezequiel Alvarez Castro[1]; A Carracedo[2]; JR Gonzalez-Juanatey[5]
[1]University Hospital of Santiago de Compostela, Cardiology, Santiago de Compostela, Spain; *[2]Fundación Pública Galega de Medicina Xenómica. SERGAS., Santiago de Compostela, Spain*; *[3]Instituto de Investigación Sanitaria de Santiago, Santiago de Compostela, Spain*; *[4]University of Santiago de Compostela, Santiago de Compostela, Spain*; *[5]University Clinical Hospital of Santiago de Compostela, Department of Cardiology, Santiago de Compostela, Spain*

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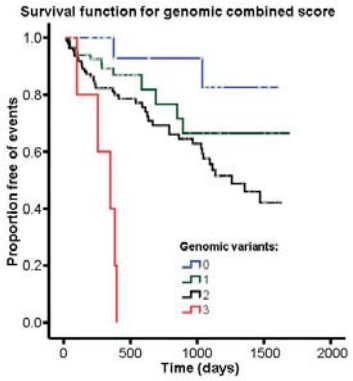
Objective: Heart failure (HF) is a complex cardiometabolic disorder resulting from the combination of genetic and environmental factors. Recent advances in genomics offer a smart option for predicting future risk of disease early in life and prognosis. The objective of this study was to examine the prognostic value of a series of single nucleotide polymorphisms (SNP) previously related with metabolic disorders and obesity.
Methods: A selection of 199 SNP found to be related with obesity, BMI, circulating lipids, HF, and cerebral infarction were genotyped in 227 patients with HF diagnosis following the current European guidelines of clinical practice. Anthropometrical and clinical variables were collected for each patient and a follow-up period was stablished for registry of death and re-hospitalization by HF as the primary endpoint. An additive genetic model was assumed, and the genotypes were analysed by Cox regression to study the association with HF prognosis.
Results: A total of 63 events (defined by the combination of death and re-hospitalization for HF) were registered. From the total of SNP, rs2107595, rs6882076, and rs737337 variants were independently associated with HF prognosis during a follow-up period of 438 (263-1077) days [median (IQR)]. Results were further adjusted for baseline characteristics (age, sex, body mass index (BMI), diabetes mellitus, hypertension, hyperlipidaemia, and blood lipid concentrations). Age and diabetes mellitus were also bad prognostic variables whereas higher total cholesterol was related with better prognosis, as expected in HF patients. Only rs737337 was related with BMI values, being the protective variant more present in normal weight (BMI $<$ 25) and obesity type I (30 $<$ BMI $\leq$ 35). A combined score of the three genomic variants was highly predictive of bad prognosis, in combination with diabetes mellitus and low levels of total cholesterol concentration.
Conclusions: Three SNP were identified as important predictors of major clinical outcomes in patients with HF, independently to age, diabetes mellitus and blood lipid concentrations. A combined score with these genomic variants could be a good independent predictor of bad prognosis in this clinical context.



Survival curve

P242
Worsening renal function in patients hospitalized for acute decompensated heart failure

E J Zaidel[1]; MI Sosa Liprandi[1]; JM Picco[1]; CN Pignataro[1]; R Villarreal[1]; HG Cestari[1]; EF Mele[1]; A Sosa Liprandi[1]
[1]Sanatorio Guemes, Cardiology, Buenos Aires, Argentina

On behalf of: Heart Failure Division, Sanatorio Güemes, Argentina

Background: It is usual to see an increase in creatinine levels in patients admitted for acute decompensated heart failure (ADHF), and renal dysfunction is a marker of adverse events in short and long term. Several pathophysiologic mechanisms have been proposed. However, there is lack of information about the rate and clinical predictors of worsening renal function (WRF).
Purpose: The aim of this study was to describe the rate of WRF in patients admitted for ADHF, and search for predictors of WRF.
Methods: A prospective registry of ADHF patients admitted to a University Hospital in the city of Buenos Aires was developed during two consecutive years (June 2013-June 2015). Baseline characteristics and daily creatinine and urea levels were registered. WRF was defined as a raise of creatinine levels ≥0.3 mg/dL or an increase of 1.5 times from baseline levels (Acute Kidney Injury Network definition). Conventional descriptive and comparative analyses were performed. The correlation between days and mean level of creatinine was evaluated with R2. Predictors of WRF were evaluated with univariate and multivariate models.
Results: 353 consecutive patients were recruited, with a median age of 75 years [IQR 67-85], and 54% were male. The most frequent etiologies were ischemic (30%), hypertensive (29%), and valvular (21%). Half of the patients had HF with preserved ejection fraction. After excluding patients on dialysis and patients included in randomized clinical trials with drugs that could potentially modify renal function (ularitide, serelaxin), 315 patients remained for the analysis. Among them, 111 (35.7%) had WRF.
Mean daily creatinine levels were 1.19, 1.22, 1.27, 1.30, and 1.35 mg/dL, respectively (R2=0.98). Mean baseline creatinine clearance was 66 ml/min/1.73 m2 (±24) (MDRD). The median hospitalization days was 9 [6-17], in WRF patients vs 7 [5-11] (p = 0.032) in non WRF, and in-hospital mortality of WRF patients was 23.4% vs 7.8% respectively (OR= 3.59; CI 95%: 1.83-7.01, p = 0.01). Five factors were related to WRF in the univariate analysis: age (75 vs 72 years), ischemic etiology (34% vs 25%), prior use of ACE inhibitors (44% vs 36%), and HF with preserved ejection fraction
(20% vs 25%), while prior use of angiotensin receptor blockers was related with a lower rate of WRF (20% vs 25%). All those factors were included in the multiple logistic regression model, and the ischemic etiology was the only independent predictor of WRF (OR=1.74; CI 95%: 1.03-3.0, p = 0.042).
Conclusions: One third of ADHF patients develop WRF, and the ischemic etiology of heart failure was the only independent predictor found. Further investigations are needed about differential mechanisms of renal dysfunction in ischemic patients.

P243
Different impact and prevalence of hyperuricemia in patients with acute heart failure with preserved ejection fraction respect to reduced ejection fraction

A Palazzuoli[1]; G Ruocco[1]; O De Vivo[1]; R Nuti[1]; PA Mccullough[2]
[1]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy; *[2]Baylor University Medical Center, Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, United States of America*

Background: The association between elevated uric acid levels and cardiovascular diseases has been known for almost half a century. Although the relationship between uric acid and chronic heart failure has also been demonstrated, the clinical and prognostic role in acute settings remains controversial and still poorly examined. Therefore, this study aims to evaluate the significance of uric acid in acute heart failure (AHF) and verify any different impact in heart failure with reduced ejection fraction (HFrEF) compared to heart failure with preserved ejection fraction (HFpEF).
Methods: This was a retrospective analysis which included consecutively 324 subjects, screened from interventional Diur-HF Trial (NCT01441245) from January 2011 to February 2016. Patients were eligible if they were admitted with a primary diagnosis of AHF. Enrolled subjects were categorized based on ejection fraction (EF): HFrEF [EF <50%], HFpEF [FE≥50%]. Blinded physicians assigned a standardized congestion score at the time of enrollment. We defined as hyperuricaemia as serum uric acid (UA) ≥ 7 mg/dL in men and ≥ 6 mg/dL in women. Patients were followed for six months after discharge with clinical visits or telephone contacts. The primary outcome was the composite of death or rehospitalization for AHF.
Results: 173 HFrEF and 151 HFpEF patients were followed and hyperuricemia was found in 160 subjects with greater proportions in HFpEF compared to HFrEF

(57% vs 43%; p = 0,01). It was significantly more prevalent in women (74% vs 60%; p = 0.008), those with diabetes (39% vs 19%; p <0.001), hypertension (62% vs 43%; p = 0.001) and atrial fibrillation (48% vs. 34%; p = 0.01). In HFrEF patients, univariate analysis showed that hyperuricemia [HR 1,48 (1,02-2,15); p = 0.04] and congestion score ≥ 3 [HR 2,83 (1,52-5,28); p < 0.001] were related to the primary outcome; after adjustment, multivariable analysis demonstrated that only congestion score ≥ 3 [HR 2,08 (1,06-4,10); p = 0.03] was independently associated with the primary outcome. On the contrary, in HFpEF patients, the only significant predictor of poor prognosis was hyperuricemia, both in univariate [HR 2,25 (1,44-3,50); p < 0.001] and multivariable [HR 2,38 (1,32-4,28); p = 0.004] analysis.
Conclusions: In Acute Heart Failure hyperuricemia is common among those with HFrEF and HFpEF. In the HFpEF subgroup, hyperuricemia was independently associated with an increased risk of death or hospitalization.

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Acid-base balance disorders are associated with increased 1-month and 3-month mortality in patients with acute heart failure

G Gabrielius Jakutis[1]; M Balciunas[2]; A Montvilaite[3]; R Norvilaite[3]; A Mebazaa[4]; A Kavoliuniene[5]; J Celutkiene[2]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; *[2]University Hospital Santariskiu Klinikos, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; *[3]Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[4]University Paris Diderot , Inserm U942, Paris, France*; *[5]Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania*

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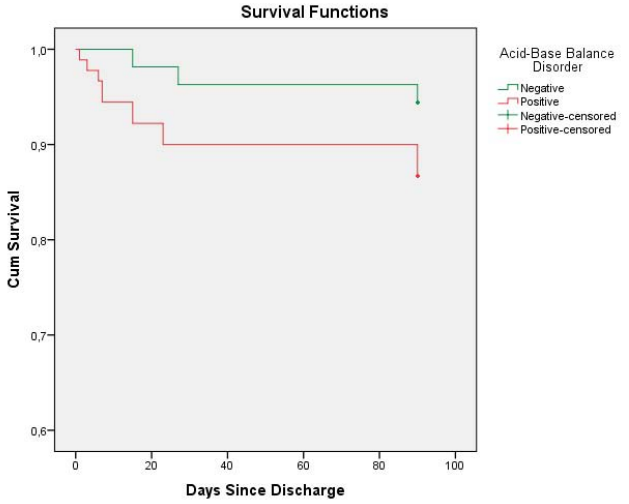
Background/Introduction: Arterial blood gas (ABG) analysis is one of the main tests for decision-making in patients with severe dyspnea. However, the significance of ABG analysis on the prognosis for the acute heart failure (AHF) patients remains unclear.
Purpose: The study evaluated whether acid-base balance disorders at the time of admission are associated with 1- and 3-month rehospitalisation and mortality rates of AHF patients.
Methods: A prospective observational cohort study enrolled consecutive patients with acute dyspnea from March, 2015 till August, 2016. The exclusion criterion was a suspected acute coronary syndrome. Data of 144 study patients with adjudicated diagnosis of AHF, available ABG and biochemical blood analyses at admission and completed 3-months follow up were included in the analysis. Outcomes were evaluated with Kaplan-Meier curves and Cox proportional hazard model to estimate survival rates, hazard ratios (HR) and 95% confidence intervals (CI). Data were analysed using SPSS v23 statistical package.
Results: 71 (49.3%) patients were male and 73 (50.7%) female. Acid-base balance disorders were found in 90 (62.5%) patients: 25 (17.3%) patients had acidosis (15 [10.4%] metabolic, 10 [6.9%] respiratory), 58 patients (40.3%) had alkalosis (7 [4.9%] metabolic, 51 [35.4%] respiratory), 7 (4.9%) patients had a mixed A-B disorder. Both respiratory and metabolic acidosis (HR=4.65, 95% CI: 1.42; 15.25, P=0.011) and mixed A-B disorders (HR=4.66, 95% CI: 1.05; 21.58, P=0.049) at admission were significantly associated with 1-month mortality (total number of deaths – 8). Metabolic acidosis (HR=7.63, 95% CI: 2.46; 23.67, P < 0.001) and mixed A-B disorders (HR=5.52, 95% CI: 1.55; 19.57, P=0.008) also displayed a significant effect on 3-month mortality (total 12 deaths). On-admission A-B disorders had no impact on 1- and 3-month rehospitalisation rates. The cumulative 90-day survival was 85% for patients with A-B disorders and 93% for individuals with normal A-B balance (p = 0.135). Patients with on-admission A-B balance disorders had a higher count of leukocytes (mean 9140/mm3 vs. 7360/mm3, p = 0.049), increased CRP (mean 29.95 mg/L vs. 12.25 mg/L, p = 0.028), glucose (mean 7.55 mmol/L vs. 6.22 mmol/L, p = 0.014), urea (mean 11.61 mmol/L vs. 7.86 mmol/L, p = 0.022) as well as high sensitivity (hs) troponin I serum concentration (mean 70.65 ng/mL vs. 45.31 ng/mL, p = 0.024) compared to patients without A-B balance disorders. No significant difference was observed in admission serum BNP concentration (mean 1554.45 pg/mL vs. 829.73 pg/mL, p = 0.065) in patients with and without A-B balance disorders.
Conclusions: On-admission acid-base balance disorders demonstrate a significant impact on 1- and 3-month mortality rates of patients with AHF. Patients with acid-base balance disorders have a distinct biochemical profile in terms of inflammatory and necrosis biomarkers. These patients require careful monitoring during first three months after the discharge.



Survival of AHF patients

P245

Short-term outcomes in heart failure patients with chronic obstructive pulmonary disease in the community

I Elhaddad[1]; K Kharbouche[1]; L Azouzi[1]; R Habbal[1]
[1]chu ibn rochd, cardiology, casablanca, Morocco

Aims: Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are common co-morbidities. The combination presents diagnostic challenges and has been linked with worse prognosis in patients admitted to hospital. There is hardly any prognostic data in patients with both co-morbidities in the community.
Methods: And Results: We evaluated 783 patients (27.2%) with left ventricular systolic dysfunction under the care of a regional nurse-led community heart failure team between June 2007 - June 2010. 101 patients (12.9%) also had a diagnosis of COPD. 94% of patients were on loop diuretics; 83% on ACE Inhibitors, 74% on b-blockers; 9.6% were on bronchodilators and 42% on aldosterone antagonists. Mean age of the patients was 77.9 + 5.7 years; 42% were females and mean NYHA
class was 2.1 + 0.6. Mean follow-up was 28.2 + 2.9 months. b-blocker utilization was markedly lower in in patients receiving bronchodilators compared to those without (overall 24.4% vs 81%; P , 0.0001). 24 month survival was 93% in patients with HF alone and 89% in those with both co-morbidities (P=NS). The presence of COPD was associated with increased HF hospitalizations [HR 1.56 (1.4-2.1); P ,0.001] and major adverse cardiovascular events [1.23 (1.03 - 1.75); P , 0.001].
Conclusions: COPD is a common co-morbidity in ambulatory HF patients in the community and is a powerful predictor of worsening HF. It does not however appear to affect short-term mortality in ambulatory HF patients.

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Clinical characteristics and outcomes of patients with acute heart failure and 'mid-range' ejection fraction: data from the IN-HF Outcome Italian Registry

F Orso[1]; A P Aldo Pietro Maggioni[2]; G Fabbri[2]; D Lucci[2]; SA Ciricugno[3]; E Giagnoni[4]; L Moretti[5]; S Valente[6]; L Tavazzi[7]
[1]AOU Careggi, Department of Geriatrics, Section of Geriatric Medicine and Cardiology, Florence, Italy; *[2]ANMCO Research Center, Florence, Italy*; *[3]F. Ferrari Hospital, Cardiology-ICU, Casarano, Italy*; *[4]Niguarda Ca' Granda Hospital, Cardiology Department, Milan, Italy*; *[5]CG Mazzoni Hospital, Cardiology Department, Ascoli Piceno, Italy*; *[6]AOU Careggi, Intensive Cardiology, Florence, Italy*; *[7]Maria Cecilia Hospital, GVM Care & Research - E.S. Health Science Foundation, Cotignola, Italy*

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Background. Recent guidelines of the European Society of Cardiology recognized as a "gray area" the patients with heart failure (HF) and an ejection fraction (EF) between 40 and 49%, defined "mid-range" (HFmrEF), and confirmed the cut-off values for HF with preserved EF (≥50%, HFpEF) and HF with reduced EF (< 40%, HFrEF).

Aims: To compare in patients hospitalised for acute heart failure (AHF) demographic and clinical characteristics as well as outcomes of HFmrEF patients with those of HFpEF or HFrEF.
Methods: Data are from the prospective nationwide Italian Network on Heart Failure (IN-HF) Outcome Registry which collects information on in-hospital and outpatients with HF.
Results: We studied 1669 patients hospitalised for AHF and with EF assessed during hospitalization: patients with HFmrEF were 19.0%, 58.4% had HFrEF and 22.6% HFpEF. HFmrEF had intermediate demographic characteristics: mean age was 73 ± 10 vs 70 ± 12 years in HFrEF and 75 ± 10 in HFpEF ($p < 0.001$), prevalence of females in HFmrEF was 43.9% compared to 30.3% and 60.0% in HFrEF and HFpEF respectively ($p < 0.001$). Ischemic etiology was more frequent in HFrEF (48.9%) and HFmrEF (47.6%) than in HFpEF patients (20.7%), $p < 0.001$, which had a higher rate of hypertensive etiology. Compared to those with HFrEF and HFpEF, patients HFmrEF had a higher prevalence of diabetes (48.0% vs 38.8% and 39.0%, $p = 0.01$), dyslipidaemia (26.2% vs 24.0% and 16.7%, $p = 0.005$) and chronic kidney disease (36.9% vs 33.0% and 25.2%, $p = 0.003$). At entry mean systolic blood pressure was significantly higher ($p < 0.0001$) in HFpEF (147 ± 34mmHg) vs HFmrEF (143 ± 33 mmHg) vs HFrEF (127 ± 30 mmHg) patients. Acute pulmonary edema was more frequent in HFmrEF (47.0%) compared to HFrEF (34.5%) and HFpEF (33.2%), $p < 0.0001$. No differences were found in the use of IV diuretics, while use of inotropes (dopamine, dobutamine, levosimendan) was higher in HFrEF (25.6%) with respect to HFmrEF (10.7%) and HFpEF (8.0%), $p < 0.0001$. In hospital mortality was higher in HFrEF patients (7.3%) compared to HFmrEF (4.1%) and HFpEF (2.9%), $p = 0.003$, but this difference was not significant at 1 year (24.6%, 23.7% and 19.6% respectively, $p = 0.16$).
Conclusions: Patients with HFmrEF represent a significant portion of patients with HF and appear to have intermediate clinical characteristics. In-hospital mortality rate was lower than that observed in HFrEF and higher than that found in HFpEF. However, this difference becomes non-statistically significant at 12 months follow-up.

P247
Evaluation of prognostic indicators of in-hospital evolution and re-hospitalization of patients admitted to the coronary unit with acute heart failure

MA Mariano Agustin Maydana Martn[1]; DE Echazarreta[1]; F Amendola[1]; LM Ortiz[1]
[1]*Hospital San Juan de Dios, Heart Failure and Pulmonary Hypertension Section, La Plata, Argentina*

Background: The term "acute heart failure" refers to the beginning of heart failure signs and symptoms, or a sudden and unexpected worsening of them. Being a life-threatening clinical condition, it demands urgent evaluation and treatment, as it often results in most of the patients having to be admitted to critical care units. In a recent research carried out in Argentina among a group of patients experiencing this situation, it was found out that 25% of them were diabetic, 20% had chronic obstructive pulmonary severe disease, and almost 10% had renal failure. The part of the population that suffers heart failure "de novo", had a tendency towards atrial fibrillation. The appropriate diagnosis of the type of acute heart failure the patient is having and the recommended treatment (e.g. reducing fluid overload and improving load conditions with diuretics, vasodilators, and even with inotropic agents to achieve better tissular perfusion), will determinate the in-hospital evolution, and/or the early re-admission at discharge; that happen in almost 25% of the patients, 30 days after being discharged, which is associated with risk of cardiovascular death. Therefore we must be meticulous and recognize variables related with in-hospital worsening, and at 30 days after discharge evolution, to prevent events in that patients.
Purpose: Identify predictors of in-hospital death from cardiovascular cause, and 30 days after discharge. Identify predictors of readmission.
Methods: We recruited fifty patients admitted to the Coronary Unit of the Hospital with diagnosis of acute heart failure since july 2016 to november 2016. We checked at admission, at discharge and 30 days the following information: filiation dates, portable x ray, cardiovascular risk factors, lab variables including biomarkers, vital signs, clinical presentation, echocardiographic variables, anthropometry, electrocardiographic findings, medications, and semiological findings.
Results: The final analysis included 50 patients with acute descompensated heart failure. The average age was 65 (SD 13), 32 p (64%) was male. 52% of patients had hypertension, and the most frequent clinical presentation was descompensated chronic heart failure. The mortality rate was 10%. Exploratory analysis indicated that hiponatremia was associated with an increased in the risk of cardiovascular mortality with a significant difference (RR=12,8 95% confidence interval 2,9-54,9 $p = 0,00002$). The creatinine clereance < 30ml/min/m2 and the serum concentration of NT-porBNP >800pg/ml was associated with an increased risk of cardiovascular death, but with no significant difference (RR=3,5 CI 0,69-17,7 $p = 0,12$ // RR=0,17 CI 0,02-0,36 $p = 0,12$ respectively).
Conclusions: In our poblation study the mortality rate was very high, and hiponatremia was a valious predictor of in-hospital and 30 day after discharge mortlity. There was not predictors associated with an increased readmission.

P248
Predictors of one year mortality in chronic systolic heart failure newly diagnosed

H M Hadj Mohammed Ali Lahmar[1]; N Laredj[1]; F Boukerche[1]; L Hammou[1]
[1]*Universitary Hospital Center of Oran, department of medecine, Oran, Algeria*

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.

P249
Incidence, risk predictors and prognosis of left ventricular systolic dysfunction after acute coronary syndrome

L Luis Santos[1]; F Montenegro Sa[1]; C Ruivo[1]; S Pernencar[1]; F Soares[1]; F Saraiva[1]; A Antunes[1]; J Correia[1]; J Guardado[1]; N Carvalho[1]; P Gomes[1]; J Morais[1]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*

Introduction: Left ventricular systolic dysfunction (LVSD) is a strong marker of worse prognosis in acute coronary syndrome (ACS) and information is lacking about independent predictors of LVSD after ACS. Thus, it is relevant to search for those determinants in order to better manage ACS patients, prevent heart failure (HF) development and improve prognosis.
Purpose: To identify predictors of LVSD after ACS and to evaluate how it influences prognosis.
Methods: Retrospective analysis of 327 patients with ACS consecutively admitted for coronariography in a non-tertiary hospital between January 2014 and December 2015. All patients underwent a routine invasive strategy and were evaluated by echocardiography, with left ventricular ejection fraction (EF) measure, before hospital discharge. Patients were divided into 2 groups according to their EF: A – EF $\geq$ 40% (n = 287; 87.8%); B – EF < 40% (n = 40; 12.2%) which defines LVSD. A one year follow-up was performed. Logistic regression analysis was used to assess independent predictors of LVSD after ACS.
Results: Overall, 141 cases (43.1%) presented with ACS without ST elevation, the mean age was 65.6 ± 13.2 years, with 97 (29.7%) being female. Patients presenting with ST elevation ACS ($p = 0.033$), heart rate >100 bpm ($p = 0.003$), and signs of heart failure (Killip-Kimball $\geq$ 2) at admission ($p = 0.001$), and those with prior history of HF ($p = 0.003$) or taking oral anticoagulants ($p = 0.038$) were significantly prone to show LVSD. Similarly, these patients showed higher levels of myocardial markers of necrosis ($p = 0.004$) and natriuretic peptides (BNP) over hospitalization ($p = 0.001$). They underwent coronariography by femoral artery access more often ($p = 0.016$), with higher rates of coronary bypass surgery referral ($p = 0.004$). One year mortality was also higher in group B ($p = 0.008$). Logistic regression showed strong association between Killip-Kimball $\geq$ 2 at admission (15.0% vs 37.5%; OR 2.6; IC95% 1.2-5.6, $p = 0.016$), maximum BNP levels $\geq$ 200 pg/mL (59.9% vs 89.2%; OR 3.9; IC95% 1.3-11.8) and LVSD.
Conclusion: Based on this unicentric data survey, LSVD after SCA, which had an incidence of 12.2%, can be predicted by assessment of HF signs at admission

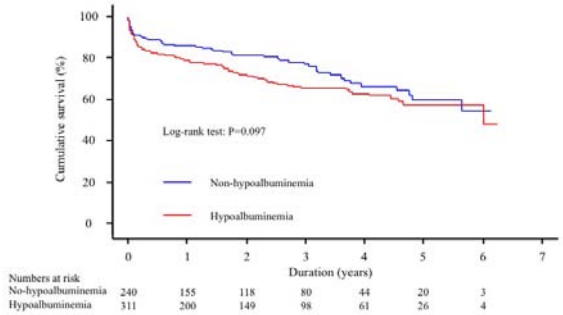
and maximum BNP levels above 200 pg/mL during hospitalization. This feature was associated with higher mortality. Therefore, this patients should be early identified and subjected to a more diligent management.

P250

Relationship between hypoalbuminemia on admission and long-term mortality in hospitalized patients following acute decompensated heart failure.

S Yatsu[1]; T Kasai[2]; H Matsumoto[2]; A Murata[1]; T Kato[1]; S Suda[2]; M Hiki[1]; A Takagi[1]; H Daida[1]
[1]*Juntendo University School of Medicine, Department of Cardiology, Tokyo, Japan*; [2]*Juntendo University Graduate School of Medicine, Cardiovascular Respiratory Sleep Medicine, Tokyo, Japan*

Background: Despite advances in specific treatments, heart failure is still recognized as one of the major public health concerns such as poor clinical outcomes. Among such HF patient population, several studies showed that HF patients with hypoalbuminemia has poorer clinical outcomes compared those without. However, in patients with acute decompensated HF (ADHF), conflicting results were reported regarding the relationship between serum albumin level and clinical outcomes. Indeed, it remains controversial whether hypoalbuminemia on admission is associated with worse prognosis in ADHF patient population. Thus, in the present study, we investigate the relationship between hypoalbuminemia on admission and long-term mortality in hospitalized patients following ADHF.
Purpose: We aimed to investigate the relationship between hypoalbuminemia on admission and long-term mortality in hospitalized patients following ADHF.
Methods: We targeted a cohort of 1684 consecutive patients who admitted to the cardiac intensive-care unit from 2007 to 2011. Among them, patients with ADHF were divided into 2 groups according to the presence or absence of hypoalbuminemia on admission defined as a serum albumin <3.4 g/dl. Relationship between admission albumin level and mortality was analyzed by univariable and multivariable Cox proportional analyses. Multivariable analysis included variables which showed <0.1 in univariable analyses.
Results: Out of the 551 patients, 311 (56%) were classified as hypoalbuminemia on admission. There were 152 deaths (27.5%) during a median follow-up of 1.9 years. Kaplan-Meier survival plots in patients with and without hypoalbuminemia are shown in the Figure. Hypoalbuminemia on admission tended to be associated with increased mortality in univariable Cox proportional hazard regression analysis (hazard ratio [HR], 1.32; P=0.098). In the multivariable Cox proportional hazard regression analysis, there was no relationship between hypoalbuminemia on admission and mortality (HR, 1.01; P=0.959). Even when we treated serum albumin levels as a continuous variable, no association between admission albumin level and mortality was observed.
Conclusion: Either hypoalbuminemia or serum albumin levels on admission was not associated with long-term mortality in patients with ADHF. These data suggest that hypoalbuminemia or serum albumin levels on admission may not be a predictor for worse long-term clinical outcomes in patients with ADHF in our patient population. Considering results of previous studies, hypoalbuminemia or serum albumin level at discharge and changes in albumin levels from admission to discharge may play some roles in relationship between albumin status in HF patients and long-term clinical outcomes.



Kaplan-Meier survival curves

P251

The prognostic value of carbohydrate antigen 125 level in patients with acute decompensated heart failure: correlation with echocardiographic parameters

JJ Sir[1]; SA Lee[1]; SM Choi[1]; SB Joo[1]
[1]*National Medical Center, Seoul, Korea Republic of*

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Background: Recently, serum CA-125 has emerged as a potential biomarker in patients with ADHF.
Purpose: The aim of this study is to investigate the prognostic value of CA-125 and to assess the association between CA-125 and clinical, biochemical and echocardiographic parameters in a population of Korean patients admitted for ADHF.
Methods: We enrolled 110 patients [59 men; median age of 72 year] admitted for ADHF. Serum CA-125, pro-BNP and other biochemical parameters were measured and all patients underwent transthoracic echocardiographic examination on admission. The MACE, defined as stroke, ACS, new-onset AF, re-hospitalization for ADHF and cardiac death were recorded during follow-up.
Results: We found that CA-125 increased accordingly as cardiac function declined from the NYHA Fc II to class III and further from class III to IV [(13.0(9.1-28.7) vs. 47.6(15.1-156.9) vs. 58.0(22.5-192.5) U/ml;$p=0.001$)]. Furthermore, the CA-125 significantly correlated LVEF($r=-0.38$,$p<0.05$), LVEDD($r=0.25$,$p<0.05$), deceleration time($r=0.41$,P=0.001), LAVI($r=-0.26$,$p<0.05$), RVSP($r=0.40$,$p<0.001$), T3($r=-0.39$,$p<0.05$), fT4($r=0.23$,$p<0.05$) and proBNP($r=0.51$,$p<0.05$). MACE developed in 34 patients during 170 ± 90 days of follow-up. The patients with MACE showed significantly elevated serum CA-125 than those without MACE [53.2(16.6-175.1)vs.28.2(11.2-91.0) U/ml,$p<0.05$]. Receiver operating characteristic curve analysis identified CA-125 for increased risk of adverse cardiac events (AUC=0.66;$p=0.01$;cut-off value:64.4 U/ml).
Conclusion: In ADHF patients, CA-125 could reflex the severity of HF and serve as prognostic biomarker for cardiovascular death and HF hospitalization, although the pathophysiology remains to be established.

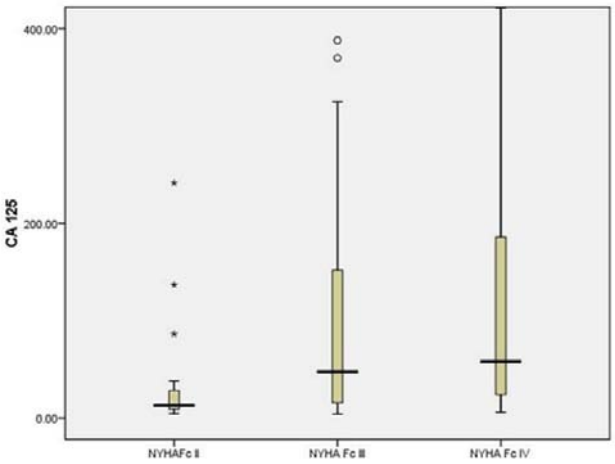


Figure 1.

P252

The prognostic value of echocardiography in early evaluation of patients with non acute coronary syndrome pulmonary edema

V Enache[1]; AC Nechita[1]; I Iordache[1]; SC Stamate[1]
[1]*University of Medicine and Pharmacy Carol Davila, Emergency Hospital St. Pantelimon, Bucharest, Romania*

Introduction: Identifying echocardiographical parameters with a prognostical value for in hospital mortality(IHM) in Acute Pulmonary Edema outside of an acute coronary syndrome (non ACS APE) of diversified ethiologies.
Methods: 92 patients with non ACS APE consecutively hospitalized in Cardiology Clinic St. Pantelimon, between 01.01-31.12.2013, distributed and analyzed according to three etiologies, based on anamnesis, clinical and paraclinical data: ischemic (ischemic coronary disease(ICD) clinically and/or imagistically documented), primary valvular (at least moderate hemodinamic valvular lessions, no ICD) and hypertensive (with preserved LVEF, without significant valvular or documented coronary artery

disease). An echocardiography was performed on admission.The IHM was analized according to echo parameters (LVEF, EDLVd, LAd, TAPSE, PAAT, DTE wave, E/E′ ratio) and ethiology.
Rezults: The following parameters have significantly corellated with IHM in our group: LVd($p = 0.006$), the cut off value 54mm at ROC curve analysis with 90 sensibility, specificity 60, 95%CI 0.58 -0.78, under the curve area 0.69, $p = 0.0003$) TAPSE ($p = 0.0002$, cut off value 17mm, sens 100, spec 48.48, 95%CI 0.66- 0.85, area 0.76, $p < 0.0001$), PAAT($p = 0.0001$, cut off value 102 ms, sens100,spec 65.71, 95%CI 0.68 -0.86, $p < 0.0001$, area 0.78), DTE($p = 0.003$, cut off value 196 ms,sens 81.82, spec 60, 95%CI 0.601 – 0.79, area 0.70, $p = 0.0002$.), E/E' ratio($p = 0.009$). The significance differs according to ethiology. Statistically significant remain: for valvular - LVd($p = 0.003$), for ischemic- TAPSE and PAAT ($p = 0.01$; $p = 0.005$) and for hypertensive - TAPSE ($p = 0.001$), PAAT ($p = 0.009$), DTE($p = 0.008$) and E/E' ($p = 0.01$).
Conclusions: A series of echocardiographical parameters, easily obtained in the first hours of admission have proven a positive predictive and independent value in our analysis for IHM. Their prognosis value changes when assessed according to ethiology, a result that gives echocardiography an important role in evaluating non ACS APE in the emergency room for identifying the ethiology, risk stratification and prognosis purpose.

P253
Echocardiography in acute heart failure: an incremental value for patient prognosis

S Pierre[1]; O Huttin[2]; S Coiro[1]; C Suty-Selton[2]; N Sadoul[2]; F Zannad[1]; N Girerd[1]
[1]*Clinical Investigation Centre Pierre Drouin (CIC-P), Cardiologie, Nancy, France*; [2]*University Hospital of Brabois , Cardiology, Nancy, France*

Introduction: Echocardiography is currently indicated in some, but not at all patients with suspected acute heart failure (AHF), mainly to identify cardiac abnormalities and refine the diagnosis of the hospitalization trigger. We intended to identify the most predictive echocardiography variables of outcome at AHF admission.
Methods: We studied a prospective cohort study of 182 patients (72 ± 14 years, 55.5% men, 31% ischemic HF), admitted for AHF between 2010 and 2013, from the ICALOR database. Each patient had benefit of a complete echocardiography at bedside within first days after admission. Clinical and biological data, with BNP value, at admission were also collected. The end-point was readmission for HF and all-cause mortality after discharge.
Results: During a mean follow-up of 9 months after discharge: 41 patients died (22.5%) and 71 (39%) were readmitted for AHF. In univariable analysis, a RV dysfunction with a TAPSE < 15mm (HR=1.69,(1.00-2.87), $p = 0.048$) and elevated PAPs (HR=3.29,(1.58-6.84),$p = 0.001$) are associated with poor outcome. After adjusting for potential confounders, high BNP value (HR=1.86,(1.17-2.97), $p = 0.009$) and PASP (HR=1.04,(1.01-1.08),$p = 0.012$) are associated with mortality whereas mitral regurgitation (HR=3.33,(1.37-8.06),$p = 0.007$) and A mitral wave velocity (HR=0.22,(0.06-0.79),$p = 0.02$) were independent predictors of readmissions for AHF. Survival was not significantly different across subgroups of ejection fraction and left filling pressures.
Conclusion: Limited sets of echo variable (PASP, mitral regurgitation and mitral A wave amplitude) quantified within first days of AHF admission were associated with mid-term outcome. These results suggest that echocardiography, mainly through congestion quantification, could help risk stratification in patients with AHF.

P254
Is arrival on the weekend associated with increased short term mortality of patients with acute dyspnea?

D Dovydas Verikas[1]; D Kuscenko[2]; D Aniulyte[1]; A Kukulskis[1]; S Damalakas[1]; K Stasaitis[1]; J Motiejunaite[1]; V Juknevicius[2]; A Mebazaa[3]; A Kavoliuniene[4]; J Celutkiene[5]
[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [2]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [3]*Hospital Lariboisiere, Paris, France*; [4]*Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; [5]*Vilnius University, Clinic of Cardiac and Vascular diseases, Vilnius, Lithuania*

On behalf of: GREAT network
Funding Acknowledgements: The work was supported by the Research Council of Lithuania, grant Nr. MIP-049/2015 and approved by Lithuanian Bioethics Committee, No. L-15-01.

Introduction: Arrival to the emergency department during the weekends might be associated with poorer care and subsequent longer hospitalisation and worse outcomes. So far few data have been published on the frequency and impact of the admission on the weekend.
Purpose: To evaluate the association of referral to the emergency department on the weekend with the short-term mortality and length of hospital stay (LOS) in patients presenting with acute dyspnea.
Methods: The prospective observational cohort study conducted in two partner institutions enrolled consecutive patients admitted to the emergency department with acute dyspnea due to acute decompensated heart failure, exacerbation of chronic obstructive pulmonary disease, pneumonia, pulmonary embolism and other causes. Data of 678 patients were included in the analysis. The death rate due to all causes was assessed after 1-month and 3-month follow-up period using Cox Regression analysis.
Results: Mean age in analysed cohort was 69.3 ± 19.9 years, 393 pts (58.0%) were male. The study revealed that 122 (18%) patients sought medical care during the weekends. During 3-month follow-up, in total 73 (10.8%) patients died, 56 of them died during the first month (8.3%). The 3-month mortality of those who came on the weekends did not differ significantly from those who came on the weekdays: 8.2% vs 11.3%, respectively, $p = 0.319$. Furthermore, 360 patients (53.1%) were hospitalised with mean LOS found to be 13.02 ± 15.06 days and 3-month death rate 7.2%.
CONCLUSION: High 1- and 3-month all-cause mortality was revealed in the prospective acute dyspnea cohort with the substantial frequency of the referral on the weekends. No impact of arrival at the weekends on the short-term mortality was found in this patient population.

P255
Survival after cardiopulmonary resuscitation by first detected electrical rhythm in patients hospitalized for acute heart failure

CI Radulescu[1]; L Antohi[1]; M Chivulescu[1]; I Cosei[1]; A Covaliov[1]; R Radu[1]; A Ambrosy[2]; C Macarie[1]; M Gheorghiade[3]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania*; [2]*Duke University Medical Center, Cardiology, Durham, United States of America*; [3]*Northwestern University, Cardiology, Chicago, United States of America*

Purpose: In patients hospitalized with acute heart failure (AHF), prognosis after in-hospital cardiac arrest is determined by prompt application of cardiopulmonary resuscitation (CPR) and by severity of cardiac structural abnormality. CPR algorhythms depend on initial electrical rhythm before CPR. Limited data exists regarding the outcome of CPR by first detected electrical rhythm (FDER), in patients hospitalized for AHF.
Methods: The Romanian AHFS (RO-AHFS) registry enrolled 3224 consecutive patients hospitalized for AHFS over a 12-month period. CPR has been considered as event on course of hospitalization and FDER before CPR was recorded in all patients. Successful resuscitation was defined as restoration of spontaneous circulation.
Results: CPR was attempted in 274 patients (8.5% of cohort) during hospitalization. FDER before CPR was recorded as VF/VT, Asystole, and PEA, respectively, for 18.7%, 28.1%, and 53.2% of attempts. Baseline characteristics at admission for CPR patients by FDER are depicted in Table 1. The proportion of patients with restoration of spontaneous circulation was 37% for VF/VT, 14.2% for asystole, and 24.3% for PEA. Only 14% of patients requiring CPR survived to discharge. The rate of survival to discharge for VF/VT, Asystole, and PEA, were, respectively, 29.6%, 7.7%, and 11.6%. Conclusions: Initial pulseless electrical rhythm reflects electromechanical and biohumoral severity of HF and may influence the success of CPR and short-term survival.

Table 1

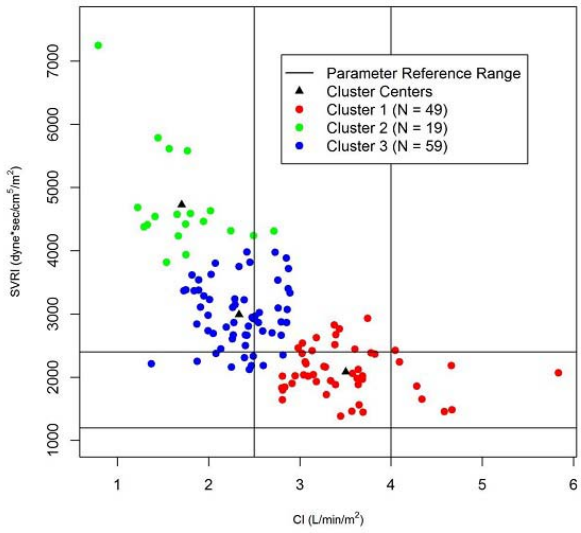
	VF/VT (n = 51)	Asystole (n = 77)	PEA (n = 146)	p
Age(years)	68.9±8	69.1±8	69.4±9	0.2
Male(%)	61	63	61	0.7
Ischemic etiology(%)	71	68	69	0.08
Na(mmol/l)	133.8±6	131±7	133.1±8	0.09
K(mmol/l)	3.81±1.1	4.4±1	3.92±0.7	0.02
BUN(mg/dl)	64±18	81±14	77±10	0.006
Creatinine(mg/dl)	1.56±0.4	1.89±0.5	1.78±0.8	0.05
LV EF(%)	33.1±7	29.2±4	30.8±5	0.03
QRS>120msec(%)	37	41	39	0.02
HR(beats/min)	105±9	91±19	99±17	0.02
SBP(mmHg)	108±22	99±17	103±19	0.001

P256
What are the differences between HFrEF, HFmrEF and HFpEF patients admitted for acute heart failure?

E Goncalvesova[1]; P Lesny[1]; M Luknar[1]; M Dankova[1]; V Simovicova[1]; M Kovacova[1]
[1]*The National Institute of Cardiovascular Diseases, Department of Heart Failure and Heart Transplant, Bratislava, Slovak Republic*

On behalf of: on behalf of SLOVASeZ investigators

Backgroud: HF Guidelines 2016 proposed new classification of heart failure based on ejection fraction – HFrEF, HFmrEF and HFpEF.
Aim of the study was to evaluate and compare the three groups of patients according LVEF admitted due to acute heart failure.**Methods:** Data from nationwide multicenter AHF surveys (SLOVASeZ I and II) with 1452 consecutive patients enrolled in 14 hospitals throughout Slovakia were analysed. Ejection fraction was measured during indexed hospitalization in 71,4% of patients and these patients were included to the further evaluation. Mean age of the patients was 72,2 ± 11,7 years, 52% of them were men. Majority of patients were admitted with decompensated heart failure (71,3%), AHF de novo was diagnosed in 28,6% of patients. We identified 41,6% patients with HFrEF, 22,2% patients with HFmrEF and 36,2% patients with HFpEF. Nineteen characteristics of these patients were selected to the statistical analysis. Patients with HFrEF were younger (mean 67,3 v.s. 73,9 years, p = 0,02), with higher proportion of men (69,7% v.s. 36,6%, p = 0,0001). Women were represented more often in HFpEF. Patients with HFrEF were admitted mostly for decompensated chronic heart failure (74,1%, p = 0,02). Coronary heart disease was considered as primary etiology in all group of patients, but the most present in HFmEF (72,3%, p = 0,001), followed by HFrEF (58,6%) and HFpEF (49,7%). Systolic blood pressure at admission was lower in HFrEF (p = 0,01) compared to other groups, with no difference in heart rate between groups. We also did not find difference in the sodium and creatinine levels. Hypertension was reffered as the most frequent comorbidity in HFmrEF and HFpEF compared to HFrEF (p = 0,001). Atrial fibrillation (p = 0,01) and anemia (p = 0,05) were more often in HFpEF. There was no difference in the incidence of diabetes mellitus and chronic kidney disease between groups. There was strong trend to higher in-hospital letalityin HFrEF, but did not reach statistical significance. **Conclusions:** The most significant differences were between HFrEF and HFpEF. Patients with HFmrEF are very close to those with HFpEF but have more CHD as dominant HF etiology.



AHF clusters using the CI and SVRI

P257

Presenting emergency department hemodynamic phenotypes of acute heart failure patients

RM Nowak[1]; S Disomma[2]; P Nanayakkara[3]; B Reed[4]; M Moyer[1]; S Millis[4]; P Levy[5]
[1]Henry Ford Health System, Emergency Medicine, Detroit, United States of America; *[2]Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy*; *[3]VU University Medical Center, Internal Medicine, Amsterdam, Netherlands*; *[4]Wayne State University, Biostatistics, Detroit, United States of America*; *[5]Wayne State University, Emergency Medicine and Physiology and Cardiovasculaer Reserach Institute, Detroit, United States of America*

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Purpose: There is little known about the baseline hemodynamic (HD) profiles (beyond pulse/blood pressure) of patients presenting to the Emergency department (ED) with acute heart failure (AHF). Assessing these baseline parameters could help differentiate underlying HD phenotypes which could be used to develop specific phenotypic specific approaches to patient care.
Methods: Patients with suspected AHF were enrolled in the PREMIUM (Prognostic Hemodynamic Profiling in the Acutely Ill Emergency Department Patient) multinational registry and continuous HD monitoring was initiated on ED presentation using noninvasive finger cuff technology (Nexfin, BMEYE, Edwards LifeSciences, Irvine, California). Individuals with clinically suspected and later confirmed AHF were included in this analysis and initial 15 minute averages for available HD parameters were calculated. K-means clustering was performed to identify out of 23 HD variables a set that provided the greatest level of inter-cluster discrimination and intra-cluster cohesions.
Results: A total of 127 patients had confirmed AHF. The final model, using mean normalized patient baseline HD values was able to differentiate these individuals into 3 distinct phenotypes. Cluster 1: normal cardiac index (CI) and systemic vascular resistance index (SVRI); cluster 2: very low CI and markedly increased SVRI: and cluster 3: low CI and an elevated SVRI. These clusters were not differentiated using clinically available ED information.
Conclusions: Three distinct clusters were defined using novel noninvasive presenting HD monitoring technology in this cohort of ED AHF patients. Further studies are needed to determine whether phenotypic specific therapies based on these clusters can improve outcomes.

P258

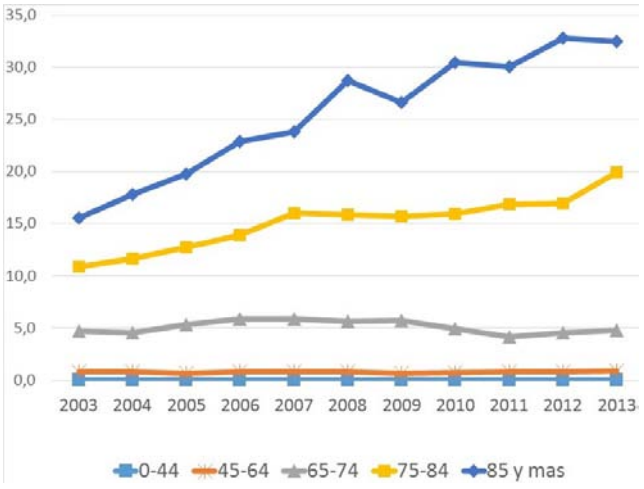
Trends of heart failure hospitalization during the period of 2003-2013.

M L Maria Lucia Fernandez Gasso[1]; J J Martinez Diaz[1]; D A Pascual Figal[2]; L Hernando Arizatela[3]; J A Palomar Rodriguez[3]; R M Soto Ruiz[1]; IA Garcia-Escribano Garcia[4]; R Rubio Paton[1]; C Fernandez Pacual[5]; J Abellan Huertas[6]; G Clavel Ruiperez[1]; P Ramos Ruiz[1]; J C Bonaque Gonzalez[1]; S Wasniewski[1]; M Merelo Nicolas[1]
[1]Hospital General Universitario de Santa Lucia, Cardiology, Cartagena, Spain; *[2]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain*; *[3]Consejería de Sanidad de la Región de Murcia, Servicio de Planificación Sanitaria, Murcia, Spain*; *[4]Hospital Comarcal del Noroeste, Cartagena, Spain*; *[5]Hospital Central De La Defensa Gomez Ulla, Madrid, Spain*; *[6]Hospital General de Almasa, Cardiology, Albacete, Spain*

Background: Heart failure represents a burden to the health-care system and it is one of the most important public health problem. Population-based studies in other countries report a reduction in recent years, but in Spain we lack data about the profile and temporal evolution in a well-defined population framework.
Purpose: To evaluate temporal trends in heart failure hospitalization in the Region of Murcia in the period comprised between 2003 and 2013.
Methods: Study based on the minimum basic hospital discharge data from all hospitals in the Region of Murcia between 2003-2013. We obtained the healthcare episodes by individual health card. For each year, were studied: crude and standardized attendance by age/ sex, ratio of feminization, length of stay, mortality, demographic and clinical variables. Results: 27 158 episodes were obtained in the period. The hospital discharges increased by 76.7%, from 1.28 ° to 2.26 ° (crude) and 1.06 ° to 1.77 ° (standardized). People ≥75 years doubled their attendance, up 19.9 ° in 75-84 years and 32.5 ° in ≥85 years, while in <74 years did not change. Arrhythmias, ischemic heart disease and valvular heart disease were the most prevalent causative disorders.The ratio of feminization was 1.34, but after standardization was matched and did not change. Length of stay was 9.4 days and in-hospital mortality was 9.2%, both of them were unchanged. Conclusions: Between 2003-2013 there is an increase in hospital discharges for HF, which affects the population >74 years, independent of population increasing. They are necessary strategies targeting this population.

Healthcare episodes Heart Failure.

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Episodes	1.754	1.948	2.253	2.472	2.614	2.592	2.723	2.819	3.019	3.323	27.158
Aged	75,0	75,6	75,8	76,3	77,0	77,2	77,8	77,9	78,0	78,4	76,9
Female	54,9	57,5	56,9	58,0	56,7	56,4	59,3	57,3	57,9	57,2	57,3
Days	9,6	9,6	9,3	10,2	9,7	9,5	9,5	9,5	9,0	8,7	9,4
Mortality	10,2	9,3	7,5	8,5	8,5	10,1	8,4	9,8	9,9	9,3	9,2
Crude-Attendance	1,33	1,44	1,63	1,75	1,82	1,78	1,86	1,91	2,05	2,26	1,75
Standarized-Attendance	1,15	1,24	1,44	1,50	1,55	1,46	1,48	1,48	1,61	1,77	1,31



Hospital attendance rates (aged)

P260

Acute heart failure in patients with stress cardiomiopathy

A Shilova[1]; M Gilyarov[1]; A Nesterov[1]; D Shchekochikhin[1]; A Svet[1]
[1]Moscow City Hospital named after N. Pirogov, coronary care unit, Moscow, Russian Federation

Background: Stress cardiomyopathy is known to be a disorder with reversible left ventricular dysfunction, regressing within few weeks. Although, prognosis of Takotsubo syndrome was initially thought to be favorable compared to myocardial infarction, recent studies show that in-hospital and long-term mortality are both consistent to STEMI. The incidence of acute heart failure in stress cardiomyopathy patients varies a lot in different regions.
Methods: We have analyzed respectively 24 cases of takotsubo (stress) cardiomyopathy according to Mayo clinical criteria, hospitalized in a City Hospital in year 2016. 20 (83,6%) of patients were hospitalized as suspected STEMI, representing 2,64% of all cases of MI in the hospital during year 2016.
Results: Of 24 patients with stress cardiomyopathy, 22 (91,7%) were women (mean age 68,54 ± 4,34). Mean EF on presentation was 41,6%. Physical triggers were more common, than emotional (50% vs 35%, $p < 0,05$), in 15% no evident triggers were found. In 36% of patients with Takotsubo syndrome psychiatric abnormalities (severe dementia, delirium or schizophrenia) were found, 3 (12,5%) patients were alcohol abused and represented with delirium tremens. In 16 (66,7%) of cases angiography showed intact coronary arteries, when in 8 (33,3%) cases multivessel atherosclerosis was found with no signs of obstructive coronary lesions. In 12 (50%) patients, takotsubo cardyomopathy caused acute heart failure (AHF). 3 (12,5%) patients developed cardiogenic shock and 5 (20,8%) patients suffered from lung edema. All alcohol abused patients suffered from severe AHF. In 5 (20,8%) of cases dobutamine administration was required, with mean duration of dobutamine infusion 7,2 days. Vasopressors (norepineprine) had to be administrated in 3 (12,5%) cases. LVOT obstruction developed in 1 case during dobutamine treatment. Mortality rate was no significantly higher, than from STEMI in our department, 2 (9,1%) vs 31 (8,4%).
Conclusions: The incidence of AHF, requiring intensive therapy is significantly high. Treatment with dobutamine seems to be safe. It seems like alcohol abused patients have worse prognosis when suffering from stress cardiomiopathy. Treatment approaches are to be further investigated.

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ExtraHF survey: the european survey on implementation of exercise training in heart failure patients: regional differences in training modalities

A Verde[1]; SM Binno[1]; U Corra'[2]; P Seferovic[3]; GQ Villani[1]; G Filippatos[4]; PP Ponikowski[5]; MF Piepoli[1]
[1]Guglielmo da Saliceto Hospital, Heart Failure Unit, Department of Cardiology, Piacenza, Italy; [2]Fondazione Maugeri, Department of Cardiology, IRCCS Scientific Institute of Veruno, Veruno, Italy; [3]University Belgrade Medical School, Department of Cardiology, Clinical Center of Serbia, Belgrade, Serbia; [4]Attikon University Hospital, Heart Failure Unit at the Department of Cardiology, Athens, Greece; [5]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland

On behalf of: Committee on Exercise Physiology & Training of the Heart Failure Association of the ESC

Background: In heart failure (HF), exercise training programmes [ETP] are well-recognised intervention to improve symptoms, but still poorly implemented. The Heart Failure Association promoted a survey to investigate whether and how cardiac centres in Europe are using ETP in their HF patients. Aim of this study is to investigate the presence of geographical difference in ETP availabilities, and modalities of 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-EU.
Results: 173 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).
Overall aerobic continuous exercise was the most common modality of training programme in all regions, (58-62%) with the exception of the northern region where this modality was implemented in only 42% of the cases, and in contrast interval low-intensity training was mostly used (85% of the cases). High intensity exercise training was implemented in around 25% of the cases, but in eastern and extra European countries this modality was employed in less than 10% of the cases. Bicycle training was used in most cases (>70%) except in the extra European countries where treadmill modality was mostly employed (60%). Other mode of aerobic endurance training with other cardio fitness facilities (e.g. elliptical trainer) was implemented in around 10% with the exception of the northern region where this modality was implemented in 30% of the cases
Conclusions: Differences in training modality implementation are evident among different European regions. Further studies should investigate ETP outcomes based on different modality of training implementation in order to identify the most effective program

P262

Severe acute heart failure complicating ST-elevation myocardial infarction. Results from the BIHOTZEZ-Gipuzkoa registry.

C Goena Vives[1]; M Telleria Arrieta[2]; L Quintas Ovejero[1]; R Garcia Martin[1]; I Lluis Serret[1]; P Morrondo Valdeolmillos[3]; JJ Artaetxeberria Zuazo[3]; K Ibarguren Olalde[4]
[1]Mendaro´s Hospital, Cardiology, Mendaro, Spain; [2]Donostia Universitary Hospital, Hemodynamic Department, Donostia, Spain; [3]Donostia University Hospital, Intensive Care Unit, Donostia, Spain; [4]Osakidetza, Emergency department, Donostia, Spain

On behalf of: BIHOTZEZ-Gipuzkoa

Introduction: Acute heart failure (AHF) complicating ST-segment elevation myocardial infarction (STEMI) is recognized as an ominous complication and studies assess the prognosis of AHF according to its timing. Purpose:We aimed to evaluate incidence and impact of severe AHF in a multicenter STEMI network patients (BIHOTZEZ) treated by primary percutaneous coronary intervention (pPCI) and also evaluate if the timing meets the recommended delays.
Methods: 254 patients included during 2015 in a prospective multicenter registry were analyzed.Patients with severe AHF (Killip III-IV) were compared to those with Killip I-II.In-hospital and 30 days mortality were the primary endpoints.Results:age, gender and anterior wall infarction did not differ between the two groups.12 patients (4.8%) presented with severe AHF.It was associated with increased in-hospital mortality rate (66.67%vs.4.6%,$p < 0.005$) and 30 days mortality rate (66.67%vs.5.9%,$p < 0.005$)(see table 1).Severe AHF patients displayed the highest mortality rate and it was the strongest predictor of in-hospital and 30-days

mortality.The Killip III-IV group had further delays due to the time required to stabilize before the transfer to hospital.This difference was no statistically significant and it is not related to mortality in our series.Conclusion:Severe AHF remains a dreadful complication of STEMI in our population and delays to achieve hemodynamic stability do not increase short-term mortality.

	Killip III-IV	Killip I-II
n	12	242
Age	65.58 (11.56)	64.82 (13.99)
Male	58 %	76 %
LVEF	43.27 (10.59)	50.46 (13.42)
Anterior AMI	41.67 %	41.91 %
Radial acces	50 %	99.6 %
In-Hospital mortality (p < 0.005)	66.67 %	4.6 %
30 days mortality (p < 0.005)	66.67 %	5.9 %
Door-to-symptoms median	14.5 (7.7-55.5)	100 (50-224)
Door-to-device < 90 min	10 %	58.38 %
Door-to-device < 120 min	60 %	79.19 %
Door-to-ECG median	3.5 (0-11)	5 (1-9.5)
Door-to-device median	105 (96-168)	81 (64-111)
Symptoms-device median	125 (100-210,5)	190 (122-358)

P263

Clinical profile and inhospital outcomes according ejection fraction in patients admitted with acute decompensated heart failure

M L Talavera[1]; A Acosta[1]; A Benavidez[1]; J Otero[1]; M Diez[1]
[1]*Cardiovascular Institute of Buenos Aires (ICBA), Heart Failure , Buenos Aires, Argentina*

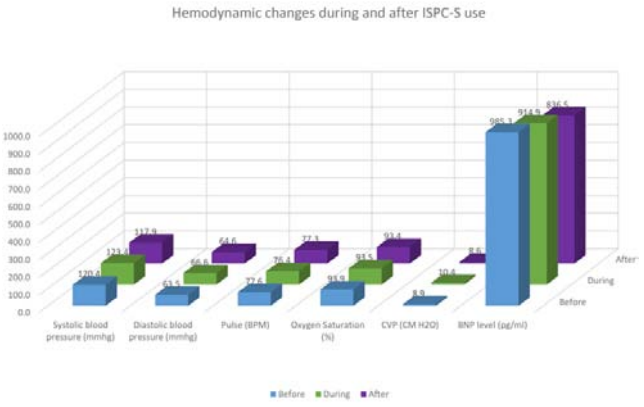
Background: The current evidence suggests that patients (pts) with heart failure (HF) and preserved systolic function (PSF) differ from those with left ventricular systolic dysfunction (LVSD) in their clinical characteristics and outcomes, but there is still a controversy about phenotypes and prognosis in both populations.
Aim: To evaluate baseline characteristics, treatments and in-hospital outcomes of pts admitted for acute decompensated heart failure (ADHF) according to left ventricle ejection fraction.
Methods: 223 consecutive pts admitted with ADHF between October-2015 and October-2016 were selected; Patients' characteristic and blood exam results were analyzed; LVSD and PSF were defined as left ventricle ejection fraction ≤45% or > 45%, respectively. Complex therapy was defined as the requirement of any of the following: inotropics, intra-aortic balloon pump, mechanical ventilation, coronary revascularization or aortic percutaneous valvuloplasty. Chi2 and Fisher tests were used to evaluate categorical variables. $p < 0.05$ was considered statistically significant.
Results: Of the total cohort, 120 (53,8%) pts had LVSD and 103 (46,2%) had PSF; pts with LVSD were more likely to be younger (74 +/-12 vs 77 +/-10, p = 0.0021), male (74% vs 53%, p = 0,001) and had a significantly higher incidence of coronary disease (47% vs 17%, p < 0,0001) than those with PSF; valvular disease was more prevalent in PSF (55% vs 22, p < 0,0001). At admission, the absence of a precipitating factor was more frequent in LVSD (44% vs 28%, p = 0,01) while uncontrolled hypertension was more prevalent in pts with SPF (22% vs 13%, p = 0,05), LVSD pts had more prevalence of low cardiac output (17% vs 2%, p = 0,0001), with higher creatinine values (1.34 IQR25-75: 1,18-1,85 vs 129 IQR25-75 1,01-1,52 mg/dl, p = 0,007) than those with PSF. During hospitalization, LVSD pts had more renal function impairment than PSF (1,7 IQR 1.34-22 vs 1,45 IQR 1.21-1,82, p = 0,003) and required more complex therapies (18% vs 2%, p = 0,01). There were no significant differences in length of stay (7 IQR25-75 4-12 vs 6 IRQ 25-75 4.12 days, p = NS) but in-hospital death or heart transplantation were more frequent in LVSD pts (14% vs 3%, p = 0,003). At discharge, LVSD pts were on of beta-bloquers: 63%, ACEi: 84% and aldosterone receptor antagonists: 43%; low cadiac output was associated to non-use of beta-bloquers (p < 0,0001) and renal impairment with non-use of aldosterone receptor antagonists (p = 0,02).
Conclusions: In this population, LVSD was associated with a more severe clinical profile at admission, a higher use of complex therapies and worse in-hospital outcomes. Nevertheless, there were no differences in length of stay, this may be related with no measurable factors in pts with SPF like fragility or complications related to invasive procedures. At discharge, LVSD pts, despite being a greater risk population, received lower rates of pharmacological treatment according to clinical practice guidelines.

P264

The safety of intermittent sequential pneumatic compression sleeves in patients with severely reduced ejection fraction.

G Gassan Moady[1]; M Khader[1]; A Shturman[1]; S Atar[1]
[1]*Galilee Medical Center, Cardiology, Nahariya, Israel*

Background: Intermittent sequential pneumatic compression sleeves (ISPC-S) are often used in bedridden patients and during laparoscopic surgery. This technique is associated with several hemodynamic changes, and its safety in patients with severely reduced left ventricular function (LVF), and its effect on Brain Natriuretic Peptide (BNP) levels have not been clearly defined yet.
Purpose: To investigate the safety of ISPC-S in patients with severely reduced LVF by measuring hemodynamic parameters and BNP levels before, during and after the use of the pneumatic sleeves.
Methods: Fourteen patients with severely reduced LVF (< 40%) who were admitted to intensive cardiac care unit in our hospital with exacerbation of heart failure symptoms were Studied. All the participants were in NYHA functional classes II-III. The ISPC-S was operated in two cycles every one minute for 1 hour by compressing sleeves which contains 10 air cells in each side. Left ventricular ejection function (LVEF), hemodynamic parameters and BNP levels were studied in each patient before, during and after the ISPC-S operation. We used the Wilcoxon signed –rank test in the statistical analysis.
Results: 11 (78.6%) of the patients were male, the median age was 65.1 ± 8.4 years, of them 11 were of ischemic etiology. The average LVEF on baseline was 31.2% with no significant change shortly after the use of ISPC-S (31.2% ± 10 vs 33.1% ± 9 p = 0.673). After using the ISPC-S system there was no significant difference in systolic blood pressure (122 ± 23 vs 118 ± 18, p = 0.158), diastolic pressure (64 ± 10 vs 66 ± 9, p = 0.567) nor in the pulse measurements (78 ± 11 vs 76 ± 11, p = 0.594). Central venous pressure measurements were 8.9 ± 3.8, 10.4, 8.7 ± 4.7 before, during and after the ISPC-S use (P=0.649). There was also no change in oxygen saturation before and after (93.9% ± 7.2 vs 93.4% ± 7.1, p = 0.683). The BNP levels were 985.3, 836.6, 762 pg/ml before, during and after the ISPC-S use, respectively (p = 0.074). There was no arrhythmic or ischemic events during or after the use of ISPC-S in any participant.
Conclusion: The use of ISPC-S in patients with severely reduced LVEF seems to be safe with no detrimental effects on hemodynamic parameters or BNP levels.



results

P265

Diastolic dysfunction is also related with the formation of left ventricular apical thrombus in patients with acute anterior ST elevation myocardial infarction

UL Choi[1]; JH Jae-Hyeong Park[1]; BJ Sun[1]; JK Oh[1]; SW Seong[1]; JH Lee[1]; SW Choi[1]; JO Jeong[1]; IW Seong[1]
[1]*Chungnam National University Hospital, Daejeon, Korea Republic of*

Background: Left ventricular (LV) apical thrombus is a clinically important complication which can cause systemic embolization in patients with acute

anterior myocardial infarction (AMI). Systolic dysfunction has been a risk factor for developing LV apical thrombus in AMI patients. However, the importance of diastolic dysfunction in the development of LV apical thrombus has been poorly proved in these patients.
Purpose: We performed to evaluate whether diastolic dysfunction can influence the development of LV apical thrombus.
Methods: We retrospectively analyzed all consecutive anterior AMI patients with available echocardiographic images within 1 month from January 2005 to April 2016. After gathering clinical characteristics from their medical records, systolic and diastolic functions were analyzed from the digitally stored images.
Results: We included total 1140 patients (813 males, 64 ± 12 years old) with anterior AMI, and 540 were diagnosed as STEMI. The incidence of LV apical thrombus was 3.2% (37/1140), and they had larger LV diastolic dimension (40 ± 9 vs 34 ± 8mm, $p < 0.01$), larger LV diastolic volume (71 ± 35 vs 105 ± 38mm, $p < 0.01$), larger LV systolic volume (105 ± 38 vs 89 ± 32mm, $p < 0.01$), and lower LVEF (34 ± 10 vs 48 ± 11mm, $p < 0.01$). Also, LV apical thrombus group showed higher mitral E velocity over mitral annular E′ velocity ratio, an indicator of LV end-diastolic pressure, (17.0 ± 9.6 vs 12.3 ± 5.6, $p < 0.01$).
After propensity score matching with age, gender and LVEF, we selected total 56 patients without LV apical thrombus as a reference group. In the LV apical thrombus group, pseudonormal (35.1 vs 19.6%,) and restrictive filling pattern (27.0 vs 5.4%) were more prevalent ($p < 0.01$). The presence of more than grade 2 diastolic dysfunction was significantly associated with the presence of LV apical thrombus (OR=2.53, 95% CI=1.28˜5.01, $p < 0.01$). Conclusions: Along with LV systolic function, LV diastolic function was also related with the presence of LV apical thrombus in patients with anterior AMI.

P266
Infective endocarditis complicated by heart failure: Prognosis and predictive factors of mortality

M Hassine[1]; M Boussada[1]; M Tahar[1]; M Mahjoub[1]; M Ben Massoud[1]; Z Dridi[1]; F Betbout[1]; H Gamra[1]
[1]*Cardiology A Department – Fattouma Bourguiba University Hospital, monastir, Tunisia*

Background: Although the progress of antibiotic prophylactic field, infective endocarditis remains a frequent pathology. Heart failure represents his main complication.
The aim of the study: was to determine the various characteristics of patients suffering from heart failure complicated by infective endocarditis and to define its impact on the mortality.
Patients and methods: From the infective endocarditis register of our service comparing 241 patients and responding to criteria of the University which collected retrospectively, we included patients with heart failure on admission, namely dyspnea greater or equal to NYHA stage II. A total of 85 patients were enrolled in the heart failure (35.2% of register).
Results: Heart failure complicating infective endocarditis of native valve had occurred in 66 cases (77.6%). The microbiological investigation was positive in 43.5 % of cases with a predominance of staphylococcus. The using of surgery was necessary in 65.8 % of cases. Hemodynamic instability was the main indication.
The total mortality in our registry was 19.5%, but higher in the group with heart failure (28.2% vs 14.7%; $p = 0.006$). In the multivariate analysis we found, as predictive factors for mortality of infective endocarditis complicated by heart failure group, the significant influence of anemia (OR= 5.2 ; IC 95% [1.6-24]; $p = 0.02$), infection by staphylococcus aureus (OR= 5.7 ; IC 95% [0.8-29.8]; $p = 0.03$) and surgery delay (OR=3.1 ; IC 95% [1.1- 14.7]; $p = 0.01$).
Conclusion: Heart failure is the most frequent complication of infectious endocarditis, and its first cause of death.

CHRONIC HEART FAILURE

P267
Semiotics of coronary vessels in patients with chronic heart failure of ischemic etiology with type 2 diabetes

AM Karimov[1]; HG Fozilov[1]; TA Abdullaev[1]; I A Igor Tsoy[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

Introduction (goals / objectives): Objective: To study the semiotics of angiographic coronary arteries in coronary heart disease with low ejection fraction in patients with type 2 diabetes.
Material and Methods: The study involved 60 patients with a diagnosis of chronic heart failure of ischemic etiology (CHF) between the ages of 40 to 80 years, including 39 men and 21 women, mean LVEF by Simpson 37,2 ± 4,6%. The patients were divided into 2 groups: 1 c. - 30 people who have had diabetes 2tipa place collateral. And 2 c. - 30 patients without diabetes 2tipa. The average duration of diabetes type 2 in one group was 6,2 ± 2,4 (5 to 8) years, while the duration HSN- 2,8 ± 2,3 (1 to 3 years). In the 2nd c., Ie, in individuals without type 2 diabetes, the average duration amounted to CHF 2,1 ± 1,8 (1.5 to 3) years.
Results: According to the CAG it found that the most common atherosclerotic lesions were located in the basin of the left anterior descending branch (LAD), amounting to - 23 (38%) cases. The second highest frequency of occurrence proved pool right coronary artery (RCA) - 12 (20%) patients. Frequency of atherosclerotic lesions of the circumflex artery (OA) and the obtuse marginal branch of OA was 11 (18.3%) and 5 (8.3%) cases, respectively. Atherosclerotic lesion in the posterior interventricular branch of the basin (ZMZHV) was observed in 3 (5%) patients. In the intermediate zone of the artery (PA), posterior-lateral branch (ZBV) and the left coronary artery (LCA) - 2 (3.33%) cases.
By the number of affected arteries revealed the following: 1 vessel disease was observed in 17 (28.3%) patients; of these patients 1g. 7 (11.6%)., Patients 2g. 10 (16.6%). ; Sosudistoe- 2s in 21 (35%) patients; 1g. 6 (10%) patients. 2 c. 15 (25%). ; and 3h- and more vascular porazhenie- in 22 (36.6%) patients; 1 of them c. 17 (28.3%) patients, 2 c. 5 (8.3%) patients.
Conclusion: CHD patients with reduced LVEF with concomitant type 2 diabetes characterized by 2s and multivessel disease compared with patients with the absence of type 2 diabetes.

P268
The membrane-modifying effect of hyperbaric oxygen therapy in chronic heart failure

V Victor Ruzov[1]; EN Altynbaeva[1]; MN Goryachaya[1]; BB Kostishko[1]; AM Vorobev[1]; M Mulenga[1]
[1]*Ulyanovsk state University, medicine, Ulyanovsk, Russian Federation*

Chronic heart failure (CHF) which complicates the course of cardiovascular diseases is accompanied by severe hypoxia, organ ischemia and platelet hemostatic disorders. The use of hyperbaric oxygen therapy for their correction is pathogenetically justified.
Purpose of the study: To study the effect of hyperbaric oxygenation on platelet membrane with different functional activity in patients with chronic heart failure of ischemic etiology.
Materials and methods: The study involved 24 patients with CHF I-III functional class (FC) of ischemic etiology.
The average age of the patients was 52,91 ± 11,54 years, mostly men (70%).
All patients for 5 days were on standard CHF medical therapy and were administered hyperbaric oxygen therapy (pressure chamber 303MK, Russia) with a duration of 30 min per session at 1.2 ATA.
Platelet aggregation was evaluated with an aggregometer “Biola 230LT” (Russia), evaluating the elastic properties of platelet membranes was done using a scanning probe of an atomic force microscope - Solver P47-PRO (Nt-MDT, Russia) in contact mode. To determine the platelet membrane elasticity, Young’s modulus was used based on the Hertz model.
Results: Prior to hyperbaric oxygen therapy (HBO) in patients with CHF, disruption of platelet aggregation in the form hyper-aggregation was found in 33.3%, hypo-aggregation - 25% and normal aggregation in 41.7%
Platelet membrane elasticity was 0.84 ± 0.19, 0.74 ± 0.22, 0.71 ± 0.20 MPa respectively.
After 5 sessions of HBO we found/revealed opposite changes the elastic properties of the membrane, depending on the functional activity of platelets
Increased platelet membrane elasticity was observed during platelet hyper-aggregation in comparison to the normal and hypo-aggregation.
The use of HBO in these patients was accompanied by a decrease in elastic modulus with 0,84 ± 0,19 to 0,42 ± 0,16 ($p = 0.04$), which indicates an increase in the elasticity of the membrane and decrease the degree of platelet aggregation activity.
Conclusion: Hyperbaric oxygen therapy in patients with CHF FC I-III is accompanied by membrane-modifying effect in the form of increasing the elasticity of the membrane with platelet hyperactivity.

P269
Assessment of the lipidic exchange at patients with chronic heart failure depending on the functional condition of kidneys

UK Kamilova[1]; ZD Rasulova[1]; DR Tagaeva[1]; VH Juraeva[1]; DR Masharipova[1]
[1]*Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, Cardiology, Tashkent, Uzbekistan*

Purpose: To study indicators of the body weight index (BWI) and condition of lipidic exchange at patients with chronic heart failure (CHF) taking into account functional condition of kidneys.

Methods: In total 120 patients with the coronary heart disease with I (37), II (43) and the III functional class (FC) (40 patients) of CHF have been inspected. The FC of CHF was estimated according to recommendations of the NYHA by means of the test of 6-minute walking. As reliable indicator of condition of food calculated the BWI on formula: BWI = weight (kg)/height2 (sq.m). Results interpreted as follows: normal BWI - 20,0-24,9 kg/sq.m, the excess body weight (preobesity) - 25,0-29,9 kg/sq.m, obesity - 30,0 kg/sq.m and above, subnutrition - is lower than 19,9 kg/sq.m. Indicators of lipidic exchange (the general cholesterol, cholesterol of lipoproteids: of the high density (LPHD) and low density (LPLD), triglycerides (TG)). To all patients determined the level of serumal creatinine (Kr), glomerular filtration rate (GFR) by formula MDRD (Modification of Diet in Renal Disease Study) in ml/min/1,732.
Results: Results of research have shown that among the inspected patients with CHF - normal BWI is revealed in 29% of cases, raised - in 62% (from them 58,5% fall to the share of obesity), lowered - in 9%. In the analysis of the BWI at patients CHF taking into account FC it is revealed that at the I FC CHF 77% investigated have the increased body weight; at the II FC CHF - 67,5%; at the III FC CHF - 46,5%. Normal BWI is available 23% of patients from the I FC CHF, for 24% - II FC CHF, for 28% - III FC CHF. Reduced BWI is available 8,5% of patients from the II FC CHF, for 25,5% of patients with the III FC CHF, at the I FC CHF such patients were absent ($p = 0,05$). At 67% (78 patients) of the inspected patients had GFRMDRD≥60 ml/min/1,732. In the analysis BWI at patients CHF taking into account GFRMDRD it is revealed that at GFRMDRD≥60 ml/min/1,732 reduced BWI had 17,9% (14 patients) of the investigated; normal BWI - 44,9% (35); the raised BWI - 37,2% (29); at GFRMDRD < 60 ml/min/1,732 (42) reduced BWI had 35,7% (15); normal BWI - 47,6% (20); the raised BWI - 16,7% (7 patients) of the investigated.
Conclusion: Among patients CHF the syndrome of dislipidemiya (DL) meets more often: the hypercholesterolemia (HHL) is noted in 45,9% of cases ($p < 0,05$ in comparison with control), hypertriglitseridemiya (HTG) - in 23% ($p = 0,03$), increase of LPLD - in 62% ($p = 0,02$), decrease in LPHD - in 15,3% of cases ($p < 0,05$). The HHL and HTG are more characteristic for patients with the II FC CHF - 62,5 and 43,6% respectively, with the III FC CHF the share of patients with this type of DL authentically decreases to 34,5 and 27,3% according to ($p < 0,05$). Specific weight of the patients having the increased LPLD level and reduced LPHD in blood tends to increase in process of increase of FC ($p < 0,05$). In our research more than a half of patients had the raised BWI (obesity and preobesity).

P270

Measurement of multiple cytokines for diagnosis and prognosis of chagas' disease and idiopathic dilated cardiomyopathy

ADNAN Khan[1]; YONG Wang[1]; NIELS Wessel[2]; HP Scultheiss[3]; MDV Consolacao[4]; THOMAS Walther[5]
[1]*Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany*; [2]*Humboldt University Berlin, Department of Physics, Berlin, Germany*; [3]*Charite - Campus Benjamin Franklin, Department of Cardiology, Berlin, Germany*; [4]*Federal University of Minas Gerais, Department of Internal Medicine, Belo Horizonte, Brazil*; [5]*Leipzig University Hospital, Department of Obstetrics, Leipzig, Germany*

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Introduction: Chagas' disease (CD), caused by the hemoflagellate protozoan, Trypanosoma cruzi, is endemic in most countries of South and Central America, where it continues to be a major source of social, health, and financial burden. Cardiac involvement is the most frequent and serious manifestation of chronic CD, and typically leads to heart failure (HF), arrhythmias, thromboembolism, and sudden death.
Purpose: HF is often a late manifestation of chronic CD, and is associated with high morbidity and mortality. Early identification of patients with CD, therefore, would be desirable as early intervention may help improve prognosis. Inflammatory biomarkers can play a vital role in early diagnosis, as inflammation mediated by cytokines plays an important role in pathogenesis and progression of CD, and may be present even in the absence of HF.
Methods: Keeping in view the inflammatory nature of CD, this study investigated the possible role of 21 different inflammatory cytokines as biomarkers for prediction and prognosis of CD. The plasma concentration of each of these cytokines was measured in a group of patients with CD, and then compared with those measured in patients with dilated cardiomyopathy (DCM) from idiopathic causes, and with control subjects.
Results: To the best of our knowledge, this is the first study to investigate cytokines such as monokine induced by interferon gamma (MIG) and stem cell growth factor beta (SCGF beta) in CD and idiopathic DCM patients. Using mono-variate analysis, plasma levels of cytokines such as SCGF beta, hepatocyte growth factor (HGF), MIG, and macrophage inhibitory factor (MIF) were significantly increased in CD patients with advanced HF, but they were unable to show any predictive or prognostic potency in CD. Further, multi-variate analysis was able to prognosticate a large proportion of CD and DCM patients, but it could not discriminate CD from idiopathic DCM.
Conclusion: It is possible that some of the cytokines that were studied here are only regulated in HF due to specific etiologies such as ischemic HF. Also, cytokines other than the ones that were investigated may play a role in causing severe inflammation and fibrosis seen in CD. Studies in future, therefore, should focus on identifying further inflammatory biomarkers that could be used as tools for early prediction and prognosis of CD. Identifying patients at an early stage of the disease may help in providing effective treatment and prevent the development of HF and thus early death.

P271

Role of obstructive sleep apnea syndrome in development of left ventricular diastolic dysfunction

A Alexey Kuchmin[1]; IV Makarova[1]; AA Kazachenko[1]; KB Evsukov[1]; AA Shevelev[1]
[1]*The Kirov Military Academy, St-Petersburg, Russian Federation*

Background: The purpose of this study was to determine the role of obstructive sleep apnea syndrome (OSAS) as a risk factor for the development of left ventricular diastolic dysfunction in middle-aged OSAS men.
Methods: We examined 38 newly diagnosed middle-aged OSAS men without conditions, affecting left ventricular diastolic function. All subjects underwent sleep study, 24-hour ambulatory blood pressure monitoring (ABPM), and an echocardiogram. Inclusion criteria for OSAS patients were: apnea-hypopnea index (AHI) ≥10 h−1 and excessive daytime sleepiness. In OSAS patients, relationships between sleep parameters, diastolic echocardiographic parameters and blood pressure recordings were also analyzed.
Results: An abnormal left ventricular filling pattern was present in 23 (60,5%) of the 38 OSAS patients. Impaired relaxation was by far the most common abnormal pattern in this group (18 (47,4%) patients), whereas a pseudonormal pattern was present only in 5 (13,2%) patients with OSAS. We analyzed separately OSAS patients with normal filling pattern and those with impaired relaxation of left ventricle. Patients with impaired relaxation had higher AHIs than those with normal pattern. LV mass, and LV mass index were also higher in OSAS patients with impaired relaxation. The study showed a significant correlation between AHI and E/A ratio ($r=-0.39$, $P < 0,01$), DT ($r=0.33$, $P < 0,05$), and IVRT ($r=0.39$, $P < 0,05$). In the model of logistic regression diastolic dysfunction was predicted only by AHI and patients age.
Conclusions: In middle-aged men OSAS can affect left ventricular diastolic function independently of other possible factors. It may be an early response to cardiac overload caused by OSAS.

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What is the incidence of elevated pulmonary artery pressure amongst patients presenting to the incident heart failure clinic?

A Abdallah Al-Mohammad[1]; L Allcock[1]; D Rogers[1]; N Lewis[1]; A Charalampopoulos[1]; D Robson[1]
[1]*Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom*

Purpose: Pulmonary hypertension (PH), defined as a systolic pulmonary artery pressure above 40mmHg is associated with increased morbidity and mortality. We investigated the frequency of pulmonary hypertension as derived by transthoracic echocardiography (TTE) amongst patients referred to our incident heart failure (HF) clinic.
Methods: Patients suspected of having new onset HF are referred to the incident HF clinic if their NTproBNP is > 400 ng/l. The clinic serves a city populated by 550,000 inhabitants. All patients undergo detailed echocardiography and are assessed by a HF consultant cardiologist. We collected data on the patients seen between April 2012 and December 2016.
Results: A total of 3939 patients were seen in this period. 779 patients (20%) had an estimated systolic pulmonary artery pressure over 40mmHg. Of this cohort, PH was the only problem identified on TTE in 188 patients (24% of those with PH). PH was found in association with HF with preserved left ventricular ejection fraction (HFPEF) in 282 patients (36% of those with PH). PH was diagnosed in association with HF with reduced left ventricular ejection fraction (HFREF) in 263 patients (34% of the patients with PH) and finally PH was detected in those with associated valvular disease in 46 patients (6%). Table 1.
Conclusions: Pulmonary hypertension is present in 1 in 5 of the patients presenting to the diagnostic HF clinic. In 76% of these patients it is found in combination with other types of heart failure, but in 24% it is the only abnormality detected on echocardiography.

Table 1

Diagnosis	2012	2013	2014	2015	2016	Total
HF PH	23	43	68	30	24	188
HF PH HFPEF	21	41	97	81	42	224
HF PH HFREF	42	77	108	22	14	263
HF PH Valve	5	17	14	8	2	46

Incidence of HF PH in 5 years

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Pulmonary and cardiac characteristics of heart failure patients comparing three groups based on left-ventricular ejection fraction

W Robaeys[1]; S Bektas[1]; JJ Boyne[1]; V Van Empel[1]; N Uszko-Lencer[1]; C Knackstedt[1]; HP Brunner-La Rocca[1]
[1]*Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*

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Background: Patients with heart failure (HF) are vulnerable to chronic obstructive pulmonary disease (COPD) and gas exchange disturbances. Vice versa patients with COPD might experience structural changes in the right heart depending on the development of pulmonary hypertension. The frequency of cardiopulmonary abnormalities is not yet investigated sufficiently in HF patients divided in the recently defined three groups based on left-ventricular ejection fraction (LVEF); i.e. HF with reduced (HFrEF), HF with mid-range (HFmrEF) and HF with preserved LVEF (HFpEF). Moreover, the influence of lung function abnormalities on the right heart is insufficiently understood.
Purpose: Therefore, the present study investigated the frequency of lung and right ventricular (RV) functions in the three HF groups. Furthermore, relations of HF and COPD were explored.
Methods: Overall, 186 consecutive stable HF patients seen in our outpatient clinic were divided into HFrEF (n = 70), HFmrEF (n = 55), and HFpEF (n = 61). Airflow limitation and gas exchange disturbance were measured by spirometry (forced exhaled volume in the first second / forced vital capacity (FEV1/FVC) (%)) and DLCO (diffusion capacity of the lungs for carbon monoxide). Standard echocardiography was performed to measure RV structure (RV diameter) and function (tricuspid annular plane systolic excursion/pulmonary artery systolic pressure (TAPSE/PASP)). Correlations were used to assess possible relations between COPD and measures of the RV.
Results: None of the investigated pulmonary parameters differed significantly between the three groups (all p>0.1); FEV1/FVC was 70 ± 12%, 70 ± 13%, and 74 ± 10% in patients with HFrEF, HFmrEF, and HFpEF (P=0.12) and DLCO was 5.7 ± 1.6, 5.7 ± 1.8, and 5.6 ± 1.6 mmol/min/kPa, respectively (P=0.95). RV structure and function did not differ either (TAPSE/PASP 0.58, 0.60 and 0.57, respectively (P=0.84)). There was only a weak correlation of DLCO (r=0.34, $p < 0.001$), and even less of AL (r=0.19, $p < 0.03$) with RV function.
Conclusion: In this outpatient clinic population pulmonary function abnormalities were comparable in the three HF groups as was RV functional impairment. Thus, identifying lung function abnormalities in stable HF is important irrespectively as to LVEF. The influence of pulmonary function abnormalities on the RV seems to be limited and not clinically meaningful.

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Comparing mildly-reduced with preserved ejection fraction heart failure patients: two flips of the same coin?

B Neves[1]; N Hammoudi[1]; F Pousset[1]; P Balagny[1]; L Legrand[1]; M Komajda[1]; R Isnard[1]
[1]*Hospital Pitie-Salpetriere, Cardiology Department, Paris, France*

Introduction: Patients with preserved ejection fraction Heart Failure (HF) are a heterogeneous group whose clinical trials have been negative so far. Heterogeneity of this population has been attributed to this systematic failure and efforts have been made to try to identify different subgroups inside this population. The most recent European Heart Failure guidelines subdivide the previously called preserved ejection fraction group into mildly reduced (MrEF) with 40-49% and preserved (PEF) with ≥50% ejection fraction. Our aim was to characterize a group of patients admitted with heart failure decompensation and left ventricular ejection fraction (LVEF) ≥40% in terms of clinical, laboratory and echocardiographic characteristics.
Methods: A cohort of patients admitted for HF decompensation between June 2015 and June 2016 on a tertiary HF center was analysed. Electronic medical records and echocardiograms were sourced for data introduction. HF was defined as current ESC criteria guidelines. Patients with HF diagnosis and EF ≥40% were included. Exclusion criteria included history of previously reduced EF, moderate valvular heart disease, constrictive pericarditis, congenital heart disease and previous cardiac transplantation.
Results: 717 patients were admitted during the study period, from what 303 fulfilled inclusion criteria. After exclusion criteria, 225 were enrolled and 211 had complete echocardiographic data for analysis. 69 (30,7%) patients had MrEF. There were no differences between groups in terms of age (p = 0,57), gender (p = 0,45) or biometrics. Coronary artery disease (CAD) and prior coronary revascularization was more frequent in MrEF (p = 0,004, p = 0,009 respectively). CAD was correlated with lower LVEF (OR 2.46 (1.36-4.51, CI 95%). Remaining comorbidities were equally present on both groups. End-diastolic and end-systolic left ventricular volumes, left ventricular end-diastolic diameter were significatively higher in MrEF patients ($p < 0,001$). Left ventricular mass showed a trend to be higher in MrEF (p = 0.052). Relative-wall-tickness was significatively higher in PEF patients ($p < 0,001$). TAPSE and tricuspid annular S′ showed a trend to lower values in MrEF patients (p = 0,07).
Conclusions: In this cohort of patients lower EF tends to be more associated with CAD and LV dilation which is consistent with a transition group between truly preserved EF and reduced EF. Further prospective studies should confirm these results and may eventually analyse CAD separately among populations with HFpEF.

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The role of sympathetic co-transmitter galanin on autonomic control in heart failure : An active player or a bystander in sympathovagal crosstalk

D Ozkaramanli[1]; M Sagbas[2]; A Akyuz[1]; S Guzel[3]; S Alpsoy[1]; N Guler[1]
[1]*Namik Kemal University Faculty of Medicine, Cardiology, Tekirdag, Turkey*; [2]*Tekirdag State Hospital, Tekirdag, Turkey*; [3]*Namik Kemal University Faculty of Medicine, Biochemistry, Tekirdag, Turkey*

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Background: Autonomic imbalance in favor of sympathetic nervous system is an important clinical feature of heart failure (HF). Sympathetic cotransmitters neuropeptide Y(NPY) and galanin, located in the adjacent vesicles to the main transmitter norepinephrine, attenuate the vagal tonus after burst sympathetic activity by a mechanism called 'sympathovagal crosstalk'. On the basis of preliminary data from animal studies suggesting increased levels of galanin in HF models and improvement in cardiac function subsequent to treatment with galanin antagonists, we examined the levels of galanin and NPY, the two main cotransmitters of sympathovagal crosstalk in chronic heart failure patients.
Purpose: We evaluated whether the levels of galanin correlated with the levels of NPY, the humoral activity expressed by Pro BNP and copeptin concentrations; and myocardial performance estimated by echocardiography in patients with HF. To our knowledge, this is the first study to document plasma concentrations of galanin in chronic HF patients.
Methods: The study population consisted of 57 patients with chronic systolic HF and 30 control subjects. Of HF patients, 68.4%(n:39) had ischemic and 31.6%(n:18) had dilated cardiomyopathy. All subjects underwent detailed transthoracic echocardiography, had their demographic characteristics recorded and blood collected for proBNP, copeptin, galanin and NPY analysis.
Results : The ProBNP, copeptin and NPY were significantly elevated in HF group.(2128.9 ± 1104.5 vs 212.6 ± 96.4 pg/mL, $p < 0.0001$; 872.3 ± 280.7 vs 640.7 ± 279 pg/mL, $p < 0.0001$; 139.8 ± 65.5 vs 79.8 ± 35.9 pg/mL, $p < 0.0001$ respectively). Galanin, on the other hand, was not statistically different between HF or control groups.(32.5 ± 19.06 vs 31.9 ± 18.4 pg/mL, p = 0.9). The correlation analysis revealed that NPY was correlated with the echocardiographic parameters of HF severity(r:-0.22, p = 0.03 for EF; r=0.3, p = 0.05 for left atrial volume index; r=0.3, p = 0.005 for Tei index of right ventricle; r=-0.23, p = 0.03 for tricuspid annular plane excursion; r=0.24, p = 0.024 for E/e′) and with proBNP(r:0.22, p = 0.047); while galanin was correlated only with humoral biomarkers ProBNP and copeptin (r=0.39, $p < 0.0001$ and 0.41, $p < 0.0001$ respectively). The NPY levels were also strongly associated with beta blocker(BB) use, in which BB significantly decreased the levels of NPY(1048.8 ± 245.1 with BB to 834.7 ± 275.6 without BB, p = 0.032). The multivariate linear regression analysis revealed that among variables like copeptin, proBNP, BMI, smoking status and beta blocker use, which were proved to be associated with galanin in univariate comparisons, only proBNP was the significant predictor of galanin levels in HF patients.(b=0.534,CI 95% 0.005-0.014, $p < 0.0001$)
Conclusions : Our findings confirmed the direct role of NPY on autonomic balance in HF and suggest that, until further evidence emerges, galanin seems not to be an active player in sympathovagal crosstalk in the failing human heart.

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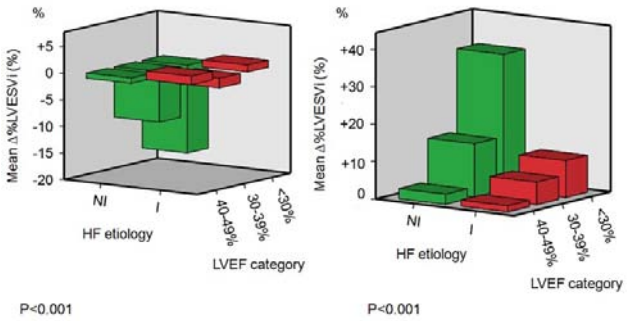
Reverse remodeling in systolic heart failure: the relevance of aetiology and baseline function

A Alberto Aimo[1]; G Vergaro[2]; V Castiglione[1]; A Barison[2]; A Giannoni[2]; V Chubuchny[2]; L Zyw[2]; C Passino[1]; M Emdin[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*

Background: Reverse remodeling (RR) refers to the complete or partial recovery of left ventricular (LV) geometry and function following guideline-recommended treatment for heart failure (HF). At present, diagnostic criteria for RR do not take into account HF aetiology or baseline function, and standardized criteria are lacking.
Purpose: To assess how aetiology and baseline function impact on RR, and to search for RR criteria with prognostic relevance in a population of patients with systolic HF.
Methods: Patients with stable systolic HF (left ventricular ejection fraction - LVEF < 50% at baseline) undergoing two transthoracic (TTE) examinations within 12 ± 4 months, were selected. The follow-up started with the second TTE. The endpoint was cardiovascular death or heart transplantation.
Results: In our population of 927 patients (age 68 ± 12 years, LVEF 34 ± 9%, ischaemic aetiology in 53%), baseline LVEF categories < 30%, 30-39% and 40-49% were similarly represented (n = 287 [31%], 324 [35%] and 316 [34%], respectively). Over the 33-month [interquartile range - IQR 15-59] follow-up, the endpoint occurred in 126 patients (14%).
Patients with non-ischaemic aetiology experienced significantly greater variations (%) in LVEF, LV end-systolic volume index (LVESVi) and LV end-diastolic volume index (all P < 0.001). %LVEF and LVESVi were significantly different across LVEF categories (P < 0.001 and 0.028, respectively), with the greatest improvement in patients with LVEF < 30%. When stratifying patients according to both aetiology and baseline LVEF category, the greatest recovery in LVESVi and LVEF was observed in patients with LVEF < 30% and non-ischaemic HF, followed by LVEF 30-39% and non-ischaemic HF, while decreasing sharply in patients with LVEF 40-49% and non-ischaemic HF. The improvements in LVESVi and LVEF were much less prominent in patients with ischaemic aetiology; LVEF recovery was greater in patients with LVEF < 30% (Figure).
When searching for RR criteria with prognostic relevance, in patients with non-ischaemic HF the highest area under the curve (AUC) values were obtained for %LVESVi, the best cut-points being -11% for LVEF < 30% (AUC 0.584), -10% for LVEF 30-39% (AUC 0.632), and -2% for LVEF 40-49% (AUC 0.680). In the ischaemic subgroup, the highest AUC values were obtained for %LVEF, the best cut-points being + 10% for LVEF < 30% (AUC 0.595), + 8% for LVEF 30-39% (AUC 0.613), and + 2% for LVEF 40-49% (AUC 0.615).
Conclusions: In stable systolic HF, the potential for recovery is greater in patients with non-ischaemic aetiology or lower baseline LVEF category. When taking into account both information and patient prognosis, the following criteria for RR were defined: -11%, -10% and -2% %LVESVi (for LVEF < 30%, 30-39% and 40-49%, respectively) in patients with non-ischaemic HF; + 10%, + 8% and + 2% %LVEF (for LVEF < 30%, 30-39% and 40-49%, respectively) in patients with ischaemic HF.



Abbreviations: HF, heart failure; I: ischemic; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume indexed; NI, non-ischemic.

Role of aetiology and baseline function

P277

Do we treat heart failure differently according to gender?

I Irene Rilo Miranda[1]; JR Beramendi Calero[1]; S Garcia Gutierrez[2]; A Anton Ladislao[2]; L Quintas Ovejero[3]; C Goena Vives[3]; M Morillas Bueno[2]; F De La Cuesta Arzamendi[1]
[1]Hospital Donostia, San Sebastian, Spain; *[2]Hospital Galdakao-Usansolo, Bilbao, Spain*; *[3]Hospital Comarcal de Mendaro, Cardiology, Mendaro, Spain*

Introduction: This study aims to determine the differential characteristics between the treatment among men and women with acute heart failure admitted to the Emergency Services 3 hospitals in our 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.
Results: The sample included 1824 patients. 48% (886) were male and 51% (938) female.
The use of antialdosteronic treatment was significantly higher in males (19% vs 13 % p = 0.0007) and it was higher too the use of antiagregants (36 % in males vs 30 % in women p = 0,0041) probably because of the higher rate of ischemic cardiomyopathy in males ((40 % vs 25 % p < 0.0001) and anticoagulant drugs (52 % in males vs 45,1 % in women p = 0,0021) although the rates of atrial fibrillation were similar in both groups (54 % vs 52 % p = 0.45)
Among men the use of betablockers was significantly higher (40 % vs 35 % p-0,05) and in the other hand, women presented a higher rate of calcium channel blockers (25 % in females vs 22 % in men p = 0.03).
Despite the higher prevalence of heart failure with preserved systolic function among females (62 % vs 38 % p < 0,0001) the use of loop diuretics was similar in both groups (63 % in women vs 61 % in men p = 0,2855).
Conclusions: 1. The use of antiagregants was higher in males probably because of the higher rate of ischemic cardiomyopathy among then.
2. The use of anticoagulant drugs was higher in men although the rates of atrial fibrillation were similar in both groups
3. Among men the use of betablockers was significantly higher and in the other hand, women presented a higher rate of calcium channel blockers probably because of the higher prevalence of heart failure with preserved ejection fraction in women
4. Despite the higher prevalence of heart failure with preserved systolic function among females the use of loop diuretics was similar in both groups

P278

Hemodynamic effects of levosimendan in advanced but stable chronic heart failure

E Emil Najjar[1]; M Stalhberg[1]; C Hage[1]; E Ottenblad[1]; A Manouras[1]; IH Lofman[1]; LH Lund[1]
[1]Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden

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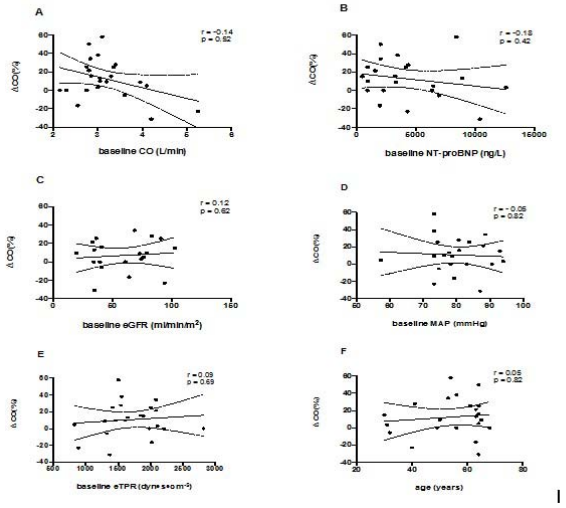
Background: Levosimendan improves hemodynamics in acute decompensated heart failure (HF). However, it is increasingly used for repetitive or intermittent infusions in advanced but stable chronic HF; without clear indication, selection criteria or effect.
Purpose: To test the hypotheses that (1) levosimendan improves hemodynamics in stable chronic HF and (2) that the response is dependent on baseline clinical and hemodynamic factors.
Methods: Twenty-three patients (median age 56 [49-64] years, 4 [17%] women) with stable New York Heart Association (NYHA) III-IV HF received a single 24-hour levosimendan infusion. Noninvasive hemodynamics (inert gas re-breathing technique), estimated glomerular filtration rate (eGFR) and N-terminal pro-brain natriuretic peptide (NT-proBNP) were assessed before and after infusion.
Results: Levosimendan had the following effects (median change): a significant increase in cardiac output (CO) (+ 9.8 ± 21.6%; p = 0.026) and decrease in NT-proBNP (-28.1 ± 16.3%, p < 0.001), estimated total peripheral resistance (eTPR) (-16.9 ± 18.3%, p = 0.005) and mean arterial pressure (MAP) (-5.9 ± 8.2%, p = 0.007) but no change in eGFR (+ 0.89 ± 14.0%, p = 0.955). There were no significant associations between baseline clinical and/or hemodynamic factors and the levosimendan effect on CO.
Conclusions: Levosimendan was associated with improved hemodynamics in patients with stable chronic HF but we could not identify any predictors of the magnitude of hemodynamic response.

Figure 3. Correlations between baseline cardiac output (A), NT-proBNP (B), eGFR (C), MAP (D), eTPR (E) and age (F) and change in cardiac output in response to levosimendan



Correlations

P279

Prevention of left ventricular diastolic dysfunction with long-term CPAP treatment in OSAS patients.

A Alexey Kuchmin[1]; IV Makarova[1]; KB Evsukov[1]; AA Kazachenko[1]; AA Shevelev[1]; AN Kulikov[1]
[1]*The Kirov Military Academy, St-Petersburg, Russian Federation*

Background: The purpose of this study was to determine the effect of hronic CPAP application on diastolic left ventricular filling in middle-aged OSAS men with diastolic dysfunction.
Methods: The study included 18 otherwise-healthy patients who had confirmed impaired relaxation of left ventricle and moderate to severe obstructive sleep apnea seen at the sleep laboratory at a single clinic. A battery of cardiac assessments, including 2D and 3D echocardiography, was done on them at baseline and after treatment with CPAP for 8 weeks. Complete measurements were available in 17 patients. ne patient failed to complete the trial.
Results: - There were no differences in blood pressure recordings, heart rate or weight at baseline and after CPAP in OSAS patients. After 8 weeks on effective CPAP, left ventricular filling pattern were not modified, but a significant increase in E/A ratio (0.69 ± 0.17 and 0.90 ± 0.13, $P < 0,01$) and reduction in DT (296.6 ± 41.3 ms and 263 ± 37.8 ms, $P < 0,05$) and IVRT (112.3 ± 8.7 ms and 101.2 ± 9.3 ms, $P < 0,01$) values were induced. Left atrial volume index also improved on both 2D and 3D echo ($P < 0.01$).
Conclusions: Chronic CPAP application can modify diastolic left ventricular filling and avoids the progression of diastolic abnormalities, and indeed, it might reverse these alterations, at least in the initial stages before severe ventricular structural changes develop. The mechanism for diastolic improvements needs further study but it may be correction in blood pressure, hypoxia, and sympathetic system activity.

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Effect of potassium/magnesium enriched salt on functional capacity and quality of life in symptomatic patients with chronic heart failure

I Iryna Voloshyna[1]; VA Vizir[1]; MA Voloshyn[1]; VI Krivenko[1]; VI Ponomarenko[2]
[1]*Zaporozhye State Medical University, Zaporozhye, Ukraine*; [2]*Institute of Ecology, Melitopol, Ukraine*

Background: Nowadays the clinical studies highlight the contradicting results regarding sodium restriction impact on outcomes in patients with chronic heart failure (CHF). Plasma magnesium and potassium concentrations are often reduced in CHF patients causing increased risk of hospitalizations and mortality.
Purpose: The present study aimed to evaluate whether potassium/magnesium enriched salt consumption could improve exercise capacity and quality of life in symptomatic patients with CHF.
Methods: A total of 64 symptomatic patients aged 66-80 years with CHF and preserved left ventricle ejection fraction were recruited. All patients were randomly assigned to 2 groups: first – with moderate (less than 5-6 g/day) salt-restricted diet ($n = 32$), second group of participants received recommendations to use potassium/magnesium enriched salt contained 30% of potassium and 5% of magnesium in their daily intake no more than 5-6 g/day. All enrolled participants were on stable treatment with 3 more drugs and initially had serum potassium level 3.9-4.7 mmol/L. Six-minute walk distance as physical function assessment, quality of life, health status, and daily activity using Minnesota Living With Heart Failure Questionnaire (MLWHFQ) were measured at baseline and at 8 weeks.
Results: There was a significant difference in change for the six-minute walk distance at 8 weeks in moderate salt-restricted diet group ($+10.5$ m; 95% CI, $+2.5$ to 26.8 m; $p = 0.02$) whereas in patients used potassium/magnesium enriched salt a slightly improved dynamic of exercise capacity had been noticed ($+17.2$ m; 95% CI, $+3.1$ to 37.2 m; $p = 0.03$) although the intergroup distinction was insignificant ($p = 0.07$). Moderate sodium salt-restricted interventions were not notably associated with quality of life enhancement. The MLWHQ overall score decreased on 15% ($p = 0.06$) mainly due to diminishing of physical subscore (-26%; $p = 0.04$). In group with potassium/magnesium enriched salt intake the greater changes of quality of life parameters had been revealed. The MLWHQ overall score reduced on 29% ($p = 0.04$), physical subscore fell on 36% ($p = 0.03$), psychosocial/symptomatology subscore decreased on 19% ($p = 0.04$). Thus, the significant correlation was found between potassium/magnesium enriched salt consumption and physical subscore of MLWHQ ($r = -0.28$; $p = 0.02$).
Conclusions: Dietary interventions concerning moderate sodium restriction either with potassium/magnesium salt enrichment lead to enhancement of exercise capacity in patients with CHF and preserved ejection fraction. Daily use of potassium/magnesium enriched salt could be a promising non-pharmacological treatment option for managing impaired quality of heart failure patient's life.

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Characteristics of newly diagnosed patients with heart failure managed in the primary care and cardiology settings in France

S Eisenring[1]; C C Proenca[2]; B Balas[3]; F Calado[3]; C Thonnelier[4]; S Bruce Wirta[5]
[1]*QuintilesIMS Switzerland, Basel, Switzerland*; [2]*Wellmera AG, Basel, Switzerland*; [3]*Novartis Pharma AG, Basel, Switzerland*; [4]*Novartis Pharma SAS, Rueil Malmaison, France*; [5]*Novartis Sweden AB, Stockholm, Sweden*

Background and purpose: This study aimed to describe and compare characteristics of newly diagnosed patients with heart failure (HF) in the primary care and cardiology settings in France.
Methods: Electronic medical records from two French databases (a general practitioner [GP] panel and a cardiologist panel) were used to identify patients. All patients (aged $\geq$18 years) who were newly diagnosed with HF from 1 January 2009 to 30 September 2013 were included. Patient histories available in the databases, from January 1994 (GP panel) or January 1998 (cardiologists) to December 2008, were used to exclude patients with a previous diagnosis of HF. Patients who were not prescribed a new treatment after diagnosis were also excluded.
Results: The study population comprised 6566 patients with newly diagnosed HF (GP panel 4940; cardiologist panel 1626). The mean $\pm$ SD age of the overall population at diagnosis was 75.0 ± 12.4 years. Patients diagnosed by cardiologists were similar in age to those diagnosed by GPs. A smaller proportion of patients diagnosed by GPs were male (54.2% vs 60.3%). Mean $\pm$ SD systolic and diastolic blood pressures of the overall population were 133.0 ± 17.5 mmHg and 75.7 ± 9.7 mmHg, respectively. Mean heart rate was higher in patients diagnosed by the GP panel than the cardiologist panel (97.5 bpm vs 82.5 bpm). At diagnosis, New York Heart Association (NYHA) functional classification was recorded for 61% of patients diagnosed by a GP and 52% of those diagnosed by a cardiologist. Overall, the majority of patients were classified as NYHA class II (56.6%), followed by class III (21.4%), class I (18.5%) and class IV (3.5%); the proportions were similar for the two panels. Insufficient data on ejection fraction were available to allow this parameter to be evaluated. In the 6-month period before diagnosis, diuretics were the most commonly prescribed cardiovascular drug by both GPs and cardiologists (54.0% and 34.4%, respectively), followed by β-blockers (44.4% and 33.7%), angiotensin-converting enzyme inhibitors (37.4% and 23.8%) and angiotensin II receptor blockers (31.7% and 19.5%). Clinical characteristics were more frequently reported at diagnosis by GPs than cardiologists: body mass index (64.0% vs 48.8%), systolic and diastolic blood pressure (77.3% vs 24.5%), potassium level (45.7% vs 18.5%), estimated glomerular filtration rate (23.9% vs 8.9%) and heart rate (78.9% vs 46.0%). N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and haemoglobin levels were rarely recorded (NT-proBNP: GP panel 6.8%, cardiologist panel 6.0%; haemoglobin: GP panel 1.1%, cardiologist panel 0.1%).
Conclusions: The age and NYHA class distributions in patients diagnosed by a GP and those diagnosed by a cardiologist were very similar. Clinical characteristics at

diagnosis were more frequently recorded by GPs than by cardiologists; however, an absence of data on ejection fraction was common to both groups.

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Comparison of office heart rate and mean 24-hours ambulatory heart rate in chronic heart failure patients

V Habenicht[1]; E Kolesnik[1]; J Schmid[1]; K Brandner[1]; A Tomaschitz[1]; S Pilz[1]; F Fruhwald[1]; D Von Lewinski[1]; K Ablasser[1]; N Verheyen[1]
[1]*Medical University of Graz, Graz, Austria*

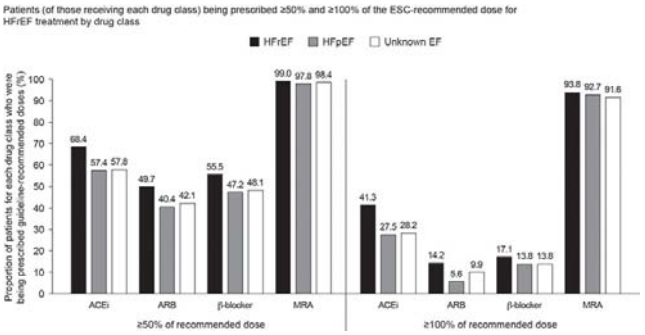
Objective: Heart rate (HR) control in heart failure patients is commonly based on single office measurements at rest. However, 24-hours ambulatory heart rate measurement may yield a more accurate surrogate parameter of individual HR than single measurements. In a pilot study, we investigated the association between measures of office HR and mean 24-hours ambulatory heart rate in chronic patients with heart failure.
Methods: Patients with stable chronic heart-failure and a left ventricular ejection fraction (EF) < 50 % were prospectively enrolled in the outpatient clinic of a tertiary care hospital. Office HR was measured after 5 minutes rest both in the sitting and in supine position, mean ambulatory HR was determined using a certified ambulatory blood pressure monitoring device (Mobil-O-Graph, I.E.M. GmbH, Stolberg, Germany) and was calculated as the mean of all successful HR measurements during 24 hours. HR >= 70 beats per minute (bpm) was considered elevated.
Results: We enrolled 28 subjects with mean age of 62.6 +/- 10.3 years (35% females) and mean EF of 34 +/- 9 %. Mean sitting HR was 69.5 +/-15.6 bpm and mean supine HR was 71.5 +/- 15.3 bpm, mean 24-hours ambulatory HR was 67.6 +/- 10.6 bpm. Ambulatory HR was correlated with sitting HR (Pearson's r = 0.620, P = 0.001) and supine HR (r = 0.398 , P = 0.044) HR was elevated in 9 subjects (33.3%) in sitting position, in 13 subjects (46.4%) in supine position, and in 13 subjects (48.1%) in ambulatory read-outs.
Among those with a normal supine HR (n = 14), 3 (21.4%) had an elevated ambulatory HR. Vice versa, 3 individuals (23.1%) of those with elevated supine HR revealed a normal ambulatory HR.
Comparing sitting HR with ambulatory HR, 5 (29.4%) had an elevated ambulatory HR, although presenting with a normal sitting HR, while 2 (22.2%) of those with elevated sitting HR had a normal amulatory HR.
Conclusion: Office HR measurements and ambulatory HR show only moderate correlation in subjects with chronic heart failure. Office HR measurements tend to be higher than ambulatory measurements. Approximately one in five patients with normal office HR has elevated ambulatory HR, while a similar proportion of subjects with elevated office HR have normal ambulatory HR. After confirmation in larger cohorts, the clinical relevance of this divergence and the usefulness of 24-hours ambulatory HR beyond office HR as target parameter in heart failure treatment should be investigated in future studies.

P283

Suboptimal dosing of common heart failure treatments in newly diagnosed patients with heart failure: a retrospective population-based cohort study in Sweden

G Wikstrom[1]; K Boman[2]; M Olofsson[2]; J Stalhammar[3]; G J Bergman[4]; M Tornblom[4]; V Wintzell[4]; B Balas[5]; S Corda[5]; K Lindmark[6]
[1]*Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*; [2]*Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden*; [3]*Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*; [4]*QuintilesIMS, Solna, Sweden*; [5]*Novartis Pharma AG, Basel, Switzerland*; [6]*Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background: Studies in real-world settings have shown that patients with heart failure (HF) often do not receive medication at doses recommended by the European Society of Cardiology (ESC). By studying dosing patterns of HF treatments in newly diagnosed patients, healthcare professionals can evaluate how well treatment guidelines are being implemented in the real world.
Purpose: To assess treatment dosing in newly diagnosed patients with HF with reduced (HFrEF), preserved (HFpEF) and unknown ejection fraction (EF) according to the ESC 2012 guidelines for HFrEF (ESC does not make recommendations for HFpEF or unknown EF), using data from the Swedish counties of Uppsala and Västerbotten.
Methods: Patients with HF were identified via electronic medical records from primary and/or secondary care in Uppsala and Västerbotten, linked via unique identifiers to the National Patient Register and Swedish Prescribed Drug Register. Local echocardiography data identified HFrEF (< 50%) and HFpEF (≥50%). Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. The date of the first diagnosis was the index date. A 10-year look-back period was used to exclude prevalent HF cases. For each drug class commonly used in HF (angiotensin-converting enzyme inhibitors [ACEis], angiotensin II receptor blocker [ARBs], β-blockers and mineralocorticoid receptor antagonist [MRAs]), this study assessed the proportion of patients who were prescribed a median maintenance treatment dose (defined as volume of drug dispensed [mg]/duration of dispensation [days]), of ≥50% and ≥100% of the recommended target dose of individual treatments within the class. Maintenance treatment was assumed to start ≤90 days after treatment initiation, and the duration of each dispensation during maintenance was 90 days.
Results: In total, 8702 patients with HF were identified (HFrEF, 23.5%; HFpEF, 12.9%; unknown EF, 63.6%; mean ± SD age, 76.6 ± 12.6 years; 46.0% female). More patients with HFrEF than those with HFpEF or unknown EF received a common HF treatment (ACEi: HFrEF, 56.3%; HFpEF, 43.8%; unknown EF, 44.1%; ARB: HFrEF, 31.6%; HFpEF, 27.0%; unknown EF, 26.9%; β-blocker: HFrEF, 80.6%; HFpEF, 64.6%; unknown EF, 63.4%; MRA: HFrEF, 48.9%; HFpEF, 32.9%, unknown EF, 26.0%). Patients with HFrEF were more likely to be prescribed maintenance treatment doses of ≥50% and ≥100% of the recommended dose than those with HFpEF and unknown EF (Figure).
Conclusions: Prescription of ESC-recommended doses of HF treatment is low. With the exception of MRAs, most patients receiving treatment were not prescribed ESC-recommended doses, highlighting suboptimal treatment of HF in Sweden. This study did not consider underlying causes of the low doses prescribed, which may be influenced by tolerability.



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Management of patients with heart failure with preserved versus reduced ejection fraction: a retrospective population-based cohort study in Sweden

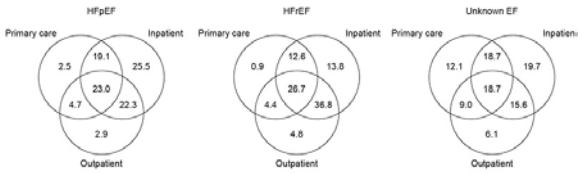
J Stalhammar[1]; K Boman[2]; M Olofsson[2]; G Wikstrom[3]; G J Bergman[4]; M Tornblom[4]; V Wintzell[4]; S Bruce Wirta[5]; C C Proenca[6]; R Schlienger[7]; K Lindmark[8]
[1]*Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*; [2]*Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden*; [3]*Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*; [4]*QuintilesIMS, Solna, Sweden*; [5]*Novartis Sweden AB, Stockholm, Sweden*; [6]*Wellmera AG, Basel, Switzerland*; [7]*Novartis Pharma AG, Basel, Switzerland*; [8]*Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background and purpose: Little is known about how patients with heart failure (HF) with preserved (HFpEF), reduced (HFrEF) or unknown ejection fraction (EF) are managed in clinical practice in Sweden. In an effort to gain a better understanding of the management of these patients, we evaluated the different care settings in which they received cardiovascular disease (CVD)-related care in the first year after diagnosis.
Methods: Patients with HF were identified via electronic medical records from primary and/or secondary care in Uppsala and Västerbotten, linked via unique identifiers to the National Patient Register. Local echocardiography data identified HFpEF (≥ 50%) and HFrEF (< 50%). Patients aged ≥ 18 years with ≥ 2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. The date of the first diagnosis was defined as the index date. Unadjusted proportions of patients treated in primary care (provided in an outpatient, office-based setting) and secondary care (provided in an inpatient or outpatient hospital setting) were assessed in the first year post-index.
Results: In total, 8702 patients with HF were identified. HF phenotype could be defined for 36.4% of patients (HFpEF, 35.4% [mean age ± SD, 74.2 ± 12.6 years; 48.8% male]; HFrEF, 64.6% [69.9 ± 13.7 years; 67.4% male]); EF was unknown for 63.6% of patients (79.5 ± 11.0 years; 50.0% male). Smaller proportions of patients with known EF than with unknown EF were treated in only a primary care setting (HFpEF, 2.5%; HFrEF, 0.9%; unknown EF, 12.1%). Small proportions of patients were seen in only an outpatient setting (HFpEF, 2.9%; HFrEF, 4.8%; unknown EF, 6.1%), while larger proportions were seen in only an inpatient setting (HFpEF,

25.5%; HFrEF, 13.8%; unknown EF, 19.7%). Most patients received CVD-related care in multiple settings, most commonly inpatient + outpatient (HFpEF, 22.3%; HFrEF, 36.8%; unknown EF, 15.6%) and primary care + inpatient + outpatient (HFpEF, 23.0%; HFrEF, 26.7%; unknown EF, 18.7%) settings. Patients with HFrEF were less commonly seen in only one setting than those with HFpEF or unknown EF (Figure). In secondary care, internal medicine wards were the most common settings for visits by patients with HFpEF (outpatient, 17.0%; inpatient, 30.7%), while cardiology clinics were the most common settings for visits by patients with HFrEF (outpatient, 26.6%; inpatient, 37.9%).

Conclusions: Patients with HFpEF, HFrEF and unknown EF are managed differently in terms of the healthcare settings in which they receive care. Patients with HFrEF are more commonly managed in an inpatient setting than those with HFpEF and unknown EF, possibly reflecting more frequent hospitalization of these patients.

Figure. Proportions of patients treated in primary care, and inpatient and outpatient settings.



EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

P285

Long-term effects of patiromer for hyperkalaemia treatment in patients with HFrEF and diabetic nephropathy on RAASi

B Pitt[1]; D Garza[2]; R Zawadzki[3]; A Romero[4]; A Conrad[4]; M Lainscak[5]
[1]University of Michigan, Ann Arbor, United States of America; *[2]Relypsa, Inc., Clinical Development, Redwood City, United States of America*; *[3]Relypsa, Inc., Biometrics, Redwood City, United States of America*; *[4]Relypsa, Inc., Medical Affairs, Redwood City, United States of America*; *[5]General Hospital Murska Sobota, Murska Sobota, Slovenia*

Purpose: Renin angiotensin aldosterone system inhibitors (RAASi) are indicated in patients (pts) with heart failure with reduced ejection fraction (HFrEF). RAASi increase the risk of hyperkalaemia (HK), particularly in pts with chronic kidney disease (CKD) and/or diabetes, and are often discontinued in HFrEF pts. Patiromer, a nonabsorbed, sodium-free potassium (K+)-binder, was previously shown in the AMETHYST-DN study to lower serum K+ (s-K+) through 52 weeks in pts with HK and diabetic nephropathy on RAASi. In this post-hoc analysis we examined the effects of patiromer on s-K+ in HK patients with HFrEF.

Methods: Patients with type-2 diabetes, CKD, and HK (baseline s-K+ >5.0– <6.0 mmol/L) were randomized to patiromer starting doses of 8.4–33.6 g/day, divided twice daily. All pts were receiving RAASi during study treatment. Changes in mean s-K+ from baseline through Week 52 were evaluated in the subgroup with HFrEF (EF ≤40%). Results: Of 306 randomized pts, 26 had HFrEF (100% Caucasian, 62% male, 69% ≥65 yr of age, mean [SD] EF: 37 [3]%, mean [SD] eGFR: 43.6 [17.7] mL/min/1.73m2. Mean s-K+ was reduced to <5.0 mmol/L at the first post-baseline visit (day 3, 48 hr after first patiromer dose) through Week 52 and stopping patiromer led to a rise in s-K+ (Table). No pts discontinued due to high s-K+. Patiromer was generally well tolerated, with 17 (65%) pts reporting ≥1 adverse event (AE) during the study. Mild or moderate gastrointestinal AEs were the most common class (occurring in 2 pts) of patiromer-related AEs, with abdominal discomfort, nausea and vomiting each occurring in 1 pt. No pts had s-K+ <3.5 mmol/L, 1 pt had serum magnesium <1.4 mg/dL (<0.57 mmol/L), and there were no reports of edema. From a baseline mean (SE) of 151.1 (2.0)/90.8 (2.1) mmHg, systolic/diastolic BP decreased by 17.0 (2.2)/ 16.2 (2.3) mmHg at Week 52. Conclusions: Patiromer decreased s-K+ through 52 weeks in HFrEF pts with HK and diabetic nephropathy. These post-hoc results, suggesting that patiromer allows continuous management of HK in HFrEF pts on RAASi, require further prospective evaluation.

Serum K+ Over 52 Weeks in HFrEF Patients	
Baseline (n=26)	5.23 (0.5)
Day 3 (n=26) Δ from baseline	4.82 (0.07) −0.41 (0.07)
Week 4 Δ from baseline	4.60 (0.08) −0.58 (0.09)
Week 24 (n=19)Δ from baseline	4.62 (0.06)−0.55 (0.09)
Week 52 (n=19) Δ from baseline	4.57 (0.08) −0.61 (0.07)
End of treatment (EOT) (n=20)	4.57 (0.10)
Follow-up Day +28 (n=17) Δ from EOT	4.97 (0.10)+0.49 (0.08)

Values are mean (SE) in mmol/L.

P286

Drug treatment patterns in patients newly diagnosed with heart failure: a retrospective population-based cohort study in Sweden

G Wikstrom[1]; K Lindmark[2]; M Olofsson[3]; J Stalhammar[4]; G J Bergman[5]; M Tornblom[5]; V Wintzell[5]; S Bruce Wirta[6]; B Balas[6]; K Boman[3]
[1]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden; *[2]Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[3]Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[4]Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*; *[5]QuintilesIMS, Solna, Sweden*; *[6]Novartis Pharma AG, Basel, Switzerland*

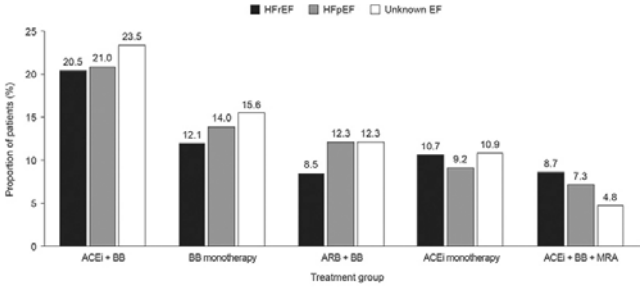
Background and purpose: Limited data are available on longitudinal drug treatment patterns in newly diagnosed patients with heart failure (HF) with preserved (HFpEF), reduced (HFrEF) and unknown ejection fraction (EF) in Sweden. We evaluated drug treatment patterns in these patients based on ESC 2012 guidelines, which recommend treatment with angiotensin-converting enzyme inhibitors (ACEis), angiotensin II receptor blockers (ARBs), β-blockers (BBs) and mineralocorticoid receptor antagonists (MRAs) for HFrEF (ESC does not make recommendations for HFpEF or unknown EF).

Methods: Patients were identified via electronic medical records from primary and/or secondary care in Västerbotten, linked via unique identifiers to the National Patient Register and Swedish Prescribed Drug Register. Local echocardiography data identified HFrEF (<50%) and HFpEF (≥50%). Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. The date of the first diagnosis was defined as the index date. A 10-year look-back period was used to exclude prevalent HF cases. ATC codes were identified from drug prescriptions. Patients with a 4-year look-back and 2 years of follow-up were included.

Results: Overall, 4357 patients were included (mean ± SD age, 76.6 ± 12.6 years; 27.7% aged ≥85 years; HFrEF, 24.6%; HFpEF, 12.9%; unknown EF, 62.5%). At the index date, 63.0% of patients were treated with an ACEi or an ARB, 62.3% with a BB and 16.0% with an MRA; 18.5% were not receiving treatment. The most common treatment groups (monotherapy or combinations) were: ACEi + BB (HFrEF, 20.5%; HFpEF, 21.0%; unknown EF, 23.5%); BB monotherapy (HFrEF, 12.1%; HFpEF, 14.0%; unknown EF, 15.6%); and ARB + BB (HFrEF, 8.5%; HFpEF, 12.3%; unknown EF, 12.3%) (Figure). The majority of patients receiving an ACEi or ARB at the index date continued to do so for the following 2 years (ACEi, 63.6%; ARB, 60.9%); most of these were receiving doses lower than those recommended by the ESC (70.8% and 88.9%, respectively). A small proportion of patients receiving an ACEi at the index date switched to an ARB over the 2-year period (4.1%) and vice versa (2.6%). Most patients were not receiving the recommended ESC dose before switching (ACEi, 81.8%; ARB, 77.8%). Similarly, most patients who discontinued an ACEi (37.3%) or ARB (39.1%) were not receiving the recommended dose before discontinuation (ACEi, 64.8%; ARB, 87.4%).

Conclusions: A large proportion of patients with HF in Sweden do not receive drug combinations recommended by the ESC. Furthermore, few patients are prescribed ESC-recommended doses of HF drugs and few undergo up-titration of treatment before switching. These findings are remarkable for HFrEF, for which guidelines are established. These findings may be partly reflective of the high proportion of elderly patients studied.

Figure. Most common treatment groups (monotherapy or combinations) received by patients with HF at index.



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BB, β-blocker; MRA, mineralocorticoid receptor antagonist.

P287

Degree of dyspnoea at admission and discharge in patients with heart failure and respiratory diseases

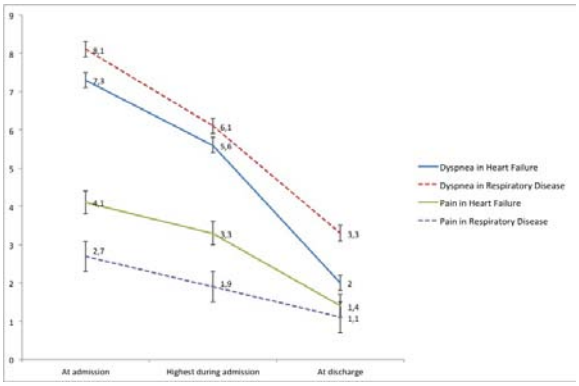
L Vicent[1]; JM Nunez Olarte[1]; L Puente-Maestu[1]; A Oliva[1]; JC Lopez[1]; R Luna[1]; A Postigo[1]; I Martin[1]; F Fernandez-Aviles[1]; M Martinez-Selles[1]
[1]University Hospital Gregorio Maranon, Cardiology, Madrid, Spain

Background: Dyspnoea is a disabling symptom in patients admitted with heart failure (HF) and respiratory diseases (RD).
Aims: The main aim of this study is to evaluate its intensity at admission and discharge and the relation with quality of life. We also describe its management, intensity, and evolution in HF and RD.
Methods: We included prospectively all patients admitted with decompensated HF and chronic obstructive pulmonary disease (COPD)/pulmonary fibrosis during 4 months. Surveys quantifying dyspnoea (Numerical Rating Scale 1-10) and quality of life (EuroQoL 5d) were administered.
Results: A total of 258 patients were included: 190 (73.6%) with HF and 68 (26.4%) with RD (62 COPD and 6 pulmonary fibrosis). Mean age was 74.0 ± 1.2 years, and 157 (60.6%) were men. Dyspnoea before admission was 7.5 ± 0.1. Patients with RD showed greater dyspnoea than those with HF both before admission (8.1 ± 0.2 vs. 7.3 ± 0.2, p = 0.01) and at discharge (3.2 ± 0.3 vs. 2.0 ± 0.2, p = 0.0001). They also presented a higher rate of severe dyspnoea (≥5) at discharge (23 [34.3%] vs. 36 [19.2%], p = 0.02). Opioids were used in 36 (15.5%), mean dose 10.3 ± 1.8 mg Morphine Equivalent Daily Dose. HF patients had worse EuroQoL 5d punctuation than those with RD, due to mobility problems (118 [62.1%] vs. 28[41.8%], p = 0.004), and lower punctuation in Visual Analogue Scale (57.9 ± 1.6 vs. 65.6 ± 1.0, p = 0.006). Progression of dyspnea and pain during hospital admission by Numerical Rating Scale are resumed in the figure. The independent predictors of severe dyspnea at hospital discharge are depicted in the table.
Conclusions: About a quarter of patients admitted with HF or RD persist with severe dyspnoea at discharge. Opioids are probably underused. HF patients have less dyspnoea than patients with RD but present worse quality of life.

Predictors of severe dyspnea

Variable	OR (95% CI)	P
Age	1.1 (1.02-1.2)	0.004
Female Sex	2.2 (1.2-2.3)	0.005
Depression	3.9 (2.1-7.2)	0.001
Non admitted in a intensive care unit	3 (1.1-8.3)	0.05
Respiratory disease	1.2 (1.1-1.4)	0.001

Independent predictors of severe dyspnea (≥5 points) at hospital discharge by logistic regression model. CI: Confidence Interval; OR: Odds Ratio



Progression of dyspnea and pain

P288

The role of IGFBP7, mimecan and osteopontin in the management of heart failure with preserved and reduced ejection fraction.

N G H M Nick Marcks[1]; S Sanders-Van Wijk[2]; HP Brunner-La Rocca[2]
[1]Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands; *[2]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*

On behalf of: TIME-CHF

Background/Objectives: Biomarkers are increasingly used in the management of heart failure (HF), where different pathophysiological pathways are involved. Thus, it is not surprising that the value is not uniform and new biomarkers are sought to better determine the underlying pathophysiology and to predict outcome. Therefore, we investigated three newly discovered biomarkers that were found to be linked with HF in a well described population to determine levels, progression and prognostic value of these biomarkers in comparison to the best established biomarker in HF, i.e. NT-proBNP.
Methods: We performed a retrospective analysis of the TIME-CHF trial, including a total of 622 patients with symptomatic HF (NYHA ≥ II), aged 60 years or older, who either received NT-proBNP or symptom-guided therapy. 462 blood samples were available at baseline (BL) for analysis. Echocardiography was performed at baseline to objectify left ventricular ejection fraction (LVEF), dividing the population in 366 patients with reduced (HFrEF, i.e. ≤45%) and 96 with preserved LVEF (HFpEF, i.e. >45%). Osteopontin (OPN), Mimecan and insulin-like growth factor binding protein 7 (IGFBP7) together with NT-proBNP were measured at baseline and after 1, 3, 6, 12 and 18 months. Follow-up (FU) was up to 5½ years.
Results: At baseline, NT-proBNP and OPN differed significantly between HFrEF and HFpEF, whereas IGFBP7 and Mimecan did not. In HFrEF patients, IGFBP7 levels showed a non-significant fluctuation between FU visits. OPN levels also showed a fluctuating progression, with a non-significant decrease after the 1-month visit and a non-significant increase after the 12-month visit. No significant differences were found between BL and month 18 for IGFBP7 and OPN. Mimecan levels showed a non-significant increase between each individual FU visit, but with an overall significant increase from BL to month 18. Secondly in HFpEF, IGFBP7 levels however did show significant fluctuations over time, with a significant change between BL and month 18. OPN levels showed a significant decrease between the 1 and 3-month visit, but no significant differences between the other individual visits. Like in HFrEF, no significant differences were found between BL and the 18-month visit. Mimecan levels did not significantly in HFpEF change during individual FU visits or the 18-month FU. OPN turned out to be the strongest predictor for overall survival without deaths due to cancer in HFrEF, shortly followed by IGFBP7, NT-proBNP, and Mimecan. In HFpEF, no of the biomarkers reached statistical significance in predicting overall survival without deaths due to cancer.
Conclusion: The three new biomarkers showed a pattern different to that of NT-proBNP despite comparable prognostic values. This supports a different underlying pathophysiological mechanism and suggests that they may be helpful in addition to NT-proBNP and stratifying new therapeutic targets, which needs to be further investigated in future studies.

P289

Coenzyme Q-10 in treatment of patients with heart failure: Results Russian multicenter double blind placebo controlled study

V Y Mareev[1]; Y V Minina[2]; Y V Mareev[3]
[1]Medical Scientific Educational Center of M V Lomonosov Moscow State University, Moscow, Russian Federation; *[2]Russian Society of Heart Failure Specialists , Moscow, Russian Federation*; *[3]Royal Brompton & Harefield Hospitals, Imperial College, London, United Kingdom*

Background: Q-10 was showed the ability to reduce mortality in HF patients in several clinical studies; however, the drug is still is not in ESC guidelines this why additional information about it effects and safety is needed to find its role in HF treatment.
Aim: To estimate clinical effects and safety of water soluble Q-10 in the form of nasal drops (90 mg/day = equivalent 225 mg/day for liposoluble tablets) in patients with heart failure.
Materials: patients with NYHA I-IV and LVEF < 45% who was on optimal medical therapy. Patients were randomized on Q-10 and placebo group. It was multicenter, randomized (ratio 2:1), placebo-controlled, double-blinded study. The Duration of study was 24 weeks. The primary endpoints were: dynamics of NYHA, and scale for HF to Optimize Clinical Status (SHOCS), distance of 6 minutes walking test.
Results: 148 patients were enrolled into the study: 101 in the Q10 group and 47 in the placebo group. There was no statistically significant difference in clinical characteristics and therapy of patients in Q10 and placebo groups. Patients in the Q10 group had greater positive dynamics of NYHA during the study (- 0.16 vs. – 0.08, =0,002), SHOCS (-1.06 vs -0.53, p = 0.036) and 6 minute walk distance (+ 32m vs + 13m, p = 0.044). Also, there were greater positive dynamics of LVEF in Q10 group (+3.1% in Q10 vs + 1.3 placebo, p = 0.038). Patients in the Q10 group have a reduction of BNP level during the study and there was an increase in BNP levels in placebo group (- 34 pg/ml vs + 34 pg/ml, p = 0.032). Safety analysis showed a similar rate of adverse reaction in Q-10 and placebo groups.
Conclusion: Results of our study support, that Q 10 showed clinical, functional, and hemodynamic improvement in clinical relevant CHF. These results can explain mechanisms by which this treatment can improve prognosis in CHF

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Effects of angiotensin receptor blocker at discharge in patients with heart failure with reduced ejection fraction

KH Ki Hong Choi[1]; GY Lee[1]; JO Choi[1]; YJ Lee[1]; ES Ju[1]; ES Jeon[1]
[1]Samsung Medical Center, Divison of Cardiology, Seoul, Korea Republic of

On behalf of: KorAHF investigators
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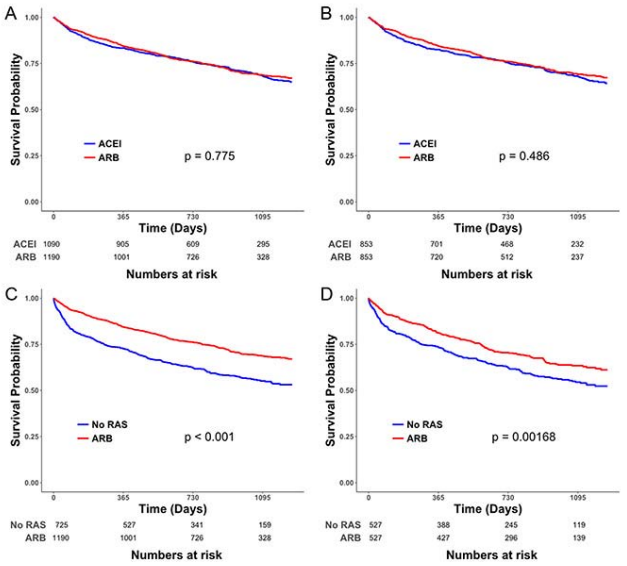
Introduction: There are limited data on comparison between the effects of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blocker (ARB) in patients with heart failure with reduced ejection fraction (HFrEF) after introduction of up-titration strategy.
Purpose: To investigate the association between treatment with angiotensin receptor blocker (ARB) at discharge and clinical outcomes in patients with HFrEF compared with treatment with angiotensin converting enzyme (ACE) inhibitors or no RAS blockade.
Methods: The Korean Acute Heart Failure registry is a prospective multicenter cohort and included patients who were hospitalized for acute heart failure (AHF) from 10 hospitals between March 2011 and February 2014. We studied 3,005 patients with HFrEF (<40%), representing 53.4% of the total study population. Our Study population was divided into an ARB (n=1,190), an ACE inhibitor (n=1,090), and a no RAS blockade (n=725) groups. Propensity score matching was performed to reduce confounding factors.
Results: All-cause death during follow-up occurred in 346 patients (29.1%) in the ARB group, 315 patients (28.9%) in the ACE inhibitor group, and 305 (42.1%) in the no RAS blockade group. After propensity score matching analysis (ARB vs. ACE inhibitor, 853 pairs), there was no significant difference between the two groups in the rate of all-cause death (hazard ratio [HR] 0.94, 95% confidence interval [CI] 0.79 to 1.12, p=0.49). The rate of all-cause death was significantly lower in the ARB group than in the no RAS blockade group in the matched population (ARB vs. no RAS blockade, 527 pairs, HR 0.73, 95% CI 0.6 to 0.89, p=0.002). The ARB group had a significantly lower discontinuation rate within 1 year than the ACE inhibitor group in the overall population (ARB vs. ACE inhibitor, 20.8% vs. 33.6%, p<0.001) and the propensity-matched population (18.5% vs. 34.0%, p<0.001).
Conclusions: For the treatment of AHF with reduced EF after hospitalization, ARB at discharge shows a mortality benefit comparable to that of ACE inhibitors. In addition, tolerability of medication was greater for ARB than for ACE inhibitor.

Outcomes according to RAS blockade use

	ARB	Comparison group	HR (95% CI)	P value
Propensity matched population				
Comparison with. ACEi (n=1706)	246 (28.8)	252 (29.5)	0.94 (0.79 to 1.12)	0.49
Comparison with no RAS (n=1054)	183 (34.7)	303 (57.5)	0.73 (0.6 to 0.89)	0.002

ACEi=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; CI=confidence interval; HR=hazard ratio; RAS=renin-angiotensin system

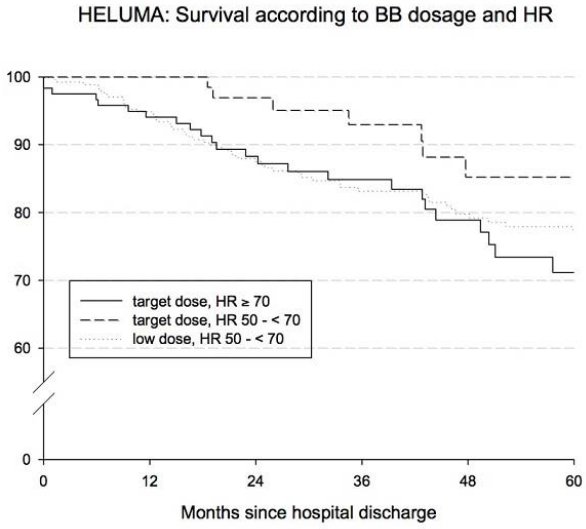


Survival curve per use of RAS blockade

P291
Beta blockers and chronic heart failure: prognostic impact of a dose targeted therapy vs. heart rate targeted strategy

A Corletto[1]; H Froehlich[1]; T Taeger[1]; M Hochadel[2]; R Zahn[3]; C Kilkofski[3]; R Winkler[3]; H A Katus[1]; J Senges[2]; L Frankenstein[1]
[1]University Hospital of Heidelberg, Cardiology and Pneumology, Innere Medizin III, Heidelberg, Germany; [2]Stiftung Institut für Herzinfarktforschung, Ludwigshafen, Germany; [3]Hear Center Ludwigshafen, Ludwigshafen, Germany

Background/Introduction: Beta blockers improve survival in patients with chronic heart failure (CHF). Whether physicians should aim for target dose or target heart rate (HR), however, is still under debate.
Purpose: Our purpose was trying to understand the different impact on survival of beta blockers on a target-dose vs. target heart-rate regimen.
Methods: We identified 1,669 patients with systolic CHF due to ischemic heart disease or idiopathic dilated cardiomyopathy from the University Hospital and the Clinic, Germany. All patients were treated with an angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) and had a history of CHF known for at least 6 months. Target dose was defined as treatment with ≥95% of the respective published guideline-recommended dose. Target HR was defined as 51-69 bpm. All-cause mortality was analysed with respect to beta blocker dosing and resting HR.
Results: 201 (12%) patients met the dose target, 285 (17.1%) the HR target, 627 (37.6%) no target and 556 (33.3%) did not receive beta blockers. During a median follow-up of 42.8 months, 733 (43.9%) patients died, 42 (20.9%), 81 (28.4%), 261 (41.6%), and 349 (62.8%) in each group (p < 0.001). The prognostic impact of being on target dose was comparable to that being on target HR. Prognosis was best in patients who met both the dose and the HR target.
Conclusions: Aiming to the guidelines recommended beta blocker dose or to HR control has a similar positive impact on survival. When on target dose, a supplemental HR control additionally improves survival.



Kaplan-meier for survival

P291 Endpoints and 5-years survival

	Target Dose (Group A) (n = 201)	Target HR (Group B) (n = 285)	No Target (Group C) (n = 627)	No Beta Blockers (Group D) (n = 556)	p-Value
Primary Endpoint					
Follow-Up (months)	42.8 (21.2-62.2)	45.6 (21.8-79.3)	44.6 (20.7-82.3)	38.4 (12.8-77.3)	< 0.05
All-cause deaths at the end of the observation-time	42	81	261	349	0.001
Survival time (months)	36.9 (17.8-57.6)	35.5 (15.6-80)	38.8 (16.3-66.4)	27.4 (9.5-53.3)	0.02
Heart transplantations	6	15	26	50	
Time-to-transplantation	20.8 (17.3-43.2)	26.2 (15-45.6)	25.7 (9.3-50.1)	17.1 (8.3-36.1)	
Mortality after discharge					
1-Year mortality	4.1%	5.1%	9.0%	20.1%	< 0.001
2-Year mortality	8.7%	12.4%	15.7%	30.6%	< 0.001
3-Year mortality	12.9%	16.8%	21.9%	41.4%	< 0.001
5-Year mortality	23.7%	22.7%	37.6%	55.6%	< 0.001

P292

The impact of digoxin on mortality in patients with chronic systolic heart failure

M May Khateeb[1]; R Odeh[1]; A Ahmed[1]; S Saker[1]; R Elshawi[1]; B Bdier[1]; M Almallah[1]
[1]*King Abdulaziz Medical City, Riyadh, Saudi Arabia*

Background / Aim: Prior Studies showed mixed results in association of digoxin use with allcause mortality (ACM). The aim of this analysis is to identify the impact of digoxin use on ACM in a contemporary heart failure (HF) cohort treated with guideline based

Methods: We included 2,298 consecutive patients seen in a HF clinic between 2000 and 2015. Patients were considered to be a digoxin user if he/she received digoxin at any point during the enrollment period in the HF clinic. Patients were matched based on digoxin utility using propensity matching in 2-3:1 fashion. The primary outcome was ACM.

Results: Of 2,298 patients, 325 digoxin users were matched with 750 non-digoxin users. Matched cohort did not have differences among demographics and clinical variables except for worse HF symptomatology and increased prevalence of AF. Overall, the prevalence of the use of guideline suggested therapies was 96%. After a median followup duration of 4 years (IQR 2 - 6 years), digoxin use was associated with increased ACM (21.8% versus 12.9%, unadjusted HR 1.81; 95 CI 1.33 to 2.45; p = 0.001). This association remained significant after adjusting for the propensity score, atrial fibrillation, ejection fraction and New York HF Class (HR 1.74; 95% CI 1.20 to 2.38; P < 0.0001).

Conclusions: In this analysis of well treated HF patients, digoxin was associated with increased ACM. Further randomized controlled trials are needed to determine whether digoxin therapy should be used in well treated HF patients. Until then, routine use of digoxin in clinical practice should be discouraged

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Comparison of outcome in systolic heart failure patients using ivabradine, digoxin or neither of them: a real life study

D Ural[1]; FO Mutluer[1]; H Kaya[2]; O Beton[2]; Y Cavusoglu[3]; A Temizhan[4]; TS Guvenc[5]; H Gungor[6]; M Refiker Ege[7]; M Zoghi[8]; K Karauzum[9]; H Altay[10]; MB Yilmaz[2]
[1]*Koc University, Istanbul, Turkey*; [2]*Cumhuriyet University, Department of Cardiology, Sivas, Turkey*; [3]*Eskisehir Osmangazi University, Department of Cardiology, Eskisehir, Turkey*; [4]*Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey*; [5]*Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Center, Department of Cardiology, Istanbul, Turkey*; [6]*Adnan Menderes University, Aydin, Turkey*; [7]*Koru Hospital, Department of Cardiology, Ankara, Turkey*; [8]*Ege University, Department of Cardiology, Izmir, Turkey*; [9]*Derince Education and Research Hospital , Department of Cardiology, Kocaeli, Turkey*; [10]*Baskent University Istanbul Hospital , Istanbul, Turkey*

On behalf of: TREAT-HF Investigators

Background and Purpose: Ivabradine is considered with a class IIa recommendation as a fourth-line therapy to reduce heart failure (HF) hospitalization and cardiovascular death in symptomatic chronic HFrEF patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite receiving maximally tolerated optimal medical therapy. Digoxin has received a class IIb recommendation to reduce the risk of hospitalization for these patients. A real-life comparison between both agents is lacking. The aim of this study was to compare their effects on cardiovascular (CV) mortality and rehospitalization in a cohort of chronic stable HFrEF patients.

Methods: The Turkish research team-HF (TREAT-HF) is a network undertaking multicenter, observational cohort studies in HF. This study is a subgroup analysis of TREAT-HF outpatient cohorts who fulfilled following criteria: (1) symptomatic HFrEF patients, (2) in sinus rhythm, and (3) using either ivabradine or digoxin on top of maximally tolerated medical therapy or (4) patients meeting ivabradine recommendation criteria but not using any of the study drugs. A total of 297 patients with available follow-up data for CV death and recurrent HF hospitalization were included in the study.

Results: A total of 61 (20.5%) patients were using ivabradine, 83 (27.9%) patients were under digoxin, and 153 (51.5%) were not using any of them despite being in sinus rhythm, and having LVEF ≤35% and a resting heart rate ≥70 bpm. During a mean follow-up of 15 ± 6 months, 59 (19.9%) patients developed CV death and 225 (76%) patients had at least one HF rehospitalization. Rate of CV death was similar among patients using ivabradine and digoxin, but higher in patients not using these agents [CV death: 8 (13.1%) in ivabradine, 13 (15.7%) in digoxin and 38 (24.8%) in neither drug users; p = 0.080]. Patients using digoxin had slightly less rehospitalization [61 (73.5%)] compared to other groups [ivabradine 47 (77%) and neither drug users [117 (77%)] but the difference between the three groups was not statistically significant (p = 0.818). Mean number of HF rehospitalization was also not different (1.5 ± 1.3 in ivabradine, 1.5 ± 1.3 in digoxin, 1.6 ± 1.4 in neither drug users; P = 0.835). In Kaplan-Meier analysis, ivabradine and digoxin had comparable effects on CV death (P = 0.087), rate of rehospitalization (P = 0.823) and combination of these endpoints (P = 0.801).

Conclusion: In this real life registry, ivabradine and digoxin had comparable effects on CV mortality and rate of rehospitalization in chronic HFrEF patients.

P294

NTproBNP in primary care: initial experience.

JL Bonilla Palomas[1]; AL Gamez Lopez[1]; M Moreno Conde[1]; MC Lopez Ibanez[1]; CJ Raez Ruiz[1]; M Cruz Ruiz[1]; E Jimenez Medina[1]; JM Abad Ortega[1]; J Leal Helmling[1]; A Villar Raez[1]
[1]*Hospital San Juan de la Cruz, Úbeda, Spain*

Introduction: The plasma concentration of brain natriuretic peptides (BNP or NTproBNP) can be used as an initial diagnostic test in patients with dyspnea or suspected heart failure (HF). Patients with normal BNP/NTproBNP concentrations are unlikely to have HF. In the other hand, elevated BNP/NTproBNP help establish an initial working diagnosis, identifying those who require further cardiac investigation. However, in Spain, the use of natriuretic peptides in primary care is not widespread.

Purpose: To describe the initial experience in our health area (a population of 150000 inhabitants) of NTproBNP use in primary care as initial diagnostic test in patients with dyspnea or suspected HF.

Methods: From april 2016 NTproBNP is available for the diagnostic evaluation of symptomatic primary care patients, specially with the goal to exclude HF using a cut-point of 300 ng/L. We evaluated the management of these patients according to the test result.

Results: During 8 months a total of 77 simptomatic primary care patients were avaluated with NTproBNP. NTproBNP was <300 ng/l in 45 patients and >300 ng/L in 32 patients. Among patients with NTproBNP<300, only 4 (9%) patients were referred to the cardiologist (No one presented abnormalities in the echocardiography study), 1 patient (2%) was referred to the pulmonologist, and 40 patients (89%) remained in

primary care, as established. Among patients with NTproBNP>300 ng/L, 15 (47%) patients were referred to the cardiologist and 17 (53%) remained in primary care. The last group of patiens presented lower NTproBNP levels than those who were referred to the cardiologist (median 960 ng/L, intercuartile range 434-1399 ng/L vs 2814 ng/L, interquartile range 967-6020 ng/L, respectively, p = 0,01).
Conclusion: In our experience, NTproBNP use among symptomatic primary care patients is particularly appropiate and useful for exclusion of the diagnosis of HF. In addition, NTproBNP use in primary care has reduced the demands of cardiac referrals and has propiciated that a significant number of patients remain managed in primary care.

P295
Ivabradine reduces rehospitalization in patients with chronic systolic heart failure: single country data from OPTIMIZE- HF program

H Sisakian[1]; H Hayrapetyan[2]; L Sahakyan[1]; M Hovhanisyan[1]; H Petrosyan[2]
[1]Yerevan State Medical University Hospital 1: University Cardiology Clinic, Department of General and Invasive Cardiology, Yerevan, Armenia; *[2]Erebouni Medical Center, Cardiovascular Center, Yerevan, Armenia*

Funding Acknowledgements: Servier

Despite advances of heart failure (HF) current therapy HF related rehospitalizations remain a challenging problem. OPTIMIZE HF program was open prospective study aiming to investigate ivabradine associated heart rate reduction influence on recurrent hospitalizations and mortality. Patients with chronic systolic heart failure who had been hospitalized for HF were randomized to ivabradine or regular recommended HF therapy (including maximized beta-blockade). In one country substudy totally 177 patients from two sites included with 12 month follow up period. The mean NYHA , EF and guideline based therapy were comparable in both groups. 58 patients were prescribed to ivabradine according to guideline based recommendations. Ivabradine was associated with fewer all cause and HF hospitalizations: 7(12 %) vs. 33 (28 %) in controls.; incidence rate ratio 0.75, 95 % confidence interval, 0,65-0,72, p = 0.001). In ivabradine treated group 3 deaths (5,2 %) vs 12 deaths (10 %) in controls were observed during 12 month period.
Conclusion: : in patients with chronic systolic heart failure treatment with ivabradine on a background of guideline based HF therapy is associated with a substantial reduction of rehospitalizations during 1 year follow up period. These effects may contribute to the quality of life and survival with reduction of health care costs.

P296
An audit exploring the effectiveness in medical data recording on implementation of an inpatient heart failure proforma

K Lattey[1]; H Bethell[1]; JS Shah[1]
[1]North West London Hospitals NHS Trust, London, United Kingdom

Background: Heart failure is an increasingly complex condition with the aging population and associated co-morbidities. Documentation in healthcare is of paramount importance for the communication of patient care. However, documentation of heart failure is complex, with multiple parameters requiring regular review on wards that may not have continuity of medical staff.
Purpose: The purpose of our project was to assess the safety and feasibility of the introduction of specific heart failure ward round proformas to standardise medical documentation in this patient group.
Methods: Based on national heart failure and ward round clinical guidelines an audit tool was developed to assess the minimum information required for a heart failure patient. The minimum data (each piece of information = 1 point) required for a new admission summary (NAS) (total score 39 points) and for a daily ward round (DWR) (total score 32 points) were collected on patients in a specialised eight-bedded heart failure unit of a cardiology ward in a busy district general hospital. The case notes of 24 patients, over a period of 15 days, before the introduction of the proformas (15 NAS and 99 DWR) and 21 case notes, over a similar period (6 NAS and 98 DWR) after the introduction of the proformas were reviewed by an independent reviewer. Scores were assigned to NAS and DWR data sets. Additionally, qualitative data was collected from members of the multi-disciplinary team using a five point likert scale questionnaire.
Results: 97% of entries included the date, patient's name, hospital number and doctor's name and 93% included documentation of a clear management plan. However, many of the clinically relevant aspects of documentation were poor, for example less than 28% of entries included the patient's past medical history and 16% included the reason for admission. The proformas resulted in a mean increase in 7 points (95% CI = 1.8,12.3; p = 0.01) for the NAS and a mean increase of 10.6 points (95% CI = 9.1, 12.1; p < 0.001) for the DWR (figure 1). Questionnaire results (n = 10) qualitatively demonstrated perceptions from the multi-disciplinary team that the proforma increased documentation. Staff on the ward previously felt that 66.5% of key outcomes were documented "always" or "most of the time", whereas this increased to 92.7% after implementing the proforma.
Conclusion: This audit demonstrates that the ward round proforma improves and standardises medical documentation in the notes for patients with heart failure. This is supported by a qualitative improvement in the medical documentation as assessed by a multi-disciplinary team. Further work is needed to determine if this kind of documentation impacts on patient outcomes.

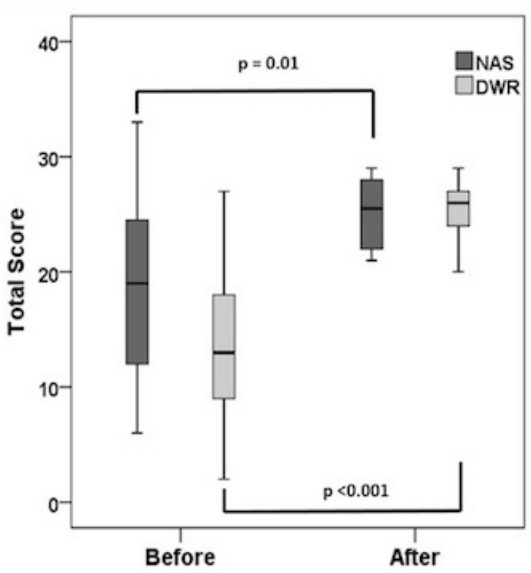


Figure 1

P297
Factors affecting medication adherence trajectories for elderly outpatients with chronic heart failure

VN Larina[1]; II Chukaeva[1]; DG Karpenko[1]; AS Bayramova[1]
[1]The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation

Objectives: To study the factors that determine adherence to threatment of elderly outpatients with chronic heart failure (HF).
Methods: In an open comparative study were included 42 outpatients aged 60 years and older (71,1 ± 9,8 yrs) with chronic heart failure NYHA II-IV class, due to coronary heart disease and/or hypertension. Patients were performed general clinical examination, ECG, EcoCG; Dual-energy X-ray absorptiometry (DEXA). Mental status was assessed using the Mini-mental State Examination scale (MMSE). Adherence to treatment was assessed by scale of complience Morisky – Green. Frailty was defined as three or more of the following: unintentional weight loss, low physical activity, frequent falls, chair stand up test >10 sec, disorders of psychological and emotional status. Results: 64,3% of patients were taking ACE inhibitors, 71,4% - beta-blockers, 9,5% - mineralocorticoid receptor antagonists. The group 1 included 25 patients (59,5%) with treatment adherence, the group 2– 17 patients (40,5%). Patients in the Group 1 were younger (68,6 ± 10 yrs) than patients in the Group 2 (74,8 ± 8,4 yrs). 56% patients of the Group 1 were with the higher education, and in the Group 1 - 64,7% patients were with the higher education. 21 patients (84%) of the Group 1 and 13 patients (76,5%) of the Group 2 were living with the family. 18 (72%) patients of the Group 1 and 8 (47%) of the Group 2 were physically active. 52% patients of the Group 1 and 64,7% patients of the Group 2 had III-IV FC NYHA. Patients of the Group 1 were taking 4,3 ± 1,5, of the Group 2 - 5,8 ± 1,7 medications. 48% and 41% of patients of two groups respectively were taking 5 or more medications. LVEF in patients of the Group 1 were 53,1 ± 13,1% and in patients of the Group 2 - 55,7 ± 13,9%. Comorbidities (anemia, diabetes, atrial fibrillation, COPD, osteoporosis on DEXA) were recorded more frequently in the nonadherence group. Frailty was found in 20% patients of Group 1 and in 35,2% patients of Group 2 and correlated with age (p = 0,003, r=0,45) and high HF FC (p = 0,003, r=0,447), that can be considered frailty as a marker of HF severity. MMSE mean score was 26,7 ± 2,4 points in patients group 1 and 25,1 ± 2,4 points – group 2 (=0,019). Severe cognitive

impairment was detected less frequently in patients of group 1 (8%), than in patients of group 2 (29,4%). Adherence to treatment correlated with impaired cognitive status (p = 0,017, r=0,36). Conclusions: Adherence to treatment of elderly outpatients was 59,5%. Patients with nonadherence to treatment were older, more often they were lonely, less physically active, and they were taking more medications. Also in this patients comorbidities and geriatric syndromes were more frequently detected, and the clinical condition was more severe than that in patients with adherence to treatment. Along with polymorbidity and polypharmacy, frailty had a significant impact in reducing the adherence to treatment, which, in turn, was associated with the frailty.

P298

Ceiling dose of valsartan improves better ventricular-vascular coupling index than usual dose in severe heart failure

W-J Wook-Jin Chung[1]; H Choi[1]; J Moon[1]; M-S Shin[1]
[1]*Gachon University, Cardiology, Gachon Cardiovascular Research Institute, Incheon, Korea Republic of*

On behalf of: VAD trial
Funding Acknowledgements: Norvatis

Background: Effects of Valsartan on LV Diastolic Function in heart failure(VaD) trial was designed as a multi-institutional, prospective and open-labeled trial in patients with stable HF who are intolerable to ACE inhibitors.
Objectives: To compare the effects of non-ceiling dose(80mg bid, NCD) vs. ceiling dose(160mg bid, CD) of valsartan in HF on surrogate markers of functional capacity, LV diastolic and systolic function.
Methods: One hundred thirty eight patients(59.3 ± 12.4 years old; 66% male; LVEF; 29.9 ± 5.9%) were forced-titrated to 160 mg of valsartan, bid for 24 weeks. Echocardiography, treadmill test, Korean activity scale index(KASI) and biochemical studies including NT-proBNP were measured at baseline and after 24-weeks therapy.
Results: Clinical examination and blinded echocardiogram showed significant improvement in NT-proBNP, LVEF, E/E′ ratio, total exercise time and KASI in all, CD(n = 72) and NCD(n = 56), respectively ($p < 0.05$). Interestingly, a significant improvement in the ventricular-vascular coupling index (VVI) was observed in CD with LVEF < 40% (2.4 ± 0.6 → 1.8 ± 0.5, $p < 0.01$). Also, CD showed improvement of symptoms as well as LV mass index compared with NCD($p < 0.05$). Conclusions: As we expected, valsartan led to a notable improvement in LV systolic and diastolic function and exercise capacity in patients with HF. The CD of valsartan showed better improvement of VVI meaning net cardiac performance in the LVEF < 40% and LV mass index, compared with NCD.

P300

Observational Study of the Therapeutic Conduct in Patients with Heart Failure in Mexico: Baseline population characteristics.

J A Jose Antonio Magana Serrano[1]; MA Gamba[2]; RC Cantero[1]; JP Nunez[2]; LR Virgen[3]; S Jimenez[4]; R Sanchez[4]; M Millan[5]; MG Jimenez[6]; P Mendoza[7]
[1]*Hospital of Cardiology at the Siglo XX National Medical Center, Division of Heart Failure and Cardiac Transplantation, Mexico City, Mexico*; [2]*Instituto del Corazon de Queretaro, Queretaro, Mexico*; [3]*Condominio el Carmen, Guadalajara, Mexico*; [4]*Hospital Angeles Puebla, Puebla, Mexico*; [5]*Centro Medico Naval, mexico city, Mexico*; [6]*ISSEMyM, Ecatepec, Mexico*; [7]*Medica Sur, mexico city, Mexico*

On behalf of: CONTEM Study
Funding Acknowledgements: Servier Laboratories Mexico

Background: We don't have a reliable Heart Failure (HF) Registry in Mexico.
Objective: To describe the clinical profile and impact of early treatment optimization after an Acute Decompensated Heart Failure (ADHF) hospitalization.
Methods: We conducted a prospective observational study in patients after an ADHF episode. All the patients were followed at 7, 30, 60 and 90 days after the hospitalization.
Results: We included 41 patients (30 men and 11 women), The mean age was 67.6 ± 12.0 years. The Left Ventricle Ejection Fraction (LVEF) was 28.5 ± 6.6%. The principal etiology was ischemic heart disease 41.5%), followed by cardiomyopathies (29.3%). Functional Class according with NYHA Classification was III (63.4%), II (19.5%) and IV (17.1%). Heart Rate at discharge was 79.2 ± 15.9 BPM, Systolic Blood Pressure 116 ± 21.1 mmHg. , The commonest comorbidities were Diabetes mellitus (29.3%), atrial fibrillation (29.3%) and renal dysfunction (29.3%). Table I show the treatment at hospital discharge.
Conclusions: The clinical profile of HF Mexican patients is similar with another countries. We discover a gap between the recommendations of HF Guidelines and its application in "Real world" scenario, especially with the use of life threatening medications. This represent an urgent call to action. The results of this study will lead us to generate national policies in terms to improve the assessment and care of HF patients in México.

Treatment after discharge

Treatment	Number (%) (N= 41)
ACEIs	15 (36.6%)
ARBs	7 (17.1%)
Beta blockers	26 /63.4%)
Aldosterone antagonists	16 (39%)
Ivabradine	11 (26.8%)
Diuretics	33 (80%)
Digoxin	15 (36%)
Nitrates	2 (4.9%)
Oral anticoagulants	17 (41.5%)
Antiplatelet agents	18 (43.9%)
Statins	19 (46.3%)
Cardiac rehabilitation sessions	21 (51.2%)
Sodium restriction	34 (82.9%)
Nutritional advice and support	30 (73.2%)

P301

The effect of ivabradine on reduction of heart rate and improvement of the quality of life in patients with angina or heart failure in morocco.

A Bennis[1]; A Kifani[1]; N Chemaou[2]; K Adnan[1]
[1]*Private Cardiology practice, casablanca, Morocco*; [2]*Private Cardiology Practice, Tanger, Morocco*

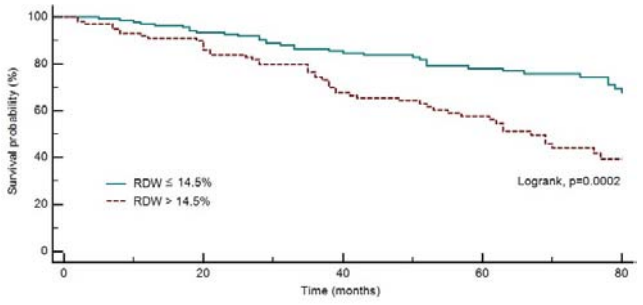
Introduction: A selective reduction of heart rate (HR) has an anti-ischemic and antianginal properties and has demonstrated beneficial effects on cardiovascular events, particularly in heart failure.
Purpose: The ESSENTIEL study aims to observe the effectiveness of exclusive heart rate reduction with Ivabradine on clinical status, LV function and quality of life in patients with angina or heart failure treated over a 4 months.
Methods: Non-interventional, observational conducted on an open cohort in Morocco, in patients with angina or heart failure. Heart rate, a current cardiovascular treatments, an Ejection Fraction, a functional classification of NYHA as well as the SEATTLE self-assessment quality of life questionnaire for angina patients, were documented after 1 and 4 months. The results were analyzed using descriptive statistical methods, by the STATA version 13.
Results: Six hundred and thirteen patients were included, their mean age was 65.77 ± 10.51 years and 60.20% of them were men. 88.11% were receiving a beta-blockers, 42.66% of which was carvedilol. Other concomitant medications included angiotensin-converting enzyme inhibitors (81.06%), long-acting nitrates (32.59%) and calcium channel blockers (37.75%). At baseline, the mean HR of patients was 90.17 ± 14.43 bpm, 14.09% of the patients were in the HR < 75 bpm, 14.96% at the 7580bpm. 37.78% and 40.34% of patients were classified as NYHA II and III, respectively. The mean value of the five SAQ domains of coronary artery disease was: physical limitation 27.91 ± 19.67, stabilization of angina 54.99 ± 29.63, angina frequency 64.25 ± 30.76, treatment assessment 42.75 ± 26.30, and perception of disease 33.96 ± 29.02. After 1 and 4 months of Ivabradine treatment the mean HR was reduced to 70.73 ± 10.65 bpm and 62.40 ± 7.60 bpm, respectively. A 4.83% improvement in mean LVEF was observed after one month of treatment and 8.27% at 4 months, accompanied by a shift in NYHA classification towards better functional class 55.85% in the V1 and 80.98% in the V2. The mean value of the five SAQ domains at 1 month and 4 months was 43.27 ± 21.09 and 55.11 ± 20.28 for the physical limitation of 77.66 ± 21.79 and 90.18 ± 14.17 for the stabilization of angina, 81.46 ± 22.15 and 91.65 ± 13.54 for the frequency of angina 69.44 ± 20.41 and 82.9 ± 17.19 for the evaluation of the treatment, 62.34 ± 26.33 and 78.37 ± 21.49 for the perception of the disease. The rate of adverse events was 1.14%.
Conclusion: over 4 months of treatment, using Ivabradine is associated with a significant reduction in HR, an improvement in the symptoms of heart failure and stable angina, these benefits were accompanied by improved QoL and good general tolerability.
Key words: heart rate, angina, Ivabradine, NYHA, Quality of life, heart failure.

P302

Red cell distribution width: an easily available parameter and an independent predictor of mortality in chronic heart failure

A R Ana Rita Marinheiro[1]; P Amador[1]; L Parreira[1]; C Sa[1]; T Duarte[1]; M Fonseca[1]; S Goncalves[1]; R Rodrigues[1]; R Caria[1]
[1]*Hospital Center of Setubal, Setubal, Portugal*

Background: Red Cell Distribution Width (RDW), a measure of the variability in the size of circulating erythrocytes, is an easily available parameter in clinical practice. In some studies a higher RDW has been described as a marker of poor prognosis in patients with heart failure (HF). However, it is unknown whether the upper limit of reference range or another cut-off value should be used in this setting.
Purpose: To evaluate the prognostic significance of RDW and to determine a cut-off value associated with an increased risk of mortality in patients with chronic HF.
Methods: We evaluate all consecutive patients admitted in a single-center HF clinic between January 2008 and December 2013. Patient baseline characteristics, laboratory values, echocardiographic evaluation and current medication were obtained in the first visit. The primary endpoint was all-cause mortality.
Results: Two-hundred and thirty-four (234) patients (mean age 65 ± 11 years, 73% male) were studied. During a mean follow-up of 57 ± 27 months, 72 patients (31%) died. The multivariate Cox regression model selected RDW (HR 1.20, p = 0.0017), creatinine level (HR 1.46, p = 0.0001) and age (HR 1.04, p = 0.0014) as independent predictors of mortality while the use of angiotensin-converting enzyme (ACE) inhibitors (HR 0.35, p = 0.0005) and angiotensin II receptor antagonists (ARAII) (HR 0.38, p = 0.0148) were independently associated with lower mortality. The optimal cut-off value for RDW by receiver operating characteristic (ROC) curve was 14.5% (AUC 0.590, p = 0.02), which corresponds to the upper limit of reference range. The Kaplan-Meier analysis demonstrated that a RDW above this value was associated with an increased long-term mortality (p [logrank] = 0.0002) (figure).
Conclusion: In this population of chronic HF patients, RDW was an independent preditor of mortality and a value greater than 14.5% was associated with an increased risk of long-term mortality.



Kaplan-Meier survival curve

P303

Prognostic significance of asymptomatic hyperuricemia and allopurinol therapy in chronic systolic HF outpatients

R Rossella Bani[1]; L Caldini[2]; A Paoletti Perini[1]; M Nesti[1]; P Pieragnoli[1]; G Ricciardi[1]; M Beltrami[1]; L Padeletti[1]
[1]Careggi University Hospital (AOUC), Arrhythmic Unit, Florence, Italy; [2]Italian College of General Practitioners, Florence, Italy

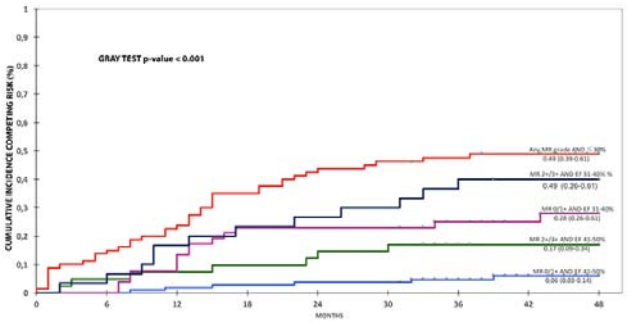
Background: Heart failure (HF) is a disease of epidemic proportions, with relevant social impact and increasing hospitalization and mortality rates. Hyperuricemia has been identified as a potential risk factor for HF development and progression. However, guidelines concerning asymptomatic hyperuricaemia (AHU) have not yet been published and specific literature is lacking. Association between high serum uric acid (SUA) levels and cardiovascular (CV) disease such as hypertension, ischemic stroke and HF has been demonstrated. Some authors underlined that xanthine oxidase inhibitors improves outcome in patients with elevated SUA. However recent findings reported opposite results.
Purpose: To evaluate the impact of AHU and of Allopurinol therapy on CV events, including hospitalizations and death, in chronic systolic HF outpatients.
Methods: We retrospectively evaluated 239 consecutive systolic HF outpatients undergoing complete clinical and instrumental cardiac examination between 2003 and 2010 at a single Cardiologic Unit. All patients were followed up to 5 years. Hyperuricemia was defined for SUA levels > 8 mg/dL and > 6 mg/dL for men and women respectively, as previously suggested. To avoid the confounding effect of treatment, the study population was divided into 2 subgroups: Group T included patients treated with Allopurinol, Group NT those not treated. The study endpoint was the combination of CV hospitalization and death. Cumulative event rates for CV events were estimated by the Kaplan-Meier method. Multivariable Cox analysis was performed to evaluate the endpoint related risk, according to SUA levels, after correction for gender and estimated glomerular filtration rate (eGFR) as covariates.
Results: Among 239 patients, (mean age 70 ± 9 years), 96 (40%) had hyperuricemia; 50 (21%) received Allopurinol therapy (Group T), whereas 189 (79%) did not (Group NT). In Group T hyperuricemic patients were 46 (40%), in Group NT 20 (24%). Baseline clinical characteristics were comparable, except for eGFR (NT: 66 ± 23 ml/min, vs T: 56 ± 20 ml/min; p = 0,004). Over a mean follow-up of 46 ± 13 months, 143 (60%) CV events occurred; 111 (78%) in Group NT, 32 (22%) in Group T. Hyperuricemic patients in Group NT showed a higher rate of CV events when compared to normouricemic patients [34 (74%) vs 77 (54%); p = 0,016)] and AUS was an independent predictor of CV events (HR:1,108; 95%CI:1,005-1,221; p = 0,039). By contrast, in Group T, CV events rate was similar between normouricemic patients (responder to Allopurinol treatment) and hyperuricemic patients (non-responder to Allopurinol treatment) [19 (59%) vs 13 (41%); p = 0.904], and CV events risk did not differ between responder and non-responder to treatment (HR:0,884; 95% CI:0,436-1,791; p = 0,733).
Conclusions: In chronic systolic HF outpatients, SUA level proved an independent predictor of major CV events. However, Allopurinol therapy is not able to improve prognosis in such patients.

P304

Clinical, humoral and echocardiographic profile of patients with heart failure can predict long-term quality of life.

M Michele Di Mauro[1]; R Petroni[1]; D Clemente[1]; A Calafiore[1]; S Romano[1]; M Penco[1]
[1]University of L'Aquila, Department of Cardiology, L'Aquila, Italy

Background. The aim of this retrospective study is to identify clinical, humoral and echocardiographic variables predicting poor QoL.
Methods. From 2009 to 2012, 310 patients were admitted forf HF with reduced ejection fraction (HFrEF). Median age was 78 years (72-84), males and females were 165 and 145. All the patients were followed by phone, calling the patients or the referring GP. The number of re-hospitalization was collected from Outpatients clinic or Hospital Administration Database. The Minnesota Living with Heart Failure Questionnaire (MLHFQ) was used as the instrument to evaluate QoL. MLHFQ < 24 is a good QoL, 24-45 is moderate QoL and >45 is poor QoL, as reported in the literature. The primary event was poor QoL at 4 year (Median follow up was 40 months), defined MLHFQ >45 and/or re-hospitalization. To avoid competing risk, Cumulative Incidence (CI) was used for univariate analysis. Multivariable analysis was performed with Cox Hazard Proportional Regression. MLHFQ was administered to all survivors. Results. Seventy-nine patients died at median time of 21months (6-35); 4-year cumulative mortality was 25 ± 2%. Re-hospitalization was recorded in 60 (19%) with a mean number of re-hospitalization of 2.6. Among 231 survivors, MLHFQ score was good in 99 (42%), moderate in 50 (21%) and poor in 88 (37%). Cumulative incidence of poor QoL was 26 ± 3% at 4 years. Univariate analysis identified following risk variables: mitral regurgitation grade stratified by EF class (Fig. 1), NT-proBNP at admission and discharge, ischemic disease and diabetes, severe tricuspid regurgitation, atrial fibrillation in presence of dilated left atrium, hypercholesterolemia, chronic pulmonary disease, age classes, left ventricular diastolic diameter, renal impairment. The multivariable analysis identified following variables: Hypercholesterolemia (HR 2.5, 1.3-4.9), chronic pulmonary disease (1.9, 1.1-3.3), ischemic heart disease and diabetes (2.1, 1.3-3,5), NT-proBNP (1.02, 1.01-1.03), severe tricuspid regurgitation (2.3, 1.3-3.9), atrial fibrillation with dilated left atrium (1.1, 1.01-1.2) and mitral regurgitation (MR) by EF: MR 2+/3+ & EF 41-50% (4.7, 1.5-15), MR 0/1+ & EF 31-40% (5.0, 2.0-12.-6), MR 2+/3+ & EF 31-40% (5.3, 2.7-10.3) and any MR grade with EF ≤30%. C-statistics of the final model was 0.78. Conclusions. Clinical, humoral and echocardiographic profile is crucial to predict long-term quality of life of patients admitted for heart failure.



Impact of MR by EF on quality of life

P305

The role of simple clinical indicators in the assessment of prognosis in patients with stable systolic heart failure

LV Prokopova[1]; MY Sitnikova[1]; EV Shlyakhto[1]
[1]*Federal Almazov Medical Research Centre, Heart failure, Saint Petersburg, Russian Federation*

Today, patients with systolic heart failure developed high-tech treatments that can improve the prognosis. Prediction of the course of the disease helps the doctor in the selection of patients for high-tech methods of treatment: the implantation of a cardioverter-defibrillator, heart transplantation, implantation of mechanical circulatory support. Objective: In a sample of patients with stable systolic heart failure reveal the routine clinical and laboratory parameters associated with the risk of an adverse outcome for 1 year.
Materials and Methods: The study included 212 patients, observed a cardiologist, a specialist in heart failure. Inclusion criteria: patients with heart failure II-IV functional class,ejection fraction of left ventricular (Simpson) less than 35% between the ages of 18 to 70 years, signed a voluntary consent to participate in the study. After 1 year, analyzed the predictive value of 200 parameters.
Results: 83% (n = 176) examined patients were men, 17% - women (n = 36). At the time of enrollment age was 49,7 ± 11,5 years. Left ventricular ejection fraction was 24,8 ± 7,4%. After 1 year, 64% of patients survived (n = 135), at 2% (n = 5) system implanted mechanical circulatory support, in 24% (n = 51) recorded fatal. In deceased patients revealed the following parameters are unfavorable outcome: speeded respiratory rate and heart rate, low blood pressure; hyponatremia, low hemoglobin, erythrocytes, lymphocytes, total cholesterol and high levels of c-reactive protein, urea, total bilirubin and erythrocyte distribution width in the serum volume; hepatomegaly, the presence of an aneurysm of the left ventricle; Statin therapy, anticoagulants (warfarin), desagregants, inotropic support. On the basis of these parameters regression analysis was performed. A model of one-prediction systolic heart failure, including heart rate (p = 0,005), systolic blood pressure orthostasis at 5 minutes (p = 0,001), respiratory rate (p = 0,001), the width of erythrocyte volume distribution (p = 0,036).
Conclusions: The model prediction of systolic heart failure consists of simple indicators. This model is available for outpatient and inpatient care.

P306

Phase angle by bioelectrical impedance vector analysis as predictor of prolonged hospital stay

L Verdeja-Vendrell[1]; D Gonzalez-Islas[2]; A Orea-Tejeda[2]; A Navarrete-Penaloza[2]; R Sanchez-Santillan[2]; A Jimenez-Cepeda[2]; G Perez-Cortes[2]; V Pelaez-Hernandez[2]; A Figueroa-Herrera[2]; S Torres-Montiel[2]; B Robles-Uribe[2]
[1]*Autonomous University of Puebla, Puebla, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Distress Clinic , Mexico City, Mexico*

Background: The phase angle (PA) is an indicator of malnutrition, functionality and integrity of cell membranes, as well as a predictor of prolonged hospital stay in patients with sepsis, cancer and cirrhosis, adverse outcomes after cardiac surgery and mortality in patients with heart failure (HF). However, in patients with HF and respiratory failure (RF) the relationship between PA and prolonged hospital stay has not been explored. Objective: To determine if PA is a predictor for prolonged hospital stay in patients with HF and RF.
Methods: A cross-sectional study was performed including hospitalized patients aged 18 years or older with a diagnosis of HF and RF. Prolonged hospital stay was defined as ≥ 7 days, while the cut-off point for the PA was 4.5°. A logistic regression was performed to determine the risk of prolonged hospital stay associated with a low phase angle. Results: 43 patients (26.3%) were men (mean age 54.02 ± 21.76 years). Patients with prolonged hospital stay had a higher prevalence of COPD (52.6% vs 10.2%, p = 0.005) and HF (42.1% vs. 10.5 %, p = 0.027), and had lower PA (4.63° ± 1.38 vs 5.78° ± 1.56, p = 0.022) compared to patients with short hospital stay. No differences were found between the groups in total body water, extracellular water or other comorbidities such as hypertension, diabetes mellitus, obesity and kidney disease. Patients with a PA < 4.5° had 7 times more risk of having a prolonged hospital stay (OR 7.65, CI 95%, 1.37 - 42.71, p = 0.020). Conclusions: A PA less than 4.5° is associated with a longer hospital stay in patients with HF and RF.

P307

The association between left ventricular ejection fraction, previous chronic heart failure and mortality in patients with acute coronary syndrome (data of Russian RECORD-3 registry)

AD Erlikh[1]
[1]*City hospital 29, Cardiac Care Unit, Moscow, Russian Federation*

On behalf of: Participants of RECORD-3 registry

Background and Purpose: As well known the low left ventricular ejection fraction (LVEF) and previous chronic heart failure (CHF) in patients with acute coronary syndrome (ACS) have association with bad prognosis. The aim of analysis was estimate of association the combination of low LVEF and previous CHF with short-term and medium-term prognosis in patients included in independent Russian ACS registry RECORD-3.
Methods: All consecutive patients with ACS symptoms hospitalized in 47 participant hospitals within 1 month (Mar-Apr 2015) were included in RECORD-3 registry. The CHF was defined as the presence of exercise dispnoe or documented CHF before ACS onset. Low LVEF (< 40%) as defined as local hospital rules. As adverse events were estimated in-hospital death and any causes death during 6 month after discharge from the hospitals.
Results: Among 2370 patients included in registry previous CHF was in 47.6%, and low LVEF – in 11.2%. 6-month follow-up was performed in 1433 patients. Among patients with previous CHF the rate of in-hospital death was 1.3% in patients with normal LVEF and 9.3% in patients with low LVEF (relative risk [RR] 7.34; 95% confidential interval [95CI] 3.36-16.08; p < 0.0001). Among patients without with previous CHF the rate of in-hospital death was 2.0% in patients with normal LVEF and 3.6% in patients with low LVEF (RR 1.81; 95CI 0.54-6.01; p = 0.23). Among patients with previous CHF the rate of 6-month post-discharge death was 4.1% in patients with normal LVEF and 13.5% in patients with low LVEF (RR 3.32; 95CI 1.72-6.39; p = 0.0006). Among patients without with previous CHF the rate of 6-month post-discharge death was 3.1% in patients with normal LVEF and 6.8% in patients with low LVEF (RR 1.81; 95CI 0.67-7.08; p = 0.38).
Conclusion: The data of Russian registry ACS RECORD-3 showed that statistically significant association of low LVEF with high in-hospital and 6-month post-discharge death was revealed only for patients with previous CHF. For patients without previous CHF this association there is only as trend.

P308

Prognostic markers in heart failure patients with mid-range ejection fraction

EE Yakubovskaya[1]; IYU Giverts[1]; MG Poltavskaya[1]; VP Sedov[1]; MV Serova[1]; MD Kuklina[1]; AA Doletsky[1]; AL Syrkin[1]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Objectives: heart failure (HF) with left ventricular ejection fraction (LVEF) in a range of 40-49% has been recently defined by 2016 European guidelines as HF with mid-range EF (HFmrEF). The data concerning prognosis and prognostic predictors in this specific type of patients is scarce. The aim of the study was to identify significant predictors of adverse outcomes among various clinical and laboratory parameters in patients with HFmrEF.
Methods: we retrospectively analyzed the subgroup of 35 patients with HFmrEF, NYHA classes II-III (26 male, mean age 59.9 ± 12,6 years, mean EF=44,3 ± 3,4%) previously included in the prospective observational study. All patients were on optimal medical treatment. At baseline the patients underwent comprehensive investigation including standard clinical examination, echocardiography, 6-minute walk test (6-mwt) and cardiopulmonary exercise testing. Average follow-up amounted 35,9 ± 22,5months. Composite end-point of cardiovascular death and hospitalization for HF was considered a primary analysis variable.
Results: Composite end-point was observed in 51,4% of patients (n = 18). Numerous clinical and laboratory variables were analyzed with respect to their prognostic value. ROC-analysis demonstrated the significant independent predictive value of left atrial volume (AUC=0,798; 95% CI 0,619 ± 0,918; p = 0,0002), E/e' AUC=0,741; 95% CI 0,533 ± 0,891; p = 0,016) and 6mwt distance (AUC=0,746; 95% CI 0,558 ± 0,884; p = 0,01).
Conclusions: In a subgroup of patients with HFmrEF left atrial volume, E/e' ratio and 6-minute walk test distance appear to be strong predictors of cardiovascular death or heart failure hospitalization similarly to HF patients with reduced or preserved EF. Further investigations are necessary to confirm this data.

P309

Can thyroid function be a predictor of poor prognosis in heart failure?

CS Catarina Sofia Soares De Sa[1]; T Duarte[1]; S Goncalves[1]; R Marinheiro[1]; MARTA Fonseca[1]; R Rodrigues[1]; D Ferreira[1]; S Correia[1]; A Lourenco[1]; F Seixo[1]; R Caria[1]
[1]*Hospital Center of Setubal, Cardiology, Setubal, Portugal*

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 in patients with heart failure are sparse.
Purpose: Evaluate the relationship between values of TSH and T4 and death/rehospitalization in a population of patients with heart failure (HF)
Methods: Retrospective study of a population of patients admitted in our heart failure clinic with mean ejection fraction of left ventriculum of 32%. Values of TSH

and T4 were divided into quartiles and the characteristics between them were compared. The occurrence of events (rehospitalization/death/combined endpoint) was determined and compared.

Results: Our population included 150 patients, aged 67 ± 11 years and mostly men (72%). Mean TSH values were 1,75 ± 0.96nmol/L and mean T4 values were 1,06 ± 0,18ng/dl. Of the patients evaluated none had abnormal values of thyroid function and 3 were treated with levothyroxine. During the follow up of these patients 8 died (5,3%) and 50 were re-admitted (33%) for decompensated HF.

We compared the quartiles of T4 and verified higher prevalence of hypertension in higher values of T4 e higher prevalence of anemia in lower values of T4. There was no difference in sex, age, ejection fraction, NYHA class or HF etiology between the quartiles.

A higher prevalence of mortality was demonstrated in patients with T4 values in the upper quartiles (1,10 a 1,22; >1,23).

There was no association between TSH values and rehospitalization, death or combined endpoint.

Conclusion: In our population we fail to verify a significative association between valued of THS and T4 and the endpoints of death and rehospitalization. Probably , a larger population will be necessary to verify a predictive association between thyroid hormones and the endpoint studied

Table I

	T4	p			
	0,99	1-1,1	1,11-1,22	>1,23	
Sex	7 (23,3%)	8 (26,7%)	9 (30%)	6 (20%)	0,743
Age	75 + -9	66 + -13	63 + -13	73 + -11	0,076
BNP	551±432	802±437	326±434	1330±1181	0,019
Hypertension	7 (24,1%)	4 (13,8%)	8 (27,6%)	10 (34,5%)	0,006
Anemia	3 (75%)	1 (25%)	0	0	0,069
Re-hospitalization	2 (16,7%)	4 (33,3%)	4 (33,3%)	2 (16,7%)	0,712
Death	0	0	1 (33,3%)	2 (66,7%)	0,059

Comparison between characteristic of population and events in the quartiles of T4 values

P310

Left ventricular remodeling and inflammation features as predicting factors of sudden cardiac death after myocardial infarction

I A Leonova[1]; S Boldueva[1]; E Bykova[1]
[1]*North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation*

The sudden death (SD) after myocardial infarction (MI) is an important issue, so this study was dedicate to comparison of patients survived and died suddenly after MI. 667 patients with MI were included. In addition to standard methods marker of apoptosis of CD 95 lymphocytes and monocytes CD 14, interleukin 1β, 2, 6, and TNF α were investigated. The patient's follow-up period was 1 - 7 years. During this period, 61 people died suddenly.

When comparing the SD and survived patients no significant differences in age, smoking, hypertension, diabetes were found. Number of male was higher (90.2% vs 74.3% p = 0.006) among SD patients, and these patients had more frequent history of repeated MI (55.7% vs 24.3% p = 0.001) and circular MI (8.2% vs. 2.8% p = 0.01). Acute and chronic heart failure, left ventricular aneurysm, ventricular extrasystole were detected significantly more frequently among SD patients compared with survived (23% and 6.3% 4*10-6; 34.4% and 8.9%3*10-9; 41% vs 19.3% 8*10-5; 48.9% vs 21.4% 8*10-5 respectively). SD patients had greater decrease in left ventricular ejection fraction (LVEF) (47,1% ± 13,6% against 56,5% ± 10,7%, p = 1*10-8), larger values of end-diastolic size (57,6 ± 8,6mm ± 6,6mm against 52,3 p = 2*10-7), end-diastolic volume (180 ± 125,8 ± 60,7ml against 38,4ml p = 2*10-5), end-systolic size (43,3 ± 12mm against 35.3 ± 7,8mm, p = 9*10-8), end-systolic volume of the left ventricle (93,9 ± 43,3ml vs. 53.1 ± 22 ml, p = 1*10-7) and left atrium (42.8 ± 4,7mm against 40.4 ± 5.3mm, p = 0.002) and more frequently recorded LV hypertrophy (3.9 % versus 57.6%, p = 0.03). Among suddenly died restrictive type of diastolic dysfunction was detected more frequently (27.3% vs. 10.8% p = 0.004). The level of lymphocyte in the first day of MI was significantly lower among SD patients than in survivors (1,3 ± 0,5 109 / l vs. 1,8 ± 0,7 10 left ventricular akinesia / L; p = 0.03). On other parameters (IL 1β, IL-2, IL-6 and TNF-α, expression of CD95 and CD14 on lymphocytes, monocytes) statistically significant differences were not found. In order to determinate the independent factors for the risk of development of SD stepwise multivariate Cox analysis was conducted. For SD development such risk factors were the most important: acute left ventricular failure III-IV class Killip (β = 1,09; OR = 2.99; 95% CI = 1,44-6,18; p = 0.003) LV end-diastolic dimension (β = 0,05; OR = 2.46; 95% CI = 1,07-2,68; p = 0.02), LVEF (β = -0,03; OR = 1.63; 95% CI = 0,40-1,75; p = 0.05) and a left ventricular akinesia (β = -0,88; OR = 2.42; 95% CI = 1,30-5 41; p = 0.006). The most important and independent factors for predicting of SD in patients after MI are the end-diastolic dimension, LVEF, LV akinesia, LV failure III-IV by Killip. Leukocytes and their classes, pro-inflammatory cytokines (IL-1.beta, IL-2, IL-6 and TNF-α), and the expression of CD95 on lymphocytes and CD14 monocytes do not have independent prognostic value in acute MI.

P311

Echocardiography parameters in heart failure patients with moderate functional mitral regurgitation and correlation with six months outcome

DR Vakilian Aghouee[1]; DR Ghaderi[1]; MR Sheikhandalibi[1]; MS Bijari[1]; MS Sahranavard[1]
[1]*Mashad University of Medical Sciences, Cardiology Department, Mashad, Iran (Islamic Republic of)*

Introduction: Heart failure is a growing problem with different etiologies. Left Ventricular Ejection Fraction (LV EF) and functional Mitral regurgitation (FMR) are important prognostic factors. This study planned to evaluate echocardiography as an available tool in differentiating etiologies of FMR and correlation with 6 months outcome.

Methods: and material: In this prospective cross-sectional study 62 HFreduced EF:less than 40%) patients with moderate FMR (40 ICM and 22 NICM) were enrolled. Patients were followed for 6 months. Primary end-points were death, re admission and NYHA class. Logistic regression and multivariate analysis was done.

Results: Mean age was 62.6 ± 11.7 and 47.4 ± 19.2 in ischemic and non-ischemic groups respectively.LV sphericity index, posterior tenting angle (PTA) and time to pick inferior S was significantly different within groups (p < 0.01). The best cut point for LV sphericity index was 1.46 and for PTA ≥40 degrees.Time to pick inferior S ≥ 140 msec and anterior Sm-velocity < 4 m/s indicate ischemic etiology(table 1). Primary end-point (readmission or death) was observed in 35.2% (17.5% and 9.1% in ischemic and non-ischemic groups, respectively). Age, diabetes, smoking, time to pick inferior Sm≥ 140 msec and ischemic etiology of FMR was associated with re admission and higher mortality(HR=3.2).

Conclusion: PTA> 40 degrees and time to peak inferior Sm>140 msec are independent predictors of MR etiology, readmission and mortality.

table 1

Parameters of Mitral valve deformity				
Anterior tenting angle (degrees)	35.2 ± 9.8	34.3 ± 11.7	34.9 ± 10.4	0.671 [b]
Posterior tenting angle (degrees)	50.7 ± 12.2	40.1 ± 11.4	43.7 ± 12.6	0.002* [a]
Medio lateral MVAD (cm)	2.8 ± 0.5	2.9 ± 0.8	2.9 ± 0.6	0.099 [b]
Antero posterior MVAD (cm)	2.8 ± 0.5	3.0 ± 0.5	2.9 ± 0.5	0.205 [a]
Tenting area (cm2)	2.2 ± 0.8	2.3 ± 0.9	2.2 ± 0.8	0.691 [b]
Coaptation depth (cm)	9.3 ± 2.0	10.4 ± 4.4	9.7 ± 3.0	0.423 [b]
TDI parameters in the level of mitral valve annulus				
Inferior S-velocity (m/s)	3.7 ± 1.1	4.8 ± 1.2	4.1 ± 1.3	0.001* [b]
Time to pick inferior S (millisecond)	194.2 ± 71.0	146.2 ± 72.9	164.2 ± 75.2	0.031* [b]
Anterior S-velocity (m/s)	3.8 ± 1.1	5.0 ± 1.5	4.2 ± 1.4	0.004* [b]
Time to pick anterior S (millisecond)	155.0 ± 67.9	151.6 ± 53.4	153.7 ± 62.3	0.857 [b]

Table-1: Echocardiography parameters of LV, RV, mitral deformity and TDI

P312

Improving heart failure care in hospitals with and without a multidiscipinary heart failure program:results from optimize Colombia project

C I Clara Ines Saldarriaga[1]; G Gonzalez[2]; S Navarrete[3]; LE Echeverria[4]; M Novoa[5]; N Murillo[6]; A Rivera[7]; MJ Rodriguez[4]; B Rolong[8]; G Trout[9]; C Martinez[1]; CV Arguello[10]; L Semanche[11]; E Contreras[12]; J Vanegas[13]
[1]*Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia*; [2]*Fundacion Santa Fe de Bogota , Cardiology - heart failure, Bogota, Colombia*; [3]*clinica fundadores, medicos asociados, cardiology, Bogota,*

Colombia; [4]*Fundacion cardiovascular, cardiology, Bucaramanga, Colombia*; [5]*clinica del norte, cardiology, medelin, Colombia*; [6]*Angiografia de occidente, cardiology, Cali, Colombia*; [7]*Clinica los Rosales, universidad tecnologica de Pereira, cardiology, Pereira, Colombia*; [8]*Fundacion cardiotoracica, cardiology, Barranquilla, Colombia*; [9]*Universidad del Magdalena, cardiology, Santa Marta, Colombia*; [10]*clinica Leon XIII, cardiology, medellin, Colombia*; [11]*Clinica del norte, cardiology, Barranquilla, Colombia*; [12]*clinica de occidente, cardiology, cali, Colombia*; [13]*Fundacion cadiovascular-instituto del corazón, cardiology, Manizales, Colombia*

On behalf of: optimize Colombia project
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Multidisciplinary Heart failure programs (MHFP) , that included a specialized staff with a cardiology and a nurse, with a training in this field are a cost effective strategy to reduce mortality, new hospitalization and to improve quality of life, however this programs are not widely available in our country and they are just focused in some hospitals. The prevalence of heart failure is increasing so it is necessary to have a strategy to improve the care of patients in hospitals with less resources.
Objective: To describe the impact of the implementation of OPTIMIZE program in the composite outcome of decompensation + hospitalizations after 30 days from hospital discharge. The OPTIMIZE program was a simple strategy implemented at hospital discharge and included: education in the hospital, a material to enhance adherence to treatment , up titration of medications in the hospital and early initiation of ivabradine to obtain a goal heart rate of 60 – 70 bpm. The outcomes were analyzed by the hospital status: with and without MHFP.
Results: 436 patients were included, 44% (N= 192) from hospitals with MHFP and 56% (n= 244) without MHFPs. 68% were male and 32% were females, the mean age was 66 years with a mean ejection fraction of 32%. 20.3% of the patients from MHFP were treated with Ivabradine vs 59.83% in hospitals without MHFP. Only 61.4% of the patients were followed in an outpatient service. After 30 days from the hospital discharge, the percentage of composite outcome of decompensations + hospitalizations was 2.2% vs 3.3 % (p = 0.530), in hospital with and without MHFP respectively.
Conclusion: The implementation of optimize program in hospitals without a MHFP improves the results of the short term prognosis of patients, with a rate of composite outcome of decompensations + hospitalizations at 30 days similar than the observed in MHFP.I,.The implementation of this program and the use of ivabradine early in the vulnerable phase, from the hospital discharge, is a good strategy to standardize the health care in all type of hospitals as a part of a quality-improvement initiative.

P313

Prognostic impact of the combined presence of anemia and chronic kidney disease on long-term mortality in patients with reduced and preserved ejection fraction following myocardial infarction

L Savic[1]; I Mrdovic[1]; M Asanin[1]; G Krljanac[1]; D Matic[1]; R Lasica[1]; D Rajic[1]
[1]*Clinical Center of Serbia, Institute for Cardiovascular Disease, Emergency Hospital, Belgrade, Serbia*

Purpose: Anemia and chronic kidney disease (CKD) are common and frequently coexist in patients with acute coronary syndrome. The aim of this study was to analyse the prognostic impact of anemia and CKD on long-term mortality in patients with reduced and preserved ejection fraction (EF) following ST-elevation myocardial infarction (STEMI).
Method: we included 2157 consecutive STEMI patients who were treated with primary percutaneous coronary intervention (pPCI). Anemia was defined as baseline hemoglobin level < 12g/dl in women and < 130g/dl in men. CKD was defined as baseline creatinine clearance < 60ml/min/m2. Reduced EF was defined as ≤ 40%. Echocardiographic examination was performed before disharge. Patients presenting with cardiogenic shock and patients on hemodyalisis were excluded.
Results: Among analysed patients 573 (26%) patients had reduced and 1496 patients (74%) had preserved EF; anemia was present in 98 (4.5%) patients, CKD in 273 (12.6%) patients and combined presence of anemia and CKD in 70 (3.2%) patients. Five year mortality rate was 21.1% and 2.9% in patients with reduced and preserved EF respectively. Estimated five year survival probability in patients with reduced and preserved EF according to the pesence of anemia, CKD and CKD + anemia is shown in the Figure 1. After multivariable adjustement in Cox regression model CKD, anemia and the combined presence of CKD and anemia were independent predictors of 5-year mortality in patients with reduced ejection fraction: CKD HR 1.89 (95%CI 1.1-3.54), p = 0.047; Anemia HR 1.83 (95%CI 1.3-4.5), p = 0.048; CKD + Anemia HR 2.4 (95%CI 1.3-4.5), p = 0.006. Other independent predictors of 5-year mortality in patients with reduced EF were older age, Killip class >1 at admission and postprocedural flow TIMI < 3. In patients with preserved EF there was no association of anemia and/or CKD with 5-year mortality and independent predictors of 5-year mortality in patients with preserved EF were only older age and Killip class >1 at admission.
Conclusion: The combined presence of anemia and chronic kidney disease is a strong independent predictor of five year mortality in patients with reduced EF following STEMI. In STEMI patients with preserved ejection fraction anemia and chronic kidney disease are not risk factors for long-term mortality.

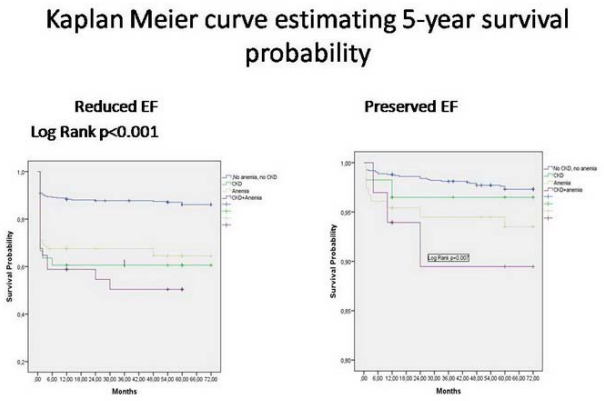


Figure 1

P314

Gender difference of obesity paradox in systolic heart failure

BS Byungsu Yoo[1]; JW Son[1]; JY Kim[1]; MS Ahn[1]; SH Lee[1]; JH Yoon[1]
[1]*Wonju College of Medicine, Yonsei University, Division of Cardiology, Department of Internal Medicin, Wonju, Korea Republic of*

Background: Obesity is often associated with better clinical outcomes in heart failure. This so called 'obesity paradox' still remains controversial. The aim of present study was to investigate the prognostic value of the obesity in patients hospitalized with systolic heart failure.
Method: We performed a pooled analysis of data from the three multi-center, observational heart failure studies, Survey of Guideline Adherence for Treatment of systolic Heart Failure in Real World; COAST, Clinical Outcomes in Relation with Serum Sodium Level in Asian Patients Hospitalized for Systolic Heart Failure]. Patients (> 18 years old) who were hospitalized with systolic heart failure (EF≤45%) were eligible for present study. We divided the subjects into 2 groups, Normal BMI group (BMI < 25) and High BMI group (BMI ≥ 25). Study endpoints included all cause mortality and any re-hospitalization within 1 year. All analysis was performed separately by gender.
Results: Total 3145 patients (male 1824, female 1321) were enrolled. In men, high BMI group (n = 563) presented more hypertension (52.9% vs. 47.9, p = 0.048). The high BMI was significantly associated with lower 1 year mortality rate (OR 0.543, 95% CI 0.355-0.833) after adjusting for age, hypertension, diabetes, ischemic heart failure, previous myocardial infarction, serum creatinine, anemia (Hb < 10g/dL) and ejection fraction. In women, patients with high BMI (n = 404) more presented hypertension (61.4% vs. 54.1%, p = 0.016), diabetes (45.2% vs. 35.2%, p < 0.001), and chronic kidney disease (12.9% vs. 8.1%, p = 0.005). After adjustment for clinical characteristics, high BMI was not significantly associated with 1 year mortality (OR 0.739, 95% CI 0.450-1.216) or 1 year rehospitalization (OR 0.958, 95% CI 0.696 - 1.319).
Conclusions: In pooled analysis from 3 Korean heart failure registries, there was a gender difference of obesity paradox. The high BMI was independently associated with lower 1 year mortality rate in systolic heart failure, especially in men.

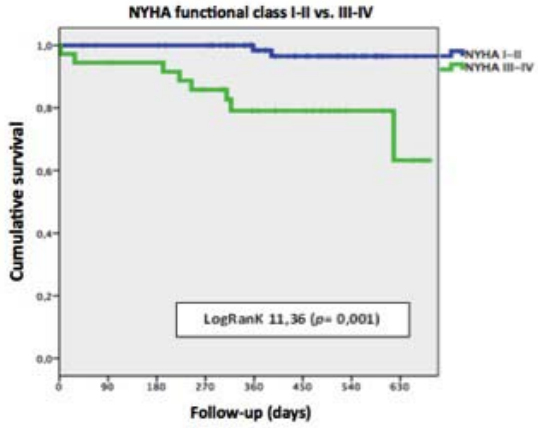
P315

Clinical predictors of mortality in patients with severe aortic stenosis undergoing surgical and percutaneous aortic valve intervention

I S S Ines Goncalves[1]; JR Agostinho[1]; IA Ricardo[1]; J Rigueira[1]; ARF Francisco[1]; T Guimaraes[1]; GL Silva[1]; R Santos[1]; A Ferreira[1]; AG Almeida[1]; F Pinto[1]
[1]*Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

Introduction: Symptomatic severe aortic stenosis (AS) presents high mortality, and the only prognosis modifiable therapy is aortic valvular intervention (AVi). There are some factors identified as predictors of mortality in patients (pts) undergoing

AVi, such as the presence of ventricular dysfunction and coronary artery disease; however, it's not known which co-morbidities and factors associated with the clinical presentation influence the prognosis most directly.
Purpose: To determine the clinical predictors of mortality in the pts diagnosed with AS submitted to AVi.
Methods: A retrospective unicentric study was made, with inclusion of consecutive pts with AS (excluding low flow low gradiente and and paradoxal aortic stenosis), diagnosed during 2015 in a tertiary center, who underwent AVi until the end of the follow-up period. Clinical data were collected and their relationship with mortality was analyzed using the Cox regression statistical method and Kaplan-Meier survival analysis.
Results: A total of 278 pts (54% women and 46% men, mean age 74 ± 9 years) were included, with a mean follow-up of 389 ± 186 days, of which 192 were submitted to intervention (51.8% women, mean age 75 ± 8.8 years; 87% underwent aortic valve replacement surgery and 13% underwent percutaneous implantation). Mortality in this subgroup was 9.7% (vs. 50% in the subgroup not submitted to AVi). The mean time from the diagnosis of AS to AVi was 59 days. In patients undergoing AVi, NYHA functional class ($p = 0.007$) and NTproBNP ($p = 0.002$) were identified as clinical predictors of mortality at diagnosis, using univariate Cox analysis. None of the cardiovascular comorbidities analyzed (hypertension, diabetes, obesity, coronary artery disease, cerebrovascular disease and chronic kidney disease) showed a significant relationship with mortality in this group. Using multivariate analysis by Cox regression, only the NYHA functional class was an independent predictor of mortality: patients in class > 2 had a 12 times higher risk of death (hazard ratio = 11.7, 95% CI, 1.37-100, P = 0.025); (P = 0.001).
Conclusions: In this group of pts with AS, the NYHA functional class was the only clinical predictor of mortality. This reflects the importance of early intervention in the course of the disease, as soon as the first symptoms appear, avoiding the delay of the intervention only for more advanced functional classes, regardless of the comorbidities or the age of the patient.



P316

Significance of NT-proBNP, TnT and soluble ST2-receptor concentrations in risk stratification in patients with acute decompensated heart failure

V N Protasov[1]; AA Skvortsov[1]; OY Narusov[1]; D E Protasova[2]; GA Tkachev[1]; VP Masenko[1]; SN Tereshchenko[1]
[1]*Russian Cardiology Research and Production Complex, Moscow, Russian Federation*; [2]*National Research Center for Preventive Medicine, Moscow, Russian Federation*

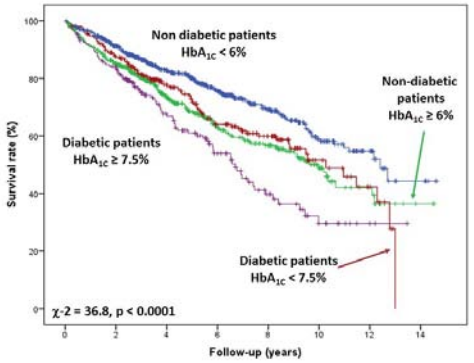
Background: sST2 and NT-proBNP are more strong predictors of adverse long-term prognosis in pts with ADHF compared TnT. Purpose: to evaluate the significance of sST2, TnT and NT-proBNP in risk stratification pts with ADHF.
Methods: In the study were included 159 pts with ADHF. Blood samples to determine NT-proBNP, sST2, hsTn-T concentrations were collected at the admission and at discharge from the hospital. 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 concentrations of NT-proBNP, hsTnT and sST2. During the period of hospitalization there was a reduction of biomarker concentrations, $p < 0,01$. During 1-year follow-up 56 pts (35,2%) had CV events. At the admission biomarker concentrations in low risk pts (without CV events) were significantly lower compared with high risk pts (with CV evnts): NT-proBNP 2819 (1233;4912,7)pg/ml vs 5215,5 (3010;8768,5)pg/ml; hsTnT 28,2 (18,85;41) pg/ml vs 41,1 (25,3;69,1) pg/ml; sST2 53,64 (37,04; 72,35) ng/ml vs 72,07 (59,27;117,75) ng/ml, $p < 0,0001$ for all. The similar trend was observed and at discharge: NT-proBNP 1439 (753,3; 2604,5)pg/ml, vs 3358 (1623,7;5432,7) pg/ml, hsTnT 24,49 (19,8;36,6) pg/ml vs 33,9 (23,2;59,2)pg/ml; sST2 31,28 (21,68;48,00) ng/ml vs 60,19 (37,25;98,35) ng/ml, $p < 0,0001$ for all.The positive predictive value was found for all tested markers. TnT concentration had the most predictive capacity in the short-term period (90 days): at the admission AUC 0,811 (0,707-0,916) and at the discharge (AUC 0,756 (0,612-0,892). In the long-term period there was a decrease of predictive capacity of TnT concentration at the admission(6 month: AUC 0,715 (0,614-0,817), 12 month: AUC 0,663 (0,567-0,758). At the discharge NT-proBNP and sST2 concentrations had the most predictive capacity relatively the primary end point during 1-year follow-up: AUC=0,726 (95% CI 0,637-0,816), AUC=0,768 (95% CI 0,682-0,854), respectively. The model with combined determination of the concentrations of the two markers at the discharge (sST2 and NT-proBNP) had the most predictive value in the medium-term (180 days), and long-term (365 days) prognosis: AUC 0,821 (0,74-0,901), R 3,33 (1,726-6,434) < 0.0001 and AUC 0,802 (0,72-0,884), OR 3,54 (2,078-6,035), < 0.0001, respectively. Including of sST2 and NT-proBNP concentrations at the discharge in the clinical and biochemical model was accompanied by increase of AUC from 0,812 (0,72-0,905); R 2,43 (1,66-3,56), < 0.0001 to 0,883 (0,816-951); R 2,86 (2,12-3,85), < 0.0001 for 6 month and from 0,747 (0,653-0,84); R 2,37 (1,657-3,389), < 0.0001 to 0,85 (0,774-0,927); OR 2,91 (2,166-3,916), < 0.0001 for 12 month. Conclusion: The TnT has a relationship with a adverse prognosis in the short -term period. NT-proBNP and sST2 at the discharge reflect the adverse prognosis in pts with ADHF in the medium-term and long-term follow-up period.

P317

Prognostic impact of glycated hemoglobin in patients with systolic heart failure

E Hebbar[1]; C Le Goffic[1]; T Mercier[1]; V Cousin[1]; H Riddon[1]; A Duva Pentiah[1]; M Fertin[1]; N Lamblin[1]; C Bauters[1]; P De Groote[1]
[1]*Lille University Hospital, Institut Coeur-Poumon, Lille, France*

Background: There are conflicting results concerning the prognostic impact of glycated hemoglobin (HbA1C) in patients with systolic heart failure.
Objectives: To analyze the prognostic impact of HbA1C in stable patients with chronic systolic heart failure.
Methods: All the patients were ambulatory, stable with optimal medical therapy at the time of inclusion. All the patients performed an echocardiography, a cardiopulmonary exercise test and a radionuclide angiography. Blood samples were drawn at rest.
Results: 1583 patients were included, of whom 436 were diabetics. Mean age was 55 ± 12 years old, left ventricular ejection fraction (LVEF) was 37 ± 12%, ischemic cardiopathy was more frequent in diabetic patients (59% vs 39%, $p < 0.0001$). During a follow-up period of 4.2 years [2.42 – 7.09], there were 508 deaths, of whom 391 were cardio-vascular related deaths, 74 non-urgent cardiac transplantations, 28 UNOS1 transplantations, 24 LVAD implantations and 11 patients were lost of follow-up. Cut-off values for HbA1C were determined by ROC curves analyses in diabetic and in non-diabetic patients. As shown in the Figure, non-diabetic patients with a HbA1C ≥ 6% had the same survival than diabetic patients with a HbA1C < 7.5% (chi-2 = 15.8, $p < 0.0001$ between the 2 subgroups of non-diabetic patients and chi-2 = 7.96, $p = 0.005$ in diabetic patients). HbA1C ≥ 7.5% in diabetic patients was an independent predictor of survival even after multiple adjustments (clinical data, LVEF, VO2 and BNP) (HR = 1.56 [1.09-2.24], $p = 0.02$). However, in non-diabetic patients, HbA1C ≥ 6% was not an independent predictor of survival.
In conclusion, HbA1C is a predictor of survival in a population of stable patients with systolic heart failure, particularly in diabetic patients.



Survival curves in different subgroups

P318

Prognostic importance of inclusion serum cystatin C level for eGFR calculation by CKD-EPI equation in patients with first decompensation of HFPEF

TV Nikiforova[1]; D Shchekochihin[1]; AS Shilova[1]; HE El Manaa[1]; AA Lomonosova[1]; PH Y Kopylov[1]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: HFPEF in a common phenotype of HF with substantial increase in incidence and prevalence. There is no direct prognostic estimator for these patients to the date. Decreased renal function is a well-known independent negative prognostic factor in heart failure patients populations. Several formulas are accepted for eGFR. The best formula for eGFR estimating in HFPEF patients regarding prognostic information remains unknown. The aim of the study is to compare prognostic significance of decreased eGFR derived by CKD-EPI equation based on serum creatinine and serum cystatin C versus CKD-EPI equation based on serum creatinine only in patients with first decompensation of HFPEF.
Materials and methods: 117 patients with first decompensation of HFPEF (average age 71,6 ± 9,1 years; 65,8% - women) were included in prospective study. 85,5% of the patients had atrial fibrillation with persistent form in 38,5%.25,6% had diabetes mellitus.32,5% had ischemic origin of HF. HFPEF was diagnosed according to ECS guidelines. All patients signed informed consent. The study was approved by ethical committee. Blood samples for biomarkers estimation erre derived during index hospitalization. The patients were mentored by phone monthly during first six months and every three months until 24 month period. Mortality, HF hospitalization and combined end point were used. Kaplan-Mayer curves with Log-rank test were used for survival analysis. P value of 0,05 or less was considered to be significant.
Results: Average eGFR at inclusion was 50,2 ± 16,9 ml/min/1.73 sq.m by serum creatinine formula and 46,4 ± 16,1 ml/min/1.73 sq.m by combined formula ($p < 0,05$). Addition of cystatin C to equation regrouped the patients by CKD classification with more numbers for 3B stage (41,0% vs 35,9%; $p < 0,05$). During follow-up 45,3% of the patients reached combine end-point, mortality was 11,9%,hospitalization due to HF was necessary in 33,3% of the patients. Study population was divided for two groups, with eGFR> 45 ml/min/1.73 sq.m or eGFR <45 ml/min/1.73 sq.m by both formulas. The groups divided by serum creatinine formula did not differ significantly in mortality, morbidity and combined end-point achievement during survival analysis ($p = 0,07$; $p = 0,7$ and $p = 0,2$). However, if the patients were divided by combined creatinine and serum cystatine C formula, the patients with eGFR <45 ml/min/1.73 sq.m demonstrated significantly increased achievement of combined end-point ($p = 0,03$) and increased mortality ($p = 0,03$).
Conclusions: Decreased baseline eGFR by CKD-EPI equation based on serum creatinine and cystatine C levels is a negative prognostic factor in patients with first decompensation of HFPEF. However decreased eGFR by CKD-EPI equation based on serum creatinine only does not. Significance of serum cystatine C level in HFPEF can be attributed to more accurate renal function measurement or GFR-independent estimation of alerted collagen turnover.

P319

A simplified bedside prognostic tool for heart failure: the proSCANNED score

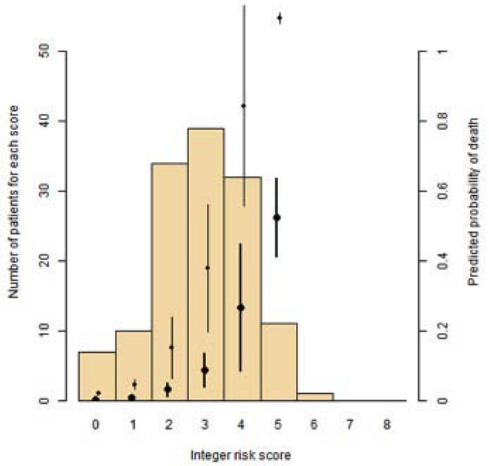
K Kamila Solecki[1]; CM Duflos[2]; B Mandoorah[1]; F Huet[1]; S Cade[1]; F Cransac[1]; A Agullo[1]; P Battistella[1]; G Mercier[2]; F Roubille[2]
[1]*University Hospital Arnaud de Villeneuve, cardiology, Montpellier, France*; [2]*University Hospital of Montpellier, economic evaluation unit, Montpellier, France*

Background: Heart failure (HF) represents a major cause of death and hospitalisation. Evaluation of the prognosis remains challenging. Various prognostic risk models have been already developed. The MAGGIC model is promising but is in reality difficult to apply in practice. Similarly to the CHADS implemented in the daily management of patients with atrial fibrillation, there is a need for a very simple tool to assess the prognosis of HF very quickly.
Purpose: To define a simplified bedside prognostic tool for HF.
Methods: All patients with stable HF were prospectively included in cardiology outpatient clinic. Based on the original mortality model of MAGGIC, some of its complicated and with poor additional-value variables were excluded and natriuretic peptides were added. The primary outcome was to predict one-year mortality.
Results: 182 patients were included. 65 (38%) patients died during a median follow-up of 42 months. 8 independent predictor variables were identified to built the integer score including: natriuretic peptides Nt-proBNP>5000 pg/mL, current smoker, chronic obstructive pulmonary disease, age ≥ 75 years-old, no betablockers, dyspnea graduated at III or IV of New York Heart Association scale, left ventricular ejection fraction ≤ 35%, diabetes. This score is able to predict 1-year survival, with an area under the curve of 0.79 (95%CI : 0.7-0.89).
Conclusion: The proSCANNED score appears as a new tool, easy to integrate in daily practice in HF patients. The power of this score has to be validated especially on larger population.

Selected variables for the integer score

	Rate ratio	95 % CI	Log Rate Ratio	p-value
Age ≥ 75 years	3.01	(1.61-5.63)	1.10	0.0006
NYHA III-IV	2.28	(1.12-4.65)	0.83	0.0228
LVEF ≤ 35 %	2.61	(1.31-5.17)	0.96	0.0061
Nt-proBNP >5000 pg/mL	3.22	(1.64-6.33)	1.17	0.0007
No betablockers	3.55	(1.70-7.42)	1.27	0.0007
Diabetes	3.32	(1.74-6.34)	1.20	0.0003
COPD	1.79	(0.84-3.82)	0.58	0.1340
Current smoker	1.83	(0.92-3.64)	0.61	0.0844

CI, confidence interval; COPD, chronic obstructive pulmonary disease; LVEF, left-ventricular ejection fraction; Nt-proBNP, Nt-pro brain natriuretic peptide; NYHA, New York Heart Association.



Predicted mortality by integer score

P320

Heart rate response to exercise in heart failure patients: the prognostic role of metabolic-chronotropic relation and heart rate recovery

J Jan Benes[1]; P Hajdusek[1]; M Kotrc[1]; E Benesova[2]; J Kautzner[1]; P Jarolim[3]; V Melenovsky[1]
[1]*IKEM, Prague, Czech Republic*; [2]*First Faculty of Medicine and General Teaching Hospital, Institute for History of Medicine, Prague, Czech Republic*; [3]*Brigham and Women's Hospital, Department of Pathology and TIMI-group, Boston, United States of America*

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Background: The dynamics of the sinus node response to exercise is linked to functional capacity and outcome in heart failure (HF). The goal of the work was to analyze determinants and impacts of cardio-acceleration, described by the concept of metabolic-chronotropic relation (MCR) and of cardio-deceleration, described by heart rate recovery (HRR).
Methods: A cohort of 25 healthy controls and 78 patients with advanced systolic HF and optimized medical and/or device therapy (97% receiving beta-blockers, 54% ICD) underwent maximal cardiopulmonary exercise test and were prospectively followed.
Results: HF patients had impaired exercise performance compared with controls (pVO2 15 ± 4 vs. 29 ± 7 ml.kg-1.min-1, $p < 0.0001$) and lower both MCR slope (0.54 ± 0.24 vs. 0.90 ± 0.15, $p < 0.0001$) and HRR (14.7 ± 7.9 vs. 18.3 ± 4.2 min-1, $p = 0.03$), representive MCR slope of a control subject and HF patients are in Fig. 1. In HF patients, MCR slope was inversely associated with beta-blocker dose (r=-0.24), NYHA class (r=-0.28) and HF duration (r=-0.25), whereas HRR with estimated glomerular filtration rate (eGFR, r= 0.39), age (r= -0.28) and BMI (r= -0.30, all $p < 0.05$). During a follow-up of 1269 ± 933 days, 64% patients experienced an adverse outcome (death, urgent transplantation, left ventricular assist device implantation). Those patients had higher NT-proBNP ($p = 0.02$), worse left ventricular

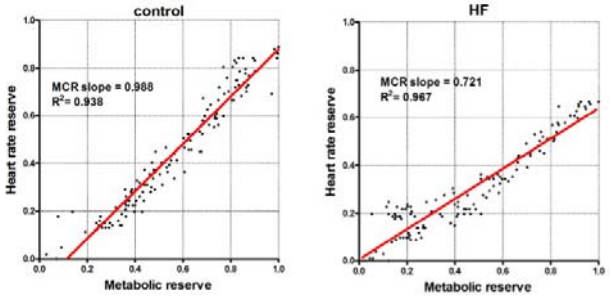
systolic function (LVEF, p = 0.03) and lower MCR slope (p = 0.02) but not HRR (p = 0.19). MCR slope (but not HRR) was a significant outcome predictor (p = 0.02 for Cox unadjusted model) even after adjustment for LVEF, serum natrium, systolic blood pressure, eGFR and NT-proBNP (p = 0.039), Table 1.

Conclusion: MCR slope is associated with different clinical variables than HRR. Compared to HRR, MCR slope provides significant prognostic information in HF patients.

Predictive power of MCR slope

	Hazard ratio	95% confidence interval	p
Model 1	0.25	0.075- 0.82	0.022
Model 2	0.19	0.036- 0.95	0.04
Model 3	0.23	0.054- 0.93	0.039

Cox proportional hazard model. Model 1. MCR slope alone; Model 2: MCR slope adjusted to left ventricle ejection fraction, serum natrium, systolic blood pressure, estimated glomerular filtration rate; Model 3: Model 2 + NT-proBNP



MCR slope in a control and HF patient

P321

A re-examination of the beta-blocker evaluation of survival trial (BEST) using composite outcomes including emergency department visits

L Shen[1]; PS Jhund[1]; UM Mogensen[2]; L Koeber[2]; JJV Mcmurray[1]
[1]University of Glasgow, the British Heart Foundation Cardiovascular Research Centre, Glasgow, United Kingdom; [2]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark

Background: We examined the influence of choice of endpoint on trial size, duration and interpretation of results in patients with heart failure enrolled in the Beta-blocker Evaluation of Survival Trial (BEST).

Methods: We used BEST to examine the effect of bucindolol on the now standard composite of cardiovascular death or heart failure hospitalization (CVD/HFH), compared with the original primary endpoint of all-cause death, expansion of this composite to include emergency department (ED) visits and the consequences for trial size and duration. We also undertook an analysis of recurrent events in addition to conventional time-to-first event analysis. The effect of treatment on death, the CVD/HFH composite, and on the expanded composite outcome (CVD/HFH/ED visit) and its components was examined using Cox regression analysis. Recurrent events were analysed using the Lin, Wei, Ying and Yang (LWYY) method.

Results: 448 placebo patients (33%) and 411 bucindolol patients (30%) died (HR 0.90; 95% CI 0.78-1.02; p = 0.11); CV deaths were 388 (29%) and 342 (25%), respectively (0.86; 0.75-1.00; p = 0.045). 730 patients (54%) experienced CVD/HFH on placebo and 624 (46%) on bucindolol (0.80; 0.72-0.89; p < 0.001). Adding ED visits increased these numbers to 768 (57%) and 668 (49%), respectively (0.81; 0.73-0.90; p < 0.001). 568 placebo patients (42%) experienced HFH compared with 476 (35%) bucindolol patients (0.78; 0.69-0.89; p < 0.001) with a total of 1333 and 1124 admissions, respectively. With the same statistical assumptions, using the composite endpoint (or expanded composite) instead of all-cause death would reduce trial size by 40% and duration of follow-up by 69%. Using the LWYY method, the rate ratio for recurrent events (CVD/HFH) was 0.83 (0.73-0.94), p = 0.003.

Conclusion: Choice of endpoint has major implications for trial size and duration, as well as interpretation of results. Use of a broader composite endpoint and inclusion of recurrent events showed a consistent benefit of bucindolol.

P322

Hospitalization for heart failure following cardiac resynchronization therapy: Impact in mortality

M Maria Trepa[1]; R Baggen Santos[1]; I Silveira[1]; B Brochado[1]; MF Oliveira[1]; C Gomes[1]; VA Dias[1]; C Roque[1]; PV Vieira[1]; H Reis[1]; S Torres[1]
[1]Hospital Center of Porto, Cardiology, Porto, Portugal

Introduction: Cardiac resynchronization therapy (CRT) in advanced heart failure (HF) is not always accompanied by improvement. Some patients fail to respond to CRT and their evolution is complicated by hospitalization for HF and decreased survival rates. We aimed to study the impact in mortality of hospitalization for HF after CRT implantation.

Methods: Single-center retrospective observational study including 303 patients who underwent cardiac resynchronization therapy (CRT). The median follow-up time was of 34.1 ± 21.1 months. Cox hazard models were adjusted for variables who proved significant (p < 0.1) in univariate regression analysis: clinical response (improvement in at least 1 NYHA class 6-12 months after CRT), echocardiographic response [improvement of > 5% in left ventricular ejection fraction (LVEF) 6-12 months after CRT], etiology (ischemic vs non-ischemic), chronic kidney disease [(CKD) defined as a creatinine clearance ≤ 60 ml/m2 determined by MDRD], diabetes and impaired right heart function after CRT. Kaplan-Meier survival curves were determined for analysis of the association between hospitalization for HF and all-cause mortality at 5 years.

Results: The study population (n = 303) had a mean age of 69 ± 10 and previous to CRT implantation, most patients (77%) were in NYHA class III. The mean LVEF was 27.5 ± 6.1% and mean QRS duration was 160 ± 24ms.

During follow-up 19% of patients (n = 57) were hospitalized for HF. In univariate analysis, they were more likely to be ischemic (p = 0.02) diabetic (p = 0.05) and have CKD (p < 0.01). Age, gender, pre-implantation LVEF, QRS duration and pattern were not statistically different between the groups. Patients who presented worst clinical and echocardiographic response to CRT were at increased risk for hospitalization (p < 0.01 in both cases), as were those with impaired right heart function after CRT (p = 0.02). In multivariate analysis absence of echocardiographic response (OR 4.58; p = 0.07) and CKD (OR 4.09; p = 0.01) proved to be independent predictors of HF hospitalization.

The primary outcome of all-cause mortality at 5 years occurred in 60% of patients with HF hospitalizations and in 22% of the control group (log rank p < 0.01). After adjusting for confounding factors by cox regression HF hospitalizations was an independent predictor of mortality (HR 5.9; 95% CI 1.6- 21.2)

Conclusions: Hospitalization for HF after CRT implantation is independently associated with mortality. Absence of echocardiographic response and CKD identified a subgroup of CRT patients who are at significantly increased risk for adverse outcomes.

P323

Long-term prognostic information of BNP levels in patients with stable systolic heart failure

T Mercier[1]; E Hebbar[1]; P Pigny[2]; M Fertin[1]; A Duva Pentiah[1]; N Lamblin[1]; P De Groote[1]
[1]Lille University Hospital, Institut Coeur-Poumon, Lille, France; [2]Lille University Hospital, Biological Department, Lille, France

BNP is a powerful prognostic parameter in pts with systolic heart failure (SHF). Few studies have analyzed the long-term prognostic power of a single determination of BNP.

Methods: BNP was measured with the Shionoria BNP RI kit. Survival analyses were performed in all the pts and in subgroups with the exclusion of deceased pts during the first yrs of follow-up (FU).

Results: We included 459 ambulatory pts: 56 ± 12 yrs, NYHA class III: 25%, ischemic:46%; LVEF:33 ± 12%, left atrial diameter:44.6 ± 8 mm, peak VO2:15.4 ± 5.1 ml/min/kg, (59.3 ± 17.3 %). BNP: 110 [41-322] pg/ml. During a FU of 7.78 yrs [0.26 - 14], there were 311 deaths (68%) of whom 245 (53%) were cardiac related, 5 pts were lost to FU, 45 had cardiac transplantation. In univariate analyses, BNP was a predictor of survival even after the exclusion of deceased pts during the 7 first years of FU. In Cox analyses, BNP was an independent predictor of survival during the 3 first yrs of FU (Table). In contrast, peak VO2 remained an independent predictor of long-term survival (at least 7 yrs).

In conclusion, in stable pts with SHF, despite the variability of its measurement, BNP was an independent predictor of survival 3 years after its determination.

Independent predictors of survival		
Variables	HR	p
All pts		
Age	1.042 [1.03 - 1.054]	< 0.0001
%VO2	0.974 [0.965 - 0.983]	< 0.0001
Left atrial diameter (LAD)	1.028 [1.012 - 1.045]	0.001
BNP	1.002 [1.001 - 1.004]	0.001
Survivors≥ 1 yr (397 pts)		
Age	1.047 [1.03 - 1.06]	< 0.0001
%VO2	0.976 [0.966 - 0.995]	< 0.0001
BNP	1.002 [1.001 - 1.004]	0.005
LAD	1.019 [1.002 - 1.036]	0.03
Survivors≥ 2 yrs (368 pts)		
Age	1.047 [1.03 - 1.05]	< 0.0001
%VO2	0.978 [0.968 - 0.988]	< 0.0001
BNP	1.003 [1.001 - 1.005]	0.004
Survivors≥ 3 yrs (328 pts)		
Age	1.05 [1.04 - 1.07]	< 0.0001
%VO2	0.975 [0.965 - 0.985]	< 0.0001

P324

Prevalence and prognostic impact of co-morbidities in heart failure: data from the Slovenian national heart failure registry

M Pusnik Vrckovnik[1]; B Jug[2]; A Marolt[1]; D Kosuta[3]; LM Hodoscek[4]; M Mulej[5]; T Ravnikar[3]; CS Pusnik[1]; M Valentincic[6]; T Vizintin Cuderman[2]; M Lainscak[7]
[1]General Hospital Slovenj Gradec, Slovenj Gradec, Slovenia; *[2]University Medical Centre of Ljubljana, Department of vascular diseases, Ljubljana, Slovenia*; *[3]Izola General Hospital, Izola, Slovenia*; *[4]General Hospital Murska Sobota, Murska Sobota, Slovenia*; *[5]General Hospital Jesenice, Jesenice, Slovenia*; *[6]General Hospital Nova Gorica, Nova Gorica, Slovenia*; *[7]General Hopsital Celje, Celje, Slovenia*

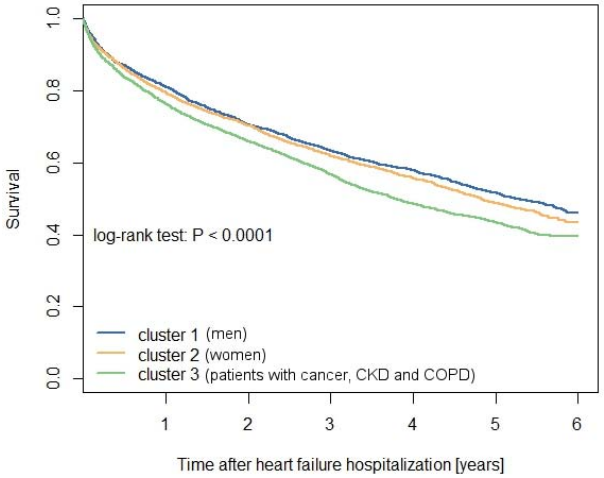
Background: Heart failure (HF) is a condition of elderly and polymorbid patients thus management is challenging.
Purpose: To prospectively assess the prevalence and prognostic impact of co-morbidities in a nation-wide population of patients with HF.
Methods: Data from the prospective registry of heart failure (started in 2014 by the national cardiology society and including a nation-wide network of general and university hospitals) were analysed. Patients with HF enrolled by June 2015 were included, and HF-related events (HF-related mortality, hospitalisations and emergency department visits) were recorded. Anaemia, atrial fibrillation (AF), depression, diabetes mellitus, coronary artery disease (CAD), chronic kidney disease (CKD) and chronic pulmonary obstructive disease (COPD) was assessed, and their respective prognostic impact was analysed using Cox multivariable model.
Results: A total of 693 patients were included (54% female, median age 78 years, interquartile range 71-83) and 46% had HF with preserved ejection fraction. CKD was the most prevalent co-morbidity (42%), followed by diabetes mellitus (35%), CAD (31%), anaemia (23%), depression (21%), and COPD (11%). During a median follow-up of 180 (interquartile range 104-264) days, 129 (19%) patients experienced a HF-related event. On multivariate analysis, anaemia (adjusted odds ratio [OR] 2.30; 95% confidence interval [CI] 1.27-4.12, p = 0.006), COPD (OR 1.95, 95% CI 1.22-3.13, p = 0.005) and CAD (OR 1.81, 95% CI 1.25-2.63) independently predicted HF-related events, while AFib and CKD showed a significant trend towards predicting unfavourable prognosis (OR 1,44, 95% CI 0.997-2.08, p = 0.052 and OR 1,45, 95% CI 0.995-2.12, p = 0.053, respectively).
Conclusion: In real-life clinical practice of unselected HF patients, co-morbidities are highly prevalent and confer unfavourable prognosis.

P325

Patient phenotypes and outcome in heart failure: a national hospitalization database cluster analysis

D Daniel Omersa[1]; J Farkas[2]; I Erzen[1]; M Lainscak[2]
[1]National Institute of Public Health, Ljubljana, Slovenia; *[2]General Hospital Murska Sobota, Department of Research and Education, Murska Sobota, Slovenia*

Introduction: Patient phenotype (e.g. sex, age, comorbidities) in heart failure (HF) varies substantially and simple descriptive analysis is often insufficient to identify patients at risk of adverse outcome.
Purpose: To identify phenotypes associated with higher risk of all cause mortality following first HF hospitalization.
Methods: We recorded all first HF hospitalizations from the Slovenian national hospital discharge registry and linked it with national death registry. Patient general characteristics and comorbidities were retrieved and all patients were followed until death or the end of year 2013. Hierarchical cluster analysis was performed using Gower's distance dissimilarity matrix that included age, sex and comorbidities. Differences between clusters were analysed using ANOVA, chi square, and Kaplan-Maier with log rank test. All statistical analyses were conducted in R 3.2.2 (R Core Development team).
Results: We identified 8248 patients (45.5% men, mean age 75.4 ± 11.1 years) that were followed for 23808 patient-years. Using the dissimilarity matrix, three clusters of patients were identified: men (cluster 1, N = 2736), women (cluster 2, N = 2693), and men and women with cancer, chronic kidney disease (CKD), and chronic obstructive pulmonary disease (COPD) (cluster 3, N = 2819). Besides sex, cluster 1 and 2 differed mostly in age (71.6 vs. 78.0 years) and prevalence of diabetes mellitus (19.6% vs. 31.2%) – P < 0.0001 for both. Cluster 3, compared to cluster 1 and 2, had higher number of comorbidities (5.5 vs 4.5 and 4.7), higher prevalence of cancer (19.2% vs. 4.3% and 0.8%), CKD (15.7% vs. 8.6% and 10.1%), and COPD (14.2% vs. 4.1% and 3.1%) - P < 0.0001 for all. During follow-up, 3727 (45.2%) deaths were recorded. Cluster 3 had the lowest survival during follow-up (P < 0.0001) - figure.
Conclusion: We identified three distinctive phenotypes and a specific combination of non-cardiovascular comorbidity (cancer, CKD and COPD), irrespective of sex, was associated with poorest survival.



P326

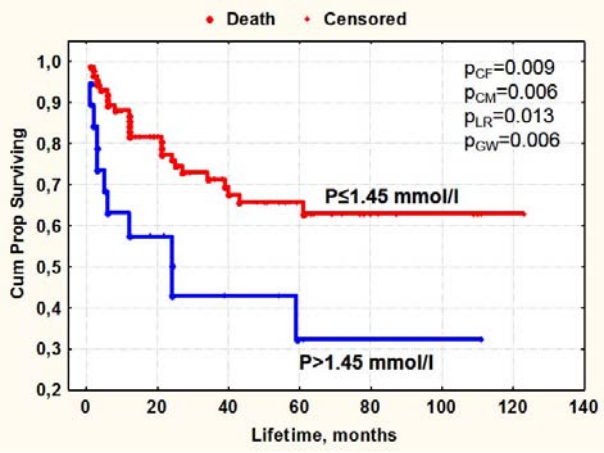
Hyperphosphatemia is a predictor of poor prognosis in patients with chronic heart failure

EV Resnik[1]; GE Gendlin[1]; IG Nikitin[1]
[1]Russian National Research Medical University, Internal Disease 2 Department, Moscow, Russian Federation

Purpose: Recent studies show that elevated serum phosphorus is associated with risk of heart failure in general population and mortality in patients with and without chronic kidney disease. Our aim was to study clinical and prognostic value of hyperphosphatemia in chronic heart failure (CHF) patients.
Methods: We evaluated serum inorganic phosphorus (P), intact parathyroid hormone (PTH), 25-OH-vitamin D, estimated glomerular filtration rate (eGFR, CKD-EPI), urinary albumin excretion (UAE), bone mineral density (dual-energy X-ray absorptiometry), Fracture Risk Assessment Tool (FRAX model) in prospective study of 212 CHF I-IV NYHA class patients with left ventricular ejection fraction (LV EF) < 45% without primary renal, endocrine, oncological and bone diseases on contemporary optimal treatment [median (interquartile range) of age – 64.0 (56.0;70.0) years; LV EF – 30.5 (25.3;36.9) %, eGFR – 61.3 (48.7;77.7) ml/min/1.73m2, UAE – 47.2 (33.0-70.0) mg/24h]. We observed the patients over 10 years. The follow-up time for death or the end of the study was 26 (12; 60) months. Survival was analysed by Kaplan-Meier method, Cox's F (CF), Cox-Mantel (CM), Log-Rank (LR) and Gehan's Wilcoxon (GW) Tests.

Results: Serum phosphorus was 1,23 (1,08; 1,41) mmol/l in CHF patients. Hyperphosphatemia (P>1.45 mmol/l) was in 23.03%. Hyperphosphatemic patients had more severe NYHA class, higher blood pressure in anamnesis, higher urinary albumin excretion, lower eGFR ($p < 0.05$). Osteoporosis (-score = or < -2.5SD) was found in 32.4(95%CI 14.7-51.9) %, osteopenia (T scores between -1.0 and -2.5SD) – in 40.5 (95%CI 22.0-59.0) % of CHF patients. PTH was 77.6 (38.2;136.0) pg/ml. 25–vitamin D was 47.3 (38.8;54.6) nmol/l. 67.8% of CHF patients died during follow-up. Survival of patients with hyperphosphatemia was significantly lower than in patients without it (Picture). In Cox regression model, it was found that serum phosphorus was one of the strongest predictors of survival and was comparable with the value of LV EF and eGFR (Table). Also there was a trend to increase the 10-year risk of any fracture in FRAX model in patients with hyperphosphatemia.
Conclusions: Hyperphosphatemia is a predictor of poor prognosis in patients with chronic heart failure. Further work is required to determine whether lowering serum phosphate levels may improve the prognosis in CHF.

Cox's regression model for CHF, =0.007			
Parameter	β	Standart error	
LV EF, %	-0.04	0.019	0.030
Serum phosphorus,mmol/l	1.02	0.54	0.046
eGFRCKD-EPI, ml/min/1,73m2	-0.016	0.009	0.050



Hyperphosphatemia and surviving in CHF

P327
Prevalence and determinant of cognitive impairment in elderly patients with heart failure - A pilot study in a geriatric hospital

S Shutaro Futami[1]; J Ishikawa[1]; C Jubishi[1]; A Suzuki[1]; A Morozumi[1]; Y Saito[1]; K Nemoto[1]; T Okawa[1]; J Tanaka[1]; T Ishiyama[1]; Y Tsuboko[1]; K Takeda[1]; H Fujimoto[1]; K Harada[1]
[1]*Tokyo Metropolitan Geriatric Hospital, Cardiology, Tokyo, Japan*

Backgrounds: In elderly patients who admitted to a hospital due to heart failure often have cognitive impairment; however, mechanisms causing cognitive impairment are unclear.
Methods: We enrolled 43 patients who admitted to a geriatric hospital because of heart failure. We excluded patients who had pre-diagnosed dementia and those who were unable to walk. We evaluated echocardiography, blood test, Mini Mental State Examination (MMSE) score and body composition using bioelectrical impedance analysis (Inbody S10) just before discharge.
Results: Mean age was 85.1 ± 8.0 (range 60-99) years (male 44.2 %). The ejection fraction was 46.9 ± 16.2 % and stroke volume was 36.5 ± 12.4 ml; median B-type natriuretic peptide was 269.1 pg/dl. The Mini Mental State Examination (MMSE) score was 20.5 ± 5.4 and there were 66.7 % of patients with cognitive impairment (MMSE < 23). MMSE score was significantly related to Age (r=-0.344, P=0.032), Regular alcohol drinking habit (r=0.437, P=0.007), uric acid (r=0.413, P=0.010), and extracelluar water per total body water (ECW/TBW) ratio (r=-0.437, P=0.007). In stepwise regression analysis that included these covariates, MMSE score was significantly associated to ECW/TBW ratio (beta=0.443, P=0.009) (i.e. body water distribution). However, when echocardiographic parameters of end-diastolic left ventricular volume (EDV) (r=0.327, P=0.048), left atrial volume index (LAVI) (r=-0.411, P=0.012), and A wave of transmitral flow (r=-0.625, P=0.001)) were included to the model, MMSE score was related to A wave of transmitral flow (P=0.001) and LAVI (P=0.015) (measures of diastolic function).
Conclusion: Cognitive function in elderly patients with heart failure might be affected by distribution of body water and cardiac diastolic function.

P328
Optimizing atrial fibrillation management in primary care by utilizing an electronic medical record dashboard for population health management

JH Michael Qiu[1]; D Ngui[2]; F Lo[3]
[1]*University of Edinburgh, College of Medicine & Veterinary Medicine, Edinburgh, United Kingdom*; [2]*University of British Columbia, Department of Family Medicine, Vancouver, Canada*; [3]*University of British Columbia, Microbiology and Immunology Undergraduate Program, Vancouver, Canada*

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Background: Systematically applying evidence based guidelines for Atrial Fibrillation (A. Fib) management in family practice can be challenging. Some physicians may benefit from automated and sustainable methods to improve patient care and outcomes leveraging the use of EMRs.
Purpose: By piloting an A. fib Electronic Medical Record (EMR) dashboard in a multi-physician family practice, our
objectives were to determine the EMR dashboard's ability to identify care gaps in Atrial Fibrillation. We also want to assess our ability to address these care gaps with 1:1 physician reviews and team based pharmacist medication reviews with patients within the practice.
Methods: We reviewed the medical literature regarding ideal design characteristics and review articles (needs reference) on utilization of EMR dashboards in health care. Also, we reviewed relevant A. fib clinical guidelines (needs reference) and developed a prototype A. Fib tool through an interactive process with feedback from physicians.
From a period of x to y, we used this dashboard to review one physicians patient roster. We recalled patients with care gaps identified by the EMR dashboard for management reassessment by a physician or alternatively, eligible patients were also seen by clinical pharmacists to review their medications. The results were tracked in real-time by the dashboard and allowed us to generate a report at the end of our intervention.
Results: A review of the dashboard for one physician resulted in identifying 15 patients who were recalled for review and we achieved the following tasks divided up into themes.
1. Patient panel/roster clean up: correctly revised atrial fibrillation in 5 patients. We had an overall increase in clinic patients identified with A. fib through improved ability to review cases.
2. Improved identification of investigation and lab monitoring care gaps: the number of A. fib patients without eGFR in 12 months decreased and the number of A. fib patients without ECHO on file decreased.
3. Improved identification of medication care gaps: the number of A. fib patients without anticoagulation agent decreased.
4. Increased referrals for shared care with team members to improve patient education
5. Improved ability to generate meaningful data for clinical audit and monitoring effect of interventions:
Conclusion: Our A. Fib EMR Dashboard allowed us to manage our A. fib patients more systematically, efficiently and effectively. This tool improved our recalls and ability to generate physician alerts increase referrals to clinic team members. The concept of utilizing the A. fib dashboard is applicable to any EMR and is a needed paradigm shift to promote the use of technology to target care gaps. This holds promise to improve the management of A. Fib in primary care, but requires further investigation.

P329
Demographic, clinical, and biological characteristics of outpatient heart failure patients in oman

M Matlooba Alzadjali[1]
[1]*Royal Hospital, Cardiology , Muscat, Oman*

Introduction: The clinical profile, and outcome of HF in western population is well demonstrated, little systematic data exist regarding the clinical profile and management of HF patients in Oman. Hence, the heart failure registry established after development of heart failure clinic to provide systematic report of the characteristics of HF patients.

Aim: To describe the demographic, clinical, and biological characteristics of outpatient heart failure patient in Oman.
Method: Outpatient heart failure registry is a prospective registry aimed to describe the clinical characteristics, management, and outcomes of consecutive patients who attended in heart failure clinic in National Heart Center in Oman since Jan 2016 until October 2016.
Results: A total of 275 patients, with mean age 57 years, were enrolled. Forty one percent females and 59% were males. With average of LVSEF 32% and pulse rate 72%. It had been noted that the average of QRSD duration among these patients were approximately 106 MS. Furthermore, serum creatinine was increased among those with LVS EF < 15-30% mean 164 mmol/l, most of the patients were on evidence based medications for heart failure treatment.
Conclusion: From this registry it's very obvious that heart failure it is burden in Oman, data on the clinical profile, management, and outcome of HF in Oman is scarce, accordingly it is highly important to evaluate the magnitude of the problem and to guide management and future plans.

P330

Probability of cardiovascular events in chronic heart failure patients with preserved and mid-range ejection fraction depending on different phenotypes of peripheral arterial system

AA Anastasia Shchendrygina[1]; YN Belenkov[1]; EV Privalova[1]; EA Zheleznykh[1]; YA Danilogorskaya[1]; VY Kaplunova[1]; MV Kozhevnikona[1]; GA Shakar'iants[1]; IS Chekneva[1]; AO Yusupova[1]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Purpose: to describe phenotypes of peripheral arterial system in heart failure (HF) patients with preserved and mid-range ejection fraction (EF) and assess their prognostic significance.
Methods: We conducted a prospective cohort study of 50 patients (pts.) with heart failure and preserved EF (HFpEF) (n = 25;male:16; mean age:65 (58;68)) or mid-range ejection fraction (HFmrEF) (n = 25;male:19; mean age:67 (61;73)) NYHA class II-III. 30 healthy controls (male:17; mean age: 57 (51;63)) were enrolled. We performed transthorocal echocardiography to estimate LVEF, E/A,Left Ventricle Mass Index (LVMI), Left Atrial Volume Index (LAVI). To determine arterial damage in different level, digital photoplethysmography and nailfold computer videocapillaroscopy during vinous occlusion were performed. Endothelial function of small (occlusion index, IO) and large vessels (phase shear, PS, ms) were estimated. Vascular remodeling of aorta (stiffness index, SI,m/s) and skin capillaries (capillary densities after vines occlusion, CDvo, cap/mm2) were determine. Followed cardiovascular events was monitoring once a year during 5 years. The study complied with the Declaration of the Helsinki regarding investigation in humans.
Results: Endothelial dysfunction and remodeling of large and small vessels were found in HF pts. IO,PS,SI was significantly higher than in controls ($p < 0.05$). The measures of remodeling of large and small vessels did not correlate (SI, CDvo (rs= - 0,15, p >0,05) as well as PS and IO (rs= -0,18, p>0,05). Individual arterial phenotype was determined by assessment of macro- and microcirculation damage associations. It was described 4 phenotypes: Type 1- functional changes of large or small vessels; Type 2-structural and functional changes of large vessels; Type 3- structural and functional changes of small vessels, Type 4 -disturbance of both small and large vessels.We found that in CHF group was 24 % pts. (n = 12) with Type1. Type2 had 8 % (n = 4). Type 3 had 2% (n = 1) and 62 % (n = 31) had Type4. There was no significant difference in types between HFpEF and HFmrEF groups. In controls only 13% (n = 4) had no changes. Type 1 had 53 % (n = 16). Type 2 was found in 7% (n = 2). Type 3 had 17% (n = 5). Type 4 was determined in 10 % (n = 3) of participants. Type 4 HF patients have significantly higher BMI, LVMI in comparison with those who has Types 1-3 (LVMI Type4 - 101 (85;125) vs. LVMI Type1-3 - 132 (106;158), p = 0,001).Cardiovascular events had 28 patients. Kaplan-Meier analysis demonstrated a significantly higher probability of cardiovascular events in HF pts. with Type 4 than those with Types 1-3 (mean follow-up: 838 days; log-rank test: $p < 0.02$).
Conclusion: It was described 4 phenotypes of arterial damage in HF pts. All the types was found in similar proportion in HFpEF and HFmrEF groups. Those who had disturbance of both small and large vessels was obese and had severe LV remodeling. Moreover, Type 4 correlated with future cardiovascular events in HF patients.

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Influence and management of diabetes mellitus in patients with heart failure with reduced ejection fraction followed in a non-tertiary hospital heart failure unit.

V Martinez Mateo[1]; L Cejudo Del Campo[1]; MJ Fernandez Anguita[1]; E Martin Barrios[1]; AJ Paule Sanchez[1]
[1]Hospital Mancha Centro, Cardiology, Alcázar De San Juan, Ciudad Real, Spain, Spain

Background/Introduction: Cardiovascular safety of oral antidiabetic drugs in patients with diabetes mellitus (DM) and heart failure (HF) with reduced left ventricular systolic function (LVSF) has not been established yet.
Purpose/Methods: We analyzed characteristics and treatment patterns in diabetic patients with symptomatic HF followed prospectively in the Heart Failure Unit (HFU) of a non-tertiary hospital.
Results: Since the begin of Unit in 2010 until 2016, 367 patients have been followed (median 44 months, 76.1% men, mean age 69.7 +/- 12.5 years [median 73]). The majority of patients presented severe LV systolic dysfunction (67.6%), functional class II (50.8%) and ischemic origin of cardiomyopathy (47.5%). Rate of treatment with beta blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers and aldosterone antagonists were 86.1%, 95.8% and 62.9% respectively without significant differences between diabetic or no diabetic patients. The prevalence of DM was 32.9%, mainly type 2 (96%). Oral antidiabetics alone were the main scheme of hypoglycemic treatment (61.5%), being metformin the main drug used (73.3%) both in monotherapy and in combination, followed of dipeptidyl peptidase IV inhibitors (40.0%). Treatment with insulin was utilized in 38.3% diabetic patients, mainly with bolus-basal regimen (52.7%). The percentage of well-controlled patients was 48.1% (according with therapeutics goals established in guidelines) with a rate of micro and macrovascular complications of 51.6% and 67.2% respectively. Regarding the prognosis, the overall accumulated survival at 65 months was 62.6%. Diabetic patients did not present a higher mortality although the subgroup of diabetic patients with worse metabolic control, those treated with insulin and those with a higher renal failure rate did present a higher mortality compared to the rest of the patients. The use of antidiabetic drugs was not associated with a worse prognosis or a higher incidence of decompensation with any of the pharmacological groups.
Conclusion: Incidence and evolution of DM in patients with symptomatic HF due to LV systolic dysfunction followed in a HFU of a non-tertiary hospital is similar to that described by other groups. Mortality was higher in those patients with worse metabolic control and impaired renal function. The use of different oral antiadiabetic drugs were safe and not associated to worse prognosis or a higher rate of decompensation.

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Characteristics of patients with chronic heart failure according to new ESC guidelines derived-LVEF classification

D Damien Logeart[1]; T Damy[2]; R Isnard[3]; M Saval[4]; C Tribouilloy[5]; F Piccard[6]; JC Eicher[7]; F Roubille[8]; JN Trochu[9]; G Roul[10]; N Naccache[11]; V Bataille[11]; P De Groote[12]
[1]AP-HP - Hospital Lariboisiere, Department of cardiology, Paris, France; *[2]University Hospital Henri Mondor, Creteil, France*; *[3]Hospital Pitie-Salpetriere, Paris, France*; *[4]University Hospital of Grenoble, Grenoble, France*; *[5]University Hospital of Amiens, Amiens, France*; *[6]Hospital Haut Leveque, Bordeaux-Pessac, France*; *[7]University Hospital Center, Dijon, France*; *[8]University Hospital Arnaud de Villeneuve, Montpellier, France*; *[9]University Hospital of Nantes Nord Laennec, Nantes, France*; *[10]University Hospital of Strasbourg, Strasbourg, France*; *[11]French Society of Cardiology, Paris, France*; *[12]Cardiology Hospital of Lille, Lille, France*

On behalf of: FRESH group

New ESC guidelines pointed out the need to specify what are heart failure (HF) patients with mid-range left ventricular ejection fraction (mrLVEF) – defined by LVEF 40 to 49%- as compared to patients with preserved LVEF (pLVEF) and reduced LVEF (rLVEF). By using French Survey on Heart Failure (FRESH), we aim to compare characteristics of these 3 subgroups in chronic HF.
Methods: FRESH is an on-going multicenter survey collecting exhaustive data in both acute and chronic HF (NCT01956539). Comparisons were performed using chi^2 or Fisher test for categorial variables and ANOVA or non-parametric Kruskal Wallis test for continuous variables. Multinomial logistic regression was performed.
Results: Among 1093 chronic HF patients, 56% had rLVEF, 22% had mrLEVF and 22% had pLVEF.
There were significant differences across LVEF subgroups in age as well as gender, underlying cardiac disease, atrial fibrillation, comorbidities, BMI, blood pressure, NYHA class, haemoglobin, natremia, BUN, creatininemia, natriuretic peptides and use of medications. The table shows significant results of the multivariate analysis.
Conclusion: Chronic HF patients with mrLVEF exhibit some significant differences with both HF-rEF and HF-pEF regarding clinical and biological characteristics, which deserves further investigations.

	Odd ratio	95%CI	p
HF-rEF versus HF-mrEF			
NYHA class 3-4	1.89	1.14-3.11	0.013
Ischemic heart disease	2.10	1.25-3.54	0.005
Dilated cardiomyopathy	3.20	1.88-5.45	< 0.001
Systolic blood pressure (by 10mmHg)	0.85	0.77-0.4	0.002
Heart rate (by 10bpm)	1.16	1.004-1.34	0.045
Hemoglobin	1.17	1.07-1.28	0.001
Natriuretic peptides (BNP or NTproBNP)2nd vs1sttertile	3.22	1.94-5.34	< 0.001
3rd vs1sttertile	4.76	2.73-8.30	< 0.001
HF-pEF versus HF-mrEF			
Age (per 10y)	1.34	1.10-1.63	0.004
Ischemic heart disease	0.27	0.15-0.49	< 0.001
Dilated cardiomyopathy	0.43	0.24-0.79	0.006
Natremia	1.08	1.02-1.15	0.014

P333

Iron and infection in patients admitted for heart failure in an internal medicine ward

J Azevedo Duarte[1]; J Almeida[1]; R Ribeiro[1]; C Henriques[1]; J Delgado Alves[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Internal Medicine 4, Amadora, Portugal*

Background: Iron deficiency (ID) is an important comorbidity in patients with chronic heart failure (CHF). Either absolute or functional, ID is an independent predictor of outcomes, even in the absence of anemia. Functional iron deficiency (FID) is defined as an inadequate iron supply when iron stores are replenished and it is present whenever the ferritin level is between 100-299mg/L and transferrin saturation is lower than 20%. Iron supplementation in patients with FID improves clinical symptoms and reduces the risk of hospitalization due to decompensated CHF. Several studies have shown that iron deficiency is associated with an impaired humoral and cell mediated immunity, thereby contributing to an increased risk of infections. Despite this, iron deficiency is still overlooked in daily clinical practice and guidelines are frequently not followed in the "real world".
Methods: Retrospective analysis of patients with heart failure admitted to an Internal Medicine ward in the period of one year (August 2015 - August 2016).
Purpose: To determine if there is any relationship between iron deficiency, iron supplementation and infection susceptibility in patients with CHF.
Results: 225 patients were included in the analysis. 201 (89%) were admitted due to decompensated cardiac insufficiency, and of these 133 (59%) had iron deficiency (ID), which in turn was functional in 43% (n = 57) of cases and absolute in 57% (n = 76). In patients with FID, the average ferritin value was 176,7mg/L, with an average transferrin saturation of 14,3%; iron therapy was administered in only 33% (n = 19) of cases. Time of admission for both cohorts was 16,2 days in patients with FID and 14,9 days in the ones with absolute ID; there was no significant difference between the two groups.
Regarding the incidence of infections, 71% (n = 49) of the patients with FID had at least one infection, whereas only 67% (n = 62) of the patients without FID were infected. Respiratory infections were the most common (46%), followed by urinary tract infections (28%); in 20% of patients more than one infection occurred during hospitalization.
Patients with decompensated HF had a significantly higher prevalence of FID (n = 55, 27%) in comparison with patients without decompensated HF (n = 2, 8%). However, there was no significant relationship between overall iron deficiency and the incidence of infection, X2 (2, N=225) = 4,313, p = 0,116. Additionally, in patients with FID there was no relationship between those who did iron therapy and the occurrence of infection, p = 0,401, two-tailed Fisher's exact test, Cramer's V=0,111.
Conclusion: Patients with CHF have a high incidence of functional iron deficiency. Whether the infection susceptibility is mainly due to the CHF itself or to the FID is difficult to differentiate, as FID cannot be seen as an independent factor from CHF. Iron deficiency might not be a relevant factor for infections in admitted patients due to the short period of time that is considered.

P334

The prevalence of rhythm and conduction disorders in three different types of heart failure

E Tamulenaite[1]; I Jonauskiene[2]; E Kavaliunaite[1]; R Zeimaite[3]; J Motiejunaite[2]; K Stasaitis[4]; D Kablucko[5]; E Paleviciute[5]; A Mebazaa[6]; A Kavoliuniene[2]; J Celutkiene[5]
[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [2]*Hospital of Lithuanian University of Health Sciences, Department of Cardiology , Kaunas, Lithuania*; [3]*Vilnius University, Vilnius, Lithuania*; [4]*Hospital of Lithuanian University of Health Sciences, Trauma and Emergency Center, Kaunas, Lithuania*; [5]*Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; [6]*Hospital Lariboisiere, U942 Inserm, Université Paris Diderot, Paris, France*

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Introduction: Cardiac arrhythmias are important co-morbidities in heart failure (HF) patients associated with worse prognosis. Given the new classification of HF presented in 2016 ESC guidelines, the prevalence of arrhythmias in particular HF types requires re-evaluation. Aim. To evaluate the prevalence of rhythm and conduction disorders in three different HF types in the population of acutely decompensated chronic heart failure (ADHF).
Methods: Prospective observational two-centre cohort study enrolled consecutive patients admitted to the emergency department with acute dyspnea. Patients with final ADHF diagnosis and available left ventricular ejection fraction (LVEF) were included in the analysis (n = 329, median of age 70 [26;96] years). Presence of atrial fibrillation (AF), left and right bundle branch block (LBBB and RBBB), combined intraventricular conduction defect and AV block were collected at admission electrocardiogram. Analysis was done by SPSS v20 statistical package using Chi Square test. The significance level was $p < 0.05$. Results. Atrial fibrillation was found in 167 (50.8%) participants, remaining 162 (49.2%) patients were in sinus rhythm, 35 patients (10.6%) had pacemakers. Intaventricular conduction disorders were detected in 76 (23.1%) patients: LBBB, RBBB and combined defects in 54 (16.4%), 11 (3.4%) and 11 (3.4%) patients, respectively. AV block was detected in 15 (4.5%) patients. Combination of cardiac rhythm and conduction abnormalities was found in 37 (11.2%) of patients. The distribution of rhythm and conduction disorders in HFrEF, HFmrEF and HFpEF are presented in the Table1. The highest prevalence of AF (54.9%) was found in HFmrEF group (n = 51), however, without significant difference. Intraventricular conduction disorders and combined abnormalities were significantly less frequent in HFmrEF group compared to HFrEF, and though not significantly different, were observed more frequently in HFmrEF compared to HFpEF. Conclusions. Even half of the patients with acutely decompensated chronic heart failure present with atrial fibrillation, which is found to be similarly frequent in different HF types. Heart failure with mid range ejection fraction demonstrates different profile in terms of rhythm and conduction disorders compared to other two types of HF.

Table1

Cardiac rhythm and conduction disorders	HFrEF(< 40%) N=156 (47.4%)	HFmrEF (40-49%) N=51 (15.5%)	HFpEF (≥50%) N=122 (37.1%)
Atrial fibrillation	80 (51.3%)	28 (54.9%)	59 (48.4%)
Intraventricular conduction abnormalities	50 (32.3%)	9 (17.6%)*	17 (13.9%)
Combined abnormalities	24 (30.4%)	4 (15.3%)*	9 (14.3%)

*p < 0.05 HFmrEF vs HFrEF

P335

The relationship between the buckberg index and functional capacity in stable chronic heart failure patients.

T Mannion[1]; S Fall[1]; M Carey[1]; L Devaney[1]; A Jago[1]; S Fay[1]; R Pharithi[1]; V Maher[1]
[1]*Adelaide & Meath Hospital, Dublin, Ireland*

Background: The Buckberg index, a diastolic to systolic pressure-time integral ratio, is a resting measure of myocardial oxygen supply and demand. It compares the delivery of oxygen to the heart muscle during diastole to the cardiac workload during systole. A suboptimal Buckberg index creates a supply–demand imbalance which may limit cardiac performance and functional capacity in patients with chronic stable heart failure.
Purpose: This study was conducted to assess the association between Buckberg index and functional capacity in chronic stable HF patients.
Methods: 156 clinically stable HF patients, whose weight, condition and medications had not changed in the previous 3 months, participated. Buckberg Index was completed using SphygmoCor system. Systolic-to-diastolic pressure shifts were assessed by the systolic and diastolic pressure-time integrals and expressed as a percentage. Patients were then categorised as follows; Group 1= Buckberg index

Table 1. P337

Parameters	6MWD, m	EF, %	CO, l/min	CI, l/min/m^2	SV, ml	ICON, 1/k	TFC, 1/k
Control group in rest	510 IQR 450 - 600	58.5 IQR 54 - 61	5.15 IQR 4.35 - 5.8	0.05 IQR 0.05 - 0.065	73.5 IQR 64.5 - 79	33.9 IQR 27.55 - 45.1	22 IQR 18.5 - 24
Control group after exercise	-	-	7.4 IQR 7.1 - 9.9	0.08 IQR 0.06 - 0.1	89 IQR 85- 96	56.8 IQR 49.2 - 68.5	23 IQR 21 - 25
HF-REF group in rest	425 IQR 360 - 450	31 IQR 24.5 - 36	4.85 IQR 4.1 - 5.75	0.06 IQR 0.05 - 0.07	71.5 IQR 58 - 81	35.1 IQR 31.4 - 49.55	23.5 IQR 18 - 27.5
HF-REF group after exercise	-	-	6.5 IQR 4.9 - 7.85	0.07 IQR 0.06 - 0.09	75 IQR 66.5 - 87.5	47 IQR 36.35 - 62.8	23 IQR 17.5 - 26

Abbreviations: 6MWD, 6-minute walk distance; EF, ejection fraction; CO, cardiac output; CI, cardiac index; SV, systolic volume; ICON, myocardial contractility; TFC, thoracic fluid content; k-thoracic impedance

≤ 150% Group 2= Buckberg index 151 - 200% Group 3= Buckberg index ≥ 201% Functional capacity was evaluated via 6 Minute Walk testing, NYHA Class, 3 day accelerometer measuring daily step count (FitBit) and Kansas City Cardiomyopathy Questionnaire (KCCQ).
Results: Univariate analysis demonstrated statistically significant correlations between Buckberg index and 6MWT distance (Pearsons r=0.23, p = 0.004), NYHA Class (r= - 0.18, p = 0.022), and the KCCQ, but not with daily step count (Fitbit). ANOVA revealed statistically significant differences among patients grouped (1-3) by Buckberg indexes in relation to 6MWT ((F (2, 155)= 8.737, p = 0.001)), NYHA Class ((F (2, 156)= 3.407, p = 0.036)), KCCQ Overall summary score ((F (2, 149)=7.516, p = 0.001) and KCCQ Clinical Summary Score ((F (2,146)=11.308, p = 0.001))
Conclusion: Buckberg index is associated with functional capacity in chronic stable HF patients. We recommend that HF patients are best managed if the Buckberg ratio is driven as high as possible.

P336

Understanding heart failure with middle range ejection fraction: results from a Colombian population

C I Clara Ines Saldarriaga[1]; GA Ortega Ramirez[2]; GE Ortega Ramirez[3]; C Gallego[1]; LA Fajardo[1]; AM Agudelo[1]; E Canas[2]
[1]Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia; *[2]Universidad Pontificia Bolivariana, Cardiology, medellin, Colombia*; *[3]Industrial University of Santander, medicine, Bucaramanga, Colombia*

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Middle range ejection fraction (HFmrEF) is a group of patients with different features and prognosis. There is no data about this population in Latin America, despite epidemiology that differs from the rest of the world.
Objective: To identify the clinical characteristics, treatment and prognosis of the HFmrEF patients in a Colombian heart failure (HF) program.
Methods: observational, retrospective study.
Results: In a population of 994 patients from a HF program, 147 patients had HFmrEF. The mean age was 67.4 +/- 13.5 years, and 44.2% were women. The mean EF was 42.8% +/- 2.7 %. Ischemic heart disease was the cause of HF (46.3%), followed by idiopathic (22.4%), and valvular disease (10.2%). The comorbidities are described in table 1. The functional class was as follows: NYHA I: 42.9%, NYHA II 36.7%, NYHA III 17%, and NYHA IV 3.4%. The total mortality was 4.8%, and cardiovascular death occurred in 85.4% of the cases. 32.7% were hospitalized at least once per year, 10.2% twice, and 3.4% three or more times. The treatment prescribed was ACE inhibitors in 50.3%, ARB in 44.9%, beta blockers 95.2%, MRA 57.1% and diuretics in 70.7%.
Conclusion: in our heart failure program, HFmrEF represents a group of mostly male patients with ischemic cardiomyopathy with a majority in NYHA I – II. They have many comorbidities, plus a rate of hospitalizations and mortality, that requires a close follow up.

TABLE 1: comorbidities

Comorbidities	Percentage
Atrial fibrillation	30.6%
Coronary disease	51.7%
Hypertension	73.5%
Diabetes	27.9%
Chronic kidney disease	27.2%

comorbidities

P337

Non-invasive cardiac output monitoring after cardiopulmonary exercise testing in patients with heart failure

E Emilia Sawicka[1]; M Marcinkiewicz-Siemion[1]; K Ptaszynska- Kopczynska[1]; M Lapinska[2]; M Szpakowicz[2]; J Skawronska[2]; W J Musial[1]; K A Kaminski[3]
[1]Medical University of Bialystok, Department of Cardiology, Bialystok, Poland; *[2]Medical University of Bialystok, Department of Community Medicine and Civilization Disease Prevention, Bialystok, Poland*; *[3]Medical University of Bialystok, Department of Cardiology, Department of Community Medicine and Civilization Disease Prevention, Bialystok, Poland*

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Introduction: Heart failure with reduced ejection fraction (HF-REF) is one of the most severe outcomes of cardiovascular diseases. Reliable non-invasive evaluation of hemodynamic parameters in rest and exercise may improve patient assessment and care. Some valuable hemodynamic variables may be obtained by continuous non-invasive cardiac output monitor (ICON) that relies on impedance cardiography. However, this metod was not tested after exercise.
Purpose: To evaluate the hemodynamic parameters obtained by ICON in HF-REF patients before and after exercise in relation to the measurements obtained in cardiopulmonary exercise testing (CPET).
Methods: The study included 24 stable, optimally treated patients (median 60.5 IQR 54.5-64 years, 4 females) with HF-REF in NYHA II, who were assessed with ICON before and after CPET. The latter hemodynamic measurement was performed within 90 seconds after the end of the exercise. Because of muscular movements during physical exercise it was not possible to make measurements during the CPET. The control group included 20 patients without history of HF-REF (median 62 IQR 57.5–65.5 years, 4 females).
Results: The study did not reveal significant differences between hemodynamic parameters measured using ICON at rest between HF-REF and controls. After CPET, however, HF-REF patients were characterized by lower cardiac output (CO) (p = 0.037) and systolic volume (SV) (p = 0.012) than controls, despite significant increase in CO (p < 0.001), SV (p = 0.006), myocardial contractility (ICON) (p = 0.001) and decrease in thoracic fluid content (TFC) (p = 0.008) after CPET in comparison to rest (Table 1).
Although CO after exercise correlated with 6-minute walk distance (R=0.5,p = 0.017), it was not significantly associated with any CPET variables. Only TFC correlated with VO2 ml/kg/min at anaerobic treshold (R=-0.42, p = 0.043).
Conclusions: Hemodynamic paramaters obtained in impedance cardiography reflected changes after physical excercise, however they did not present association with the well-established parameters in CPET. The usefulness of ICON monitor after exercise, remains to be further investigated.

P338

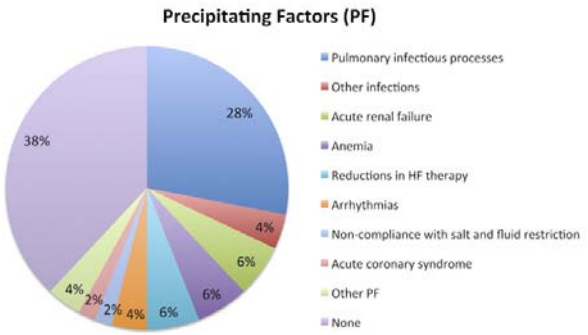
Change in the precipitating factors of heart failure admission in patients included in a heart failure unit

Z Blazquez Bermejo[1]; D Iglesias Del Valle[1]; E Garcia[1]; J De Juan[1]; E De La Cruz[1]; R Cadenas[1]; V Martinez[1]; C Casanova[1]; A Garcia[1]; A Martin[1]; E Prieto[1]; R Cano[1]; I Plaza[1]
[1]University Hospital Infanta Sofia, Cardiology, Madrid, Spain

Background: Avoidable precipitating factors (PF), such as non-compliance with pharmacologic therapy for heart failure (HF) or with salt and fluid restriction, have been identified in 32-54% of HF admissions. Moreover, multidisciplinary programs that focus on enhancing patient self-care activities reduce HF hospitalizations.
Purpose: The aim of this study was to review the different PF of decompensated HF admissions in patients that are closely monitored in a HF unit.
Methods: 112 patients with HF diagnosis were prospectively included in the HF unit at our institution between May 2014 and December 2016. Self-care education and a telephone contact were provided. Patients were systematically followed-up in the

HF outpatient clinic. All changes in clinical status, admissions and deaths were documented.
Results: Baseline characteristics and HF therapy are summarized in the table. A total of 50 episodes of decompensated HF in 25 different patients were attended during a median follow-up of 13 ± 8.4 months. 70% required hospitalization and 30% were discharged from the emergency department. The PF of the episodes are shown in the figure. Pulmonary infectious process was the most common known PF (28%) and only 8% of the 50 episodes were considered avoidable.
Conclusions: Avoidable PF of HF admissions are low in the context of multidisciplinary management programs. A better self-care education and closer follow-up may explain the reduction of HF hospitalizations in these programs.

Baseline characteristics and HF therapy	
Age (years)	64.3±13.2
Male sex	70.5%
Arterial hypertension	66.1%
Diabetes mellitus	36.6%
Significant coronary artery disease	37.5%
GFR < 60mL/min/1.73m^2	35.7%
COPD	17.0%
Anemia	27.7%
LVEF < 40%	83.0%
Beta-blockers	91.1%
ACE-I or ARB or ARNI	87.5%
MR antagonist	73.2%
ICD	19.6%
CRT	17.0%

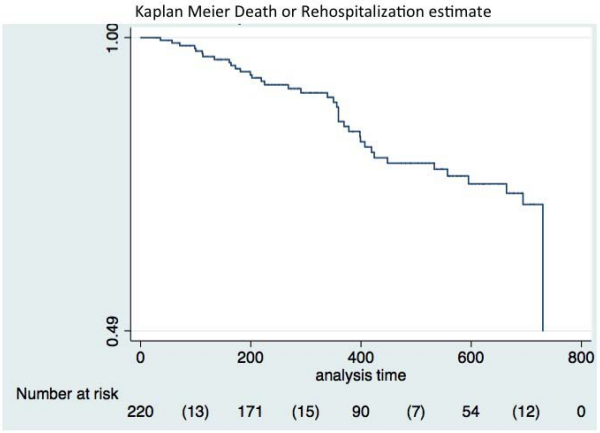


Precipitating factors of HF admission

P339
Optimize Brazil - Analysis of a multidisciplinary approach in a multicenter brazilian cohort to optimize heart failure treatment

P Schwartzmann[1]; HT Moreira[1]; R Mourilhe-Rocha[2]; H Villacorta[3]; JD Souza-Neto[4]; T Sickler-Cruz[5]; D Albuquerque[2]; MV Simoes[1]
[1]Medical School of Ribeirao Preto, University of Sao Paulo, Internal Medicine, Ribeirao Preto, Brazil; *[2]State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil*; *[3]Universidade Federal Fluminense - RJ, rio de janeiro, Brazil*; *[4]Hospital de Messejana Dr Carlos Alberto Studart Gomes, Fortaleza, Brazil*; *[5]Santa Helena Saúde, São Paulo, Brazil*

Introduction: Heart Failure (HF) is a major health problem worldwide, with elevated proportion of deaths, hospitalizations and morbidity. In Brazil, a national prospective registry demonstrated an even higher rate of death and re-hospitalizations. The treatment is challenging and requires a multidisciplinary initiative to improve pharmacological and non-pharmacological treatment in this population. This comprehensive multidisciplinary approach is the main goal of the Optimize Program and is focused beyond the pharmacological treatment in educating patients and their families about the disease and providing information for self-monitoring.
Purpose: We aimed at assessing the clinical effect of Optimize-HF Program in a retrospective multicenter Brazilian cohort of heart failure patients.
Methods: We retrospectively included a total of 219 patients (124 males, 59.9 ± 13.5 y.o.) with heart failure and reduced left ventricular ejection fraction (LVEF) mainly with non-ischemic etiology (151 patients – 68.9%). Patients were followed in HF clinics of five Brazilian HF centers and received the multidisciplinary orientations contained in the Optimize program.
Results: The baseline characteristics were: LVEF = 29.8 ± 0,09%, systolic arterial pressure = 111 ± 21 mmHg, heart rate = 72,2 ± 14 bpm, 38.3% of the patients were in NYHA functional class II and 48% of the patients were in NYHA functional class III, NT-ProBNP 2973 ± 3216 pg/mL, 7% had implantable cardioverter defibrillator or cardiac resynchronization therapy. Patients were treated following the recommendations of the guidelines: 84% were using betablockers, 78% ACE inhibitors or ARBs, 15.9% ivabradine. The follow-up time was 414 ± 223 days, with 5% of mortality and 21.3% of the combined outcome of death or rehospitalization. The low mean LVEF, the worse functional class (more than a half of patients were from NYHA III-IV) and the high mean NT-ProBNP level suggest that this is a high risk HF population. The outcome rate of death and a combined outcome of death or rehospitalization were markedly lower in comparison to the Brazilian National Registry of HF, which showed more than 50% of mortality and rehospitalization over a year.
Conclusion: The optimization of HF treatment using a multidisciplinary program in this multicenter Brazilian cohort presented a lower rate of death and death or rehospitalization. These results suggest the potential benefit of this multidisciplinary strategy to improve prognosis of patients with heart failure and reduced LVEF.



P340
Stroke prevention with combination of ivabradine with low dose of carvedilol versus optimized dose of carvedilol alone in chronic heart failure patients.

NARESH Sen[1]; SONAL Tanwar[2]; ASHOK Jain[3]
[1]NARAYANA HRUDAYALAYA INSTITUTE OF MEDICAL SCIENCE, BANGALORE, India; *[2]Rajasthan University of Health Sciences, Cardiology, Jaipur, India*; *[3]Fortis Escorts Heart Institute, Jaipur, India*

Background: According to proved cardiac physiology high heart rate in patients with chronic heart failure (CHF) is linked to adverse cardiovascular events like arrythemia or stroke and worsening of dyspnea. Carvedilol and Ivabradine both are recommended in CHF for heart rate reduction. However, Carvedilol also role in reduction of blood pressure which compromises cerebral perfusion pressure and may risk for stroke events.
Purpose: Our aim is to access stroke evidence in chronic heart failure patients with comparison between Ivabradine with Low dose of Carvedilol and optimized dose of Carvedilol alone.
Method: 3 years randomized observational study performed at three different cardiac centres. We have divided two groups : group A(n = 1084) treated with low dose 3.125 to 6.25 mg Carvedilol with Ivabradine 5 to 7.5 mg twice daily and group B (n = 890) treated with Carvedilol 12.5 to 25 mg twice daily. We observed stroke events rate and exercise test for functional capacity.
Result: In our study, 1974 patients of chronic heart failure were enrolled. Age of patients - 39 to 71 yrs, Systolic Blood pressure -128 to 168 mmHg , Diastolic Blood pressure - 78 to 108 mmHg, Heart Rate - 92 to 138 beat/min. Heart rate was reduced in both groups, but a greater reduction of blood pressure in group B optimized dose of Carvedilol was observed. There was significant reduction in stroke rate in group A(n = 21) versus group B (n = 48) (1.9% vs 5.4% , p < 0.004). The distance walked on

the 6-min walking test and the exercise time on MVO(2) test significantly improved in combination group A ($P < 0.02$).
Conclusion: Ivabradine with low dose of Carvedilol has better results in stroke rate reduction in chronic heart failure patients as compared to optimized dose of carvedielol alone.

P341
Outcome of a transitional care clinic to reduce heart failure readmission in high-risk inner city population

J Justin Lee[1]; F Reyes[1]; M Ramirez[1]; M Rahman[1]
[1]*SUNY Downstate Medical Center, Internal Medicine, Brooklyn, United States of America*

Background: Heart failure (HF) is a worldwide problem with an astronomical amount of burden on healthcare expenditure that is only projected to increase in the future. Previous studies have shown that black population with low socioeconomic status has significantly higher rates of HF than other ethnicities. Population at our institution consists of 80% black ethnicity, with 31% living below poverty level. Managing our patients with chronic medical conditions is particularly challenging as many of them do not fully understand the complexity of their illness and the importance of adherence with medical treatment plan. Reasons for hospital admissions for HF exacerbation include not only medication non-compliance, but also failure to follow up with primary care appointments and inappropriate use of the emergency room as the medium for immediate aid during crisis.
Our institution has established a transitional care clinic (TCC) in May 2015, with aims to aid patients with chronic medical conditions by providing early post-discharge follow up regardless of patient's financial or insurance status.
Methods: Retrospective review was conducted for patients who were scheduled for TCC with a diagnosis of HF, from May 2015 to October 2016. Our TCC model includes, follow-up appointment within 7 days post-discharge and reminders via phone calls a day before TCC appointment, post clinic follow up phone calls and additional TCC clinic visits as needed to bridge patient over to his or her primary care clinic. A 30-day readmission rate was calculated and compared between patients who followed up with their TCC and who did not, by using Fisher's exact test. Also, readmission rates were compared for patients who followed at TCC vs. cardiology clinic.
Results: Total of 204 admissions for HF were identified in the study period. Majority of patients were black (91%) with a mean age of 65 years and median length of stay of 5 days. Out of 137 patients who did not follow up with our TCC, 44 were readmitted (32.12%) within 30 days of discharge. From the 67 patients who followed with our TCC, 7 were readmitted (10.45%). Forty percent of patients who did not show up to neither TCC nor cardiology clinic were readmitted, compared to 8% who showed up to either TCC or cardiology and 6% who followed up with both.
Conclusions: Our transitional care clinic model demonstrates early success with 22% decrease in 30-day all-cause HF readmission in patients who were followed up at the clinics. Rate of readmission did not differ significantly on patients who were followed at TCC, compared to those who were followed by their cardiologists. Future study design can be directed towards cost analysis, comparison to historical data from other inner-city population and interventions focused on ways to increase compliance with TCC appointment, including more frequent reminders using emails, text messages, etc.

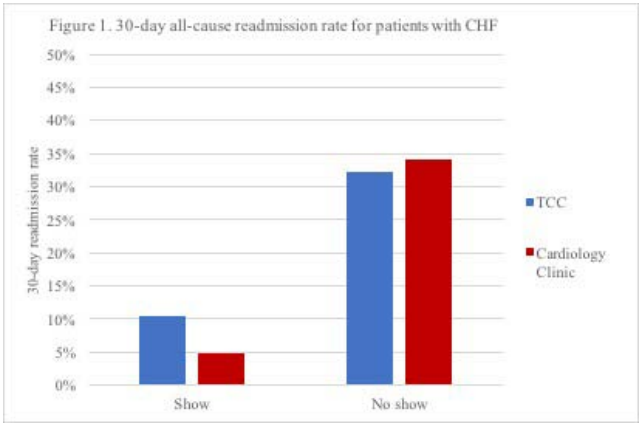


Figure 1.

P342
NO metabolism in patients of elderly age with chronic heart failure.

I Ime Etukudo[1]; L Abugu[2]
[1]*Kharkov National University of V.N. Karazina, Internal Medicine , Kharkov, Ukraine*; [2]*Kharkov National Medical University, Internal Medicine , Kharkov, Ukraine*

Important role in pathogenesis of chronic heart failure (CHF) is the disturbance of vasodilatory function of endothelium, determined by level of synthesis and metabolism of nitric oxide (NO). S-nitrosothiol – complex: made as a result of introducing NO into dinitrozol complexes of iron with thiol ligands forming a physiological oxidation that reflects the intensity of its synthesis.
Aim of investigation: determination of peculiarities of NO metabolism in patients of elderly age with CHF.
Matherial and methods: 68 patients with ischemic heart disease of age from 60 to 92 were examined. CHF of II functional class (FC) was determinated in 44 (64%), CHF of III FC–in 24 (35%) patients (NYHA). 29% had hypertensive disease (HD), 19% patients diabetes mellitus (DM). Nitrates and nitrites were determinated in serum by method of Griss' diasoreaction with determination of nitric junction. S-nitrosothiol was determinated by fluorometric method.
Results: there was a significant decrease of S-nitrosotiol levels comparing to control group. Comparing level of S-nitrosothiol in groups 60-75 and >75 years, in men and women, depending on presence of HD and DM in anamnesis meanings of this metabolite had no difference. Nitrate levels in patient with II and III FC of CHF was significantly less of those in control ($< 0{,}05$; $< 0{,}05$). Nitrites level in patients with CHF II FC was lower ($< 0{,}05$), in CHF III FC – had no difference from normal one. Level of nitrates and nitrites in CHF III FC was significantly higher CHF II FC($< 0{,}01$; $< 0{,}05$). At the age of > 75 years, level of nitrates and nitrites were significantly lower than at the age of 60-75 years ($< 0{,}05$; $< 0{,}05$). Indices of NO were significantly higher in patients with HD and DM comparing to patients without HD and DM in anamnesis ($< 0{,}05$).
Conclusion: Depression of NO metabolites formation testify about decreasing of intensity of NO metabolism and reflects physiological and pathological processes caused by CHF, endothelial dysfunction. In CHF III FC, HD and DM in anamnesis, they were significantly higher rates of nitrites and nitrates. This fact can be related to induction of iNOS with increasing formation of NO that due to CHF can be caused by growing ischemia, due to HD – increased endothelial dysfynction and high blood pressure, due to DM – metabolic disturbances, which connected to unbalance of pressors and depressors acting of insulin. In such way, changes of vasodilatory function in patients of elderly age depend on severity of CHF, age of the patient and presence of polymorbide background.

P343
State of the thromboxane-prostacykline system in patients with chronic heart failure

V Valery Vishnevsky[1]
[1]*Medical Institute of Orel State University, Departament of Internal Diseases, Orel, Russian Federation*

Background: In recent years in the study of the pathogenesis of several diseases of the cardiovascular system, and chronic heart failure (CHF) in particular, careful attention is drawn to the prostanoids, because keeping active physiological balance between thromboxane and prostacyclin is one of the main conditions for maintaining optimal blood flow in the myocardium.
Aim: To study thromboxane-prostacyclines system (TPS) in patients with coronary heart disease (CHD) complicated by the CHF.
Methods: The status TPS was analyzed among 82 patients with CHD and CHF at the age of 42-60 years. Investigated in blood plasma the stable metabolites of prostacyclin – 6-keto-prostaglandin F1a (6-keto-PGF1a), prostaglandin E – PGE1, thromboxane A2 – TxB2 immunoenzyme method sets of reactants of company IBL. Depending on the functional class (FC) of the CHF patients were divided into 3 groups: 1 gr. – with the CHF FC I (34 patients), 2 gr. – with the CHF FC II (27 patients), 3 gr. – with the CHF FC III-IV (21 patients).
Results: In the control group content of TxB2 in blood plasma amounted to $147{,}2 \pm 2{,}9$ ng/ml, 6-keto-PGF1a – $87{,}3 \pm 2{,}8$ ng/ml, PGE1 – of $0{,}62 \pm 0{,}07$ ng/ml, the ratio of TxB2/6-keto-PGF1a – $1{,}65 \pm 0{,}26$. With progression of CHF biosynthesis prostacyclin was significantly decreasing, level of TxB2 and the ratio of TxB2/6-keto-PGF1a in patients of 2 gr. and 3 gr. was significantly higher compared to the control group and 1 gr. Thus, in patients of 2 gr. and 3 gr. the content of prostacyclin amounted to $70{,}2 \pm 5{,}6$ ng/ml and $64{,}6 \pm 4{,}9$ ng/ml, respectively ($p < 0{,}05$, $p < 0{,}01$). Level of TxB2 in 2 gr. was $183{,}4 \pm 8{,}1$ ng/ml, 3 gr. – $226{,}4 \pm 9{,}3$ ng/ml ($p < 0{,}01$); the ratio of TxB2/6-keto-PGF1a in 2 gr. and 3 gr. – $2{,}61 \pm 0{,}29$ and $3{,}43 \pm 0{,}36$, respectively ($p < 0{,}01$).
Indicators of PGE1 in patients of 1 gr. were higher than in the control group, but in patients of 2 gr. and 3 gr. the level of PGE1 was declining, however, it exceeded targets. Reduction of the level of 6-keto-PGF1a, increase of TxB2 in plasma with

increasing FC CHF indicates their involvement in the mechanism of progression of heart failure and breach response the TPS as the exacerbation of the pathological process. Comment: The decrease of prostacyclin level in blood plasma, increased thromboxane and their ratio in patients with coronary heart disease probably reflects not only the severity of coronary insufficiency, but also chronic heart failure.

P345

Impact of ejection fraction on the clinical features in heart failure patients with concominant chronic obstructive pulmonary disease

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

The problem of management heart failure (HF) patients with concominant chronic obstructive pulmonary disease (COPD) is relevant and understudied. The research continues for clinical markers for aggravating both diseases, as well as criteria for their unfavorable course and prognosis. It is proved that the state of left ventricular systolic function, determined by the size of the ejection fraction, largely affects the survival of patients with heart failure. It is expected that adherence to heart failure, COPD significantly change clinical phenotype.

Purpose: To investigate the clinical features of heart failure in association with chronic obstructive pulmonary disease, depending on the value of left ventricular ejection fraction.

Methods: We enrolled 105 HF patients in association with COPD (average age – 68,4 ± 9,4 years, left ventricular ejection fraction – 53,8 ± 11,4%, I-II FC – 43,9%, III-IV –56,1%). Duration of heart failure did not exceed 6 years. In the study we used Questionnaire Minnesota living with heart failure for assessment quality of life, walk test, clinical assessment scale.

Results: All patients, depending on the value of left ventricular ejection fraction (LVEF), were divided into 3 groups according to recommendations of the European Society of Cardiology (2016.): 1. preserved left ventricular ejection fraction –81 patients (77,1%), 2. midrange –12 (11,45%), reduced left ventricular ejection fraction – 12 (11,45%). The frequency of severe course COPD was higher in the second group than in the others – 62,5%. The most unfavorable cohort was a group with a reduced left ventricular ejection fraction, which was confirmed by the worst results of the test distance (190,6 ± 96,1 m) and clinical assessment test (6,9 ± 2,1 points), worse quality of life (62,3 ± 20,9 points). The direct correlation of moderate intensity was determined between LVEF and Tiffno index ($r = 0,354$, $p < 0,05$), functional vital capacity of the lungs (FVC) – $r = 0,322$, $p < 0,05$, and also between heart failure functional class (FC) and clinical features of COPD, measured by clinical assessment test (CAT) and MRC ($r = 0,444$, $p = 0,01$ and $r = 0,344$, $p < 0,05$).

Conclusions: The results of this study indicate mutual influence on the clinical characteristics of both heart failure and bronchial obstructive disease on the formation of the clinical phenotype of the patient. The study showed that LVEF in patients significantly affects on the course of both diseases. At the same time, the clinical criteria for COPD have an impact on the course of both diseases, evidenced by a correlation between CCQ and clinical assessment scale ($p < 0,05$, $r = 0,473$), CCQ and CHF FC ($p < 0,05$, $r = 0,344$). The positive correlation between the results of COPD Assessment Test – CAT, reflecting the clinical condition of the patient at the time of the study, and CHF FC ($p < 0,05$, $r = 0,346$), clinical assessment scale ($p < 0,05$, $r = 0,410$), quality of life ($p < 0,05$, $r = 0,49$) was founded.

P346

The effectiveness of tolvaptan does not correlate with the severity of hyponatremia

R Rissa Setiani[1]; R Soerarso[1]; N Hersunarti[1]; BB Siswanto[1]
[1]*Harapan Kita Hospital, Jakarta, Indonesia*

Background: Heart failure is a disease associated with high morbidity and mortality rates, as well as increasing costs. Patients with heart failure often develop hyponatremia due to the changes in neurohormonal system. Hyponatremia has been associated with longer hospital stay, increased complications, larger costs, as well as increased rate of hospitalization. Tolvaptan is a selective, competitive vasopressin receptor 2 antagonist used to treat hyponatremia associated with congestive heart failure.

Purpose: This study aims to assess the effects of tolvaptan in heart failure patients with various severity of hyponatremia.

Methods: Prospective cohort study design was used. Patient recruitment was done in our Cardiovascular Center from 2015 to 2016, resulting in 31 in-hospital subjects. Inclusion criteria was adult patients who had heart failure and received tolvaptan. Data was collected through interview, physical examination, medical record, and laboratory examinations. The outcome of tolvaptan administration was assessed from the decrease in body weight and edema, as well as 24-hour urine volume. Data analysis was done using SPSS 20.0. The severity of hyponatremia is classified into below or above 120 mEq/L.

Results: Thirty-one subjects were included in this study. Seventy-one percent of the subjects were male, with average age of 51.2 ± 2.3 years old. NYHA classes of the population were as following: II (6.4%), III (61.3%), IV (32.3%). The median baseline sodium level was 131 (103-138) and median LVEF was 29% (14%-71%). All of the participants were prescribed furosemide (median dose 332 [40-840] mg) and 38.7% were prescribed spironolactone (median dose 25 [12.5-50] mg). Thirty percent of the participants had comorbid conditions. Tolvaptan effects on participants with hyponatremia below ($n = 6$) or above ($n = 25$) 120 mEq/L are not significantly different ($p > 0.05$), with average diuresis of 3021 (SD 1279) cc/day.

Conclusion: Tolvaptan can effectively improve diuretic effects of furosemide in heart failure patients despite various severity of hyponatremia.

ADVANCED HEART FAILURE

P347

Influence of a continuous veno-venous hemofiltration on the long-term prognosis in patients with an advanced heart failure and an acute coronary syndrome

O Oksana Trebacz[1]; K Zbierska[2]; J Nessler[1]; K Zmudka[3]; A Gackowski[1]
[1]*John Paul II Hospital, Department of Coronary Artery Disease and Heart Failure, Krakow, Poland*; [2]*John Paul II Hospital, Krakow, Poland*; [3]*John Paul II Hospital, Department of Interventional Cardiology, Krakow, Poland*

Introduction: Heart failure (HF) is one of the most common and challenging therapeutic problems. Coronary artery disease (CAD) can lead to HF and coronary angiography followed by PCI are utilized for its diagnosis and treatment. The use of contrast media could impair renal function while prophylactic fluid infusion is a standard of care. An adequate hydration in overloaded HF patients with urgent indications for intervention in acute coronary syndrome (ACS) setting is challenging. Periprocedural use of continuous veno-venous hemofiltration (CVVH) in such patients could be a valuable option.

Purpose: To analyze the long-term prognosis of patients with an advanced HF, undergoing PCI with periprocedural CVVH use.

To assess safety of CVVH and identify patients at increased risk for complications.

Methods: We performed prospective interventional study, which included 52 patients with chronic HF (NYHA II-IV), reduced ejection function (EF < 45%) and chronic kidney disease (stages III-IV), referred for coronary angiography/PCI due to ACS.

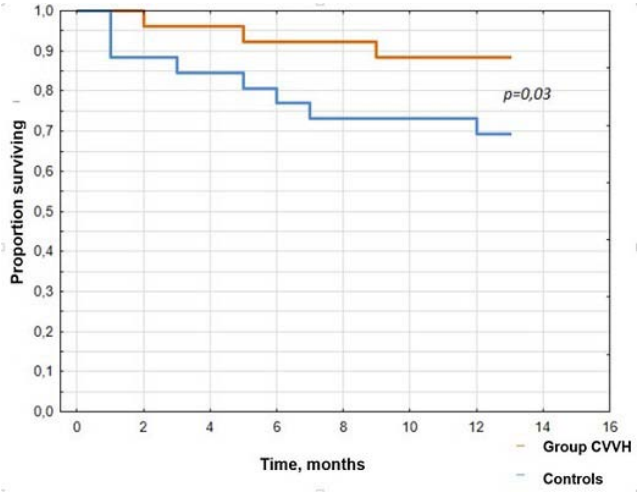
In 26 patients CVVH was used during the PCI procedure and 24h afterwards as an addition to a standard care. Another 26 patients received only standard treatment.

We measured serum creatinine levels at 24, 48 and 72h post PCI in both groups as well as NT-proBNP levels at 24 and 48h in CVVH group. In 3,5 years follow-up we assessed the risk of cardiovascular death and mortality from any cause.

Results: Patients in CVVH group were more often diabetic (73,1% vs. 38,5%, $p = 0,025$), active smokers (38,5% vs. 7,7%, $p = 0,02$), had history of previous PCI (57,7 vs. 23,1%, $p = 0,023$), were in significantly higher NYHA class ($p = 0,03$) and had pulmonary edema at admission (46,1% vs 11,5%, $p = 0,01$). Both groups were similar in routine laboratory measurements, except for higher initial creatinine ($p = 0,017$) and potassium levels ($p = 0,018$) in CVVH group. In CVVH group creatinine level significantly declined at 24h after the PCI (161,87 ± 63,4 vs. 124,71 ± 39,8 μmol/l, $p = 0,003$) with subsequent nonsignificant rise at 48 and 72h. In controls, the lowest observed creatinine level at admission (129,9 ± 38,1 μmol/l) significantly increased at 24h (136,4 ± 43,6, $p = 0,049$ μmol/l). NT-proBNP levels significantly decreased at 24 and 48h after the CVVH ($p = 0,015$). In CVVH group we observed a trend toward higher bleeding rate and need for transfusion (19,2 vs. 7,7%, $p = 0,42$). All bleeding events were related to vascular access site and occurred exclusively in female patients (100%, $p = 0,004$).

We observed significantly higher probability of survival at one year in CVVH group patients (88,5 vs. 73,1%, for CVVH and control groups respectively, $p = 0,03$), but this difference lost statistical significance at 3,5 years follow up.

Conclusions: Use of CVVH in patients with an advanced HF might result in a decrease of 1-year mortality with no such effect at a longer follow up. The use CVVH in women could increase the risk of bleeding complications.



survival probability in 1-year follow-up

P348

Beta-blockers uptitration between infusions predicts event-free survival in advanced heart failure treated with repeated cures of low-dose levosimendan

N Barras[1]; J Regamey[1]; P Vogt[1]; R Hullin[1]; PO Yerly[1]
[1]*University Hospital (CHUV), Department of cardiology, Lausanne, Switzerland*

Background: Prognosis of Advanced heart failure (AHF) is very poor. Because of low blood pressure (BP) and fluid overload, uptitration of Angiotensin converting enzyme inhibitors (ACEi), Angiotensin receptor antagonists (ARA), beta-blockers (BB) and mineralocorcticoid receptor antagonists (MRA) is not tolerated. Intermittent levosimendan (levo) infusions may then be a of value to alleviate symptoms and possibly improve outcome.
Purpose: The goal of this study was to find out factors predictive of 1 year event-free survival in 42 AHF patients (LVEF < 40%, NYHA 3-4 despite optimal therapy>3 months) treated with repeated low dose Levo (0.05 µg/kg/min during 24h every 4 wks) (4.37 + /-1.9 infusions/ pat).
Methods: Medical files were reviewed for the composite endpoint of mortality, re-hospitalization or LVAD implantation during 1 year after first infusion. Patients' baseline characteristics and status at inclusion and after 3 infusions were compared between the 14 who reached the endpoint (33%) and the 28 event-free survivors.
Results: Nor patients' characteristics (age 61.4 + 8.9y vs 59.7 + 7 y, P=0.62; female 17.85% vs 7.14%, P=0.64; IHD 50% vs 64.3%, P=0.51; LVEF 0.21 + 0.05 vs. 0.22 + 0.06) nor patients' baseline status predicted outcome (Table). Only BB therapy, percent of BB target dose and heart rate after 3 infusions predicted endpoint occurrence (Table). After adjustement for HR and BB, only BB dose >35% target dose remained significant (OR=0.64; 95%CI 0.07-0.87).
Conclusion: repeated levo infusions offer the opportunity tu uptitrate HF background therapy, particularly BB, which in turn may predict mid-term outcome.

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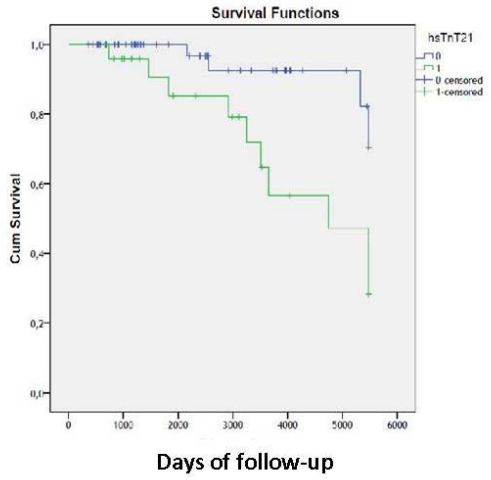
Utility of cTnT-hs and sAXL for prognosis evaluation after heart transplantation

S Sonia Mirabet Perez[1]; J Ordonez Llanos[1]; P Garcia Frutos[2]; V Brossa Loidi[1]; L Lopez Lopez[1]; M Tauron[1]; E Sole[1]; A Ferrero[1]; E Roig Minguell[1]
[1]*Hospital de Sant Pau, Barcelona, Spain*; [2]*Department of Cell Death and Proliferation, IIBB-CSIC, IDIBAPS , Barcelona, Spain*

Cardiac allograft vasculopathy (CAV) is one of the main limiting factors for long-term survival after heart transplantation (HTx). Once CAV is established it is associated with worse outcomes, but the progression of the disease is very variable and the prediction of cardiovascular events sometimes is uncertain. Some patients with CAV have a rapid deterioration while others remain stable for long periods of time despite being diagnosed with CAV. The aim of this study was to evaluate the usefulness of sAXL, Lp-PLA2, GDF-15 and cTnT-hs to assess prognosis in HTx recipients.
Methods: This is an observational single center study that include HTx patients who had undergone routine CAV assessment, by coronary angiography or by coronary multi-slice computed tomography (MSCT) between January 2012 and April 2015. CAV was classified according the recomendations of the ISHLT. Blood samples were collected at the time that angiography or MSCT was done. sAxl (protein involved in vascular remodeling) , Lp-PLA2 (marker of atherosclerosis), cTnT-hs (marker for myocardial necrosis) and GDF 15 (marker associated with cardiovascular events) were assessed and were correlated with the development of cardiovascular events during the follow-up (until December 2016). Cardiovascular events (CV) were defined as a combined endpoint that included cardiovascular death, acute myocardial infarction or angina, heart failure or EF < 50% not due to rejection.
Results: A total of 96 HTx patients were included. Mean time after HTx was 9 ± 7 years. CAV was diagnosed in 49 patients (CAV1 in 26, CAV2 in 6, and CAV3 in 17 patients). During the follow up nineteen patients (20%) presented cardiovascular events. Five patients died, 6 had angina or AMI, and the remaining 8 had heart failure or EF < 50%. All the patients that presented cardiovascular events had CAV (13 were CAV3, 2 CAV2 and 4 CAV1). There were significant differences in cTnT-hs values between patients with and without cardiovascular events (50 ± 41 vs 19 ± 19 ng/L; p < 0.01) and sAXL values (104 ± 67 vs 69 ± 27 ng/L; p < 0.04). cTnT-hs ≥21 ng/L predicted the development of cardiovascular events with a specificity of 78%, sensitivity of 68%, positive predictive value of 43%, and negative predictive value of 91%. In the multivariate analysis cTnT-hs and sAXL were independent predictors of increased risk for cardiovascular events after HTx. Survival without cardiovascular events in HTx patients with cTnT-hs >21 ng/L was 47% compared with 70% in patients with cTnT-hs < 21 ng/L (p < 0.01) (Figure 1). Lp-PLA2 and GDF15 had no correlation with cardiovascular events.
Conclusions: sAXL and cTnT- hs could be useful biomarkers to assess the prognosis of Heart transplantation recipients. In our study, values of cTnT-hs ≥ 21 ng/L have a high negative predictive value for cardiovascular events in patients with CAV. Therefore, the routine assessment of cTnT-hs after HTx may help to improve the management of chronic HTx patients.

table P348

	Baseline			After 3 infusions		
Variable	No endpoint (n = 28)	Endpoint (n = 14)	P	No endpoint (n = 28)	Endpoint (n = 14)	P
NYHA class	3.03 +/- 0.6	3.36 +/-0.6	0.11	2.37 +/- 0.9	2.83 +/- 0.43	0.15
SBP (mmHg)	102 +/-11	106 +/- 17	0.41	104 +/- 6	99 +/- 12	0.58
HR (bpm)	78 +/- 8	82 +/- 6	0.85	71 +/- 10	81 +/- 14	0.039
Creatinine (µmol/L)	116 +/- 31	138 +/- 38	0.18	108 +/- 22	147 +/- 50	0.13
NTproBNP (ng/L)	5233 +/- 2244	7765 +/- 3506	0.56	2910 +/-4002	6085 +/-1728	0.21
ACEi/ARA	89.2%	85.7%	1	92.9%	80%	0.27
% target dose ACEi/ARA	0.175 +/-0.125	0.175 +/-0.145	0.94	0.3 +/- 0.12	0.175 +/- 0.12	0.11
BB	96.4%	71.4%	0.65	96.4%	60%	0.012
% target dose BB	0.12 +/- 0.12	0.08 + /-0.06	0.14	0.35 +/- 0.08	0.09 +/- 0.037	0.046
MRA	100%	85.7%	0.11	92.8%	80%	0.28
% MRA target dose	0.5 +/- 0.25	0.5 +/- 0.25	1	0.5 +/- 0.375	0.5 +/- 0.25	0.96



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Predictors of mortality at six months after in advanced heart failure patients attended in primary care

JM Verdu-Rotellar[1]; MA Munoz[1]; E Calero[1]; N Farre[2]; R Abellana[1]; C Checa[1]
[1]Primary Care Research Institute (IDIAP), Barcelona, Spain; *[2]Hospital del Mar, Cardiology, Barcelona, Spain*

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Background: To know the predictors of survival in patients with advanced heart failure is crucial to decide end-of-life options.
Purpose: to determine the factors related to the six months mortality of heart failure patients at functional status New York Heart Association (NYHA) IV attended in primary care.
Methods: Retrospective cohort study including 726 heart failure patients at NYHA IV functional status in Catalunya (Spain) was carried out. Demographic and clinical data, laboratory tests, treatments, comorbidity and vital status were drawn from primary care electronic medical records.
Logistic regression models and multiple imputations were performed.
Results: Mean age was 83.2 years (SD 7.8) and 62.9% were women, 43,0% were diabetic, 32.8% had coronary heart disease, 15.6% had history of stroke, atrial fibrillation was present in 49.7%, and 19.1% of patients had cancer.
Adjusted multivariate analysis found that: age (OR 1.04, 95% CI 1.01-1.06), low systolic blood pressure (OR 3.75, 95% CI 1.68-8.33),low body mass index (OR 4.62 95% CI 2.19-9.76), heart rate > 100/min (OR 2.14, 95% CI 1.05-4.35), renal impairment (OR 1.80, 95% CI 1.11-2.93), limitations in daily living activities (OR 1.68, 95% CI 1.02-2.75) and furosemide dosis (mg/day) (OR 1.007, 95% CI 1.003-1.02) were related to a higher mortality.
Conclusion: : A small number of variables easily obtained from primary care can predict which kind of patients are more probably going to be death in the six months after reaching the NYHA IV functional status.

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Low dose of basiliximab for induction immunosuppresion therapy for heart transplant results in favourable outcomes

V Veraprapas Kittipibul[1]; P Tantrachoti[1]; P Ongcharit[1]; A Ariyachaipanich[1]; S Siwamogsatham[1]; T Chaemchoi[2]; S Sritangsirikul[2]; S Puwanant[1]
[1]Chulalongkorn University, Department of Medicine, Faculty of Medicine, Bangkok, Thailand; *[2]King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

Background: Basiliximab 20 mg IV on Day 0 and Day 4 has been used as induction immunosuppression therapy for heart transplant. This simplified two-dose regimen was adopted from the studies in renal transplant. Little is known about the efficacy and safety of a low-dose regimen of Basiliximab (10 mg IV on Day 0 and Day 4) for induction immunosuppression therapy for heart transplant.
Methods: We studied safety and efficacy outcomes of Basiliximab 10 mg IV on Day 0 and Day 4 for induction immunosuppression therapy in 17 consecutive adult heart transplant recipients. All patients received cyclosporine or tacrolimus, mycophenolic acid, and prednisolone.
Results: Of 17 recipients (age 42 ± 14 years, 82% male, weight 54 ± 10 kg, height 166 ± 7 cm, body surface area 1.6 ± 0.2 m2, 100% CMV of D+/R+, ischaemic time 228 ± 78 minutes) receiving Basiliximab 10 mg IV on Day 0 and 4 for induction immunosuppression therapy, no rejection or mortality reported within 2 weeks post-operation. The efficacy and safety were shown in Table 1.
One death was attributed to Acinetobacter Baumanii infection occurring at 3 months post-transplant. No CMV disease, malignancy, or Post-transplant lymphoproliferative disorder detected at 1-year follow-up. None of 17 patients had adverse reactions (flushing, hypotension, serum sickness, or anaphylaxis). Mean serum creatinine at 6 months was 1.27 ± 0.41 mg/dl. Compared with previous studies using Basiliximab of 20 mg, the rejection, mortality, and infection rates were comparable.
Conclusions: Low dose of Basiliximab (10 mg IV on Day 0 and Day 4) for induction immunosuppression therapy for heart transplant results in no rejection or mortality within 2 weeks post operation in all patients. At 6 months post-transplant, moderate acute cellular rejection (ISHLT grade ≥ 2R) event-free rate was 86%. One-year survival was 90%. Further study comparing two induction regimens of Basiliximab (20 mg vs. 10 mg) on Day 0 and Day 4 along with CD25 and pharmacodynamic/kinetic profiles in heart transplant recipients is needed.

Table 1: Efficacy and safety outcomes

Post-HTx duration	Survival	≥2R ACR event-free rate	Graft failure event-free rate	CMV infection even-free rate	Treated infection event-free rate
2 weeks	100%	100%	100%	100%	94%
1 month	100%	88%	100%	83%	94%
3 months	94%	88%	100%	65%	75%
6 months	93%	86%	100%	57%	71%
12 months	90%	70%	100%	40%	50%

HTx, heart transplant; ACR, acute cellular rejection; CMV, cytomegalovirus.

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Intermitent treatment with levosimendan in outpatients with chronic advanced heart failure: our experience.

DJ Daniel Jose Elena Aldana[1]; MLG Miguel Antonio Lopez Garrido[1]; PCC Maria Del Pilar Cardila Cruz[1]; LJM Laura Jordan Martinez[1]; VBM Victor Manuel Becerra Munoz[1]; NAM Nasiba Abdeselam Mohamed[1]; AGC Ana Guijarro Contreras[1]; ARM Ainhoa Robles Mezcua[1]; RJA Rafael Jimenez Arjona[1]; RCA Rafael Campos Arjona[1]; AMR Ana Molina Ramos[1]; VGR Maria Victoria Garcia Ruiz[1]; LMH Luis Morcillo Hidalgo[1]; JMGP Jose Manuel Garcia Pinilla[1]
[1]University Hospital Virgen de la Victoria, Cardiology, Malaga, Spain

Introduction: Intermitent treatment with levosimendan might be a alternative for patients with chronic advanced heart failure, since there is not enough cientific evidence according to this. The aim of this study was to reach the clinical evolution of the patients undergo this therapy in our hospital.
Methods: We studied all the outpatients with chronic advanced heart failure treated with intermitent levosimendan therapy, recording clinical features, analytical values and events during the follow-up.
Results: From the 23 patients we have studied (65 years, 35% women), 11 (47,8%) of these had an isquemic ethiology. The mean of LVEF was 28% and the mean of Charlson Comorbidity Index was 5,5. 14 patients (60.9%) were admitted due to heart failure episode in the previous year before starting the therapy, and 9 (39,1%) had descompensated heart failure episodes. The mean of NT-proBNP pre-therapy was 3798 pg/ml, decreasing in 56,5% of the patients in the next 3 months and getting better in the 21.7% in the next 6 and 12 months. The median follow up duration was 11 months (IQR 5-18), recording at the 12th month an improvement of functional class in 10 patients (43,5%), 3 (13%) descompensated heart failure, 4 (17.4%) readmitted at hospital, 7 (30.4%) deaths and 3 (13%) heart transplantation. Patients with anemia had more descompensated heart failure episodes (37.5%vs0%, p = 0.032).
Conclusions: -NT-proBNP levels decreased in a high percentage of patients at the third month and less at the sixth and twelfth month of the follow-up.
-The prevalence of readmission and descompensated heart failure after intermitent therapy with levosimendan decreased according to the previous year pre-treatment.

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The safety and the efficacy of opioid agents for palliative care in patients with advanced heart failure

Y Nishihata[1]; H Mochizuki[1]; M Ono[1]; I Komatsu[1]; T Fukuda[1]; M Mizuno[1]; N Nakaoka[1]; Y Kijima[1]; Y Shiina[1]; N Komiyama[1]
[1]*St. Luke's International Hospital, Department of Cardiology, Tokyo, Japan*

Background: Palliative care for patients with advanced heart failure is recommended in the guidelines for the acute and chronic heart failure and it has been the focus of attention in this pandemic of heart failure. Because cardiologists are not familiar with opioids, there might be the underuse of those drugs for fear of those negative effects.
Purpose: To investigate the safety and the efficacy of opioid agents for palliative care in patients with advanced heart failure.
Methods: We investigated 4640 patients admitted to our cardiovascular center from January 2013 to September 2016, and extracted 28 patients with advanced heart failure treated with opioid agents to palliate their dyspnea. We examined patient´s background, starting dosage and maintenance dosage of opioids, concomitant drugs and clinical responses.
Results: About all 28 patients, their mean age was 79.4 years-old and 13 (46.4%) were male. Of those patients, 25 (89.3%) had renal dysfunction defined as estimated glomerular filtration rate (eGFR) of under 60 ml/min and 20 (71.4%) had severe renal dysfunction defined as eGFR of under 30 ml/min. Morphine hydrochloride, fentanyl and oxycodone were administered for 22, 3, and 3 patients respectively. The mean starting dosage of morphine, fentanyl and oxycodone were 5.8 ± 3.2, 0.71 ± 0.50, and 4.7 ± 0.58 mg/day, and the maintenance dosage were 8.7 ± 7.6, 0.77 ± 0.40, and 14.7 ± 13.6 mg/day, respectively. Inotropic agents, diuretics, and sedative medication were administered in combination with opioids in 89.3%, 17.9%, and 25.0%. Systolic and diastolic blood pressure did not change significantly after administration of opioids (97 ± 22.1 to 98.1 ± 20.2 mmHg and 49.9 ± 13.6 to 52.3 ± 14.1 mmHg). Heart rate and respiratory rate were significantly reduced by opioids (87.8 ± 25.2 to 83.8 ± 24.3 bpm, $p < 0.01$, and 27.3 ± 7.9 to 22.0 ± 6.5 bpm, $p < 0.01$) but nobody experienced significant respiratory depression nor symptomatic bradycardia. Their dyspnea score assessed by 'Face Scale' was significantly improved by opioids (2.9 ± 1.0 to 1.5 ± 0.9, $p < 0.01$).
Conclusions: Low dose opioids were relatively safe and effective for palliative care in patients with advanced heart failure and renal dysfunction.

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End of life care and symptom control in the final year preceding mortality from end-stage heart failure - Observations from a heart failure disease management programme.

V Voon[1]; S Chew[1]; C Craig[2]; D White[1]; E Wong[1]; C Cahill[1]; B Meany[1]; F Twomey[1]; T Kiernan[1]
[1]*University Hospital Limerick, Limerick, Ireland*; [2]*University of Limerick, Iimerick, Ireland*

Background: End of life care (EOLC) preceding end-stage heart failure (ESHF) death is poorly described, even within the context of a HF disease management programme (HF-DMP). It is thought that extending this period of recognition may provide greater opportunity for better care, particularly specialist palliative care (SPC). Therefore, we aimed to characterize EOLC, especially symptom control, during the final year preceding ESHF deaths.
Methods: All patient deaths (n = 53) within University Hospital HF-DMP in 2014-2015, were identified and categorized as ESHF and non-ESHF deaths. We retrospectively compared medical record data between both groups for demographics, HF clinic visits, hospitalizations and SPC referral during 12 months preceding death. Missing data was excluded. Data were expressed as mean ± SD or %.
Results: All ESHF deaths had at least NYHA III dyspnea prior to last hospitalization/HF clinic visit. None were eligible for heart transplant. No significant differences were observed between ESHF (n = 21) vs Non-ESHF (n = 20) deaths in terms of age, gender or nursing home admission within last year of life. Left ventricular ejection fraction in all patients was 30 ± 13% with approximately a third of patients in both groups with implantable cardiac defibrillators (ICD). Within last 12 months of life, ESHF deaths had more HF clinic visits for HF symptom control with diuretics, versus non-ESHF deaths (1.2 ± 2.0 vs 0.3 ± 0.4, p = 0.04). However, there were no significant between-group differences in HF and non-cardiovascular hospitalizations. In both groups, less than a quarter of patients had documented ICD deactivation discussions and less than a third of patients had documented SPC referrals, which were only initiated within the last 3 months of life. During this period, reported symptoms for control in ESHF deaths were dyspnea (86%), pain (19%), fatigue (57%) and oedema (67%), and were not significantly different to comparator group.
Conclusion: A low incidence of documented SPC referral for symptom control and ICD deactivation discussions was observed during EOLC of ESHF deaths. This is despite greater HF symptom burden during final 12 months of life within the ESHF deaths group. More work is required to explore these observations, including the use of structured assessment to document such parameters.

ARRHYTHMIAS AND TREATMENT

P355

Prolonged P-wave duration is associated with atrial fibrillation recurrence after radiofrequency catheter ablation

Y-S Wang[1]; G-Y Chen[2]; X-H Li[2]; X Zhou[2]; Y-G Li[1]
[1]*Xinhua Hospital of Shanghai Jiao Tong University School of Medicine, Department of Cardiology, Shanghai, China People's Republic of*; [2]*Xinhua Hospital of Shanghai Jiao Tong University School of Medicine, Clinical Research Unit, Shanghai, China People's Republic of*

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Background/Objectives: A change in the P-wave duration (PWD) was approved in patients with atrial fibrillation recurrence (AFR) after radiofrequency catheter ablation (RFCA). The correlation between the PWD and AFR and the potential utilization of a prolonged PWD in the prediction of AFR after RFCA remains unclear.
Methods: A meta-analysis of clinical studies that investigated the relationship between PWD and AFR after RFCA was performed. Studies regarded PWD in patients with or without AFR after RFCA, and also studies concerned with the predictive effect of prolonged PWD on AFR after RFCA, were included and summarized. Outcome measures are reported as absolute risk differences with 95% confidence intervals. A receiver operating characteristic (ROC) curve was used to evaluate the potential cut-off value of PWD for AFR. Summary receiver operating characteristic curve (SROC) analysis was performed to show the overall predictive efficiency of PWD for AFR.
Results: Nine studies were included in the meta-analysis. An overall effect test based on 8 studies that contained a total cohort of 1,010 patients showed a highly significant association between prolonged PWD and AFR after RFCA ($Z = 14.20$, $P < 0.000$). A statistic summary included 4 studies that included a total of 593 patients indicated an obviously higher risk of AFR among patients with prolonged PWD ($Z = 5.86$, $P < 0.000$). ROC curve analysis indicated 149.5 ms as the potential cut-off value of PWD for AFR after RFCA. SROC analysis suggested an acceptable predictive efficiency of PWD for AFR (AUC = 0.66)
Conclusions: The risk of AFR after RFCA is strongly related to a prolonged PWD. PWD is one potential low-cost and feasible predictor for AFR after RFCA.

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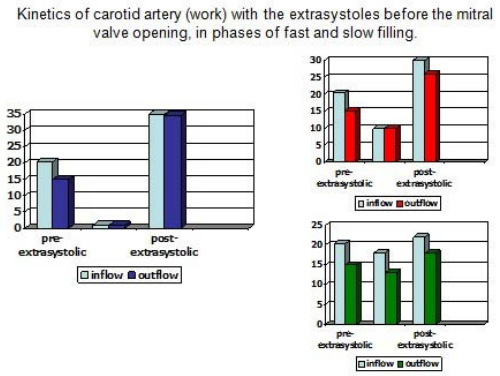
Extrasystoles from the point of view of its functional importance

O A Olga Germanova[1]; NN Kryukov[1]; AV Germanov[1]
[1]*Samara State Medical University, Samara, Russian Federation*

Atrial fibrillation is considered to be a risk factor of thromboembolic events because of the high probability of mural thrombus in auricles with ability of its further fragmentation. The majority of researches acknowledge the kardioembolic nature of stroke. However it's not paid attention to the role of elastic and muscle-elastic arteries on the background of multifocal arterial atherosclerosis with extrasystoles and atrial fibrillation in tromboembolic danger.
Aim: To determine the influence of intra-arterial hemodynamic and kinetic disorders of main arteries on the probability of thromboembolic events in the patients with different types of extrasystoles and atrial fibrillation.
Methods: We examined 186 patients with the permanent form of atrial fibrillation and supraventricular and ventricular extrasystoles. We used extrasystoles classification in accordance to the moment of their appearance in cardio cycle. We have identified:
Extrasysoles before the mitral valve opening.
Extrasystoles in rapid ventricular filling phase before the transmitral blood flow peak. Extrasystoles in rapid ventricular filling phase after the transmitral blood flow peak. Extrasystoles in slow ventricular filling phase.
We registered sphygmograms and doppler -ultrasound of carotid, radial, ulnaris, posterior tibia, arch of foot arteries. We analyzed the peak speed direct blood flow, blood flow volume. To know the moment of extrasystoles appearance in cardio cycle and ectopic center localization we used apex-cardiography and electrocardiography. The volume of cardiac output and transmitral blood flow were measured by echocardiography. We determined the parameters of heart biomechanics and main arteries kinetics, which characterized speed, acceleration, capacity and work in each phase of heart cycle in systole and diastole, and also the periods of dominance of outflow over inflow. We valued the contribute to the circulation of the premature contraction and first post-extrasystolic contraction.

Conclusion: The main importance to the hemodynamics changes has the moment of extrasystole appearance in cardio cycle and the ability of the first post-extrasystolic contruction to reestablish an adequate resulting blood flow. On the background of multifocal lesions of main arteries the main importance has the first post-extrasystolic contraction. It is accompanied by the sharp increase of hemodynamic and kinetic parameters of arteries and the increased deformation of vascular wall. The maximums of these parameters are revealed in first post-extrasystolic contruction in case of extrasystoles before the mitral valve opening and before the transmitral peak flow. In atrial fibrillation the main danger are the first ventricular contractions after the maximum time pauses. It causes the significant increase of cardiac output, arteries diameter as well as non-stability of atheromas and mural thrombus fragmentation with high embolism probability.



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Ventricular tachycardia and atrial fibrillation complicating the clinical course of takotsubo cardiomyopathy

B Schneider[1]; A Athanasiadis[2]; J Schwab[3]; U Gottwald[4]; W Toepel[5]; R Schoeller[6]; U Sechtem[2]
[1]Sana Kliniken, Luebeck, Germany; *[2]Robert-Bosch-Krankenhaus, Stuttgart, Germany*; *[3]Klinikum Nuernberg, Nuernberg, Germany*; *[4]Allgemeines Krankenhaus, Celle, Germany*; *[5]Klinikum Idar-Oberstein, Idar-Oberstein, Germany*; *[6]DRK Kliniken Berlin | Westend, Berlin, Germany*

Background: Takotsubo cardiomyopathy (TTC) has increasingly been recognized over the past years. Most studies, however, are fairly small. A German TTC registry has been initiated to further characterize this syndrome in a larger patient population.
This study evaluated the incidence and clinical relevance of ventricular arrhythmias (VA) and atrial fibrillation (AF) as a complication of TTC.
Methods: From 37 heart centres, 324 pts (296 f, 28 m, age 68 ± 12) were included 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. During hospitalisation, 7/324 pts (2.2%) died (cardiogenic shock n=4; myocardial rupture, stroke and asystole n=1 each).
Results: During the first 48 hours, 209 pts were continuously monitored and had daily ECG recordings. Ventricular tachycardia and/ or ventricular fibrillation was documented in 17 pts (8%) and newly diagnosed AF in 32 pts (15%). TTC pts with and without arrhythmias were compared.
In pts with VA, time from symptom onset to hospital admission was shorter (3.8 ± 3.2 vs 8.7 ± 7.3 hours, $p < 0.001$). Pulmonary oedema (29% vs 12%, $p < 0.05$), need for intraaortic balloon pumping (6% vs 0.5%, $p < 0.05$) or resuscitation (18% vs 3%, $p < 0.002$) and left ventricular thrombi (12% vs 3%, $p = 0.05$) were seen more frequently. The QTc interval was only slightly more prolonged (476 ± 45 vs 470 ± 55 ms day 1, 521 ± 80 vs 510 ± 57 ms day 2, 533 ± 93 vs 508 ± 60 ms day 3, all p = ns). Heart rate and other ECG parameters (ST- segment elevation, T- wave inversion, Q waves) were similar. Regarding age, sex, symptoms, trigger events, cardiac markers, ejection fraction, ballooning pattern, pre- and acute medication and mortality there was no significant difference among pts with and without VA.
Pts with AF frequently were on a pre-medication with diuretics (50% vs 12%, $p < 0.005$), had a lower ejection fraction (45 ± 14% vs 52 ± 15%, $p < 0.02$) und presented more frequently with pulmonary oedema (25% vs 11%, $p < 0.05$) and cardiogenic shock (16% vs 5%, $p < 0.05$). Age, sex, symptoms, trigger events, cardiac markers, ECG changes, ballooning pattern, pre- and acute medication other than diuretics, and mortality were not significantly different among pts with and without newly diagnosed AF.
Conclusion: During the acute phase of TTC, ventricular arrhythmias are observed in 8% and atrial fibrillation in 15%. Patients with arrhythmias have a more complicated clinical course, however, mortality is not increased.

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Life threatening ventricular arrhythmias in patients hospitalized for acute heart failure

Cl Radulescu[1]; L Antohi[1]; M Chivulescu[1]; I Cosei[1]; R Radu[1]; A Covaliov[1]; A Ambrosy[2]; C Macarie[1]; M Gheorghiade[3]; O Chioncel[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; *[2]Duke University Medical Center, Cardiology, Durham, United States of America*; *[3]Northwestern University, Cardiology, Chicago, United States of America*

Background: During hospitalization for acute heart failure (AHF), some patients may experience life-threatening ventricular arrhythmias, including sustained ventricular tachycardia (sVT) and ventricular fibrillation (VFib), placing them at high risk of in-hospital mortality.
Aim: To identify clinical variables independently associated to incidence of sVT/VFib during hospitalization for AHF.
Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients admitted for AHF in 5 academic and 8 community hospitals, over a 12-month period. A multivariate logistic regression model was developed to identify baseline clinical variables predictive of incident sVT/VFib.
Results: During hospitalization for AHF, the incidence of sVT and VFib was 3.6% and 3%, respectively. Patients who experienced sVT/VFib had higher in-hospital mortality compared to patients who did not (24.8% vs 5.7%; $p < 0.001$). The incident sVT/VFib was associated to in-hospital mortality in the whole cohort (HR=3.82;95%CI=1.59-5.21) and this association has been maintained event after adjustment by 18 baseline clinical variables (HR=2.60; 95%CI= 1.03-6.75). Patients who experienced sVT/VFib in a ICU/ICCU setting had a lower mortality compared to patients who had arrhythmias on regular ward (21.5% vs 26.7%; $p = 0.03$). Using a multivariate logistic regression model, creatinine at admission (HR=1.06;95%CI= 1.03-1.11), diabetes (HR=1.20;95%CI= 1.09-1.35), EF < 40% (HR=1.64;95%CI= 1.53-1.72), without beta-blocker at admission (HR=1.79;95%CI= 1.63-1.85), history of previous revascularization (HR=1.91;95%CI= 1.82-2.05) , need of inotropic agents (HR=2.70;95%CI= 1.93-3.65) were found to be independent risk factors for incident sVT/VFib during hospitalization.
Conclusions: Clinical variables commonly measured at the time of admission may help to identify at-risk patients for VT/VFib during hospitalization. Early disposition decision-making, as well as intense monitoring may help to prevent mortality in this group of patients.

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Left atrial remodeling and ventricular-arterial coupling in patients with recurrent atrial fibrillation: effects of amiodarone and sotalol

A Shavarov[1]; EV Kokhan[2]; GK Kiyakbaev[1]; VS Moiseev[1]
[1]RUDN University, Moscow, Russian Federation; *[2]Lomonosov Moscow State University, Moscow, Russian Federation*

Background: Impaired left ventricular-arterial coupling (VAC) might lead to diastolic dysfunction (DD) and therefore structural and functional changes of the left atrium (LA) that are substrate for atrial fibrillation (AF). The effects of amiodarone and sotalol on LA remodeling and VAC parameters remain unclear.
Purpose: To compare the effects of amiodarone and sotalol on LA remodeling and VAC parameters in patients with recurrent AF and preserved left ventricular systolic function.
Methods: The study included 60 hypertensive patients [45% male, median age 65 (61; 72) years] with paroxysmal and persistent AF and preserved left ventricular systolic function. The patients were treated with amiodarone (A) 200 mg + metoprolol 50 mg daily (n = 30) or sotalol (S) 160 mg daily (n = 30). All the patients underwent echocardiography and speckle tracking analysis before and 3 months after treatment. Global peak LA longitudinal strain (PALS) and strain rate (PALSR) in the reservoir (r) and contractile (c) phases were assessed using 6 segments in the 4-chamber and 2-chamber views. To estimate VAC arterial elastance index (Eal), left ventricular end-systolic elastance index (Eesl), Ea/Ees, systemic vascular resistance index (SVRI) and total arterial compliance (TAC) were calculated.
Results: A and S had comparable favorable effect on most clinical and echocardiographic parameters. Both A and S significantly reduced Eesl (from 1.41 to 1.25 and from 1.7 to 1.6 mm Hg/ml/m^2, respectively, p for all < 0.001) and increased TAC (from 1.15 to 1.35 and from 1.11 to 1.40 ml/mm Hg, respectively, p for all < 0.001). There were no significant changes in Eal and SVRI in A and S groups. The reduction of LA size was significantly greater in A group compared to S group (: -2.0 vs

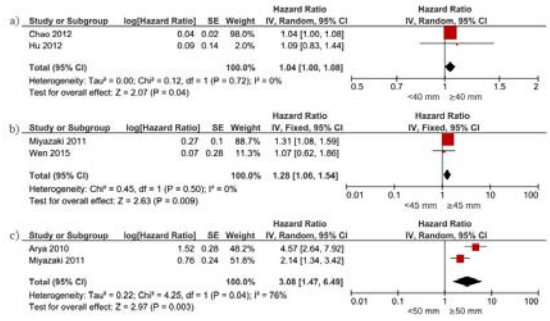
-1.1 mm, p = 0.02). Both A and S similarly improved PALSRc (: -0.23 vs -0.28 1/s, p = 0.35) that was independently associated with the efficacy of antiarrhythmic therapy.
Conclusion: A comparable change in VAC parameters was observed in both groups. Amiodarone and sotalol had comparable antiarrhythmic effect due to similar influence on PALSRc. The effect of amiodarone on LA reverse remodeling was, however, more favorable.

ATRIAL FIBRILLATION

P360
Left atrial size as predictor of recurrences after catheter ablation in paroxysmal atrial fibrillation: a systematic review and meta-analysis

I Ibadete Bytyci[1]; G Bajraktari[1]; MY Henein[2]
[1]University Clinical Centre of Kosova, Clinic of Cardiology, Pristina, Kosovo Republic of; *[2]Umea University, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background and Aim: Left atrial (LA) enlargement is associated with paroxysmal atrial fibrillation (PAF) incidence and outcome. The predictive role of the LA size in AF treatment with catheter ablation is still controversial. The aim of this meta-analysis was to analyze the potential association between LA diameter in patients with PAF undergoing ablation and AF recurrence after ablation.
Methods: We systematically searched PubMed-Medline, EMBASE, Scopus, Google Scholar and the Cochrane Central Registry, up to December 2016 in order to select clinical trial and observational studies, which assessed the predictive role of LA diameter in AF recurrence after catheter-ablation. 2962 patients from 16 studies with paroxysmal AF (PAF) were included.
Results: The pooled analysis showed that after a follow-up period of 19. 66 ± 8.31 months, patients with AF recurrence had larger LA size compared with those without AF recurrence, with a weighted mean difference (WMD) 2.31 ([95% CI 1.27 to 3.34], P < 0.0001).
LA diameter ≥40 mm predicted AF recurrence HR:1.04 [95% CI 1.00 to 1.08], P=0.04), but the best cut-off value, in all included patients, was ≥50mm HR:3.08 [95% CI 1.47 to 6.49], P=0.003).
Conclusions: Enlarged left atrium in patients with PAF undergoing catheter ablation predicts recurrences. The diameter more than 50 mm is the best cut-off of the recurrences of AF, but diameter of 40 mm also can predict recurrences in these patients.



Multivariate HR (Hazard ratio) of AF rec

P361
Step by step treatment of patients with congestive heart failure and long-standing persistent atrial fibrillation using combining of crt and catheter ablation

E Zhelyakov[1]; A Ardashev[1]; A Kocharyan[1]; Y Belenkov[1]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation

Aim: to assess clinical results of combining CRT-D and catheter ablation in long-standing persistent atrial fibrillation (AF) pts with congestive heart failure (HF) and reduced ejection fraction (EF).
Material and methods: We studied 8 consecutive patients (2 women, 51.4 ± 13.6 years of age) with long-standing persistent AF, congestive HF who underwent CRT-D placement as the first step of treatment. After CRT-D placement biventricular pacing mode (VVI from 70 to 85) was activated and rate control drugs dose was titrated. As the second step all patients underwent catheter ablation (RFA) for AF 3 mos. later. The ablation performed using 3D mapping system and included antral isolation of the PVs with additional left atrial linear ablation of the roof, mitral isthmus and substrate modification of the left atrium posterior wall. Switch of mode pacing from biventricular VVI to DDD was performed at the end of procedure after sinus rhythm restoration. Follow up included repeat echocardiography, device interrogation with percent of pacing and ventricular events checks, NYHA HF functional class (FC) evaluation at baseline and at months 3, 6, and 12.
Results: At the first step there were no complications associated with CRT-D implantation. At the 3 month of follow up the NYHA FC improved from 3.1 ± 0.4 to 2.3 ± 0.6, percent of biventricular pacing ranged from 72 to 99 (mean 88 ± 7%). Echocardiography showed a mean LV EF of 32.9 ± 7.5%, an increase from a baseline of 29.2 ± 7.8%. There were no complications associated with RFA of AF. At 6 months of follow up 6 of 8 pts were free from AF. Two pts had 3 episodes of AF which required external cardioversion performing. NYHA FC improved from 2.3 ± 0.6 to 1.9 ± 0.6, a mean LV EF increased from 32.9 ± 7.5% to 42.1 ± 4.8%. At 12 months of follow up 5 of 8 pts were free from AF. Three pts had 7 episodes of AF which required external cardioversion performing (3 pts) and redo ablation of AF (2 pts). NYHA FC improved from 1.9 ± 0.6 to 1.6 ± 0.6 to, a mean LV EF increased from 42.1 ± 4.8% 45.6 ± 5.2%. Device interrogation showed 5 episodes of nonsustained ventricular arrhythmias (1 episodes of ventricular fibrillation and 4 episodes of ventricular tachycardia) without therapy in 2 pts during all period of follow up.
Conclusion: Combining CRT-D and catheter ablation in patients with congestive HF and long-standing AF may be reasonable approach, although there is little data supporting its use.

P362
Maze III procedure in patients with heart failure, atrial fibrillation and valve disease.

AA Kulikov[1]
[1]Cardiology Research and Production Center, Moscow, Russian Federation

Research objective: To estimate effectiveness of Maze III procedure combined with a mitral valve operation in patients with heart failure and long-standing atrial fibrillation.
Methods: In the study were included 100 adult patients (48 men) with heart failure, persistent and longstanding persistent forms of AF and valvular pathologies. Average age of patients was 59 years. Average AF duration was 4 years.
Functional class of heart failure on NYHA 2,7 ± 0,75. The size of the left atrium 5,1 ± 1,5 cm, average left ventricular ejection fraction 61 ± 8,6%.
Antiarrhythmic therapy was tried to all patients, however it was inefficient.
All patients had mitral valve pathology. Also 80% of patients had the tricuspid valve insufficiency.
To all patients the electric cardioversion was made. After restoration of a sinus rhythm, the EP was executed. Then, on the first or second day after EP, correction of valve pathologies combined with "Maze III" procedure was carried out.
Results: Following the results of Maze III procedure combined with correction of valve disease, disposal of AF was observed in 95% of patients. 46% of patients had stable sinus rhythm to the moment of discharge from the hospital. 24% of patients had atrial rhythm with the maximum heart rate of 80-110 bpm (according to results of 24-hour Holter monitoring). For 25% of patients, it was necessary to implant a pacemaker. According to results of EP study, 13% of these patients suffered from sick sinus syndrome before operation. For 9% of the remaining 12% of patients, the indications for pacemaker implantation were atrioventricular nodal rhythm with low heart rate and pauses more than 3 sec long. For 1% of patients the indication was second degree AV block (type 2) and second degree SA block (type 2); for 1% the indication was complete heart block, and for 1% it was atrial rhythm and pauses more than 3 sec long.
13% of patients with an atrial rhythm and normal heart rate developed typical atrial flutter (AFL) in the early postoperative period. For all of them the RF catheter ablation with linear ablation of the right atrial isthmus and creation of isthmus block was effective, and further recurrence of AFL was not observed.
Conclusions: In the early postoperative period Maze III procedure combined with a mitral valve operation proved to be an effective surgical technique of treatment of persistent and long-standing persistent forms of AF in patients with heart failure. NYHA class II heart failure was not an obstacle for surgical treatment of AF.

P363

A new predictor of atrial fibrillation after coronary artery bypass graft surgery: HATCH score

M Mithat Selvi[1]; H Gungor[1]; C Zencir[1]; S Gulasti[1]; M Akpek[1]; U Eryilmaz[1]; C Akgullu[1]
[1]*Adnan Menderes University, Cardiology, Aydin, Turkey*

Background: The aim of this study was to investigate the association between HATCH score and atrial fibrillation (AF) after coronary artery bypass graft (CABG) surgery.
Methods: 369 patients (103 patients with AF and 266 patients without AF) undergoing isolated CABG surgery were analyzed. Complete medical records were retrospectively collected to investigate HATCH score.
Results: The median age of patients with AF was significantly higher than the median age of sinus rhythm group (60.8 ± 10.0 years vs. 67.8 ± 9.5 years, p < 0.001). HATCH score was significantly higher in patients who developed AF after CABG surgery than the sinus rhythm group (p = 0.017). Multivariate logistic analysis showed that, HATCH score [odds ratio (OR): 1.334; 95% confidence interval (CI), 1.022-1.741, p = 0.034] was independent predictor of AF after CABG surgery (Table 1). Receiver operating characteristic curve analysis showed that the cut-off point of HATCH score related to predict AF was 1, with a sensitivity of 42% and specificity of 70%.
Conclusion: Patients with elevated preoperative HATCH score may have higher risk for AF after CABG surgery.

1

Variables	Adjusted OR*	95% CI*	p value
HATCH score	1.334	1.022-1.741	0.034
Triglycerides	0.996	0.992-1.000	0.030
Furosemide usage	1.632	0.560-4.757	0.370
Distal anastamosis	1.415	0.942-2.126	0.094

OR: odds ratio CI: confidence interval

P364

Results from a comparison of cryoballoon vs radiofrequency ablation using carto 3 system for paroxysmal atrial fibrillation, (the first algerian experience af ablation with

DR Bouame[1]; DR Tebache[1]
[1]*Central Hospital of the Army, Algiers, Algeria*

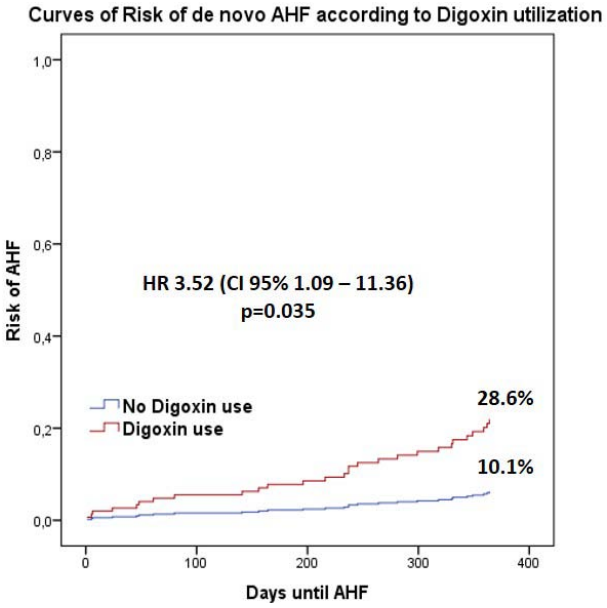
Introduction: Cryoballoon ablation has emerged as a new alternative for the treatment of symptomatic drug-refractory atrial fibrillation (AF) , comparative data of early recurrence rates of atrial fibrillation (ERAF) following second-generation cryoballoon (CB-G2) and radiofrequency current (RFC, using the carto 3 system with smartouch) ablation for pulmonary vein isolation (PVI) in paroxysmal AF (PAF) are rare. We randomized PAF patients into either PVI with CB-G2 (group 1) or PVI with a combined RFC-approach applying contact force (CF, smartouch) with the endpoint of unexcitability (group 2) to investigate ERAF (for a duration of six months).
Methods: In group 1 (n = 19), CB-G2-PVI was performed. After CF-PVI in group 2 (n = 15), bipolar pacing on the ablation line and additional ablation until unexcitability was conducted. Follow-up included 72 h of in-hospital monitoring followed by 15-day Holter ECGs (24h) 3, and 6 months, , post ablation to evaluate ERAF.
Results: Acute PVI was reached in 98% of group 2 and in 97% of group 1. Shorter procedure durations (114.5 ± 13.9 vs. 167.3 ± 18.7 min, P < 0.05) but extended fluoroscopy times (22.5 ± 11,5min vs. 17.5 ± 10.3 min, P < 0.05) were found in the CB-G2 group. Six non-severe complications occurred (4 vs 2 in group 1 and 2, P = 0.73). In group 2, three patients suffered from ERAF vs. three patients in group 1 (P = 0.67). The time until the occurrence of ERAF was shorter in group 2 when compared with group 1 (P = 0.025).
Conclusion: ERAF rates were equal among groups at six months; however, they occurred earlier in the initial phase (the first month) after RFC ablation when compared with CB-G2 (the third month). PVI utilizing cryoablation is associated with shorter procedure durations but extended fluoroscopy time while being similarly secure.
We acknowledge an absence of superiority in the efficiency and safety of one technique compared to another.

P365

Chronic digoxin utilization in patients with atrial fibrillation is associated with hospitalization for de novo acute heart failure

J B Augusto[1]; M Borges Dos Santos[1]; D Roque[1]; D Faria[1]; H Ferreira[1]; J Urzal[1]; C Santos[2]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal*; [2]*Hospital Santo Andre, Leiria, Portugal*

Background: The treatment of atrial fibrillation (AF) is complex. There are conflicting data regarding the effects of digoxin used for rate control in these patients.
Purpose: We aimed to evaluate the incidence of hospitalization for de novo acute heart failure (AHF) at 12-month follow-up in patients with atrial fibrillation who were under digoxin therapy.
Methods: We included retrospectively 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period. Among them, 423 patients were admitted for in-hospital management. Patients who had previous known heart failure (n = 101) were excluded. We determined the proportion of digoxin prescription at discharge. Primary outcome was the incidence of hospitalization for de novo AHF 12 months after discharge.
Results: We included 253 AF patients who were successfully discharged and followed for 12 months (mean age of 70.7 ± 12.6 years, 37.5% males). A total of 5.9% (n = 15) had digoxin prescribed at discharge. Kaplan-Meier analysis (Figure) showed that patients with AF who were taking digoxin had a higher incidence of de novo AHF 12 months after discharge (28.6 vs. 10.1%; log-rank p = 0.027). Multivariable Cox regression analysis controlled for age, gender, systemic hypertension, diabetes mellitus, pattern of AF (paroxysmal or non-paroxysmal), successful cardioversion at discharge, CHA2DS2VASc score, chronic kidney disease and glomerular filtration rate at discharge showed that digoxin therapy was an independent predictor of de novo AHF (HR 3.52; CI 95% 1.09 – 11.36; p = 0.035). There was a trend towards a higher mortality rate 12 months after discharge in AF patients taking digoxin (26.7 vs. 10.5%; p = 0.079).
Conclusions: Digoxin may be harmful in AF patients, as it is associated with hospitalization for de novo AHF, as well as a tendency towards higher mortality. This finding could have an impact on the management of patients with AF who are at risk of developing heart failure.



Risk of de novo AHF

P366

Why don't beta-blockers work in patients with heart failure and atrial fibrillation? Pauses?

Y Mareev[1]; AR Lyon[1]; R Lane[2]; P Rogers[2]; C Butcher[1]; R Smith[2]; J Cleland[1]
[1]*Royal Brompton & Harefield Hospitals, Imperial College, London, United Kingdom*; [2]*Royal Brompton & Harefield NHS Foundation Trust, London, United Kingdom*

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Background: Recent analyses suggest that patients with heart failure and a reduced left ventricular ejection fraction (HFrEF) who are in atrial fibrillation (AF) do not benefit from beta-blockers. This might be because the benefits of beta-blockers are offset by induction of arrhythmias, particularly pauses.
Aim: To quantify, in patients with heart failure who are either in sinus rhythm (SR) or AF, the burden of brady- and tachy-arrhythmias and provide insights into the relationship between them and heart rate measured at clinic.
Methods: Ambulatory patients with symptomatic chronic heart failure treated with loop diuretics but with no implanted device were invited to wear a patch to record

their ECG for up to 14 days. Baseline differences between those with AF and SR were made using Mann–Whitney U or Fisher's exact tests. The primary endpoint was a composite; bradycardia ≤30bpm for ≥ one minute; high-degree atrioventricular (AV) block; pauses ≥3 seconds; average of >1,000 ventricular ectopics beats per day; ventricular tachycardia (VT) with ≥100 bpm for ≥5 beats.
Results: Patients were predominantly in NYHA class II with a median LVEF of 37%; 30 were in AF and 47 in SR. Patients with AF were older (77 vs. 68 years), had higher heart rate (73 vs. 64 bpm) and were less likely to receive beta-blockers (53% vs. 87%) and ACEi/ARA (70% vs.96%) and more likely to receive digoxin (43% vs. 4%). The median duration of monitoring was similar between groups (331 hours). Of patients in AF, 23 (77%) met the primary endpoint compared to 22 (47%) in SR ($p = 0.02$). Compared to patients in SR, more patients in AF had pauses (20% vs. 2%, $p = 0.01$) or heart rate <30bpm (6% v 0%). The median clinic heart rate for those with AF and pauses was 70bpm (IQR: 67-76) bpm. The rate of brady-related VT was similar in AF and SR (6.6% vs. 8.5%; $P = 1.0$). One patient in SR developed an idio-ventricular rhythm at 40bpm during recording, then symptomatic VT and ventricular fibrillation from which they were resuscitated.
Conclusions: Although patients with heart failure and AF have higher clinic heart rates than those in SR, they have a high incidence of brady-arrhythmias, some of which are followed by episodes of VT. Whether this accounts for the failure of beta-blockers to improve prognosis in patients with HFrEF requires further research.

CARDIOMYOPATHY

P367
Pregnancy in women with hypertrophic cardiomyopathy: data from the European Society of Cardiology initiated Registry of Pregnancy and Cardiac disease (ROPAC)

S Sorel Goland[1]; IM Van Hagen[2]; G Elbaz-Greener[3]; U Elkayam[4]; A Shotan[5]; WM Merz[6]; SC Enar[7]; IR Gaisin[8]; PG Pieper[9]; MR Johnson[10]; R Hall[11]; A Blatt[3]; JW Roos-Hesselink[2]
[1]Kaplan Medical Center, Rehovot, Israel; *[2]Erasmus MC, Rotterdam, Netherlands*; *[3]Assaf Harofeh Medical Center, Zerifin, Israel*; *[4]University of Southern California, Los Angeles, California, United States of America*; *[5]Hillel Yaffe Medical Center, Hadera, Israel*; *[6]University Bonn Medical School, Bonn, Germany*; *[7]Turkiye Hospital, Istanbul, Turkey*; *[8]Izhevsk State Medical Academy, Izhevsk, Russian Federation*; *[9]University Medical Center Groningen, Groningen, Netherlands*; *[10]Imperial College School of Medicine, Chelsea and Westminster Hospital,, London, United Kingdom*; *[11]Norwich Medical school, University of East Anglia, Norwich, London, United Kingdom*

Aims: We report the maternal and fetal outcomes at birth and after 6 months in a cohort of pregnant women with hypertrophic cardiomyopathy (HCM).
Background: Although most women with HCM tolerate pregnancy well, there is an increased risk of obstetric and cardiovascular complications.
Methods: All pregnant women with HCM entered into the prospective worldwide Registry of Pregnancy and Cardiac disease (ROPAC) were included in this analysis. The primary endpoint was a major adverse cardiovascular event (MACE), which included death, heart failure (HF), thromboembolic event and arrhythmia. Baseline and outcome data were analysed and compared for patients with MACE versus without MACE and for patients with obstructive HCM versus non-obstructive HCM.
Results: Sixty pregnant women (mean age 30.4 ± 6.0 years) with HCM (41.7% obstructive) were included. No maternal mortality occurred in this cohort. In 14 (23%) patients at least one MACE occurred: 9 (15.0%) HF and 7 (12%) an arrhythmia (6 ventricular and 1 atrial fibrillation). MACE occurred most commonly during the 3rd trimester and postpartum period. In total, 3 (5.0%) women experienced fetal loss. Women with MACE had a higher rate of emergency Caesarean delivery for cardiac reasons (21.4% vs. 0%, $p = 0.01$). No significant differences in pregnancy outcome were found between women with obstructive and non-obstructive HCM. NYHA functional class of ≥ II and signs of HF before pregnancy, were associated with MACE.
Conclusions: Although most women with HCM tolerated pregnancy well, cardiovascular complications were not uncommon and predicted by pre-pregnancy status facilitating pre-pregnancy counselling and targeted antenatal care.

P368
Serum NT-probrain natriuretic peptide and high-sensitivity cardiac troponin I levels in carriers of myosin-binding protein C founder mutation

G Gunnar Thor Gunnarsson[1]; B Adalsteinsdottir[1]; CY Ho[2]; BJ Maron[3]; MA Burke[4]; R Danielsen[5]; JG Seidman[4]; CE Seidman[4]
[1]University of Iceland, Faculty of Medicine, Akureyri, Iceland; *[2]Brigham and Women's Hospital, Department of cardiology, Boston, United States of America*; *[3]Minneapolis Heart Institute Foundation, The Hypertrophic Cardiomyopathy Centre, Minneapolis, United States of America*; *[4]Harvard Medical School, Department of Genetics, Boston, United States of America*; *[5]Landspitali University Hospital, Reykjavik, Iceland*

On behalf of: The Icelandic HCM project

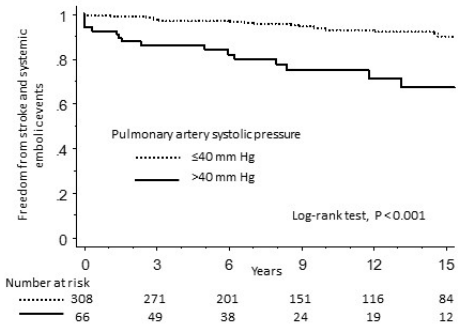
Background: Increased levels of serum NT-probrain natriuretic peptide (NT-proBNP) and cardiac troponins have been observed in patients with overt hypertrophic cardiomyopathy (HCM) and are associated with various clinical features such as severity of left ventricular hypertrophy (LVH), symptoms of heart failure and degree of fibrosis. Additionally NT-proBNP concentration predicts overall prognosis and survival in HCM. However, limited data exists on the role of cardiac biomarkers in sarcomere mutation carriers with normal left ventricular (LV) wall thickness.
Purpose: The aim of this study was to determine if serum NT-proBNP and high-sensitivity cardiac troponin I (hsTNI) may play a role as markers of LV remodeling in MYBPC3 mutation carriers before the development of LVH.
Methods: In total of 290 genotyped individuals were studied from Icelandic families with the MYBPC3 c.927-2A>G founder mutation. Subject were divided into 3 groups based on genotype status and the presence or absence of LVH (≥12mm). NT-proBNP and hsTNI levels were compared between 60 genotype-positive individuals without LVH (G+/LVH-; age 33 ± 17), 108 genotype-positive with LVH (G+/LVH+; age 52 ± 17), and 122 healthy control relatives (G-/LVH-; age 41 ± 18).
Results: A stepwise increase in mean NT-proBNP levels was observed between groups; 37.5 ± 1.09 pg/mL in controls, 65.3 ± 1.1 pg/mL in G+/LVH- subjects and 179 ± 1.14 in G+/LVH+ (values expressed as means + SE, adusted for age and gender; $p < 0.0001$ between each group). However, there was a substantial overlap in NT-proBNP levels between the G+/LVH– and control groups. In G+/LVH+ subjects, hsTNI was significantly higher (5.46 ± 1.12 pg/mL) compared to the other groups. There was not a significant difference in hsTNI levels between G+/LVH- subjects (1.71 ± 1.24 pg/mL) and controls (1.26 ± 1.11 pg/mL; $p = 0.113$).
Conclusions: Higher concentration of NT-proBNP in G+/LVH- subjects compared to controls may reflect early LV remodeling process in HCM. A follow-up study is needed to determine if serum concentrations of NT-proBNP in genotype-positive individuals can predict the risk of developing LVH.

P369
Echocardiographically estimated pulmonary artery systolic pressure predicts progressive heart failure and systemic embolic events in patients with hypertrophic cardiomyopathy

K Kanbayashi[1]; S Shintaro Haruki[1]; Y Minami[1]; R Maeda[1]; K Haruki[1]; R Itani[1]; A Suzuki[1]; T Suzuki[1]; K Ashihara[1]; T Shiga[1]; N Hagiwara[1]
[1]Tokyo Women's Medical University, Cardiology, Tokyo, Japan

Background: Echocardiographically estimated pulmonary artery systolic pressure (PASP) is a non-invasive widely available method that is used to estimate pulmonary arterial pressure. Although elevated PASP predicts mortality in patients with hypertrophic cardiomyopathy (HCM), the details of adverse events is not available. This study aimed to determine whether elevated PASP is predictive of progressive heart failure and systemic embolic events in a tertiary referral HCM cohort.
Methods: This study included 374 clinically diagnosed patients with HCM. PASP was estimated from tricuspid regurgitant jet velocity using the modified Bernoulli equation at the initial evaluation.
Results: The median (interquartile range) PASP was 33 (28–37) mm Hg, and elevated PASP (>40 mm Hg) was observed in 66 (17.6%) patients. Patients with elevated PASP had a higher proportion of female sex, were more likely to have atrial fibrillation, and had a larger left atrial dimension than those without elevated PASP (≤40 mm Hg). Twenty of the 66 (30.3%) patients with elevated PASP and 30 of the 308 (9.7%) patients without elevated PASP experienced episodes of progressive heart failure with an increase to ≥3 New York Heart Association functional class ($P < 0.001$). In addition, 17 of the 66 (25.8%) patients with elevated PASP and 24 of the 308 (7.8%) patients without elevated PASP experienced stroke and systemic embolic events during the 10.3 ± 7.4 years of follow-up ($P < 0.001$; Figure). Multivariable analysis showed that PASP >40 mm Hg was independently associated with progressive heart failure (adjusted odds ratio, 2.08; P=0.049) and embolic events (adjusted hazard ratio, 2.66; P=0.008).
Conclusions: PASP estimated by Doppler echocardiography could help risk stratification for progressive heart failure and embolic event in patients with HCM.

Figure



Figure

P370

Characterization of circulating miRNA21 in young and elderly patients with symptomatic hypertrophic cardiomyopathy

VG Victoria Davydova[1]; TG Bezhanishvili[2]; EN Semernin[1]; AA Poliakova[1]; S Pyko[3]; EV Kiseleva[2]; AA Zakharenco[2]; MI Zaraiskii[2]; AY Gudkova[2]
[1]Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation; *[2]Saint Petersburg Pavlov State Medical University, Saint Petersburg, Russian Federation*; *[3]Saint Petersburg Electrotechnical University "LETI", Saint Petersburg, Russian Federation*

Background: The level and function of circulating miRNA21 in genetic cardiac diseases have been studied not enough.
Aim: Our aim was to study the level of circulating miRNA21 in patients with familial hypertrophic cardiomyopathy (HCM) in different age groups.
Methods: 72 individuals were examined. The study group included 27 probands with HCM at the age 19 - 70 years (45,67 ± 3,23 years). The diagnosis of HCM was established according to the guideline of the European society of cardiology on the diagnosis and treatment of HCM, 2014. The control group included 45 healthy donors without cardiovascular diseases and other severe pathologies, matched by age and sex with the studied group. Total RNA was extracted from plasma of patients. miRNA21 and reference RNA U6 cDNA was prepared based on StemLoop-technology. Expression was examined using semiquantitative RT-PCR protocol. Calculation of the relative gene expression level of miRNA21 was done according to the standard procedure 2-ΔCt.
Results: The level of the miRNA21 in the group of patients with HCM compared to control group ranged from 0.66 to 337,79 (37,73 ± 13,51) versus from 0.01 to 9,85 (1,84 ± 0,40), p < 0.001, respectively. 16 patients had symptomatic HCM and in 11 cases there was diagnosed asymptomatic HCM. In patients with symptomatic HCM the level of miRNA21 compared to asymptomatic HCM ranged from 1.87 to 337,79 (57,87 ± 21,46) versus from 0.66 to 45,25 (8,45 ± 3,85), respectively. Elevated levels of circulating miRNA21 were found in patients with symptomatic HCM (p < 0,004). Patients with symptomatic HCM were divided into 2 subgroups: 1 — young patients at the age from 19 to 43 (30,56 ± 3,09); 2 - elderly patients at the age from 51 to 68 (63,14 ± 2,38). The main symptoms in young patients were dizziness, syncope, ventricular arrhythmia (III-V class according to Lown classification). The risk of sudden death corresponded to the intermediate and high risks according to the 5-year risk of SCD using the HCM Risk-SCD model (a Web-based calculator is provided with the Guidelines, 2014).
The leading syndrome in older patients was heart failure NYHA II-III. In both groups the majority of patients had an adverse cardiac remodeling. In young patients with symptomatic hypertrophic cardiomyopathy the level of miRNA21 ranged from 7 ,46 to 337,79 (83,64 ± 34,61) and it was higher (p < 0.042) than in the group of patients with symptomatic HCM older than 45 years, in which the level of miRNA21 ranged from 1.87 to 119.43 (24,73 ± 15,92).
Conclusion: The significant increase of the level of miRNA21 was found in young patients with HCM with a high risk of sudden cardiac death and adverse cardiac remodeling. Age is an important determinant of the clinical course of the HCM.

P371

Can plasma proteomic profiling differentiate patients with hypertrophic cardiomyopathy from other cardiovascular patients?

R Radek Pudil[1]; S Stulik[2]; H Rehulkova[2]; P Rehulka[2]; A Fucikova[2]; L Horakova[1]
[1]Charles University Prague, Faculty of Medicine in Hradec Kralove, 1st Department of Medicine, Hradec Kralove, Czech Republic; *[2]Faculty of Military Health Sciences, University of Defence, Department of Molecular Pathology and Biology, Hradec Kralove, Czech Republic*

Introduction: Hypertrophic cardiomyopathy (HCM) is a hereditary cardiovascular disease with a prevalence of 1:500. Even if numerous genetic mutations were described and many diagnostic methods are used, some method that could help with early diagnosis would be beneficial. Proteome discovery analysis represents a promising outlook in an effort of identification novel disease specific markers of different cardiovascular diseases.
Purpose: The aim of this study was to compare plasma profiles of patient cohort suffering from non-obstructive HCM and group of healthy donors and also other cohorts of selected cardiovascular diseases: dilated cardiomyopathy (DCM), aortic valve stenosis (AS), chronic stable coronary artery disease (CAD) and stable arterial hypertension (AH). The next aim was to identify disease-unique protein markers that could be potentially used in early diagnosis of HCM.
Methods: In this study were analyzed pooled plasma samples of patient individuals. All these samples were depleted from fourteen most abundant proteins in human plasma. Proteomic labeling with isobaric tags for relative and absolute quantitation (iTRAQ) was applied to all of these samples. Firstly, plasma reduction, alkylation and trypsin digestion was done according the manufacturer's protocol. Secondly, all samples were labeled with iTRAQ reagents and mixed. Sample mixtures were purified and fractionated using reverse phase chromatography with mobile phase buffered at pH = 10. Acidified, evaporated and reconstituted fractions were further submitted to LC-MS/MS analysis using Q-Exactive mass spectrometer.
Results: Out of the high number of identified proteins, 293 proteins showed significant up- or down- regulation at least in one cardiovascular cohort in comparison to control group of healthy donors. We have focused only on 128 disease-uniquely shifted proteins in plasma concentration. More than sixty disease-unique proteins were identified in DCM cohort and almost fifty proteins in AS cohort., and only seven disease-unique markers were detected in HCM group, whereas all of them are related to this disease as was confirmed by the search in the published literature. Both principal component analysis and hierarchical clustering analysis identically divided the disease groups into two main clusters: first involving HCM, AH and control group of healthy donors; second cluster containing DCM, AS and CAD.
Conclusion: The aim of this study was a plasma profiles comparison of selected cardiovascular diseases. Many proteins with significant differences and also proteins with disease-unique plasma profile differences were identified. These proteins are intended to be consequently validated via targeted proteomic analysis and some of these proteins (in case of successful verification) could later serve as potential markers of HCM or other studied cardiovascular diseases.

P372

Heart fatty acid binding protein and glycogen phosphorylase bb are associated with the morphologic and functional parameters in patients with non-obstructive hypertrophic cardiomyopathy

R Radek Pudil[1]; M Vasatova[2]; L Horakova[1]; P Rehulka[3]; H Rehulkova[3]; J Stulik[3]; V Palicka[2]
[1]Charles University Prague, Faculty of Medicine in Hradec Kralove, 1st Department of Medicine, Hradec Kralove, Czech Republic; *[2]University Hospital Hradec Kralove, Institute of Clinical Biochemistry and Diagnostics, Hradec Kralove, Czech Republic*; *[3]Faculty of Military Health Sciences, University of Defence, Department of Molecular Pathology and Biology, Hradec Kralove, Czech Republic*

Background: Hypertrophic cardiomyopathy (HCM) is mostly autosomal dominant disease of the myocardium, which is characterized by myocardial hypertrophy. The association of increased myocardial structural markers and the severity of left ventricle outflow tract obstruction are very well know.
Purpose: The aim of study was to analyze the clinical significance of these markers in structural and functional changes in patient with non-obstructive type of HCM.
Methods: In the group of 47 patients (58.4 ± 12.4 years, 12 females) with non-obstructive HCM, we assessed plasma concentrations of glycogen phosphorylase BB (GPBB), cardiac troponin T (hsTnT) and heart type of fatty acid binding protein (hFABP) and analyzed its association with morphological and functional parameters.
Results: Left ventricle mass was 344.8 ± 129.9 g, and it exceeded reference values for two-dimensional method in all patients. Left ventricle mass index was 171.4 ± 60.2g.m-2, and it exceeded reference values in all patients. The mean of the left ventricle ejection fraction was 67.1 ± 9.9%, and, only in 2 (4%) patients, the LV ejection fraction was below the reference values. Left ventricle fractional shortening was 33.7 ± 8.7, and it exceeded the reference values in 3 (6%) patients. None of the patients had left ventricle outflow tract obstruction. Compared to healthy controls, plasma levels of structural markers were increased [hsTnT: median: 9ng/L (IQR: 5 - 16 ng/L), vs. 7 (5 - 9) ng/L, p 0.03; hFABP: 1.8 (1.4 - 3.3) μg/L vs. 1.6 (1.3 - 2.1) μg/L, p 0.05; GPBB: 3.9 (2.5 - 6.3) μg/L vs. 2.3 (1.9 - 4.2) μg/L, p 0.001]. We found significant association of plasma cardiac markers levels and left ventricle mass index (hFABP: r 0.41, 95% CI: 0.07-0.66, p 0.01; GPBB: r 0.21, 95% CI: 0.12-0.51, p

0.05; hsTnT: r = 0.39, 95%CI: 0.12 - 0.62, p 0.008) and LV ejection fraction (hFABP: r -0.31, 95% CI: -0.57 - -0.02, p 0.05; GPBB: r -0.46, 95% CI: -0.68 - -0.14, p 0.004).
Conclusions: Increased hFABP, GPBB and hsTnT levels are associated with structural and functional parameters in patients with HCM and could serve as a potential tool for diagnostic process of these patients.

P373
Clinical risk factors of new onset atrial fibrillation in patient with hypertrophic cardiomyopathy.

J-H Jung-Hyun Choi[1]; BW Kim[1]; SH Lee[1]
[1]*Busan National University Hospital, Busan, Korea Republic of*

Backgrounds: Atrial fibrillation(AF) is common clinical manifestation of HCMP patients. Prevalence of AF in HCMP patients is known to approximately 20%. There are limited data available to predictive factor of AF in patient of HCMP. The aim of this study is to investigate of clinical risk factor of AF in HCMP patients.
Methods: This study is retrospective observational study. We investigated the HCMP patients who performed echocardiography and had sinus rhythm at presentation (n = 40) from 2011 to 2015 at our 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 ± 14.89 vs 31.00 ± 7.99, p = 0.001, LAVI(59.01 ± 24.09 vs 43.58 ± 16.37, p < 0.001, Mitral E velocity(77.03 ± 27.78 vs 61.74 ± 17.56, p < 0.001) and AEMDi (72.07 ± 15.90 vs 63.08 ± 15.43, p = 0.004), AEMDp(152.41 ± 27.59 vs 141.98 ± 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 HCMP patients.
Conclusion: This observational study shows AEMDi by PW Doppler may have an additional predictive value to LAVI of new onset AF in HCMP patients.

P374
The course of dilated cardiomyopathy, depending on the availability of ECG changes

NA Kurbanov[1]; TA Abdullaev[1]; I A Igor Tsoy[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

Objective: The study of the clinical and functional status of pts with dilated cardiomyopathy (DCM) with and without pathological changes on ECG.
Methods: The study included 274 pts with DC at the age of 17 to 61 years (mean age 42,9 ± 1,1 years). In addition to the clinical examination all pts underwent ECG, Holter ECG monitoring (HMECG), echocardiogram, 6MWT. All pts were divided into 4 grs. Gr 1 included 47 pts in whom the ECG recorded blockade of the left leg bundle branch block (LBBB). Pts of the 2 gr (44) in the ECG were detected pseudo-Q wave. The 3 gr consisted of 124 pts, which were characterized on the ECG by decreasing of R wave amplitude, a deep S wave in the right leads, and high R wave in the left precordial leads. 4 gr of pts on the ECG were found complete blockade of right bundle branch block (n = 16) or a bundle branch block (44 pts), which were excluded from the study of this fragment.
Results: Source FC HF in the I and II gr was significantly higher than in gr III. (3,5 ± 0,1 and 3,3 ± 0,1 versus 3,1 ± 0,1; p < 0.01). the clinical status of pts found that in gr III. 6MWT parameters were significantly higher (232 ± 9m) than in grs I and II, respectively (196 ± 12 m and 202 ± 11m p < 0.01). A number of indicators, indicating the presence of right ventricular heart failure, such as ascites, peripheral edema were significantly more frequent in the gr with LBBB pseudo Q-wave and ECG changes. Analysis of the parameters of intracardiac hemodynamics revealed an increase in the linear dimensions of the left heart of pts I and II: improving performance of EDD - on 9.2% and 3.2% (both p < 0.01), ESD - on 12.5%, and 5,1% (p < 0.01), while LVEF was lower on 12.1% and 16% (both p < 0.01) in gr I and II, respectively. Analysis of conduction disorders according HMEKG showed that I st. AV block significantly more common in the I and II grs (32% and 39% vs. 12%; p < 0.01), respectively. It should be noted that the progression of heart failure in the 15 pts with AV- blockade of I degree in 4 cases, the AV-conduction violation worsened up to the III degree, requiring pacemaker implantation in the future, in the absence of this kind of dynamics in the other grs. Analysis of the frequency of occurrence of heart rhythm disorders has shown that high grade ventricular arrhythmias were significantly more frequent in gr I and II, amounting to 68% and 77% versus 28.9% (p < 0.01). However, it noted the prevalence of the number of pts with atrial fibrillation in gr III (p> 0.05).
Thus, in pts with dilated cardiomyopathy and LBBB with the presence of the ECG pseudo-Q-wave observed more pronounced destructive changes in the myocardium, as evidenced by the low contractility function, the prevalence of the presence of high grade ventricular arrhythmias and conduction atrioventricular violation and also a high incidence of registration signs of right heart failure compared with pts without the presence of these changes.

P375
Genetic meta-analysis in idiopathic diated cardiomyopathy: can gene expression repositories offer a new insight?

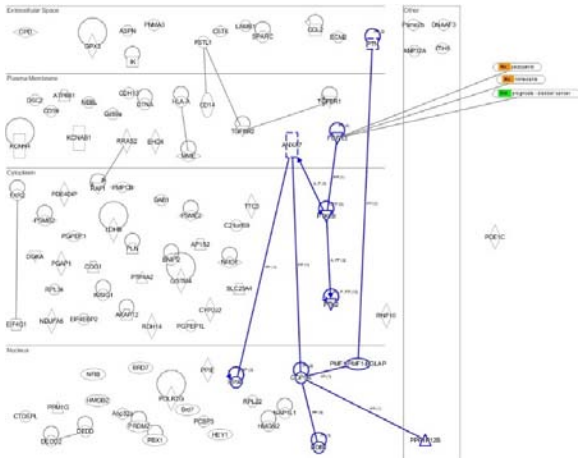
C T Cormac O'connor[1]; M E O'callaghan[2]; D O'hare[1]; T Kiernan[1]
[1]*University Hospital Limerick, Cardiology Department, Limerick, Ireland*; [2]*University of Limerick, Research Department, limerick, Ireland*

Introduction: Despite advances in genetic analysis and the increasing availability of analytical technologies, the genetics of Idiopathic (non-familial) Dilated Cardiomyopathy (DCM) is poorly understood. Microarray analysis allows the simultaneous analysis of up to 40,000 gene products. Public gene expression repositories (PGER) house microarray expression data from over 50,000 individual experiments.
Purpose: To utilise PGERs to identify genetic differences between normal and cardiomyopathic hearts, and use this data to identify dysregulated intracellular pathways.
Methods: Search was conducted differentiating hearts with idiopathic DCM and normal controls. Nine experiments were considered suitable for analysis. Raw genetic expression data was extracted and analysed using R statistical software. Genes that were dysregulated from controls were compared across all nine experiments using de novo visual basic script (VBS) code. Enrichment analysis was conducted using Ingenuity pathway software.
Results: A total of 23,967 genes were dysregulated across all experiments (table 1). Frequency analysis identified genes occuring most commonly across experiments. Enrichment analysis allowed the identification of specific pathways which were observed to become up- and down-regulated in at least 66% (6 out of nine experiments). Pathways which were seen to be up-regulated in DCM have been associated with: 1) Immune cell infiltration effects seen in rheumatoid arthritis, 2) c-AMP signalling, 3) Cardiac B-Adrenergic signalling and , 4) HGF signalling (Figure 1). Pathways down-regulated were 1) PTEN signalling, 2) Protein Kinase A signalling, and 3) the STAT3 Pathway.
Conclusions: PGERs successfully established a genetic consensus in identifying intracellular pathways which have become dysregulated in idiopathic DCM. This novel type of meta-analytical technique shows promise in establishing intracellular aetiology in systemic pathology.

Genes most frequency of dysregulated

Gene	Number of Experiments gene was dysregulated (out of Nine experiments).	Up or down -regulated	Known Intracellular function
LAMB1	9	UP	Laminin B1, extracellular matrix protein
CD14	8	DOWN	Innate immune protein involved with bacterial surveillance
PDE4DIP	8	DOWN	C-AMP mediated immunomodulation
DSC2	8	UP	Cell-cell adhesion protein previously associated with with arrhythmogenicright ventricular dysplasia
HEY1	8	UP	Associated with embryonic cardiovascular development
INSIG1	8	UP	Mediates feedback control of cholesterol synthesis in cells.
KCNAB1	8	UP	Voltage-gated Potassuim channel, shaker-related subfamily.
NAP1L1	8	UP	Nucleosome assembly protein (NAP) family, involved in cell proliferation

Genes most frequency of dysregulated



Pathway analysis of most frequent genes

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Clinical significance of excessive myocardial trabeculation in dilated cardiomyopathy patients

A Sousa[1]; T Pinho[2]; O Azevedo[3]; L Lopes[4]; M Campelo[2]; B Moura[5]; A Madureira[2]; F Rocha Goncalves[1]; J Silva Cardoso[1]; E Martins[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; [2]H. São João, Porto, Portugal; [3]Guimares Hospital, Guimaraes, Portugal; [4]Garcia de Orta Hospital, Lisbon, Portugal; [5]Regional Military Hospital nº1, Porto, Porto, Portugal

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Introduction: Left ventricular noncompaction (LVNC) is characterized by extreme morphologic variability and considerable overlap with other cardiomyopathies. Whether LVNC is a distinct pathological entity or a merely an anatomical phenotype shared by different cardiomyopathies remains a matter of debate.
Purpose: The goal of this study is to evaluate the clinical relevance of excessive myocardial trabeculations in dilated cardiomyopathy (DCM) patients.
Methods: We included 80 consecutive idiopathic and familial DCM patients, followed at 5 national referral centers, that underwent a comprehensive CMR study as part of their diagnostic work-up. Ventricular volumes, ejection fraction and mass were measured using dedicated software. Late gadolinium enhancement (LGE) presence, pattern and location were assessed. We compared clinical, electrocardiographic, imagiological and molecular data and outcomes between patients with or without noncompaction criteria at CMR.
Results: Nine patients (11%) fulfilled noncompaction criteria. They presented similar age (47 ± 13 vs 46 ± 12, p = 0.829; at diagnosis 42 ± 8 vs 38 ± 14, p = 0.652), gender (56% males vs 52%, p = 1.000) and identical clinical profile (symptoms at presentation, cardiovascular risk factors, previous hospitalizations, NYHA class, congestion, heart-failure medical therapy, devices, heart transplant and family history of DCM, heart transplant, sudden death or heart failure death – p NS for all comparisons). Mean left ventricular ejection fraction was 32 ± 11% vs 34 ± 11% (p = 0.514) and end-diastolic volume 129 ± 29 mL/m2 vs 127 ± 37 mL/m2 (p = 0.889). LGE was present in similar proportion of patients, although in patients with LVNC, LGE was preferentially located in apical-lateral and apical-anterior segments. There was no difference in any electrocardiographic parameters. At least one genetic variant was found in 44% pts with LVNC vs 19% of those without, although the difference was not statistically significant. At a median follow-up of 32 months (IQR 16), nine patients experienced an adverse event, but the presence of LVNC was not a predictor of those (OR 2.86, 95%CI [0.48-17.0], p = 0.248).
Conclusion: In our series of patients the presence of excessive trabeculations was neither associated with major differences in clinical presentation, molecular profile, functional parameters, nor it was a predictor of worse prognosis. This argues against LVNC being a distinct form of cardiomyopathy or being associated with a more severe form of DCM.

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Clinical markers of LMNA-associated DCM and prognostic predictors of life-threatening ventricular tachyarrhythmias

T G Vaikhanskaya[1]; N G Danilenko[2]; L N Sivitskaya[2]; O G Davydenko[2]
[1]Republican Scientific and Practical Center "Cardiology", Minsk, Belarus; [2]Institute of Genetics and Cytology, National Academy of Science, Minsk, Belarus

Lamin-related phenotype of DCM associated with a high risk of sudden cardiac death (SCD) even in the absence of significant dilatation and left ventricular contractile dysfunction.
Purpose: The aim of this study was to evaluate clinical predictors of the LMNA-associated DCM phenotype and non-invasive prognostic markers of life-threatening ventricular tachyarrhythmic events.
Methods and results. The study included 165 patients with DCM who had a heart rhythm disorder and conduction disturbance (aged 49,2 ± 11,5 years; 135/81,8% male; NYHA 2,67 ± 0,45; LVEF 27,6 ± 10,1 %; follow-up 39,7 ± 12,4 months). All patients underwent clinical studies, screening of lamine A/C (LMNA) gene, CPK and NT-proBNP levels definition, neuromuscular investigation. LMNA mutations were detected in 45 (27,3%) patients. As a result of ROC analysis only ECG predictors (PR ≥ 215 ms: AUC 0.987, 95% CI 0.973 - 0.999, p = 0.0001, sensitivity 95 %, specificity 95 %; pathological mTWA test ≥ 25 % : AUC 0.775, 95% CI 0.701 - 0.848, p = 0.0001; QRS ≥ 122 ms: AUC 0.773, 95% CI 0.689 – 0.857, p = 0.0001) were demonstrated a priority predictive significance to assess LMNA-positive phenotype compared to laboratory tests (serum CPK level ≥ 118 u/l: AUC 0.671, 95% CI 0.548 - 0.793, p = 0.009; sensitivity 65%, specificity 69%; NT-proBNP: AUC 0.538, 95 % CI 0.275 - 0.802, = 0.75) and echocardiography parameters (LV GLS: AUC 0.645, 95% CI 0,548 - 0.793, p = 0.092; LVEF: AUC 0.473, p = 0.75). Events of sustained ventricular tachycardia (sVT) and/or ventricular fibrillation (VF), and documented SCD were accepted as a primary endpoints to the multivariate Cox regression model. By analysis independent predictors of life-threatening tachyarrhythmias were revealed such as nsVT episodes (beats ≥5, bpm ≥ 150: HR 2.23; 95% CI 1.03-4.96; p = 0.033) and changes in LMNA gene (missense mutations and/or rs4641, s.1698C>T: HR 1.87; 95% CI, 1.09 - 3. 01; p = 0.02).
Conclusions: Our findings support an important position of genetic research LMNA mutations in DCM patients for an early prediction of adverse clinical outcomes. According to the Cox regression analysis were detected an independent predictors (cumulative effect of the combination identified predictors such as nsVT events and LMNA-positivity: HR 5.23; 95% CI 1.45-16.9, p = 0.013) that should be used to improve the risk-stratification of SCD and optimization of the general management for DCM.

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Implantable cardioverter/defibrillators for primary prevention in dilated cardiomyopathy post-DANISH: an updated meta-analysis and systematic review of randomized controlled trials

A Karathanos[1]; G Wolff[1]; Y Lin[1]; M Brockmeyer[1]; S Wolters[1]; B Nowak[2]; A Fuernkranz[1]; H Makimoto[1]; M Kelm[1]; V Schulze[1]
[1]University Hospital Dusseldorf, Department of Cardiology, Pneumology and Angiology, Dusseldorf, Germany; [2]Cardiology Centre Bethanien (CCB), Frankfurt am Main, Germany

Background: Sudden cardiac death (SCD) is frequent in patients with heart failure due to dilated cardiomyopathy (DCM). Implantable cardioverter/defibrillator (ICD) device therapy is currently used for primary prevention. However, publication of the DANISH trial has recently given reason for doubt, showing no significant improvement in all-cause mortality in comparison to contemporary medical therapy.
Methods: We performed a meta-analysis of all randomized controlled trials comparing ICD therapy to medical therapy (MT) for primary prevention in DCM. The primary outcome was all-cause mortality; secondary analyses were performed on sudden cardiac death, cardiovascular death and non-cardiac death.
Results: Five trials including a total of 2,992 patients were included in the pooled analysis. Compared to contemporary medical treatment there was a significant mortality reduction with ICD device therapy (odds ratio (OR) 0.77, confidence interval (CI) 0.64-0.93; p = 0.006). SCD was decreased significantly (OR 0.43, CI 0.27-0.69; p = 0.0004), while cardiovascular death and non-cardiac death showed no differences. Sensitivity analyses showed no influence of amiodarone therapy on overall results. Analysis of MT details revealed the DANISH population to adhere best to current guideline recommendations.. Furthermore, it was the only study including a substantial amount of CRT devices (56%).
Conclusions: Our meta-analysis of all available randomized evidence shows a survival benefit of ICD therapy for primary prevention in DCM. DANISH results suggest an attenuation of this ICD advantage when compared to contemporary medical and cardiac resynchronization therapy. ICD therapy should remain the recommendation for primary prevention of SCD in DCM according to current literature.

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Arrhythmogenic phenotype of dilated cardiomyopathy: predictors of life-threatening ventricular tachyarrhythmias

T G Vaikhanskaya[1]; L N Sivitskaya[2]; N G Danilenko[2]; T V Kurushka[1]; O G Davydenko[2]
[1]Republican Scientific and Practical Center "Cardiology", Minsk, Belarus; [2]Institute of Genetics and Cytology, National Academy of Science, Minsk, Belarus

Patients (pts) with dilated cardiomyopathy (DCM) are developing a life-threatening ventricular tachyarrhythmias (VTAs) sometimes in the early stages even in the absence of symptoms of severe heart failure and a free linked with systolic dysfunction. This clinical phenotype is arrhythmogenic and associated with an increased risk of sudden cardiac death (SCD)

The aim of this study was to evaluate a clinical prevalence of arrhythmogenic DCM and identify a non-invasive prognostic predictors of life-threatening ventricular tachyarrhythmic events.

Methods and results. One hundred sixty patients with a recent diagnosis of DCM (aged 47,3 ± 11,4; 132\82,5% male; NYHA 2,35 ± 0,49; LV EF 29,6 ± 9,13%) were comprehensively evaluated and followed for 47,9 ± 12,4 months. Arrhythmogenic DCM phenotype was dened by Holter 24h monitoring ECG (or CRT-D/ICD device interrogation) as at presence ≥1 of the following signs: non-sustained or sustained ventricular tachycardias (nsVT\sVT), ≥1500 premature ventricular contractions/24 hours, and ≥50 ventricular couplets/24 hours. Of the 160 patients, 92 (57,5%) pts demonstrated these criteria. In 45 (28,1%) pts with DCM were identified changes in Lamin A\C gene (LMNA). As a primary end points to the multivariate Cox analysis were accepted a successful resuscitation, ICD-shock, documented SCD, sustained ventricular tachycardia (sVT) or ventricular brillation (VF). By the Cox regression multivariable model analysis criteria as a nsVT (5 beats with HR≥150 bpm: HR 2.24; 95% CI 1.02-5,49; p = 0.029) and LMNA missense mutations (≥ 1 nucleotide changes: HR 1.99; 95% CI, 1.09 - 3.97; p = 0.032) were identified as independent and cumulative predictors (HR 5.63; 95% CI 1.63-17.5, p = 0.011) of life-threatening VTAs.

Conclusions: Thus, more half of DCM patients developed an arrhythmogenic phenotype associated with increased risk of VTAs during follow-up. Independent predictors (a fast nsVT and LMNA missense mutations) predicts a poor prognosis and an increased risk of SCD and therefore to improvement of risk-stratification should be used purposely to select of potential candidates for preventive ICD therapy.

P380

Idiopathic dilated cardiomyopathy shows increased circulating levels of soluble low-density lipoprotein receptor-related protein 1

S Roura[1]; C Galvez-Monton[1]; D De Gonzalo-Calvo[2]; A Valero[3]; P Gastelurrutia[1]; E Revuelta-Lopez[1]; C Prat-Vidal[1]; C Soler-Botija[1]; A Llucia-Valldeperas[1]; I Perea-Gil[1]; O Iborra[1]; FE Borras[3]; J Lupon[4]; V Llorente-Cortes[2]; A Bayes-Genis[4]
[1]ICREC research group, Institut d'Investigació en Ciencies de la Salut Germans Trias i Pujol, Badalona, Spain; *[2]Cardiovascular Research Center, CSIC-ICCC, IIB-Sant Pau, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*; *[3]Germans Trias i Pujol Health Science Research Institute, Innovation in Vesicles and Cells for Application in Therapy Group, Badalona, Spain*; *[4]Germans Trias i Pujol Hospital, Cardiology Service, Badalona (Barcelona), Spain*

Introduction: Idiopathic dilated cardiomyopathy (IDCM) is a frequent cause of heart transplantation. Potentially valuable blood markers are being sought and low-density lipoprotein receptor-related protein 1 (LRP1) has been linked to the underlying molecular basis of the disease.

Purpose: This study compared circulating levels of soluble LRP1 (sLRP1) in IDCM patients and healthy controls, and elucidated whether sLRP1 is exported out of the myocardium through extracellular vesicles (EVs) to gain a better understanding of the pathogenesis of the disease.

Methods: LRP1 α chain expression was analyzed in samples collected from the left ventricles of explanted hearts using immunohistochemistry. sLRP1 concentrations were determined in platelet-free plasma by enzyme-linked immunosorbent assay. Plasma-derived EVs were extracted by size-exclusion chromatography (SEC) and characterized by nanoparticle tracking analysis and cryo-transmission electron microscopy. The distributions of vesicular (CD9, CD81) and myocardial (caveolin-3) proteins and LRP1 α chain were assessed in SEC fractions by flow cytometry.

Results: LRP1 α chain was preferably localized to blood vessels in IDCM compared to control myocardium. Circulating sLRP1 was increased in IDCM patients. CD9- and CD81-positive fractions enriched with membrane vesicles with the expected size and morphology were isolated from both groups. The LRP1 α chain was not present in these SEC fractions, which were also positive for caveolin-3.

Conclusions: The increase in circulating sLRP1 in IDCM patients may be clinically valuable. Although EVs do not contribute to higher sLRP1 levels in IDCM, a comprehensive analysis of EV content would provide further insights into the search for novel blood markers for these patients.

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Association between bisphenol A exposure and dilated cardiomyopathy

M Moustafa Kamal Saad[1]; K Elkhashab[1]; N Elsherbiny[2]; H Ebeid[1]
[1]Fayoum University, cardiology, Fayoum, Egypt; *[2]Fayoum University, community medicine and public health department, Fayoum, Egypt*

Background: Bisphenol A (BPA) has become a common environmental chemical released into food or beverage over time, especially under heat and acidic solutions. BPA exposure also occurs in human through inhalation. Studies have suggested potential links between BPA exposure and diseases including cancer, obesity, diabetes, reproductive disorders, neuroendocrine, immune systems and Cardio-Vascular system disorders. BPA exposure may be a risk factor for a range of CVS abnormalities as cardiomyopathies and cardiac arrhythmias. Aims: This study aimed to determine serum (BPA) concentrations in patients with dilated cardiomyopathy (DCM) as well as the serum level of estradiol and testosterone compared with a healthy control group.

Materials and Methods: Fifty DCM patients and thirty healthy controls subjects were included. A thorough physical examination, ECG and a complete echocardiographic assessment was performed. Serum BPA levels, estradiol and testosterone were measured by using corresponding ELISA Kits. RESULTS: BPA was significantly more detected in the DCM groups than in the normal group (P value = 0.048). Patients with DCM and detected BPA had more significant right side chambers affection (in terms of dimensions and function) and left atrial dilation (P value=0.0001 and 0.05 respectively). Atrial fibrillation was significantly detected in the DCM patients than in the normal group (P value = 0.004). Estradiol level was significantly higher in the DCM patients' than in the normal group. CONCLUSION: Our findings demonstrated that BPA exposure increased in DCM patients compared with healthy controls, which raise the possibility that BPA exposure might be responsible for some of the cases of dilated cardiomyopathy.

prevelance of BPA in the study groups

Variables	Cases(N=50)	Control(N=30)	P-value
BPA (bisphenol A)	N (%)	N (%)	
Detected(found but level not incorporated into the comparison)	12 (24 %)	2 (6.7%)	0.048
Not detected	38 (76 %)	28 (93.3%)	

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Risk stratification of life-threatening ventricular tachyarrhythmias in patients with dilated cardiomyopathy

T G Vaikhanskaya[1]; O P Melnikova[1]; A V Frolov[1]
[1]Republican Scientific and Practical Center "Cardiology", Minsk, Belarus

The study of prognostic factors of life-threatening ventricular tachyarrhythmias with tightly related sudden cardiac death (SCD) remains the cornerstone issue still.

Purpose: Design of prognostic model to define personalized risk of life-threatening ventricular tachyarrhythmias in patients with dilated cardiomyopathy (DCM) was the aim of this study.

Material and methods. The study enrolled and followed up 53,1 ± 12,6 months 268 pts with DCM (74,6% male, aged 47,2 ± 11,7 years, LVEF 28,7 ± 10,1%; NYHA class 2,7 ± 0,4). We analyzed age, gender, NYHA, 6-MWT, peak VO2, EchoCG, Holter ECG (PVEs, sVT, nsVT, VF), QRS width, device interrogation and high definition ECG (Intecard-7) with assessment of HRT, mTWA, JTd, and QTd. For multivariate ROC analysis and binary logit-regression model as a primary endpoints were accepted SCD documented, successful resuscitation, sustained VT, and CRT-D\ICD appropriated discharges.

Results: Predictors and their cut-off parameters defined as a result of ROC analysis were included in the binary logit regression model (table). As a result binary logit regression analysis of independent risk factors (PVES, sVT, mTWA, HRT, JTd and LV GLS mean) predictive model was constructed (F=31,2; χ2=143,2; p = 0,0001) eventually:

P = 1/(1 + e^(-(7,25-0,38×LV GLS-0,76×PVEs-4,35×nsVT-1,46×JTd-4,28×HRT-5,03 ×mTWA)))

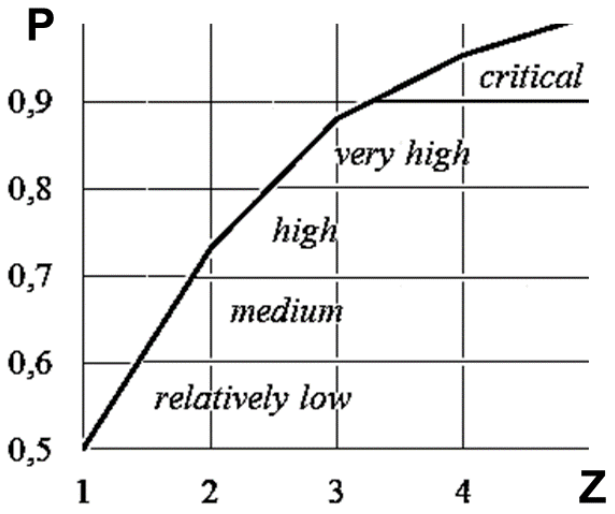
The range of probability of P was divided into the risk level quintiles: 0.5 to 0.6 for low risk; 0.61 to more than 0.91 high risk. Risk grading is presented in Figure 1.The classification matrix demonstrated a high prognostic significance of discriminant function (F=31.2; χ2=143,2; p < 0.0001; sensitivity of 80.8 %; specificity 99.1 %).

Conclusion: The proposed risk stratification allows to classify correctly to 93.9% DCM pts. Non-invasive and an individualized method enable to stratify patients with higher risk of life-threatening VTA by standard clinical investigations (ECG, Echo, Holter ECG) that allows to select of potential candidates for preventive ICD therapy.

Binary logistic regression model

Parameters	Constant	LV GLS ≥ -6,5%	PVEs ≥1500/24h	nsVT*	JTd ≥70 mc	HRT**	TWA***
Coefficients	7.25	-0.38	-0.76	-4.35	-1.46	-4.28	-5.03
Hazards Ratio(χ2)	1414.5	0.68	0.46	0.01	0.23	0.01	0.01

Note: * nsVT ≥ 5 PV Es complexes with HR ≥ 150 bpm; **TO ≥ 0% and/or TS< 2,5 ms/RR; *** mTWA ≥ 25 % test abnormal > 46 mcV



Risk grading of P-values

P383

Women vs. men in takotsubo cardiomyopathy

M Margarida Oliveira[1]; D Bento[2]; R Santos[3]; MJ Vieira[4]; H Antunes[5]; L Reis[6]; C Ruivo[7]; R Faria[8]; A Marreiros[9]; AR Almeida[10]
[1]Alto Ave Hospital Center, Guimaraes, Portugal; *[2]Faro Hospital, Faro, Portugal*; *[3]Hospital Centre do Tamega e Sousa, Penafiel, Portugal*; *[4]Hospital of Santarem, Santarem, Portugal*; *[5]Hospital Sao Teotonio, Viseu, Portugal*; *[6]University Hospitals of Coimbra, Coimbra, Portugal*; *[7]Hospital Santo Andre, Leiria, Portugal*; *[8]Centro Hospitalar do Médio Ave E.P.E, Vila Nova de Famalicao, Portugal*; *[9]Universidade do Algarve, Ciências Biomédicas e de Medicina, Faro, Portugal*; *[10]Hospital Garcia de Orta, Almada, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo cardiomyopathy (TCM) is a cardiac syndrome characterized by transient left ventricular dysfunction in the absence of coronary artery disease. It usually affects postmenopausal women but it can also affect men. Differences between genders regarding TCM are still not clearly defined.
Aim: To determine the differences between men and women regarding clinical presentation, evolution and complications in TCM.
Methods: We performed a multicentre study involving 12 Portuguese hospitals including every patient diagnosed with TCM in the last 12 years. Clinical, electrocardiographic and echocardiographic data were collected and analysed in order to establish the differences between genders. SPSS 23.0 was used for statistical analysis.
Results: We included 234 patients, 24 men and 210 women (168 were postmenopausal). Physical stressor was mainly observed in men (54.2% vs 14.3%, $p < 0.001$) and emotional stressor in women (50% vs 16.7%, $p = 0.002$). Symptoms at presentation were also different between genders, being chest pain more prevalent in females (90.5% vs. 58.3%, $p < 0.001$) and syncope in males (25% vs. 3.3%, $p < 0.001$). Mean follow-up was 33 ± 33months. Mortality was significantly higher in men (20,8% vs 4,8%, $p = 0,002$) and due to cardiac causes in all men and non-cardiac in women ($p = 0,002$).
Conclusion: This study showed significant differences between men and women regarding type of precipitating factor, clinical presentation and prognosis of TCM. Men, compared to women, have more commonly a physical stressor, present more often with syncope and less frequently with chest pain and have higher mortality from cardiac causes.

P384

Development of tachycardia is not related to ejection fraction in patients on clozapine with suspected cardiotoxicity

G George Joy[1]; M Bolstridge[2]; A Porras-Segovia[3]; E Whiskey[2]; S Shergill[2]; C Plymen[4]
[1]King's College Hospital, London, United Kingdom; *[2]South London and Maudsley NHS Foundation Trust, London, United Kingdom*; *[3]University of Granada, Granada, Spain*; *[4]Imperial College Healthcare NHS Trust, London, United Kingdom*

Introduction: Clozapine is the most effective management for treatment-resistant schizophrenia however, its use is limited due to side effects. Tachycardia is a common side effect, although considered relatively benign but, clozapine-associated myocarditis & cardiomyopathy are associated with significant mortality. Patients on clozapine who develop tachycardia are often referred due to concern of cardiotoxicty. In such patients we assessed the relationship between heart rate (HR) & ejection fraction (LVEF).
Method: Retrospective study of 27 patients on clozapine referred to a cardiology tertiary unit with suspected cardiotoxicity. Echo, ECG & demographic data were analysed by students t test & linear regression analysis.
Results: There was no significant correlation between HR & LVEF; in fact, a higher LVEF was associated with a marginally higher HR ($r=0.148$ $p = 0.058$;Fig 1).
There was no significant difference in age, gender, length of time on clozapine, QRS or QTc durations between these two groups (Table 1). Clozapine was frequently discontinued in both groups, but earlier in those with reduced LVEF, see table1. During a follow-up period of 6.1 ± 5 years no patient suffered cardiac mortality.
Discussion: We find that clozapine associated tachycardia is associated with a normal LVEF. We isolated two distinct manifestations of cardiotoxicity related to clozapine: those with tachycardia had normal LVEF & those with reduced LVEF did not exhibit significant tachycardia.
This confirms that the development of tachycardia is not sensitive for cardiomyopathic process but might infer a benign cardiac course to treatment. We suggest that management of these patients should be interdisciplinary with close liaison between cardiologists & psychiatrists to prevent unnecessary cessation of an effective psychiatric medication.

Table 1

	Clozapine 'Cardiomyopathy' group (n = 11)	Clozapine 'Tachycardia' group (n = 16)	Clozapine Total group (n = 27)	pvalue
Age, years	41± 15	44± 11	43± 12	0.51
Gender (% female)	4 (36%)	5 (31%)	9 (33%)	-/-
Length of time on drug at review, median (IQR) years	4.9 (0.4-13)	7.2 (1.3-10)	6.6 (0.8-10)	0.51
Heart rate Median (IQR) bpm	83 (76-90)	103 (97-115)	98 (85-114)	0.0006
QRS durationMedian (IQR) ms	90 (88-98)	90 (85-95)	90 (86-95)	0.66
QTc interval Median (IQR) ms	431 (416-440)	441 (418-468)	434 (418-458)	0.47
LVEFMedian (IQR) %	45 (37-50)	55 (52-55)	52 (44-55)	< 0.001
Clozapine discontinued	8 (73%)	4 (25%)	13 (45%)	0.027
Time to discontinuation from referral (months)	2 IQR 10	19 IQR 56	3 IQR 15	p = 0.016

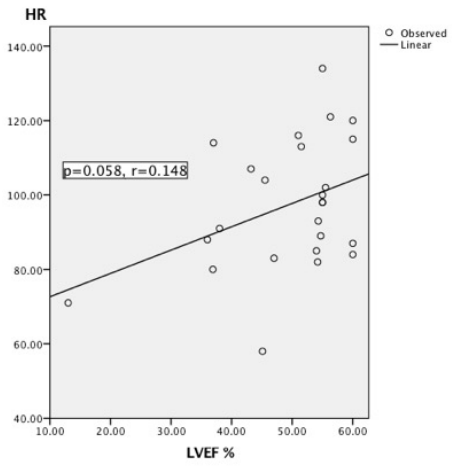


Figure 1

P385

Cardiological evaluation of patients with Becker muscular dystrophy

A Markman[1]; M Markman[1]; B Markman[2]; A Miranda[3]; A Lordsleem[2]; M Vianna[4]; V Van Der Linden[3]
[1]Agamenon Magalhães Hospital, Cardiology, Recife, Brazil; *[2]Federal University of Pernambuco, Cardiology, Recife, Brazil*; *[3]AACD - Disabled Child Care Association, Recife, Brazil*; *[4]University of Pernambuco, Recife, Brazil*

Background: Becker muscular dystrophy (BMD) is a genetic disease linked to X and is associated with a defect in the gene encoding a protein, dystrophin. Progressive weakness of the skeletal muscles, cardiomyopathy and respiratory failure are the most prominent features, with heart disease being the main cause of morbidity and mortality.
Objectives: our aim is to present the cardiological characteristics of a series of cases of patients with BMD in a specialized center in Brazil.
Methods: between May 2013 and November 2016 were attended 14 men with BMD. They underwent rest electrocardiogram (ECG), 24-hour Holter monitoring and two-dimensional transthoracic echocardiography (2D TTE) during follow up.
Results: the mean age was 23.2 years. Six patients (42.8%) reported heart disease as antecedent, nine (64.2%) were asymptomatic. Symptoms of palpitation and dyspnea were present in 42% and 60%, respectively, in the symptomatic ones. Twelve patients (85.7%) presented abnormal ECG, from which right bundle conduction disorder (33.3%), sinus tachycardia (16.6%) and left ventricular hypertrophy (16.3%) were the most frequent pathologic changes. Nine patients underwent echocardiography and systolic dysfunction was present in five (55.5%) with mean ventricular ejection fraction of 39.5%, diastolic dysfunction in one (11%) and left ventricular hypertrophy in one (11%). Holter monitoring were done in 28.5% of the patients and one (25%) showed nonsustained ventricular tachycardia.
Conclusion: the majority of patients in this group had resting ECG changes and more than half of them appeared to have myocardial dysfunction. We conclude that an early cardiologic evaluation is necessary in patients with BMD.

P386

Clinical characteristics and outcome of patients admitted by alcoholic cardiomyopathy to a university hospital from western spain

C Carbonell Munoz[1]; C Herrera Flores[2]; R Antunez Conde[2]; C Santos Jimenez[2]; R Casin Bricio[2]; P Segovia Alonso[1]; FJ Laso Guzman[1]; M Marcos Martin[1]
[1]Hospital Clínico Universitario, Internal Medicine, Salamanca, Spain; *[2]University of Salamanca, Medicine, Salamanca, Spain*

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Background: Alcoholic cardiomyopathy is a form of heart disease caused by chronic alcohol abuse. There is a paucity of data regarding clinical and epidemiological characteristics of this disease.
Purpose: The aim of this study was to analyse clinical and echocardiographic characteristics as well as long-term follow-up of patients admitted by alcoholic cardiomyopathy at a tertiary university center.
Methods: Retrospective study of a case series of patients admitted during a thirteen year period to a tertiary universitary center with alcoholic cardiomyopathy as main diagnosis (International Classification of Diseases, 9th revision code: I42.9). Data were obtained from the Admission Department and from medical records. For patients with several admissions, the first episode was considered.
Results: We identified 30 patients with alcoholic cardiomyopathy as main diagnosis during the study period. Mean age was 55.83 years (standard deviation [SD] = 10.20), and 29 patients (96.7%) were men. Twenty-three patients (76.67%) were admitted in the Cardiology Department and six (20.0%) in the Internal Medicine Department. Reason for admission was to perform cardiac procedures (11 patients, 36.70%), followed by heart failure (10 patients, 33.33%). Mean hospital stay was 9.27 (SD = 7.69) days. During a median follow-up of 44.80 months, five patients died (16.67%) and twenty patients were readmitted for a total of 47 hospital readmissions.
ECG showed signs of ventricular hypertrophy in 8 patients (26.67%) and atrial fibrillation in 8 cases (26.67%). Ischemic heart disease was present in 5 patients (16.67%) and alteration of liver function tests in 10 patients (33.33%). Echocardiogram showed left ventricular dysfunction in 27 patients (93.10%), with a mean left ventricular ejection fraction of 38.90% (SD=14.56%); left ventricular dilatation was found in 23 patients (79.31%), with an average end-diastolic volume of 167.65 (SD = 83.35) mL.
Alcohol consumption before admission was quantified in 19 patients, with a mean consumption of 565.3 grams per week [SD = 333.2]). Alcohol consumption was qualitatively recorded in 9 patients and was not recorded in one patient. Only 16 discharge reports (53.33%) recommended patients not drink alcohol.
Conclusion(s): The clinical characteristics of our patients are similar to those found in the medical literature. The lack of quantification of alcohol consumption and the percentage of discharge reports not recommending abstinence may suggest a low awareness towards alcohol-induced cardiac damage. Quantitative recording of alcohol intake and promoting abstinence should be promoted among patients with alcoholic cardiomyopathy.

P387

Meta-analysis on the diagnosis of inflammatory cardiomyopathy in endomyocardial biopsies - Comparison of immunohistology with histology and cardiac magnetic resonance

M Noutsias[1]; J Katzmann[1]; P Schlattmann[2]; E Noutsias[3]; C Konstas[1]; JG Westphal[1]; P Aftanski[1]; B Bigalke[4]; C Tschoepe[5]; PC Schulze[1]
[1]University Hospital of Jena, Department of Internal Medicine I, Division of Cardiology, Pneumology, and Intensive Medical Care, Jena, Germany; *[2]University Hospital of Jena, Institute of Medical Statistics, Informatics and Documentation (IMSID), Jena, Germany*; *[3]Theodor-Wenzel-Werk, Department of Psychiatry, Berlin, Germany*; *[4]Charite - Campus Benjamin Franklin, Cardiology, Berlin, Germany*; *[5]Charite - Campus Virchow-Klinikum (CVK), Cardiology, Berlin, Germany*

Funding Acknowledgements: DFG SFB TR 19 “DCMi” and UKGM 10/2009 “T cell functionality in DCMi”

Background: Diverse immunohistological (IHC) concepts have been elaborated for the sensitive detection of inflammatory cardiomyopathy (DCMi) in endomyocardial biopsies (EMB).
Purpose: Meta-analysis on the immunohistologic diagnosis of DCMi in EMB.
Results: We included n=61 investigations, with 10,491 patients (mean age: 47.1 years; men: 66%) who underwent EMB obtainment and IHC-diagnostics for infiltrate density and/or endothelial cell adhesion molecule (CAM) expression. In these studies, n=460 control patients were devoid of IHC-proof of DCMi. The mean IHC-detection rate of DCMi was 50.8% (95% CI: 47.7–53.8%; range: 18.4–91.7%). A substantial publication bias was excluded (Funnel Plot: $p = 0.4264$). This IHC-detection rate was significantly ($p < 0.0001$) higher compared to the mean detection rate of myocarditis according to the histological Dallas criteria (mean: 8.04%; 95%-CI: 5.08–12.5%; subset of n=3,274 patients in n=30 publications). However, 13 different criteria were described in the various publications, with various thresholds of diverse phenotypes of infiltrates, and expression of diverse CAM, quantified either visually or by digital image analysis (DIA). The comparison of IHC and cardiac magnetic resonance (CMR) data available in a subset of n=13 publications with 1,185 patients revealed a sensitivity of 69% (95%-CI: 58-79%), a specificity of 73% (95%-CI: 59-84%), and a ROC-AUC of 0.77 (95%-CI: 0.73-0.81) (Figure 1).
Conclusions: The results of this meta-analysis encompassing 10,491 patients confirm that the IHC-detection of DCMi has significantly higher sensitivity compared to the histological Dallas criteria, and cannot be fully substituted by CMR. However, standardization of the different IHC-diagnostic protocols seems pertinent.

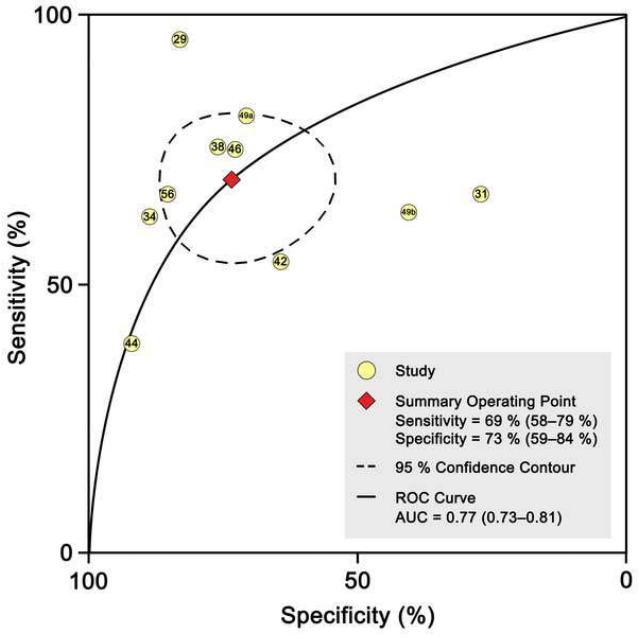

Figure 1

P388

Using longitudinal strain to identify wild type transthyretin amyloidosis in patients with aortic stenosis

G Robin[1]; T Cognet[1]; M Galinier[1]; D Carrie[1]; M Elbaz[1]; I Berry[2]; G Victor[2]; O Lairez[3]
[1]*Toulouse Rangueil University Hospital (CHU), Cardiology, Toulouse, France*; [2]*Toulouse Rangueil University Hospital (CHU), Nuclear Medicine, Toulouse, France*; [3]*Toulouse Rangueil University Hospital (CHU), Cardiology and Nuclear Medicine, Toulouse, France*

Introduction: Wild-type transthyretin amyloidosis (ATTRwt) and degenerative severe aortic stenosis (sAS) are both age-related pathologies with influence on prognosis. Diagnostic of cardiac amyloidosis may be confusing with the consequences of sAS on the left ventricle. Our aim was to describe a specific echocardiographic pattern for a better screening of cardiac amyloidosis in patients with severe aortic stenosis (sAS).
Methods: Echocardiography with speckle tracking analysis of 65 sAS without ATTRwt was compared to 15 ATTRwt with AS (moderate/severe = 8/7) and 31 ATTRwt with no AS.
All patients received 740 MBq of 99mTc-DPD intravenously. Genetic test with transthyretin gene sequencing was indicated in all patients with positive 99mTc-DPD scintigraphy to distinguish hereditary from ATTRwt.
Results: Specific echocardiographic pattern in patients with combined ATTRwt and AS was defined by more pronounced left ventricular hypertrophy (LVH) ($p < 0.001$), lower global longitudinal strain (GLS) ($p < 0.001$) and higher proportion of patients with longitudinal apical sparing (LAS) with a ratio > 0.93 (100% in sAS and 88% in moderate AS), as a consequence of severe decrease in basal ($p < 0.001$) and mid ($p < 0.001$) longitudinal strain. Low-gradient sAS despite preserved left ventricular function was observed in 43% of sAS with ATTRwt versus 9% in sAS without ATTRwt ($p < 0.05$).
Conclusion: ATTRwt in sAS may be suspected in patients with specific echocardiographic pattern combining lower GLS with exacerbated LAS, in presence of LVH and low-flow, low-gradient profile.

Echocardiographic data

2D strain parameters	ALL (n = 111)	Severe AS (n = 65)	AS/ATTRwt (n = 15)	ATTRwt (n = 31)	p
			Moderate (n = 8)	Severe (n = 7)	
GLS	-12.2±4.2	-14.0±4.3	-9.1±2.4	-8.3±2.8	-10.8±3.2	< 0.001
Mean basal LS	-6.8±5.2	-8.9± 5.6	-3.2±3.1	-2.0±2.5	-5.4±3.9	< 0.001
Mean medial LS	-11.5± 4.8	-13.4±5.2	-8.4±2.9	-7.6±2.6	-10±3.4	< 0.001
Mean apical LS	-17.5±5.5	-18.7±6.4	-15.9±3	-15.1±4	-16.5±4.4	0.11
LAS > 0.93 (%)	41 (42.2%)	11(17%)	7 (87.5%)	7 (100%)	16 (51.6%)	< 0.001

GLS, global longitudinal strain ; LS, longitunal strain ; LAS, longitudinal apical sparing ; AS, aortic stenosis ; ATTRwt, wild type amyloidosis transthyretin

P389

Remodeling of vascular walls in different levels of arterial system in patients with progressive course of hypertrophic cardiomyopathy

VYU Kaplunova[1]; GA Shakaryants[1]; MV Kozhevnikova[1]; EO Korobkova[1]; MA Kiryupina[1]; AI Malakhov[1]; EV Privalova[1]; YUN Belenkov[1]
[1]*I.M. Sechenov First Moscow Medical State Universityul. Trubetckay , 8, str. 2, 119992 Moscow, Russia, therapy, Moscow, Russian Federation*

Purpose: to assess the relationship between remodeling of large and small vessels and markers of endothelium dysfunction and growth factors in patients with progressive course of hypertrophic cardiomyopathy (HCM) by photoplethysmography, nail fold computer videocapillaroscopy and applantation tonometry.
Methods: 54 patients with progressive course of HCM were included in the study. All of them had heart failure with preserved ejection fraction. Group 1 included HCM patients (n-30; male: 12, mean age 47,96 + 16,97) and group 2 – HCM patients with metabolic syndrome (MS) (n-24; male: 18, mean 50,18 + 18,56). Digital photoplethysmography and nail fold computer videocapillaroscopy at baseline and with arterial and venous occlusion tests were performed. We estimated endothelial function of large vessels (phase shear (PS, ms) and microcirculation (occlusion index (IO)). Remodeling of large vessels (stiffness index (aSI, in/s) and skin capillaries (capillary densities (CD, cap/mm2) were evaluated. The levels of biological markers (TGF-α, IGF-1, von Willebrand factor and NT-proBNP, TIMP-1, endothelin) were estimated. Rheocardiography was performed on RheoCardioMonitor system. To asses aortic stiffness the applantation tonometry were performed.
Results: Central aortic systolic pressure (CASP) was above normal level in both groups (group1 - 125,00 + 3,86; group2- 128,00 + 3,55; norm 80-120 mmHg) by applantation tonometry was founded in both groups. Capillary densities was decreased in HCM patients 29.37 cap/mm2 (26.87;31.87). Significant reduction of system vascular resistance (SVR) measured by rheocardiography (9,14 + 6,82; $p < 0.05$) was found in HCM patients.A positive correlation between TIMP-1 level and RI (r=0,517; $p < 0,05$), and negative correlation between TIMP-1 level and CD (r=-0,413; $p < 0,05$) in group 1 was determined. IFR level associated with RI (r=0,517; $p < 0,05$). A positive correlation between VEGF-A level and SI (r=0,699; $p < 0,05$) in group 2 was identified. CASP correlated with TGF level (r=-0,401; $p < 0,05$).
Conclusion: 1. The tendency for enlargement of large vessels vascular stiffness and capillary remodeling was found in patients with progressive course of HCM. 2. Remodeling of small and large vessels correlates with growth factors.

P390

Coronary calcium scoring in patients with takotsubo syndrome - Is takotsubo protective against coronary atherosclerosis?

E Elmir Omerovic[1]; J Lundgren[1]; A Ali[1]; Y Shao[1]; B Redfors[1]
[1]*Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: Takotsubo syndrome is an increasingly recognised clinical entity with signs and symptoms similar to acute myocardial infarction and acute heart failure. Coronary artery calcium (CAC) score reflects the severity of coronary artery disease and is a predictor of future coronary events. The aim of this study was to evaluate CAC score in patients with takotsubo syndrome.
Methods: We included 73 patients diagnosed with takotsubo syndrome at Sahlgrenska university hospital (Gothenburg, Sweden) between 2005 and 2013. All patients underwent CT examination on a multi-slice CT scanner (Siemens Definition Flash). In addition to calcium scoring, we also performed contrast CT angiography (Omnipaque 350 mg/ml, 325 mg iodine/kg) in 43 patients without contraindications. The CT scans were performed during a breath hold and with ECG-gating. Each coronary vessel was identified with a multiplanar reconstruction technique. Calculation of total CAC score was done according to the standard scoring system. The area (mm2) of each calcified lesion was multiplied by a density factor depending on the maximum computed number Hounsfield units (HU) in the lesion; 1= 130-199 HU, 2= 200-299 HU, 3= 300-399 HU and 4= ≥ 400 HU. The total CAC score was determined by calculating the sum of all calcifications in each patient.
Results: The mean age was 65.7 years and 9 (12%) were male. The distribution of the traditional risk factors for coronary artery disease was similar to age and gender matched population. Successful CT examination was achieved in 72 (99%) patients. Of these, 35 patients (49%) had no calcifications in coronary arteries. The median total calcium score was 1.5 . This value is lower than median calcium score (˜8) reported previously in healthy volunteers in Sweden. Only 5 patients (7%) had a total CAC score of >400. We found significant stenosis (>50%) in two (4.6%) patients.
Conclusions: Patients with takotsubo syndrome have low total CAC score. The takotsubo phenotype may confer protection against progression of atherosclerosis in coronary arteries.

P391

Severe heart failure due to development of cardiac sarcoidosis in the patient with familial sarcomeric cardiomyopathy

O V Olga Blagova[1]; AV Nedostup[1]; VP Sedov[1]; SA Alexandrova[2]; MV Yakovleva[3]; ME Polyak[3]; EV Zaklyasminskaya[3]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*; [2]*Bakoulev Center for Cardiovascular Surgery RAMS, Moscow, Russian Federation*; [3]*B.V. Petrovsky Russian Scientific Center of Surgery of the Russian Academy of Medical Sciences, Moscow, Russian Federation*

Purpose: to evaluate diagnosis stages and treatment of severe heart failure in a patient with familial form of cardiomyopathy and associated sarcoidosis.
Methods: male patient, 64 y.o., suffers dyspnea and paroxysmal atrial fibrillation from age 61 years. One year later, the patient first noted appearance of cough. X-ray revealed intrathoracic lymphadenopathy. A month ago, the patient significantly increased dyspnea, also appears edema of the lower limbs. Patient's daughter 35 y.o. and son 39 y.o. has been established the diagnosis of non-obstructive hypertrophic cardiomyopathy. Echocardiography (Echo-CG), Holter ECG monitoring, computer tomography (CT), cardiac magnetic resonance imaging (MRI), and DNA diagnostic were performed in the father.
Results: The examination revealed mild jaundice, symmetrical edema of the lower limbs, increased respiratory rate (24 per minute) and a little crepitation, irregular heart rhythm with a heart rate of 40-50 per minute, blood pressure 110/70 mm Hg, a slight increase in liver size. ECG showed sinus bradycardia (42 beats per minute), ventricular premature beats (PVBs), decreased amplitude of R wave. Holter monitoring showed signs of sick sinus syndrome, episodes of atrial fibrillation, PVBs

and nonsustained ventricular tachycardia. Echocardiography revealed signs of a noncompact myocardium, restrictive cardiomyopathy with reduced ejection fraction (36%), and also mitral regurgitation grade 2, tricuspid regurgitation grade 3. Systolic pulmonary artery pressure was 45 mm Hg, the thickness of the left ventricular myocardium 13 mm. The level of anti-heart antibodies was increased by 2-3 times. MRI showed definite signs of noncompact myocardium (22% of myocardial mass), intramyocardial gadolinium enhancement in the early and late phase in the interventricular septum, right ventricle, anterolateral wall of the left ventricle and papillary muscles; volume of fibrosis was 26%. During electrophysiological study induced ventricular fibrillation (VF), cardioverter defibrillator (ICD) was implanted. CT scan has shown the lymphadenopathy without pulmonary lesions, the diagnosis of sarcoidosis confirmed using thoracoscopic biopsy. In the patient and his two children was identified MYBPC3-p.Q1233* mutation. The patient receives a steroid and cardiotropic therapy for 2.5 years, symptoms of heart failure reduced. After ICD shock due to VF sotalol was replaced on amiodarone.
Conclusions: One mutation in the gene sarcomeric proteins (myosin binding protein C) has a different phenotype in the same family: myocardial noncompaction in the father and similar non-obstructive hypertrophic cardiomyopathy in two children. The development of sarcoidosis in the father led to a worsening of myocardial dysfunction. The cardiac sarcoidosis is confirmed by the presence of restrictive cardiomyopathy, specific pattern of gadolinium enchancement by MRI, high titers of ant-heart antibodies, and the positive effect of steroid therapy.

P392
Predictors of outcome in takotsubo cardiomyopathy, a multicenter study

A L Ana Calvo[1]; O Azevedo[1]; J Bispo[2]; I Cruz[3]; RP Santos[4]; MJ Vieira[5]; B Marmelo[6]; L Reis[7]; C Ruivo[8]; A Marreiro[2]; R Faria[9]
[1]Alto Ave Hospital Center, Cardiology, Guimaraes, Portugal; *[2]U.Algarve, Algarve Biomedical Center, Algarve, Portugal*; *[3]Hospital Garcia de Orta, Almada, Portugal*; *[4]Hospital Centre do Tamega e Sousa, cardiology, Penafiel, Portugal*; *[5]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[6]Hospital Sao Teotonio, Viseu, Portugal*; *[7]University Hospitals of Coimbra, Coimbra, Portugal*; *[8]Hospital Santo Andre, Leiria, Portugal*; *[9]Centro Hospitalar Medio Ave, Cardiology, Famalicao, Portugal*

Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction in the absence of significant coronary artery disease. The predictors of prognosis of TC are not yet fully established.
Purpose: To identify predictors of outcome in patients (P) diagnosed with TC.
Methods: Multicenter study involving 13 hospital centers that included all patients diagnosed with TC in the last 12 years. We assessed demographic data, precipitating factors and clinical presentation, trying to establish the predictors of after discharge outcomes. We define the occurrence of an outcome in the follow-up of TC patients as a variable that combine the occurrence of death, stroke/TIA, acute myocardial infraction (AMI) and TC recurrence.
Results: We included 234 P diagnosed with TC predominantly female (89.7%). During hospitalization occurred complications: heart failure (24.4%), cardiogenic shock (6.8%), atrial fibrillation (9.0%), complete atrioventricular block (2.1%), acute pulmonary edema (4.3%), stroke / TIA (1.7%), LV thrombus (1.3%) and death (2.2%). Over a follow-up of 33 ± 33 months, there were: TC recurrence (4.3%), stroke / TIA (3.0%), AMI (0.4%) and death (6.4%). An outcome in the follow-up occurred in 12.4% of patients.
The following variables were identified by the CHAID technic as predictors of complications at follow-up: (i) Presentation without an emotional stress factor (p = 0,019); (ii) Presentation with dyspnea (p = 0.049).
Conclusion: TC has a relatively low rate of complications in the follow-up. Presentation without an emotional stress factor or dyspnea are independent predictors of complications in the follow-up of TC patients.

P393
Will patients with a history of psychiatric disease be different from the rest of the patients with takotsubo cardiomiopathy?

N Craveiro[1]; J Bispo[2]; L Calvo[3]; R P Santos[4]; C Ruivo[5]; L Reis[6]; A C Gomes[7]; S Carvalho[8]; A Marreiros[2]; E Correia[9]
[1]Hospital of Santarem, Department of Cardiology, Santarem, Portugal; *[2]Algarve Biomedical Center, Centro hospitalar do Algarve, Department of Cardiology, Faro, Portugal*; *[3]Hospital Guimaraes, Department of Cardiology, Guimaraes, Portugal*; *[4]Hospital Centre do Tamega e Sousa, Department of Cardiology, Penafiel, Portugal*; *[5]Hospital Santo Andre, Department of Cardiology, Leiria, Portugal*; *[6]Centro Hospitalar e Universitário de Coimbra, Department of Cardiology, Coimbra, Portugal*; *[7]Hospital Garcia de Orta, Department of Cardiology, Almada, Portugal*; *[8]Hospital Center of Tras-os-Montes and Alto Douro, Department of Cardiology, Vila Real, Portugal*; *[9]Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo Cardiomyopathy (TCM) is increasingly been described as a "stress" cardiomyopathy that can be triggered by physical and emotional factors. A higher prevalence of neuropsychiatric disease has been described in these patients but little is known about their characteristics.
Objectives: To evaluate and characterize a population of patients with TCM and history of psychiatric disease.
Methods: Multicenter retrospective study including 234 patients hospitalized with TCM. Two groups were formed: Group A, with a history of psychiatric disease (n = 17, 7.3%), and Group B, without psychiatric history disease (n = 217, 92.7%). The groups were compared in terms of their demographic characteristics, comorbidities, precipitating factors, clinical presentation, electrocardiographic, echocardiographic changes and in-hospital evolution. Statistical analysis was performed using SPSS version 23.0.
Results: Patients with a history of psychiatric disorder did not present significant differences in gender, comorbidities or postmenopausal status compared to the rest.
These patients do not present more frequently a precipitating factor (47.1% vs 60.4%, p 0.282), nor factors associated with emotional stress (35.3% vs 47.5%, p 0.333).
The clinical presentation of the patients did not differ between the two groups, with chest pain being the main complaint at presentation (100% vs 86.2%, p 0.139). Also the characteristics of ECG and echocardiogram did not differ significantly between the 2 groups, including the type of TCM.
During hospitalization, patients with psychiatric conditions did not present a significant difference in the new event rate compared to the rest.
Conclusions: In our study, patients with Takotsubo Cardiomyopathy with a psychiatric history did not present significantly different characteristics when compared with the remaining TCM patients.
The in-hospital prognosis of patients with psychiatric conditions seems to be similar to that of the remaining TCM patients.

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Will patients with a history of neurological disease be different from the other patients with takotsubo cardiomyopathy?

N Craveiro[1]; J Bispo[2]; B Faria[3]; R P Santos[4]; C Ruivo[5]; L Reis[6]; A C Gomes[7]; S Carvalho[8]; A Marreiros[2]; E Correia[9]
[1]Hospital of Santarem, Department of Cardiology, Santarem, Portugal; *[2]Algarve Biomedical Center, Centro Hospitalar do Algarve, Department of Cardiology, Faro, Portugal*; *[3]Hospital Guimaraes, Department of Cardiology, Guimaraes, Portugal*; *[4]Hospital Centre do Tamega e Sousa, Department of Cardiology, Penafiel, Portugal*; *[5]Hospital Santo Andre, Department of Cardiology, Leiria, Portugal*; *[6]Centro Hospitalar e Universitario de Coimbra, Department of Cardiology, Coimbra, Portugal*; *[7]Hospital Garcia de Orta, Department of Cardiology, Almada, Portugal*; *[8]Hospital Center of Tras-os-Montes and Alto Douro, Department of Cardiology, Vila Real, Portugal*; *[9]Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo Cardiomyopathy (TCM) is a clinical entity associated with changes in the brain-heart connection, culminating in transient, sometimes fatal, left ventricular dysfunction. It appears to be triggered by physical and emotional factors and a higher prevalence of neuropsychiatric disease has been described in these patients.
Objectives: To determine if patients with TCM and a history of neurological pathology have different in-hospital clinical features and prognosis.
Methods: A multicenter retrospective study including 234 hospitalized patients with the diagnosis of TCM. Two groups were formed: a Neuro group, including patients with a history of neurological disease (n = 10; 4.3%); A non-Neuro group without history of neurological disease (n = 224, 95.7%). The groups were compared in terms of their demographic characteristics, comorbidities, precipitating factors, clinical presentation, electrocardiographic, echocardiographic alterations and evolution in hospitalization. Statistical analysis was performed using SPSS 23.0.
Results: Patients with a history of neurological disease did not present significant gender or age differences.
With regard to comorbidities, patients in the Neuro group were more often smokers than those in the non-Neuro group (40% vs 12.9% p 0.037). There were no differences regarding the remaining comorbidities.
No significant differences were found between the groups regarding the existence of precipitating factors. Patients in the Neuro group presented more frequently with syncope (20% vs 4.9%, p 0.042). There were no differences in the other modes of presentation. Regarding the ECG and echocardiogram characteristics, the Neuro group presented less frequently atrial fibrillation (AF) at the initial ECG (10% vs 45.1%, p 0.046).There were no differences between the two groups regarding the in-hospital evolution.
Conclusions: Patients with Takotsubo Cardiomyopathy with known neurological disease were more often smokers, more frequently presented syncope at

admission and less frequently atrial fibrillation at the initial ECG AF. No differences were found regarding the in-hospital prognosis of TCM patients.

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Clinical features and prognosis of amyloidosis cardiac

J Joffrey Eduardo Lujan Valencia[1]; L Madrona Jimenez[1]; M Chaparro Munoz[1]; B Prado Gotor[1]; A Recio Mayoral[1]
[1]*Virgen Macarena University Hospital, Sevilla, Sevilla, Spain*

Introduction: The amyloidosis cardiac is an entity of great clinical relevance, often underdiagnosed with potentially curable medical treatment, its diagnosis requires a high clinical suspicion and a compatible anatomopathological sample. Our objective is to describe the etiology of the disease, presentation form, diagnostic methods, therapeutic strategy and follow-up.
Methods: Retrospective analysis of a series of patients at our center between 2007-2015.
Results: We analyzed 10 patients with a mean age of 64 (38-95) years, 5 (50%) were women. The etiology responds in 8 (80%) to primary amyloidosis (LA), 1 (10%) senile, 1 (10%) secondary. The main symptoms were dyspnea in 11 (91.7%), edema in 9 (75%), cachexia in 4 (33.3%), hepatomegaly in 3 (25%), splenomegaly in 2 (16.7%), pleural effusion in 6 %) And cardiomegaly in 4 (33.3%). NYHA at diagnosis was III-IV in 8 (66.6%) and I-II in 4 (33.3%). Renal insufficiency was found in stage I in 2 (16.7%), stage II in 8 (66.7%), stage III-IV in 2 (16.7%). Cardiac MRI was performed in 8 (66.7%) patients, of whom they presented subendocardial late enhancement 6 (50%). Other diagnostic procedures included bone marrow biopsy in 7 (58.3%), abdominal fat in 10 (83.3%), cardiac biopsy in 1 (8.3%) and rectum in 1 (8.3%). Protein electrophoresis was also performed, which was diagnosed in 6 patients (50%). Regarding the treatment, 7 (58.3%) were treated with Inhibitors of the angiotensin-converting enzyme, being interrupted in one of them (8.3%) for symptomatic hypotension; Moreover they also received beta-blockers 4 (33.3%), loop diuretics 11 (91.7%), antialdosteronic 4 (33.3%) and thiazide 1 (8.3%). Oral anticoagulant therapy was performed 4 (33.3%). The chemotherapist was, melphalan in 1 patient (8.3%), cyclophosphamide in 2 (16.7%) and therapy with immunomodulatory drugs in 3 (25%). Dexamethasone was associated in 3 patients (25%), other types of corticoid in 4 (33.3%). Bone marrow transplantation was performed in 3 patient (25%) and cardiac transplantation was performed in 1 patient (8.3%). The NYHA at the end of follow-up was I-II in 4 (33.3%) and III-IV in 5 (4.7%). During the follow-up, 4 (33.3%) patients died, with an average survival of 18.67 months.
Conclusions: The prognosis of cardiac amyloidosis remains uncertain, presenting a significant deterioration of the functional class at follow-up and a high mortality rate. Further studies with recent immunomodulatory drugs may improve outcomes.

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Mortality predictors in patients with takotsubo cardiomyopathy

B Bebiana Faria[1]; B Marmelo[2]; P Azevedo[3]; C Ruivo[4]; R Santos[5]; A Gomes[6]; M Vieira[7]; L Teles[8]; A Marreiros[9]; A Almeida[6]; L Calvo[1]; J Portugues[1]
[1]*Hospital Guimaraes, Guimaraes, Portugal*; [2]*Hospital Sao Teotonio, Viseu, Portugal*; [3]*Faro Hospital, Cardiology, Faro, Portugal*; [4]*Hospital Santo Andre, Cardiology, Leiria, Portugal*; [5]*Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*; [6]*Hospital Garcia de Orta, Almada, Portugal*; [7]*Hospital of Santarem, Cardiology, Santarem, Portugal*; [8]*University Hospitals of Coimbra, Coimbra, Portugal*; [9]*Algarve University, Cardiology, Faro, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo cardiomyopathy (TC) is characterized by transient left ventricular dysfunction in the absence of artery coronary disease. The prognosis is generally favorable but there are cases of death. TC is a rare disease with a low number of events and because of that, there are few studies that describe mortality predictors.
Objective: Identify mortality predictors in Takotsubo cardiomyopathy.
Methods: Retrospective study, including all patients (P) with diagnosis of Takotsubo Cardiomyopathy in 12 portuguese hospitals in the last 12 years. Demographic, clinical, electrocardiographic (ECG) and echocardiographic data were collected to identify mortality predictors during follow-up.
Results: The sample consisted in 234 P, composed mainly by women (89.7%). In 59% of cases it was possible identify the precipitating factor, in 18.4% was physical stress and 47% refers an emotional stress. The most frequent clinical presentation was chest pain in 87% of the P and 89% had elevation of troponin at admission. About 24% developed heart failure (HF) during hospitalization, and 6.8% of P presented in Killip IV class. The average follow-up was 33 ± 33 months and overall mortality rate was 6.4%.
The factors that were significantly associated with death during follow-up were male gender ($p = 0.002$), angina history ($p = 0.024$), presence of chronic renal failure ($p = 0.26$), presence of precipitating factor ($P = 0.08$), namely emotional stress ($p = 0.001$), dyspnea at presentation ($p = 0.002$), atrial fibrillation at admission ECG ($p = 0.016$), Killip class at admission ($p = 0.004$), as well as the development of HF during hospitalization ($p < 0.001$). After multivariate analysis, the only independent mortality predictor was the development of HF during hospitalization ($p < 0.001$).
Conclusion: These results allowed to confirm the low mortality rate associated with Takotsubo cardiomyopathy. The results suggest the existence of a strong association between the development of HF during hospitalization and mortality in Takotsubo cardiomyopathy.

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Cardiac function and endothelial progenitor cells recruitment in recovered patients with takotsubo cardiomyopathy

L Liaz Zilberman[1]; A Zalik[1]; I Fugenfirov[1]; G Gandelman[1]; S Shimoni[1]; J George[1]; S Goland[1]
[1]*Kaplan Medical Center, heart institute, Rehovot, Israel*

Background: Takotsubo Cardiomyopathy (TCM) is a transient cardiomyopathy and endothelial dysfunction has been proposed as the main potential mechanism involved in the pathogenesis. Post-recovery cardiac function and endothelial function including endothelial progenitor cells (EPCs) were not evaluated in TCM yet.
Aim: To evaluate the measures of endothelial function, inflammatory markers and to assess cardiac function using comprehensive echocardiographic techniques such as Tissue Doppler Imaging (TDI) and 2-dimentional strain (2DS) imaging in post-TCM patients.
Methods: Twenty five post-TCM patients were included in this study. All patients underwent echocardiographic evaluation including left ventricle (LV) and right ventricle (RV) function assessment using standard echocardiography, TDI, and 2DS techniques. The number of EPCs: CD34+ cells, CD34+KDR cells, vascular endothelial growth factor (VEGF) levels and inflammatory markers: hsCRP, IL6 and Ox-LDL antibodies were quantified in 12 patients. All echocardiographic and laboratory measures were compared to age-matched controls.
Results: All patients recovered from TCM and were evaluated at mean follow-up of 3.7 ± 1.8 months from the acute event. The mean age was 60 ± 13 years, 24 women, and the mean LV ejection fraction (EF) at follow-up was 58.1 ± 11.5%. Although there was no difference in LVEF between the two groups ($p = 0.13$), patients with post-TCM had significantly lower early velocities E' septal (6.3 ± 1.7 versus. 8.8 ± 2.4 cm/s, $p = 0.003$) and systolic velocity S' septal (6.4 ± 1.7 versus 7.5 ± 1.5 cm/s, $p = 0.02$) by TDI. Lower LV global longitudinal strain (-18.8 ± 3.9 versus -21.1 ± 3.1%, $p = 0.03$), RV global strain (-20.9 ± 4.2 versus -23.3 ± 3.3%, $p = 0.07$) and significantly lower early diastolic strain rate (1.0 ± 0.3 versus 1.28 ± 0.4 1/s, p0.001) were obtained in post-TCM patients. Compared to controls, post-TCM patients had higher concentration of circulating CD34+KDR levels (0.18 ± 0.05 versus 0.07 ± 0.04, $p = 0.01$), with no difference in VEGF, hsCRP, IL6 and Ox-LDL between the groups.
Conclusions: In this pilot study comprehensive echocardiographic techniques such as TDI and 2DS were able to identify altered cardiac function in recovered patients with TCM. Enhanced recruitment of EPCs, cells that have been implicated to improve endothelial regeneration after initial vascular injury was evident even after LV recovery in patients with takotsubo cardiomyopathy.

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Diastolic function in Crohn patients _a study of strain analysis by speckle_tracking

M Oliveira[1]; MR Lourenco[1]; O Azevedo[1]; T Curdia Goncalves[1]; MJ Moreira[1]; F Castro[1]; L Calvo[1]; B Faria[1]; P Von Hafe[1]; J Portugues[1]; J Cotter[1]; A Lourenco[1]
[1]*Hospital Guimaraes, Guimaraes, Portugal*

Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease that affect the gastrointestinal tract but has also extraintestinal manifestations. Cardiac involvement is considered rare and limited to sporadic cases of myocarditis, endocarditis and pericardial effusion. Myocardial deformation imaging is the most sensitive technique to evaluate left ventricular function. E/SRe ratio has been considered to be a better index of left ventricular filling pressures and a prognostic predictor in many pathologies. There are no studies in literature evaluating diastolic function in CD by myocardial deformation imaging.
Objective: The aim of this study was to evaluate left ventricular diastolic function in CD patients using conventional 2D echocardiography, tissue Doppler imaging and strain analysis by speckle tracking.
Methods: Cross-sectional study including 40 patients with CD, followed in hospital consultation of Gastroenterology, and no other causes of left ventricular dysfunction. We collected clinical and demographic data. We performed 2D transthoracic echocardiogram including conventional echocardiography and tissue Doppler imaging. We performed 2D strain analysis by speckle-tracking and determined early diastolic strain rate (SRe) and E/SRe ratio.

Results: Patients were mainly female (57%), with mean age of 34,4 ± 10,3 years and mean disease duration of 8,2 ± 6,4years. Harvey-Bradshaw activity index showed that 30 patients were in remission, 8 patients had mild disease activity and 2 patients had moderate disease activity. 32,5% patients had already been submitted to surgery because of CD complications.
CD patients had significantly lower ejection fraction than controls (58,18 ± 0,66 vs. 65,58 ± 0,82 %, p < 0.001). Regarding diastolic function parameters: E/A ratio (1,49 ± 0,07 vs. 1,49 ± 0,08; p = 0,982), lateral E' velocities (16,65 ± 0,65 vs. 16,76 ± 0,66 cm/s; p = 0,908), septal E' velocities (13,34 ± 0,42 vs. 14,55 ± 0,64 cm/s; p = 0.111) and mean E/E′ ratio (6,08 ± 0,23 vs. 6,09 ± .0,22, p = 0,993) were normal for age without diferences between CD patients and controls.
Indexed left atrial volume was significantly higher in CD patients (23,3 ± 0,7 vs. 19,8 ± 1,1 ml/m2, p = 0.007) although within normal range.
E/SRe ratio was significantly higher in CD patients than controls (48,0 ± 7,5 vs. 42,4 ± 7,4cm, p = 0.005). This difference neither correlates with disease activity (p = 0.790) or disease duration (p = 0.990) nor was associated with past complications (p = 0.224), previous surgery (p = 0.106) or medication (p = 0.870).
Conclusion: This is the first study evaluating left ventricular diastolic function in CD by myocardial deformation imaging. Our study showed that CD, like other systemic inflammatory diseases, results in subclinical left ventricular diastolic dysfunction.

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Prognostic Value of Echocardiography in Peripartum Cardiomyopathy - Speckle tracking study

K Hristova[1]; R Marinov[1]; G Stamenov[2]; K Chacheva[2]; M Michova[2]; S Persenska[2]; N Dimova[2]; A Racheva[2]
[1]National Heart Hospital, Sofia, Bulgaria; *[2]Nadezhda Women's Health Hospital , Sofia, Bulgaria*

Normal pregnancy is associated with reversible changes in both systolic and diastolic mechanics, consistent with an increase in preload and decrease in afterload and systemic vascular resistance. The aim of the study is to evaluate left ventricular cardiac mechanics via speckle tracking echocardiography in a population of pregnant women with per partum cardiomyopathy and preeclampsia(PE) after invitro fertilization (IVF) during different stages of pregnancy.
The study population included 42 pregnant women with PE, after IVF, 10 of them with multiple pregnancy (46.5 ± 3 years) and 20 healthy nonpregnant women (33 ± 4years).Apical and basal short axis and apical view for three, two and four chamber for 2D images were acquired (65 ± 7 frames/s) during the first, second and third trimester of the pregnancy, as well as up to two months post partum. The curves of longitudinal(GLS), circumferential(GCS), radial strain(GRS) and LVT /LVUR were extracted using a commercial software.
Results: Peak LVT and LVUR increased significantly in the 3rd trimester in both pregnancy groups (13.48 ± 2.90°,13.12 ± 3.30°,16.83 ± 3.61°,P < 0.001; and -111.52 ± 23.54°/sec,-107.40 ± 26.58°/sec,-144.30 ± 45.14°/sec, P < 0.001; in the 1st, 2nd, and 3rd trimester, respectively.The pregnants with twins have the highest value for LVT and LVUR compare with other pregnants (p < 0.01), but in the last trimester, the time to peak LVUR is prolonged. An independent correlation was found between the change in LVT and LV end-systolic volume in 1st and 3rd trimester (r = 0,56). Peak LVUR at the 3rd trimester correlated significantly with LV end-diastolic volume. Multiple regression analysis indicates that only systolic blood pressure (r = 0.394, P = 0.005) was an independent predictor for increased LV torsion. Arterial hypertension (AH) and prevalence of preeclampsia (PE) are more often in IVF group. Longitudinal strain decreased significantly (p < 0.001) during 3th trimester in women with AH and PE. Global longitudinal strain measures of the LV were non-significantly different between the different groups in first and second trimester (GLS-20.6 ± 3,14 vs.-19,29 ± 2,17).There are not found significant differences for GCS and GRS during pregnancy. Conclusions: During pregnancy LV twist and peak untwisting rate increase in the 3rd trimester and correlate with end-systolic and end-diastolic volume, respectively. Blood pressure and condition of multiple pregnancy are independently associated with increased torsion during pregnancy and may predict the new onset heart failure and perinatal cardiomyopathy. Global longitudinal strain is the main predictor of new onset peripartum cardiomyopathy

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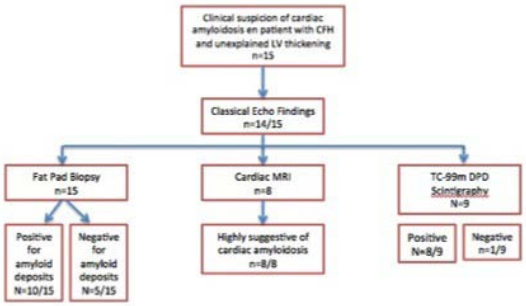
Multimodality non-invasive imaging diagnosis of cardiac amyloidosis

M Groba-Marco[1]; A Cardenes-Leon[1]; A Garcia-Quintana[1]; M Blanco-Nuez[1]; I Menduina-Gallego[1]; H Mendoza-Lemes[1]; J Hernandez-Ramirez[1]; R Sakhrani-Gobind[1]; V Quevedo-Nelson[1]; JD Marin-Esmenota[1]; J Garcia-Salvador[1]; D Valeron-Hernandez-Abad[1]; E Caballero-Dorta[1]
[1]University Hospital Dr Negrin, Cardiology, Las Palmas De Gran Canaria, Spain

Background: Cardiac amyloidosis (CA) is a common underdiagnosed cause of restrictive cardiomyopathy and heart failure. Two major types of CA are cardiac amyloid light-chain (AL) and transthyretin-related cardiac amyloidosis (ATTR, mutant and wild types). An early diagnose determines prognosis and therapeutic options.
Purpose: To determine the role of different non-invasive imaging techniques in the diagnosis of CA and its ability to differentiate between subtypes.
Methods: We analysed the use of a 2D- echocardiography, a cardiac MRI and a 99m-Tc-DPD-cardiac-scintigraphy in patients with unexplained left-ventricle thickening that resulted on the diagnosis of CA. The cohort included 15 patients admitted at the University Hospital between March 2011 and June 2016, 9 (60%) had ATTR wt, 5 had AL (33%), and 1 (6%) was confirmed but untyped. Mean age was of 81.3 ± 3.4 and 66.8 ± 6.3 years of age in the group with ATTR wt and AL respectively (p < 0,001).
Results: A 12-lead ECG and 2D-transthoracic echocardiography were done firstly. Significant low voltage and poor R-wave progression with significant LV thickening was observed in 47% of the patients (n = 7/15), and 93% (n = 14/15) had classical echocardiographic signs of infiltrative cardiomyopathy.
In 8 patients a Cardiac-MRI was performed, all highly suggestive of CA with diffuse late gadolinium enhancement, without significant difference of the pattern observed in both subtypes (ATTR n=4, AL n= 3, untyped n=1). In 4 patients the MRI was not done due to having a cardiac pacemaker (n = 1, AL), significant renal failure (n = 2, 1 AL and 1 ATTR) or both (n = 1, ATTR), and in 1 patient it had to be postponed until further clinical improvement due to supine position intolerance (n = 1, ATTR). In 4 of these 5 patients, the cardiac scintigraphy was done, presenting positive myocardial uptake of Tc-99m-DPD in 3 (75%, all ATTR).
Fat pad biopsy was taken in all of the patients, observing amyloid deposits in 10 studies (67%, n=15). In the other 5 patients with negative results, 3 patients (all ATTR) had both MRI and scintigraphy suggestive signs of CA, 1 patient (AL) only a suggestive cardiac MRI, and 1 patient (ATTR) only a positive cardiac-scintigraphy.
Conclusions: Although endomyocardial biopsy with immunostaining is considered the gold standard, multimodality non-invasive imaging techniques provide an attractive alternative for the detection of CA. Cardiac-scintigraphy, especially in ATTR, is an effective and safe technique to be used in patients with significant renal failure and cardiac pacemaker. No significant differences were observed in these modalities to distinguish between ATTR and AL cardiac affectation, but the age of the patient should be taken into consideration for a diagnostic approximation. We advocate for a multimodality imaging approach for the diagnosis of an underdiagnosed CA.



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Meta-analysis for the value of colchicine for the therapy and prevention of pericarditis and postpericardiotomy syndrome

JG Westphal[1]; P Schlattmann[2]; LL Lutschinger[1]; C Konstas[1]; P Aftanski[1]; T Bekfani[1]; PC Schulze[1]; M Noutsias[1]
[1]University Hospital of Jena, Department of Internal Medicine I, Division of Cardiology, Pneumology, and Intensive Medical Care, Jena, Germany; *[2]University Hospital of Jena, Institute of Medical Statistics, Informatics and Documentation (IMSID), Jena, Germany*

Introduction: Colchicine inhibits mitotic processes via interference with formation of microtubule, which eventually also inhibits the activation of immunocompetent cells. Colchicine has been used for the treatment and secondary prevention of pericarditis (PC) and of postpericardiotomy syndrome (PPS).
Aim: Meta-analysis of investigations on the clinical effects of colchicine for the treatment and secondary prevention of PC and PPS.
Methods and Results: By systematic literature search pathways, we identified n=10 relevant prospective trials, with 1,981 patients (mean age: 57.8 + 7.3 years; men: 62.5%; mean follow-up: 13.6 + 91 months). Two studies with n=981 patients (mean age: 57.6 + 6.7 years) used an open label design, in which the patients were randomized to the respective study group. The remaining eight trials were randomized controlled trials (RCT). The n=1.000 control patients (mean age: 57.9 + 8.0 years) had a conventional therapy. In the colchicine treated study patients, the daily dose of colchicine was 0.5-1.0 g (depending on tolerance) in n=7 trials, 1.0 g daily in n=2 trials, and 1.0 g daily in one further trial. Colchicine treatment was associated with a significant reduction of a recurrence of pericarditis (OR: 0.33; 95%-CI: 0.25-0.44), and of rehospitalization both for PC and PPS (OR: 0.25; 95%-CI: 0.13-0.49). The rate of gastrointestinal adverse effects was significantly higher in the colchicine treated patients (OR: 2.6; 95%-CI: 1.82-3.72).

Conclusions: the results of this meta-analysis based on 1,981 patients confirm the efficacy of colchicine for the treatment and secondary prevention of pericarditis (PC) and of postpericardiotomy syndrome (PPS).

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Chronic heart failure as a specific form of the arrhythmogenic right ventricle dysplasia/cardiomyopathy and a consequence of associated myocarditis.

Y A Yulia Alexandrovna Lutokhina[1]; O V Blagova[1]; A V Nedostup[1]; S A Alexandrova[2]; E A Mershina[3]; A G Shestak[4]; EV Zaklyazminskaya[4]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Bakoulev Center for Cardiovascular Surgery RAMS, Moscow, Russian Federation*; *[3]Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*; *[4]Russian Research Center of Surgery, Petrovsky, Moscow, Russian Federation*

Background: Arrhythmogenic right ventricle dysplasia/cardiomyopathy (ARVD) was described in 1977, however, generally accepted clinical classification of the disease is still missing. Frequency and factors of the development of chronic heart failure (CHF) in various forms of ARVD are not determined.
Purpose: To evaluate the frequency and factors of the development of CHF in three main clinical forms of ARVD and to relate CHF with the presence of associated myocarditis.
Methods: forty seven patients (mean age 38,8 ± 15,8 y 40.4% males) with ARVD according to Revised Task Force Criteria 2010 (TFC) were evaluated (22 patients with definite, 13-with borderline and 12 with possible diagnosis). All patients underwent ECG, 24h-Holter monitoring, echocardiography, blood tests for detection of anti-heart antibodies and DNA of cardiotropic viruses. Mutations were identified by Sanger sequencing. Also were performed magnetic resonance imaging (MRI, n=40), signal-averaged ECG (n = 15), morphological study of the myocardium (endomyocardial biopsy, n=2, and autopsy, n=2).
Results: According to the features of clinical course of ARVD, we identified three clinical forms of the disease. I. Latent arrhythmic form - characterized by frequent premature ventricular contractions and/or nonsustained ventricular tachycardia (VT) in the absence of sustained VT (SVT) and syncope. II. Manifested arrhythmic form – SVT/ventricular fibrillation. III. ARVD with progressive CHF (as the main manifestation of the disease). These forms were diagnosed in 24, 10, and 13 patients respectively. These three groups were compared by 4 main parameters: 1) confidence of diagnosis; 2) structural-functional characteristics; 3) presence/absence of myocarditis; 4) the results of the DNA-diagnostics. Patients with the III form (severe CHF) differed from others patients with higher confidence of diagnosis, significantly larger size of the right ventricle, lower ejection fraction of both ventricles, low voltage ECG but with a lower incidence of SVT. Significant differences in the frequency of detection of mutations have not been detected, however, in patients with the III form are dominated by mutations in DSP gene, which are associated with CHF and left ventricle involvement. The frequency of associated myocarditis in patients with III form was not significantly higher than in patients with manifested arrhythmic form (61.5% and 30.0%). Probably, in patients with CHF the presence of myocarditis facilitated the realization of abnormal genetic program, which resulted in more severe clinical course: congestive CHF, greater requirement in implantable cardioverter defibrillator (53.8 v 11.8%), presence of lethal outcomes (15.4 v 0%).
Conclusions: It is reasonable to allocate the patients with ARVD with CHF in a separate clinical form, characterized by the presence of mutations, associated with CHF, that in combination with associated myocarditis result in the severe clinical course and worse prognosis.

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Electrocardiographic changes in takosubo cardiomyopathy: differences between apical and mid-ventricular involvement

B Schneider[1]; K Peters[1]; U Desch[1]; J Stein[1]
[1]Sana Kliniken, Luebeck, Germany

Background: Besides the typical presentation of apical ballooning (AB), a variant form of takotsubo cardiomyopathy (TTC) with mid-ventricular ballooning (MB) has been recognized. This study assessed if there are electrocardiographic differences between these two TTC variants.
Methods: Over a 9-year period, we observed 76 TTC patients (69 f, 7m; 70 ± 12 years). By angiography, 45 patients (59%) had AB and 31 (41%) MB. ECG on admission, at the time of maximal T-wave inversion, before discharge and the daily QTc-interval were compared.
Results: Time from symptom onset to first ECG (8.8 ± 7.7 vs 7.9 ± 9.9 hours, p = ns) and heart rate (88 ± 21 vs 90 ± 25/min, p = ns) were not different in patients with AB and MB. At presentation, most patients had ST elevation (AB 96%, MB 84%, p = ns). In AB there was a trend towards a higher number of leads with ST elevation (4.3 ± 2.1 vs 3.4 ± 2.5 leads) and a greater magnitude of ST elevation (0.65 ± 0.41 mV vs 0.47 ± 0.4 mV, both p = ns). The number of patients with ST-elevation in V2 (87% vs 68%, p < 0.05), V3 (93% vs 65%, p < 0.002) and V4 (73% vs 32%, p < 0.001) was greater in AB whereas ST-elevation in aVL occurred more frequently in MB (11% vs 29%, p < 0.05). The occurrence of a Q wave was similar in both groups (AB 33%, MB 29%, p = ns) but the number of leads with a Q wave was higher in AB (2.3 ± 0.7 vs 1.6 ± 0.7, p < 0.02). Reciprocal ST segment depression was similar (AB 24%, MB 29%, p = ns).
During follow-up, AB patients showed more leads with T-wave inversion (8.2 ± 1.17 vs 6.1 ± 2.7 leads, p < 0.001), and the magnitude of T-wave inversion (3.3 ± 1.5 vs 1.6 ± 1.0 mV, p < 0.001) was larger. The presence of T-wave inversion was similar in lead I, aVR, aVL and V2 but AB patients developed more wide spread T-wave inversion in lead II (80% vs 45%, p < 0.002), aVF (AB 58%, MB 32%, p < 0.05), V3 (AB 97%, MB 71%, p < 0.001), V4 (AB 98%, MB 58%, p < 0.001), V5 (AB 98%, MB 61%, p < 0.001) and V6 (AB 93%, MB 52%, p < 0.001). The QTc interval on day 2 was longer in AB (538 ± 66 vs 508 ± 52 ms, p < 0.05). Ventricular arrhythmias (AB 7%, MB 13%) and atrial fibrillation (AB 22%, MB 13%, both p = ns) were similar. Time to ECG normalization was significantly longer in AB (86 ± 98 vs 45 ± 30 days, p < 0.04).
Conclusion: In patients with TTC, ECG changes are much more pronounced in AB than in MB. At presentation, ST-segment elevation in lead V2–V4 and the number of leads with abnormal Q waves are higher in AB. During follow-up, the QTc interval on day 2 and the extent of T-wave inversion is greater in AB than in MB, and time to complete ECG normalization is longer in AB.

P404

Incidence and clinical relevance of left ventricular thrombus in patients with takotsubo cardiomyopathy

B Schneider[1]; A Athanasiadis[2]; J Schwab[3]; U Gottwald[4]; W Toepel[5]; R Schoeller[6]; U Sechtem[2]
[1]Sana Kliniken, Luebeck, Germany; *[2]Robert-Bosch-Krankenhaus, Stuttgart, Germany*; *[3]Klinikum Nuernberg, Nuernberg, Germany*; *[4]Allgemeines Krankenhaus, Celle, Germany*; *[5]Klinikum Idar-Oberstein, Idar-Oberstein, Germany*; *[6]DRK Kliniken Berlin | Westend, Berlin, Germany*

Background: Takotsubo cardiomyopathy (TTC) is increasingly recognized all over the world. Left ventricular thrombi (LVT) complicating TTC have been reported only sporadically. This study evaluated the incidence and clinical relevance of LVT in patients (pts) of a large TTC registry.
Methods: From 37 hospitals, 324 pts (296 f, 28 m, age 68 ± 12) were included 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.
Results: Within the first week of symptom onset, 301 pts were studied by echocardiography (echo, n=276) and/or cardiac MRI (n = 147). In 8 female pts (incidence 2.7%), LVT was diagnosed between day 1 and day 5. Apical ballooning was present in 7 pts and mid- ventricular ballooning in 1 pt. Multiple mobile thrombi were seen in 3 pts, and in 1 pt spontaneous echo contrast was present within the dyskinetic apex. In 3 of 4 pts studied by both echo and CMRI, LVT were detected only by CMRI. No pt had right ventricular thrombus.
Pts with LVT were significantly older (76 ± 12 vs 67 ± 12 years, p < 0.05). Symptoms, triggering events, time from symptom onset to hospital admission and cardiac markers were not different among both groups. The admission ECG in pts with LVT more frequently displayed negative T-waves (100% vs 66%, p < 0.05); heart rate, ST-segment elevation and Q waves were similar.
The QTc was longer (491 ± 67 vs 465 ± 52 ms day 1, 539 ± 87 vs 500 ± 64 ms day 3) and ventricular tachycardia (29% vs 8%, p = 0.05) occurred more frequently in pts with LVT, whereas atrial fibrillation was similar (14% vs 15%).
LV ejection fraction (48 ± 21% vs 49 ± 14%) was not different, but right ventricular involvement (50% vs 17%, p < 0.02) and the need for an intraaortic balloon pump (12.5% vs 0.7%, p < 0.001) were significantly more frequent in pts with LVT. Acute medication (ASS, clopidogrel, heparin, beta-blocker, ACE-inhibitor, catecholamines) was similar in both groups. In 2 of 8 pts (25%) LVT were progressing despite therapeutic doses of heparin, aspirin and clopidogrel. Both suffered a large stroke, 1 pt died.
One additional pt had a stroke on day 2 after TTC onset; echo did not show LVT. CMRI, however, had not been performed.
Conclusion: LV thrombi occur in 2.7% of pts with TTC and a severe clinical course. CMRI is the imaging method of choice as echo underestimates the incidence of LVT. Despite therapeutic anticoagulation, LVT may grow and embolize, resulting in disabling stroke.

COMORBODITIES

P405

Sequential cyclophosphamide-bortezomib-dexamethasone (CyBorD) unmasks the harmful cardiac effect of dexamethasone in primary (AL) cardiac amyloidosis

T Damy[1]; F Lebras[1]; V Moulinier-Frenkel[1]; A Guellich[1]; S Guendouz[1]; A Hulin[1]; M Kharoubi[1]; K Ayad[1]; A Jaccard[2]; D Bodez[1]
[1]GRC-Amyloid Research Institute - APHP - INSERM, Créteil, France; *[2]University Hospital of Limoges, Limoges, France*

On behalf of: GRC Amyloid Research Insitute
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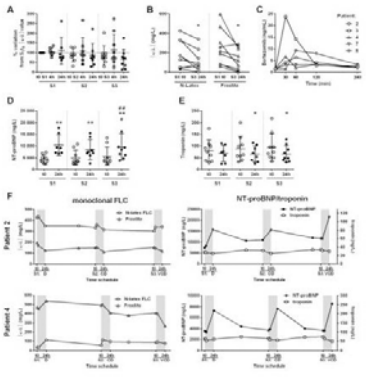
Background: Cardiac Amyloidosis (CA) is a rare disease. Therefore, cardiac involvement in systemic light-chain (AL) amyloidosis is more frequent than expected and carries poor prognosis. Chemotherapy combining (at the same time) cyclophosphamide, bortezomib and dexamethasone (CyBorD) is widely used in CA and improves long-term outcome in mild CA. However, chemotherapy might destabilize severe cardiac amyloidosis (CA) particularly during the early phase of administration leading to death. Indeed, 26 of the 67 patients with CA who were treated in our center between 2010 and 2014, 11 died within the first month all in the score III of the Mayo Staging. These disappointing results led to a change in the protocol i.e., escalation-sequential treatment regimen with the hypothesis that the combination of the drugs might increased the cardiac toxicity: Dexamethasone is known induced fluid retention, bortezomib is suspected of direct cardiac toxicity and both three drugs might induced an acute release of free light chain that might increase the amyloid burden.
Methods and Findings: In an attempt to understand the underlying mechanisms, the first nine patients with the new protocol were closely followed. The first cycle of this protocol consisted of three sequences, with weekly successive introduction of low-dose dexamethasone, cyclophosphamide and bortezomib. Serum cardiac biomarkers including NT-proBNP and troponin HS as well as free light chains were quantified at time 0, 4h and 24h for each sequence. Kinetic of Serum Bortezomid concentration was also measured at 0, 4h and 24h after administration of this drug. Interestingly, NT-proBNP serum concentrations increased 2-folds at 24h for each of the three sequences following Dexamethasone. No significant variation was observed for troponin, light chains and bortezomib concentration and no patient died during the first month.
Conclusions : Corticoids may destabilize the frail heart function of patients with CA most likely through fluid retention. Strategies that limit abrupt exposition to corticoid during the first cycles may be preferred in CA. Larger studies are needed to define the best sequence and dose of chemotherapy in these patients.

Table 1 Biological and clinical characte

Patient	1	2	3	4	5	6	7	8	9
mFLC type	kappa	lambda	lambda	lambda	lambda	lambda	kappa	lambda	kappa
mFLC level (mg/L; N Latex assay)	35	369	161	43	130	326	50	175	235
Troponine at diagnosis (ng/L)	92	27	117	75	40	91	86	35	110
Nt pro BNP at diagnosis (ng/L)	3995	7328	4500	4371	2260	6321	2260	2500	11600
Mayoclinic score	III	II	III	III	II	III	III	II	III



Dynamic quantification of FLC, NT-proBNP

P406

Detection of cardiac dysfunction in asymptomatic cancer survivors with exercise strain echocardiography

K Kaitlyn Lam[1]; F Lee[2]; T Long[3]; L Naylor[3]
[1]Fiona Stanley Hospital, Advanced Heart Failure and Cardiac Transplant Service, Perth, Australia; *[2]Fiona Stanley Hospital, Cardiology, Perth, Australia*; *[3]The University of Western Australia, Perth, Australia*

Background: Cardiac dysfunction can have a latency period when patients are asymptomatic for several years after the completion of cancer therapy. Abnormalities may not be detected until the process is advanced & costly therapy is required.
Purpose: The purpose of this study was to use stress echo to detect pre-clinical stages of cardiac disease in young adult survivors of childhood cancer.
Method: 15 asymptomatic survivors of ALL had exercise Vo2 /stress echocardiography. Echo images obtained assessed chamber size & biventricular function by 2D, 3D imaging, 2D speckled strain analysis & Doppler assessment.
Results: 10 Males, 5 Females with mean age 18.8± 3 years. The mean VO2ml/kg.min was 40.72± 12.42. The stress echoes showed significant reductions in cardiac strain at peak exercise & recovery. When compared to baseline values, global longitudinal strain reduced by 21.8% & 7.6%, global circumferential strain by 16.5% & 10.5% at peak exercise& recovery respectively.
Conclusion: Exercise stress strain echocardiography can detect early cardiotoxicity in asymptomatic cancer patients.

Exercise Echo Parameters			
	Baseline	Peak	Recovery
Global Longitudinal Strain(%)	-21.1± 2.7	-16.5±3.8**	-19.5± 2.7*
Strain AP4 (%)	-21.3± 2.9	-16.7± 2.6**	-19.5± 3.8
Strain AP2 (%)	-21.3±3.0	-16.4± 4.7**	-19.1± 2.9*
Strain AP3(%)	-20.9±3.3	-17.9±5.1	-19.8±2.4
Global Circumferential Strain (%)	-21.9±4.4	-18.3± 4.6#	-19.6± 3.6#
Strain SAX Base (%)	-19.1±5.0	-17.7±6.8	-18.3± 4.3
Strain SAX Mid Wall (%)	-23.4± 4.8	-18.0± 5.3**	-19.2±3.8**
LV Diastole (cm)	5.0± 0.5	4.5± 1.3	4.7±0.5*
LV Volume diastole mL (2D Biplane Simpson)	95.9± 22.9	79.0±19.5#	82.1± 20.4#
LVEF % (2D Biplane Simpson)	64.3± 7.0	71.4±2.9#	64.6± 6.2
LVEF (3D)	50.0± 7.1	62.1± 18.7#	56.4±8.0
RVS′ (cm/s)	12.6± 1.6	16.9±3.0**	12.4± 2.5

# $p < 0.05$ *$p < 0.01$ ** $p < 0.001$: significance when compared to baseline values.

P407

Echocardiography parameters as predictors of left ventricular ejection fraction reduction in cancer patients

M Laufer Perl[1]; A Milwidsky[1]; B Sadeh[1]; D Ravid[1]; N Amrami[1]; G Keren[1]; Y Topilsky[1]; Y Arbel[1]
[1]Tel Aviv Sourasky Medical Center, Cardiology, Tel Aviv, Israel

Background: Advances in treatment have led to improved survival of cancer patients, but with the price of increased morbidity and mortality, mainly due to cardiac causes. Echocardiography is the method of choice for the detection of myocardial dysfunction during and after cancer therapy. Early identification of Left Ventricular (LV) Dysfunction may prevent the development of Heart Failure. Currently, diastolic parameters are known to be common among cancer patients, but have not been found to be prognostic for Left Ventricular Ejection Fraction (LVEF) reduction.
Objectives: To evaluate Echocardiography parameters as predictors of LVEF reduction (defined as EF reduction ≥5%) in cancer patients with normal baseline LV function.
Methods: A retrospective, single-center observational study that included 82 consecutive patients evaluated in the Cardio-oncology clinic from January 2015

to September 2016. Clinical and echocardiographic variables were evaluated for all patients. All patients performed at least two echocardiography exams and excluded were patients with reduced LV function (Ejection Fraction < 60%) at baseline.
Results: Among 82 consecutive patients, 18 patients (22%) developed LVEF reduction. Several echocardiography parameters were found to be a significantly predictors of LVEF reduction, including larger LV end diastolic diameter (LVEDD) (49 ± 5mm vs 46 ± 5mm, p = 0.002), lower e' septal (6.1 ± 2.2cm/s vs 7.7 ± 2.4 cm/s, p = 0.019), lower e' lateral (8 ± 2.5 cm/s vs 10.1 ± 2.7 cm/s, p = 0.015), higher E/e' septal (13.8 ± 6.6 cm/s vs 11 ± 5.3 cm/s, p = 0.046). However, E/A and deceleration time were not predictive of deterioration in EF (p = 0.520, 0.627).
Conclusions: Early identification of cardiac dysfunction is essential for the prevention of symptomatic heart failure. Our study demonstrates that parameters associated with depressed diastolic function, and larger LV size may identify early cardiac dysfunction which may lead for early cardio protective treatment and prevention of irreversible LVEF reduction and heart failure.

P408
Characterization of the clinical and echocardiographic profile of a population of women with breast cancer.

J Joao Pais[1]; B Picarra[1]; RA Guerreiro[1]; A Bernardo[2]; C Tata[2]; D Bras[1]; J Carvalho[1]; K Congo[1]; AR Santos[1]; R Matos[1]; C Cruz[1]; J Aguiar[1]
[1]*Hospital Espirito Santo de Evora, Departement of Cardiology, Evora, Portugal*; [2]*Hospital Espirito Santo de Evora, Evora, Portugal*

Introduction: Cancer patients are treated with several therapies with potential harmful cardiotoxic effects. Carrying out appropriate cardiovascular therapy to the clinical profile of these patients may minimize the risk of such cardiotoxicity.
Purpose: To characterize the clinical and echocardiographic profile of a population of women with breast cancer.
Methods: In a 2-year period, all women with breast cancer who underwent an echocardiogram in our echocardiography laboratory were evaluated. All women had started some type of oncologic therapy (chemotherapy or radiotratherapy). Cardiovascular risk factors, echocardiographic data and type of chemotherapy and / or radiotherapy were recorded.
Results: The study included 116 women, with a mean age of 60.5 ± 13.0 years. 99% of these women underwent chemotherapy and 70% were submited to radiotherapy. The prevalence of cardiovascular risk factors was hypertension - 34.7%, Diabetes Mellitus - 20.8%, dyslipidaemia 30.7%, smoking - 7.9%, smoking habits in the past - 5, 0%, and coronary disease - 3.0%. The echocardiographic evaluation revealed that the great majority of the women had good left ventricular function (93.3%) and that only 1.9% had moderate or severe left ventricular function depression. In 58.7% of the women, minor valve disease were reported, but in only 8.2% of these patients the disease were moderate or severe. The presence of pericardial effusion was found in 4.8% of the women, and in all cases the effusion was slight.
Conclusions: In our population of women with breast cancer there was a low prevalence of cardiovascular risk factors. Most of these patients have good left ventricular function, with no significant valve disease.

P409
Basal renal function and its evolution in patients admitted for decompensated heart failure.

L Secco[1]; SM Mettini[1]; F Jaliff[1]; J Zubiri[1]; DA Fernandez[1]; L Lapadula[1]; C Cejas[1]; G Sumay[1]; MG Masuelli[1]; SM Pereiro Gonzalez[1]
[1]*Hospital Center Churruca-Visca, Buenos Aires, Argentina*

Background: The worsening of renal function (RF) is very common in patients hospitalized because of decompensated heart failure, it is associated with high prevalence of events on the follow up..
Methods: It is a prospective analysis of 474 patients (p) admitted for decompensated of heart failure, consecutively, in our Cardiology Department, from June 2012 to November 2016, with a median follow up of 26 months (Q1 13 - Q3 33). We divided two groups (G): G1 with basal normal RF (n 236) and G2 (n 226) with basal abnormal RF. We defined normal RF those with serum creatinine levels < 1.3 mg/dl and creatinine clearance >60 ml/min/1.73m2; those which lower clearance and/or higher creatinine serum levels were classified as abnormal basal RF. We also classified as worsening renal function, those with increased serum creatinine greater than 0.3 mg/dl and/or decrease in creatinine clearance > 10 ml/min/1,73 m2. Quantitative variables with normal distribution were expressed with medium and with standard deviation (analyzed by test Fisher's Test); those with not normal distribution, were expressed with median (m) and quartiles (analyzed by Mann Whitney's Test). Dichotomous variables were analyzed by Chi^2.
Results: We observed that G1 had more worsening RF that G2, with differences statistically significant (DSS) (p = 0.0000, G1 57.2% vs G2 36.7%-table 1), we analyzed the median of maximum furosemide dose and it was 80 mg/day, for both, without DSS. Hospital mortality was higher for those in G2 with DSS (p = 0.0421, G1 3% vs G2 7.1%) as the amount of p older than 75 years old (p = 0.00005, G1 46.2% vs G2 62.4%). There were no differences in the rehospitalization, follow-up mortality, combination of both, or if they had ejection fraction higher than 50%.
Conclusions: The cardiorenal syndrome was present in the older patients and had more hospital mortality (DSS). There were no differences between groups in rehospitalizations or mortality in the follow-up. Nevertheless, we observed, that those with better renal function worsen it, despite not having differences in the doses of furosemide. Our next step is analyze it.

Table 1

Basal RF	% (n)	Worsening	
Normal	51,1 % (236)	57,2 %	p = 0,0000OR 0,43IC 95% 0,29-0,63
Abnormal	48,9 % (226)	36,7 %	

P410
Prevalence and prognostic value of comorbidities in patients with decompensated heart failure and acute kidney injury

A Klimenko[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: Patients admitted with acute decompensated heart failure (ADHF) often have multiple concomitant diseases that complicate management and may adversely affect outcomes. Up to 70% of ADHF patients had at least 1 noncardiac comorbidity (CoM), of which the most common are chronic kidney disease (CKD), anemia, diabetes mellitus (DM) and chronic obstructive pulmonary disease (COPD).
Purpose: The aim of the study was to determine the prevalence of CoM in ADHF patients depending on the presence of acute kidney injury (AKI) and to evaluate the impact on short-term (30-days mortality) and long-term (6 months rate of ADHF rehospitalizations) outcomes.
Methods: in 183 patients admitted with ADHF (125 male, 69 ± 9 years (M ± SD), arterial hypertension 87%, ischemic heart disease 56%, myocardial infarction 53%, atrial fibrillation 51%, DM 36%, known CKD 40%, COPD 29%, anemia 20%, ejection fraction 44 ± 15%) the prevalence of AKI and main CoM was assessed. AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney and multiple logistic regression analysis were performed. P < 0.05 was considered statistically significant.
Results: Patients with AKI versus patients without AKI had higher rates of DM (40 vs 26%, < 0.05) and anemia (33 vs 11%, p < 0.001). 41% of patients developed AKI and 79% of them had at least 1 CoM and 5% pts all 4 of them. AKI in patients with COPD versus without COPD was transient (76 vs 48%, p < 0.05), had higher rate of long-term outcomes (71 vs 41%, p < 0.05) and there was tendence to more frequent community-acquired (presenting on admission) AKI (76 vs 50%, p>0.05). There was not found any difference in prognosis between anemic and non-anemic pts. AKI in DM patients versus AKI without DM was persistent (87 vs 18%, p < 0.001), had higher risk of 30-days mortality (30 vs 9%, p < 0.05) and tendence to higher 6 months rate of ADHF rehospitalizations (53 vs 44%, p>0.05). Development of AKI in the presence of CKD versus AKI de novo less often was transient (45 vs 71%, p < 0.01), had lower risk of 30-days mortality (11 vs 29%, p < 0.05) and higher 6 months rate of ADHF rehospitalizations (60 vs 29%, p < 0.01). Evaluation the impact of CoM on outcomes demonstrated the increasing risk of long-term outcomes in parallel with the increasing number of CoM (1CoM-44%, 2- 50%, 3- 76%, 4- 100%, p < 0.05).
Conclusions: 79% of ADHF patients with AKI had at least 1 main comorbidity. The presence of comorbidities is the independent risk factor for adverse short- and long-term outcomes in ADHF patients with AKI.

P411
Prognostic impact of renal dysfunction in the patients with acute heart failure

E Mezhonov[1]; Y Vyalkina[2]; S Shalaev[1]
[1]*GBUZ TO "Regional clinical hospital", Tyumen, Russian Federation*; [2]*Tyumen State Medical University, Tyumen, Russian Federation*

Background: Renal disease as a target organ is often found in patients with cardiovascular disease patients. The question of influence on the state of renal function during acute heart failure (AHF), as well as the extent to which these disorders

determine the prognosis of patients becomes urgent. Purpose. To estimate the prevalence of renal dysfunction and its prognostic value in patients with AHF.
Materials and methods. The study included 141 patients (mean age 57.4 ± 9.86 years, 75.2% men), admitted to the hospital due to the development of symptoms of AHF, left ventricular ejection fraction of 15% to 80% (mean 37.8 ± 14.19%). Indicators of renal function were divided into 6 categories according to the estimated glomerular filtration rate (GFR) using a calculation formula CKD-EPI. Acute kidney injury (AKI) diagnosed according to the KDIGO recommendations (2012). The primary endpoint was defined as rehospitalization due to symptoms of AHF or death from cardiovascular causes. Result. Analyzed the frequency of occurrence of the endpoint, depending on the level of GFR and microalbuminuria (MA). With the decline of GFR levels increased in direct proportion to the frequency of rehospitalization due to AHF, so if GFR greater than 90 ml/min it amounted to 37.5%, 60-89 ml/min – 33.9%, while the GFR 45-59 ml/min – 48.9%, 15-44 ml/min – 78.6%, less than 15 ml/min - 100% (p = 0.027). Reduced GFR of less than 45 ml/min was associated with an increase in death from cardiovascular causes - 43.8%, while in patients with GFR over 45 ml/min death from cardiovascular causes registered with 12,8% (p = 0.005). Increased MA to levels of over 300 mg/l was associated with a poor prognosis, the endpoint and death from cardiovascular causes was reported in 81.8% and 36.4% of patients, and in patients without MA – 39.8% and 12.0% respectively (p = 0.012 and p = 0.036). Analyzed OR of the primary endpoint of the depending on the level of GFR and MA. GFR of less than 60 ml/min increases the risk of an endpoint of 2.5 times (OR 95% 2.541 (1.284-5.028), p = 0.007), and GFR less than 45 ml/min - 10 times (OR 95% 10.157 (2.213-46.622), p = 0.003). GFR of less than 45 ml/min increases the risk of death from cardiovascular causes of 5 times (OR 95% 5.299 (1.732-16.214), p = 0.003). The presence of MA over 300 mg/l increases the risk of the primary endpoint in 6 times (OR 95% 5.946 (1.236-28.611), p = 0.026). Development AKI associated with an increase of the frequency of the primary endpoint as compared to patients without AKI, 85.7% and 41.7% respectively (p = 0.003). The frequency of death in patients with AKI also increased to 57.1%, whereas in patients without AKI – 11.8% (p < 0.001). The AKI increases the risk of the primary endpoint in 8 times (OR 95% 8.377 (1.8-38.996), p = 0.007) and the risk of death from cardiovascular causes of 10 times (OR 95% 9.956 (3.035-32.652), p < 0.001). Conclusion. Reduced GFR and MA is important predictors of cardiovascular morbidity and mortality in patients with AHF.

P412
The interaction between heart failure and renal failure

AN Anass Inchaouh[1]; A Hadadi[1]; R Habbal[1]
[1]*Ibn Rochd University Hospital, Casablanca, Morocco*

Introduction: Heart failure (HF) is an important public health problem whose incidence and prevalence are progressively increasing. Multiple comorbid conditions are common in patients with HF. Renal failure (RF) is one of the important comorbid condition that shares common cardiovascular risk factors with HF. The interaction between HF and RF has been suggested to cause a deterioration of each of these conditions. Moreover, the interaction between these conditions has been suggested to form a vicious cycle, termed cardio-renal syndrome, which increases mortality.
Aim: Our aim was to investigate the prevalence, the clinical characteristics of HF patients with different deg rees of renal dysfunction
Methods: This is a retrospective study of all HF patients registered in the therapeutic Unit of Chronic Heart failure in the cardiology department over a period of 2 years. Renal function was determined from the estimated glomerular filtration rate (GFR), and patients were divided into 4 stages : GFR 60-89(Mildly reduced kidney function), GFR 30-59 (Moderately reduced kidney function), GFR 15-29 (Severely reduced kidney function) and GFR < 15 mL/min per 1.73 m^2 or on dialysis (endstage kidney failure).
Results: The study was conducted in 1280 patients with a mean age of 68.6 years and male predominance (60,1%). RF was found in 62% of the patients. Patients with moderate RF were characterized by the higher prevalence of strokes, myocardial infarction and the lowest ejection fraction. Patients with severe RF had the worst cardiovascular risk profile : older age, higher prevalence of cardiovascular risk factors, diabetes, hypertension, dyslipidemia, the lowest walking parameter of the 6-minute walk test and the most prescription of diuretics. Patients with endstage RF had more anemia and less prescription of angiotensin-converting enzyme (ACE) inhibitors.
Conclusion: RF seem to be highly prevalent in HF patients with a worse risk profile. The presence of cardio-renal syndrome highlights the necessity of early treating these comorbidities.

P413
Cardiohepatic syndrome is driven by congestion rather than hypoperfusion in decompensated heart failure

A Soloveva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Department of Internal Disease Propaedeutics, Moscow, Russian Federation*

Objective: Abnormal liver function tests (LFT) are associated with specific clinical, biological and prognostic features in decompensated heart failure (DHF) and defined as cardiohepatic syndrome (CHS), but their predictors are still unknown. The aim of this study was to assess the prevalence and predictors of CHS in DHF.
Methods: In 322 patients with ADHF (190 male, 69.5 ± 10.6 years (M ± SD), arterial hypertension 87%, myocardial infarction 57%, atrial fibrillation (AF) 65%, diabetes mellitus 42%, known chronic kidney disease 39%, chronic anemia 29%, left ventricular ejection fraction (EF) 37.6 ± 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) were measured on admission. CHS was considered when at least one LFT level exceeded upper normal limit. Multivariate logistic regression analysis was performed. p < 0.05 was considered statistically significant.
Results: CHS occurred in 274 (85.1%) of patients with DHF. Increase of ALT was detected in 50 (15.5%), AST in 46 (14.3%), DB in 262 (81.4%), TB in 192 (59.6%), AP in 90 (27.9%) and GGT in 102 (31.7%) of patients with DHF. Most of LFT elevations were moderate (≤ 3UNL) - ALT in 38 (76%), AST in 42 (91.3%), DB in 150 (57.3%), TB in 186 (96.9%), AP in 86 (96.7%), GGT in 74 (72.5%) of alterations cases. The independent predictors of CHS were severe tricuspid regurgitation (odds ratio (OR) 32.3, 95% confidential interval (CI) 7.7-135.7, p < 0.001), right ventricular end diastolic volume >31 mm (OR 11.7, CI 5.2-26.2, p < 0.05), heart rate on admission >115 per minute (OR 10.9, CI 2.6-45.9, p < 0.05), EF<31% (OR 6.7, CI 2.4-19.3, p = 0.02), chronic AF (OR 5.7, CI 2.7-11.8, p < 0.05), hydrothorax (OR 4.3, CI 1.9-9.4, p < 0.05) and ascites (OR 2.7, CI 1.3-5.7, p < 0.05).
Conclusions: severe tricuspid regurgitation and right ventricular dilation were more powerful predictors of cardiohepatic syndrome in DHF than heart rate on admission >115 per minute and EF<31%.

P414
Nonalcoholic fatty liver disease and increased risk of 1-year all-cause and cardiac hospital readmissions in elderly patients admitted for acute heart failure

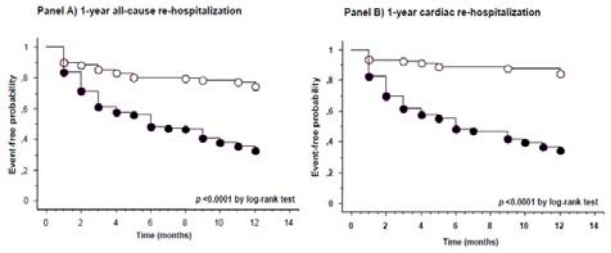
F Filippo Valbusa[1]; D Agnoletti[1]; S Bonapace[2]; L Scala[1]; C Grillo[1]; P Arduini[3]; E Turcato[3]; G Targher[4]; G Arcaro[1]
[1]*Sacro Cuore - Don Calabria Hospital, Internal Medicine, Negrar-Verona, Italy*; [2]*Sacro Cuore - Don Calabria Hospital, Division of Cardiology, Negrar-Verona, Italy*; [3]*Sacro Cuore - Don Calabria Hospital, Division of Geriatry, Negrar-Verona, Italy*; [4]*University and Azienda Ospedaliera Universitaria Integrata of Verona, Section of Endocrinology, Diabetes and Metabolism, Verona, Italy*

Background: Nonalcoholic fatty liver disease (NAFLD) is an emerging risk factor for heart failure (HF). The rates of hospital readmissions and the related costs continue to rise dramatically. The aim of this study was to investigate whether NAFLD diagnosed at hospital admission was independently associated with 1-year all-cause and cardiac re-hospitalizations in patients admitted for acute HF (AHF).
Methods: We studied 212 elderly patients who were consecutively admitted with AHF to our hospital over a 1-year period. NAFLD was diagnosed by ultrasonography. Patients with known acute myocardial infarction, severe valvular heart diseases, endstage renal disease, cancer, known liver diseases or decompensated cirrhosis were excluded. Cox regression was used to estimate hazard ratios (HR) for the associations between NAFLD and the outcomes of interest.
Results: The cumulative rate of 1-year all-cause re-hospitalizations was 46.7% (n = 99). Patients with NAFLD (n = 109; 51.4%) had remarkably higher 1-year all-cause and cardiac re-hospitalization rates compared with their counterparts without NAFLD. NAFLD was associated with an approximately 5-fold increased risk of 1-year all-cause re-hospitalization (adjusted-HR 5.26, 95% CI 3.03-9.08, p < 0.0001) after adjustment for established risk factors and potential confounders. Similar results were found for 1-year cardiac re-hospitalization (adjusted-HR 8.33, 95% CI 3.98-16.7, p < 0.0001).
Conclusions: NAFLD was independently associated with increased risk of 1-year all-cause and cardiac re-hospitalization in elderly patients admitted with AHF.

Table 1

Cox regression analyses - Association between NAFLD and risk of 1-year all-cause or cardiac re-hospitalization rates in hospitalized patients with AHF at baseline			
CoxHazard Models	Hazard ratio(s)	95% CI	p value
1-year all-cause re-hospitalization: NAFLD (yes vs. no) (n: 212)			
Unadjusted model	3.50	2.23-5.49	< 0.0001
Adjusted model	5.26	3.03-9.09	< 0.0001
1-year cardiac re-hospitalization: NAFLD (yes vs. no) (n: 187)			
Unadjusted model	5.86	3.27-10.4	< 0.0001
Adjusted model	8.33	3.98-16.7	< 0.0001

Data are expressed as hazard ratios ± 95% confidence intervals (CI) as assessed by either univariable (unadjusted) or multivariable Cox hazard models. Covariates included in multivariable regression models, with NAFLD, were: age, sex, hospital ward, pre-existing diabetes, CHD, LV-ejection fraction, eGFR and NT-proBNP, serum sodium and GGT levels.



P415

Mixed phenotype of cardiohepatic syndrome is common and associated with worse prognosis in patients with decompensated heart failure

A Soloveva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Department of Internal Disease Propaedeutics, Moscow, Russian Federation*

Objective: Over the last several years different mechanisms of cardiohepatic syndrome (CHS) in decompensated heart failure (DHF) have been discussed. The purpose of the study was to assess the prevalence and associations of different phenotypes of CHS in patients with DHF.
Methods: In 322 patients with DHF (190 male, 69.5 ± 10.7 years (M ± SD), arterial hypertension 87%, myocardial infarction 57%, atrial fibrillation 66%, diabetes mellitus 42%, known chronic kidney disease 39%, chronic anaemia 29%, ejection fraction (EF) 38 ± 13%, EF<35% 39%) liver function tests (LFT) - alanine transaminase (ALT), aspartate transaminase (AST), direct and total bilirubin (DB and TB), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT) were measured on admission.
LFT were considered abnormal when levels exceeded local upper normal limit (UNL). Only ALT and/or AST increase was considered as hepatocellular CHS. Isolated increase of GGT, AP, DB and TB (with DB increase) – as cholestatic CHS. The simultaneous increase of markers of cytolysis and cholestasis was considered as mixed CHS. Mann-Whitney test was performed, $p < 0.05$ was considered statistically significant.
Results: Abnormal LFT occurred in 274 (85.1%) of patients. Hepatocellular, cholestatic and mixed CHS were detected in 0.4, 32.8 and 66.8% of patients with DHF and CHS. Patients with mixed vs cholestatic CHS had higher levels of AST (median 32 (interquartile range 23;49) vs 21 (18;27) U/l,), ALT (30 (15;53) vs 17 (12;25) U/l), DB (12 (7;17) vs 6 (4;9) μmol/l,) and TB (33 (25;41) vs 19 (15;22) μmol/l), $p < 0.001$ for all comparisons. Patients with mixed vs cholestatic CHS had higher cholestatic markers increase incidence (DB (97 vs 93%, $p < 0.05$), TB (90 vs 31%, $p < 0.001$), GGT (44 vs 24%, $p < 0.01$) and AP (39 vs 20%, $p < 0.01$)) and severity: incidence of increase >2UNL of DB (82 vs 40.5%, $p < 0.01$), TB (24.4 vs 0%, $p < 0.01$), GGT (60 vs 54.6%, p>.05) and AP (18 vs 11%, $p < 0.01$). Patients with mixed vs cholestatic CHS had higher NT-proBNP level (9200 ± 7985 vs 7122 ± 6572 pg/ml, $p < 0.05$), incidence of EF<35% (47 vs 36%, $p < 0.05$), severe mitral regurgitation (51 vs 31%, $p < 0.01$), vasopressor therapy (11 and 4%, $p < 0.05$), lower systolic blood pressure (SBP) (132 ± 17 vs 144 ± 21 mmHg, $p < 0.001$) and pulse BP (51 ± 14 vs 60 ± 15 mmHg, $p < 0.001$) on admission. No significant differences in signs of congestion were observed between groups. Mixed CHS was associated with higher all-cause death in 6 months (30 vs 23%, $p < 0.05$).
Conclusions: The prevalence of mixed CHS in patients with DHF was 66.8%. Patients with mixed vs cholestatic CHS had higher LFT and NT-proBNP levels, incidence of LFT increase, severe mitral regurgitation, EF<35%, vasopressor therapy, lower SBP and pulse BP on admission and had worse prognosis.

P416

In-hospital changes of liver stiffness and biomarkers of liver fibrosis in patients with acute decompensated heart failure

AA Balashova[1]; PV Lazarev[1]; IV Garmash[1]; VS Moiseev[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Purpose: To assess the dynamic changes in liver stiffness measurements (LSM) and direct fibrosis markers in patients hospitalized with acute decompensated heart failure (ADHF) receiving standard heart failure therapy according to the international guidelines.
Methods: 35 patients [8 female, median age 58 (IQR 47-68) years, NYHA III class n=16 (46%), NYHA IV class n=19 (54%)] were included. Transient elastometry measurements (FibroScan®) and direct markers of fibrosis were analyzed at baseline and discharge from hospital. The median duration of hospitalization was 14 days. Serum concentration of direct markers of fibrosis [matrix metalloproteinase-9 (MMP-9), N-Terminal Propeptide of Type III Collagen (PIIINP), laminin] was determined by means of immunosorbent assay.
Results: Heart failure therapy resulted in the reduction of signs of congestion [weight loss 5.5 (4.0-7.0) kg]. There was a significant decrease in LSM (26,3 [19-48] vs. 16.6 [11-21.8] kPa; $p < 0.01$) from baseline to end of hospitalization, although they remained elevated (grade 4 METAVIR score). A decline in LSM significantly correlated with weight loss (rho 0.4, < 0.05) and reduction of leg circumference (rho 0.3, < 0.05). On admission direct markers of fibrosis were elevated above reference values [MMP-9 850 (525.0-1390.0) ng/ml, PIIINP 33.4 (24.4-55.2) ng/ml, laminin 218 (167.0-248.5) ng/ml], and no significant changes occurred during hospitalization [ΔMMP-9 50 (-420 - 260) ng/ml, ΔPIIINP 5 (-0.7 - 13.7) ng/ml, Δlaminin 12 (-33 - 50) ng/ml, p>0.05 for all comparisons].
Conclusion: Increased LSM in patients with ADHF is not explained by fibrosis alone, and tends to be overestimated due to the presence of congestion This is confirmed by the absence of dynamic changes in fibrosis markers. Therefore, the application of transient elastometry for assessment of fibrosis in patients with ADHF is limited.

P417

Improvement of heart failure symptoms through novel implantable remede central sleep apnea treatment device: first long-term experience

H Fox[1]; T Bitter[1]; D Horstkotte[1]; O Oldenburg[1]
[1]*Herz- und Diabeteszentrum NRW, Ruhr-Universität Bochum, Clinic for Cardiology, Bad Oeynhausen, Germany*

Background: Sleep-disordered breathing (SDB) and Cheyne-Stokes respiration (CSR) are associated with shorter survival periods in patients with heart failure (HF). A novel treatment method for this patient group is unilateral phrenic nerve stimulation by the remedē system, a transvenously implantable neurostimulation device, which has recently been studied in a short-term randomized, controlled trial. Previous literature has shown the efficacy and safety of the treatment with this first-generation device, but hardly any data is available on long-term clinical parameters in HF patients.
Methods: We performed remedē® device replacement in the first three consecutive HF patients for battery depletion and documented observations on clinical parameters, longevity, operation procedure, complications and difficulties with this novel device therapy.
Results: All patients were on permanent neurostimulation treatment by phrenic nerve neurostimulation when device replacement became necessary. Apnoea-hypopnoea index (AHI from 45 ± 4/h to 9 ± 4/h), oxygen-desaturation index (ODI from 35 ± 7/h to 7 ± 6/h) and time spent with oxygen saturation of < 90% (T < 90% from 5 ± 7 to 0 ± 0%) were improved and improvements remained constant throughout the four-year follow-up. Mean battery life was 4.2 ± 0.2 years, mean replacement procedure time was 25 ± 5.1 minutes. Using conventional X-ray

stable lead positions in a long-term setting were documented and no major complications occurred. In addition, clinical exercise capacity and sleepiness symptoms improved.
Conclusions: The novel remedē® device shows a sustained therapy efficacy and safety in terms of stable lead positions over four years. Long-term phrenic nerve neurostimulation therapy for central SDB/CSR in HF appears feasible in a clinical routine setting to improve HF symptoms.

P418
Sleep disorders and quality of life in patients with heart failure

I Uchmanowicz[1]; J Orzepowska[2]; M Wleklik[1]; MH Magdalena Hanna Lisiak[1]
[1]Wroclaw Medical University, Department of Clinical Nursing , Wroclaw, Poland; *[2]Wroclaw Medical University, Cardiology Department, Wroclaw, Poland*

Introduction: Population aging dynamics contribute to increasing numbers of elderly individuals, including heart failure (HF) patients. Age is a risk factor for a multitude of diseases, including cardiovascular disorders, as well as a factor affecting sleep quality and quantity. Patients with HF commonly experience poor sleep quality, which reduces both total sleep quantity and sleep effectiveness, and increases sleep and awakening latencies, compared to individuals without HF. The sleep disorders seen in HF patients significantly affect their quality of life and self-care capabilities.
Purpose: To analyze correlations between sleep disorders and quality of life in HF. To analyze the impact of socio-demographic and clinical factors on sleep disorders in HF.
Material and methods: The study included 100 patients (40 female and 60 male, mean age: 68.69 ± 14.27 years) hospitalized in a Cardiology Ward. Material was collected using a socio-demographic questionnaire, the patients' clinical data, and standardized research instruments: the Epworth Sleepiness Scale, the Minnesota Living with Heart Failure (MLHF) questionnaire specifically evaluating quality of life in HF, and the general WHO Quality of Life (WHOQoL) questionnaire. Correlations and differences at $p < 0.05$ were considered statistically significant.
Results: Patients with sleep disorders were shown to have a lower quality of life than those without sleep problems, both in the MLHF ($p < 0.001$) and in the WHOQoL (r=1.36, $p = 0.002$) scales. Sleep disorders indicated by the Epworth scale were correlated with NYHA functional class (r=3.917, $p = 0.003$), left ventricular ejection fraction – LVEF (r=-0.056, $p = 0.029$), the use of diuretics (r=1.208, $p = 0.034$), and the use of digoxin (r=1.854, $p = 0.015$).
Conclusions: 1. Sleep disorders adversely affect quality of life in heart failure patients. 2. Increased use of diuretics and digoxin contributes to sleep disorders in HF patients. 3. Sleep disorders in HF patients are correlated with higher NYHA class, lower LVEF, and higher proBNP levels.

P419
Sleep apnea in peri-partum cardiomyopathy patients admitted in acute heart failure: a longitudinal study in Mozambique

M Machava[1]; I Mbanze[1]; P Deyoung[2]; J Orr[2]; A Malhotra[2]; E Calua[1]; R Banze[1]; C Muianga[1]; V Govo[1]; N Jessen[1]; A Fabula[1]; A Oliveira[1]; A Damasceno[1]
[1]Eduardo Mondlane University, Maputo, Mozambique; *[2]UCSD, S. Diego, United States of America*

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Background: There are very few studies on sleep apnoea in Sub Saharan Africa and much lees in peripartum cardiomyopathy. We reported previously that sleep apnoea was common in patients admitted with acute heart failure in a cardiac service in Mozambique despite being younger and leaner than the ones usually studied in other series. Moreover, longitudinal follow-up also show that sleep apnoea improved in some treated and compensated patients but not in all.
Purpose: Peripartum cardiomyopathy is common in Sub Saharan Africa and occurs in young patients. Furthermore, Cheyne-Stokes respiration is uncommon in women. Therefore, we sought to examine the prevalence and outcomes of sleep apnoea in peripartum cardiomyopathy patients admitted with decompensated acute heart failure recently diagnosed.
Methods: Subjects were recruited from an acute care cardiology unit in Mozambique. Consenting acute decompensated heart failure subjects admitted to our service underwent type III portable sleep testing (ApneaLink, Resmed) and echocardiography at both baseline and at 6 month follow up. Follow up evaluation was performed after heart failure treatment according to local practice. Sleep studies were scored by a RPSGT using a modified Chicago criteria (3% desaturation).
Results: To date, 153 subjects have undergone baseline evaluation. Mean age was 41 ± 16 years, 60% were female, 26% known HIV positive and BMI was 23.7 ± 7 kg/m2. Of these, 13% of subjects had peripartum cardiomyopathy. Peripartum patients were younger (28 ± 6 versus 43 ± 17 years; $p < 0.001$), with similar BMI, but lower LVEF (26 ± 3% versus 36 ± 2%; $p = 0.02$) and smaller left atrial size (44 ± 1 versus 53 ± 1 cm3; $p = 0.001$). Baseline AHI was not significantly different between those with peripartum and non-peripartum aetiology (17.8 ± 2.6/hr versus 19.3 ± 1.7/hr; $p = 0.403$). Similarly, there was no difference in OAI, CAI, hypopnea index, %CSR, baseline or nadir Sp02, or %time SpO2 < 90%.
Follow up data at 6 months were available for 77 subjects, including 16 subjects that had died. Using fixed effect modelling, the AHI decreased by a mean of 6.2 ± 3.0/hr ($p = 0.037$). There was no significant difference in this change in the peripartum group ($p = 0.736$) as well as in change in AHI from baseline to 6 months between the peripartum and non-peripartum groups. LVEF improved non-significantly by a mean of 4.7 ± 3.0% with no significant difference between the two groups.
Conclusion: Sleep apnoea is similarly severe in acutely decompensated heart failure patients with peripartum cardiomyopathy compared to other aetiologies, despite younger age, female gender, and differences in echocardiographic measures. Although the sample size is small, we found no differences in the improvement of sleep apnoea in peripartum patients compared with the whole group.

P420
Identification of cognitive impairment and delirium in patients with decompensated heart dailure

S Mitchell[1]; K Jones[2]; J Taylor[2]; T Quinn[2]
[1]University of Glasgow, Glasgow, United Kingdom; *[2]Glasgow Royal Infirmary, Glasgow, United Kingdom*

Background: Delirium is common in older hospitalized patients and associated with morbidity and mortality. The majority of patients admitted with acute decompensated heart failure (ADHF) are older but there has been limited study of delirium in this group. The local target is to perform cognitive screening in all older unscheduled admissions and implement delirium prevention/management in all at risk.
Purpose:We aimed to benchmark cognitive screening of in-patients with ADHF and identify patients with delirium.
Methods: Patients admitted to a cardiology ward with ADHF were screened over 5 weeks. The ward admits unselected adults with cardiovascular pathologies not requiring level 2 care. Cases were identified by case-note review. Preferred cognitive screens in our centre are the 4 point Abbreviated Mental Test (AMT) and 4AT for delirium. The Think, Investigate, Manage, Explore (TIME) bundle is used to initiate delirium prevention/management. We recorded any completed cognitive assessment. We then assessed ADHF patients using the 4AT, 10 point AMT and an informant questionnaire for cognitive impairment (AD8).
Results:We identified 43 patients, mean age 78.7 years (range 52-95). Two patients refused to participate, 1 was terminally ill. Of 40 patients assessed, AMT4 and 4AT were completed by ward staff in 85% and 45% respectively. The TIME bundle was initiated in 42.5% of patients, none fully completed. Four patients had an established diagnosis of cognitive impairment. Following our assessment, a further 11 patients were identified as having cognitive impairment, 8 of these had not been identified by the treating team. Eight patients (20%) screened positive for delirium of whom 5 were assessed as also having likely underlying cognitive impairment.
Conclusions: Cognitive impairment, in particular delirium, is common in patients hospitalized with ADHF, but recommended screening and management bundles are infrequently completed. This has important implications for the training of healthcare professionals around recognition and management of these conditions.

P421
Heart failure and cardiogenic shock are predisposing factors for nosocomial infections in an intensive cardiac care unit.

M Carrington[1]; J Pais[1]; B Bruno Cordeiro Picarra[1]; AR Santos[1]; R Guerreiro[1]; J Carvalho[1]; K Congo[1]; D Bras[1]; J Aguiar[1]
[1]Hospital do Espírito Santo, Évora, Portugal

Introduction: Patients with heart failure (HF) usually had multiple comorbidities and could be more susceptible to nosocomial infections. Currently, there is a lack of information regarding its prevalence and prognostic impact of nosocomial infections in patients admitted to an Intensive Cardiac Care Unit (ICCU).
Purpose: To determine the prevalence of nosocomial infections in patients hospitalized in an ICCU and to identify possible predictors of their appearance.
Methods: Prospective study, which included all patients consecutively admitted to the ICCU within 4 years. We considered 2 groups: Group 1 - patients who developed nosocomial infections and Group 2 - patients who did not develop nosocomial infections. We registered demographic data, patient's provenience (emergency department (ED), other general intensive care units (ICU), outpatient clinic or other hospitals), diagnosis of admission, duration of hospitalization and destination of the patient (cardiology ward, ambulatory or death).
Results: From a total of 1633 patients admitted to the ICCU, 150 patients (9,1%) developed nosocomial infections, of these 40,0% were respiratory, 26,7% urinary, 16,0% had fever without an identified infectious focus, 14,0% were severe sepsis

and septic shock, and 3,3% had infection of another etiology. These patients were older (72,4 ± 11,8 vs 67,7 ± 14,2 years, p = 0,001), with no differences between genders. The main diagnosis of admission was acute coronary syndrome in both groups (Group 1: 53,3% vs 52,8%, p = ns); however, Group 1 patients were more frequently admitted for decompensated heart failure (16,7% vs 6,4%, p = 0,001) and cardiogenic shock (6,0% vs 0,6%, p = 0.001), with no differences in the nosological groups of arrhythmias, valvular heart disease or disease of the myocardium or pericardium. The majority of patients in both groups were admitted from the ED (Group 1: 56,0% vs 57,9%, p = ns); however, Group 1 patients were more frequently admitted from general ICU (17,3% vs 8,8%, p = 0,002), and less frequently from the outpatient clinic (2,7% vs 9,7%, p = 0,014), p = 0,006). Patients with nosocomial infection had longer hospitalizations (6,8 ± 5,2 vs 3,0 ± 2,0 days, p = 0,001), higher mortality (9,3% vs 3,1%, p = 0,001), and lower direct ambulatory discharges (4,7% vs 15,8%, p = 0,001).
Conclusions: Nosocomial infections are frequent, being presented 9,1% of patients hospitalized in our ICCU and were associated with a 2,3-fold increase in days of hospitalization and 3-fold increase in mortality. Heart failure and cardiogenic shock seems to be predisposing factors for its appearance.

P422
The relationship between employment status and depressive symptoms and minnesota living with heart failure questionnaire

G Guliz Kozdag[1]; K Hebert[2]; D Ural[3]; I Gogichaishvili[4]; L Arcement[5]; O Argan[6]
[1]Kocaeli University, Faculty of Medicine, Department of Cardiology, Kocaeli, Turkey; *[2]General Electric, Wakasha Wisconsin, United States of America*; *[3]Koc University, Cardiology, Istanbul, Turkey*; *[4]Cleveland Clinic, Cleveland, Ohio, United States of America*; *[5]Chabert medical center, Houma Louisiana, United States of America*; *[6]Kocaeli Government Hospital, Cardiology, Kocaeli, Turkey*

Background: The association between unemployment and depression is explained by both causation and selection. The aims of this study were to identify the relationship between employment status and depressive symptoms and to determine the effects of work status on the score of Minnesota living with heart failure questionnaire (MLHFQ).
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).
Methods: and Results: This is a prospective, nonrandomized, cohort study of outpatients with heart failure (HF) and ejection fraction 40% by echocardiography. Patients in this study were enlisted in the country of Georgia from a hospital-affiliated outpatient HFDMP for systolic HF located at Central University Hospital, Tbilisi, 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. 22% of unemployed patients had depressive symptoms, 19% of currently employed patients had depressive symptoms and 9% of previously employed patients had depressive symptoms. The difference was statistically significant between unemployed patients and previously employed patients (p = 0.004). Unemployed patients' MLHFQ score was 66 ± 16, currently employed patients' MLHFQ score was 62 ± 13 and previously employed' patients MLHFQ score was 56 ± 12. There was a statistical difference between currently employed patients' MLHFQ score and previously employed patients' score (p = 0.005). It was determined a statistical difference between previously employed patients' MLHFQ score and unemployed patients' MLHFQ score (p < 0.001).
Conclusion: Unemployed patients' group had the highest MLHFQ score and the highest ratio of depressive symptoms in this cohort.

P423
Comparison of sleep quality disturbances between patients with chronic heart failure and cancer patients

V Bistola[1]; E Keka[1]; E Danousi[1]; G Bakosis[1]; J Parissis[1]; J Lekakis[1]; G Filippatos[1]
[1]Attikon University Hospital, Heart Failure Unit, Cardiology Department, Athens, Greece

Background: Severe chronic diseases including heart failure (HF) and cancer are frequently associated with sleep quality disturbances. However, differences in the severity and individual components of such disturbances between different diseases are not known.
Aim: To compare severity and individual components of sleep quality disturbances between patients with HF and cancer.
Methods: One hundred patients hospitalized for HF (assessed at pre-discharge) and 100 cancer patients were included in the study. Sleep quality was assessed by Athens Insomnia Scale (AIS), a self-administered questionnaire that includes 8 items, 5 of which assess night sleep features and 3 assess daytime functional impairment due to insomnia. Each item has 4 possible answers, graded 0-3, higher rating denoting worse sleep quality.
Results: HF patients were 80% males, of age (mean ± SD) 72 ± 12 years, while cancer patients were 32% males, aged 61 ± 11 years. HF patients had higher scores in all individual components of night sleep quality and associated daytime functioning compared to cancer patients, including (mean ± SD): sleep induction (2.91 ± 1.02 vs 2 ± 0.98, p < 0.001), awakenings during the night (3.26 ± 0.836 vs 2.52 ± 0.904, p< 0.001), final awakening (2.20 ± 1.27 vs 1.63 ± 1.04, p = 0.001), total sleep duration (2.61 ± 1.12 vs 1.71 ± 0.945, p < 0.001), sleep quality (2.67 ± 1.11 vs 1.80 ± 0.921, p < 0.001), and well-being (2.73 ± 0.851 vs 1.95 ± 0.833, p < 0.001), functioning capacity (2.73 ± 0.862 vs 1.95 ± 0.821, p < 0.001) and sleepiness during the day (2.50 ± 0.969 vs 1.92 ± 0.917, p < 0.001).
Conclusion: Nighttime sleep quality and associated daytime functioning is worse in patients with HF as compared to cancer patients.

P424
Impact of chronic obstructive pulmonary disease on left ventricular geometry

A Milovancev[1]; M Kojicic[1]; S Puskar[1]; A Stojsic Milosavljevic[2]; M Stefanovic[2]; A Ilic[2]; S Tadic[2]; I Srdanovic[2]
[1]Institut of Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia; *[2]Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia*

Background: Left ventricular hypertrophy (LVH) represents significant risk factor for cardiovascular mortality. LVH impairs myocardial relaxation and causes diastolic dysfunction which may lead to heart failure (HF). The prevalence of HF especially HF with preserved ejection fraction (HFpEF) in chronic obstructive pulmonary disease (COPD) patients is high but often underdiagnosed and undertreated. The aim of our study was to assess left ventricular geometry in COPD patients with no previous history of cardiovascular (CVD) diseases.
Methods: We performed a prospective cohort study of 120 male patients with stable previously diagnosed COPD. All patients underwent spirometry and transthoracic echocardiography. LVH was defined as left ventricular mass index (LVMI) of >115 g/m2. Exclusion criteria were formerly diagnosed CVD including arterial hypertension.
Results: The mean value of forced expiratory volume in one second (FEV1) was 54.7 ± 27, 94% of the predicted value. The mean LVM index (LVMI) was 103. 4 ± 27.3 g/m2. The prevalence of LVH was 37. 2 % in COPD patients, 25. 2% had concentric LVH and 12% had eccentric LVH. There was a positive linear correlation between left atrial volume (LAV) and LVMI (r=0.32, p = 0.0004). The overall prevalence of HFpEF was 23, 3 % in COPD patients.
Conclusion: The frequency of LVH as an early sign of left ventricular remodeling is high in COPD patients with no history of CVD and HFpEF is present in majority of those patients.

P425
Outcome predictors for short and long-term evolution in patients with prosthetic valve endocarditis and prior heart failure with initial conservative intention to treat

MM Baluta[1]; E Panaitescu[2]; MM Vintila[3]
[1]Carol Davila University of Medicine-St Pantelimon Clinical Emergency Hospital-Cardiology Department, bucharest, Romania; *[2]Carol Davila University of Medicine and Pharmacy , Medical Informatics and Biostatistics, Marketing, Medical Technology , Bucharest, Romania*; *[3]St. Pantelimon Emergency Hospital, Cardiology, Bucharest, Romania*

Introduction: Short and long-term mortality in prosthesic valve endocarditis (PVE) remains high and strongly dependent on patients characteristics, disease course and on initial therapeutic strategy.
Purpose: The aim of our work was to identify common factors for short-term and long-term outcome in patients with PVE and initial conservative intention to treat, managed in infection disease departments.
Methods: We analyzed retrospectively 56 PVE patients (age 54.64 ± 11.34, 20 women and 36 men), diagnosed with modified Duke criteria along 5 consecutive years (2000-2004). They had either early PVE (n = 29) or late PVE (n = 27). Initial follow up was performed at the end of antibiotic treatment (EoAT). Long-term follow up (LTFU) was performed after 12.87 ± 0.97 years (15 years maximum). Final vital status was verified in National Insurance Database. Variables analyzed: demography, comorbidities, etiology, clinical, biochemical, echocardiography data and outcome. Ten patients were lost to LTFU (6 from early and 4 from late PVE group) and excluded from our analysis.
Results: Conservative therapy was successful in 71% of patients admitted in infectious diseases departments, with only one case of in-hospital death.

21.4% patients were transferred for early surgery due to conventional antibiotic treatment failure. The perioperative death rate was 33%. At the end of antibiotic cure of all studied patients, survival was 90.4% with a total duration of antibiotic therapy (AT) of 33.55± 12.8 days. Early valve surgery was determined by perivalvular extension of infection (p < 0.001), prostheses dysfunction (p = 0.00009), embolism (p = 0.007), persistent fever (p = 0.03). Factors strongly related to mortality overall at EoAT were age (p = 0.04), diabetes (p = 0.016), coexistence of ischemic heart disease (p = 0.07), prior heart failure (p = 0.07), ischemic left ventricular (LV) systolic dysfunction (p = 0.0002), hemodynamic instability (p = 0.04), persistent fever (p = 0.06), anemia (p = 0.001). We found at long-term follow up a reduced survival in remaining patient, only 44% (52.4% early PVE, 35% late PVE). Factors related to long-term mortality: advanced age (p = 0.0009), diabetes (p = 0.038), mid range LV ejection fraction 40% ≤EF < 50% (p = 0.038) and staphylococcus infection (p = 0.053). NYHA class at baseline does not influenced outcome statistically significant. Conclusions: We observed a very high long-term mortality in patients admitted in infectious diseases departments with an initial conservative intention to treat. Common outcome factors determined for both short-term and long-term survival in PVE patients were diabetes and advanced age. Short-term only poor prognosis factors were nonresponsive infection with valve dysfunction, embolism, prior heart failure, and anemia. Long-term only prognosis factors were staphylococcus infection, ischemic left ventricular systolic dysfunction, and mid range LVEF at baseline.

P426

Osteoporosis, frailty and non-adherence to the treatment in patients with chronic heart failure

VN Larina[1]; Il Chukaeva[1]; DG Karpenko[1]; AS Bayramova[1]; AV Pozdnyakova[2]
[1]*The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation*; [2]*M.V. Lomonosov Moscow State University, Faculty of Fundamental Medicine, Moscow, Russian Federation*

Non-adherence to guidelines is prevalent among elderly CHF patients, despite guideline-adherent treatment being independently associated with lower risk of all-cause and CV deaths. Efforts to improve adherence would lead to better outcomes for elderly HF patients. According to the World Health Organization, the adherence to the CHF treatment is the extent to which a patient's medication taking coincides with the prescribed treatment. The objective to determine the factors related to non-adherence to the treatment in elderly outpatients with CHF.
Methods: 40 female and 13 male, aged 60-88 yrs, suffering from NYHA FC II-III CHF entered the study. All patients had clinical, laboratories evaluation, Echo CG. The participants were identified as frail according to the frailty criteria of Fried. Frailty was diagnosed in patients with a score 3 or greater: unintentional weight loss (more than 10 pounds within the past year), self-reported exhaustion, slow walking speed, MMSE < 24 points, weakness. Validated questionnaire Morisky Medication Adherence Scale (MMAS-4) is being used to evaluate treatment adherence. Bone mineral density (BMD) in the lumbar spine (LI-LIV) and femoral neck (FN) were examined using dual-energy X-ray absorptiometry. Results. Osteoporosis (OP), T-score < -2.4 SD, was present in 62,3% (group 1), absent- in 37,7% patients (group 2). Patients of 2 groups did not differ with respect to the age, education, family presence, working status, NYHA FC, systolic/diastolic BP, AF cases or 6 min WT. Diabetes was found in 45% patients with OP and in 18,2%-without OP, =0,036. HbA1 was higher among patients without OP compared with those with OP (6,3 ± 0,7% vs 5,9 ± 1,3%, =0,047). N-proBNP was 1418 ± 170 pg/ml in patients with OP, 229 ± 180 pg/ml – without OP, =0,001. Patients with OP had higher rates of past bone fractures compared to those without OP, < 0,001. Treatment adherence was 42,4% in patients with OP and 45% - without OP. MMAS mean score was 3,3 ± 0,9 in patients with OP and 3,25 ± 0,8- without OP. There was correlations between high adherence and severity of CHF symptoms (=0,027, r=0,42), MMSE (=0,017, r=0,36), systolic BP (< 0,001, r=-0,44), low density cholesterol (=0,044, r=-0,33), diastolic BP (=0,04, r=-0,27) and past OP bone fractures (p = 0,039, r=0,46). Frailty associated with NYHA FC (=0,003, r=0,45), CHF hospitalization (=0,009, r=0,40), LVEF (=0,025, r=-0,37), OP (p = 0,019, OR 4,5, 95%CI 1,3-15,8) and past MI (p = 0,001, OR 6,8, 95%CI 2,2-20,8). Conclusion. These findings indicate that non-adherence was similar in two groups of patients and correlated with disease severity and past OP bone fractures. Due to fact that frailty in this population significantly associated with OP, we can suppose that the frailty influences on elderly patient's adherence. Our finding raises the fact that OP fractures and frailty could be a mere marker of HF severity and should become a routine additional assessment of HF outpatients' adherence to treatment.

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Prevalence and risk factors of venous thromboembolism in acute heart failure patients

T Titaya Sukhupanyarak[1]; T Yingchoncharoen[1]; P Sritara[1]; P Vathesatogkit[1]; S Yamwong[1]; P Angchaisuksiri[1]; T Panpikoon[1]
[1]*Mahidol University, medicine cardiology, Bangkok, Thailand*

Background: Venous thromboembolism is one of the consequences of heart failure and also impacts mortality and quality of life. However, the previous studies of VTE in heart failure in Thailand were small and the data was limited.
Objective: To evaluate the prevalence of VTE and risk factors in acute heart failure patients in Thailand.
Method: The prospective cohort study was conducted from December 2015 to July 2016 in Ramathibodi hospital, Mahidol university, Thailand. The patients who were hospitalized due to acute heart failure were enrolled and screened for deep vein thrombosis (DVT) by Doppler ultrasonography beyond 5 days and computed tomography angiography (CTA) if clinical suspected pulmonary embolism. Multiple logistic regression was performed to identify risk factors of VTE.
Results: 80 patients were enrolled in the study, 41 were male (51.3%), mean age was 73 years old, mean BMI was 22.4 kg/m2, primary etiology of heart failure were ischemic (37.5%) and hypertensive cardiomyopathy (25%), mean NT pro-BNP was 6637 pg/mL, mean D-dimer was 1139 ng/mL, mean EF was 50 %. Among 80 patients, 36 patients (45%) had history of prior heart failure, 4 patients (5%) had history of prior VTE and 7 patients (8.8%) had history of cancer. The prevalence of VTE was 10% (8 patients). Multiple logistic regression showed history of prior VTE as an independent risk of VTE in our population (OR 71.795 (95% CI 4.161-1238.679, P value 0.003).
Conclusion: In Thailand, the prevalence of VTE in hospitalized heart failure patients is 10%. The history of prior VTE increases risk factor of VTE in hospitalized heart failure.

multivariable analysis

Patient characteristics	Odd ratio	95% CI	P-value
History of cardiovascular condition: Venous thromboembolism	71.795	4.161-1238.679	0.003
History of non cardiovascular condition: anemia	5.579	0.850-36.634	0.073
ICU admission	6.567	0.645-66.819	0.112

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Intensive statin therapy has no impact on cognition in high cardiovascular risk patients

M Vorobyeva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Objective: The recent cholesterol guidelines recommend aggressive statin therapy in patients at high cardiovascular (CV) risk. Rates of cognitive impairment are relatively high in populations with CV diseases and risk factors. The relationship between statins and cognition remains unclear. The aim of the study was to investigate the cognitive dysfunction (CD) and effects of intensive statin therapy on cognition in patients at high CV risk.
Methods: In 187 patients with history of clinically evident CV disease and fasting low-density lipoprotein cholesterol (LDL-C)>1.8 mmol/l or non-high-density lipoprotein cholesterol (non-HDL-C)>2.6 mmol/l (64% male, 60.8 ± 8.6 (M ± SD) years, >65 years 37.4%, current smoking 42%, abdominal obesity 65%, arterial hypertension 90%, myocardial infarction 73%, percutaneous coronary intervention 58%, coronary artery bypass surgery 13%, non-hemorrhagic stroke 30%, diabetes mellitus 22%, symptomatic peripheral arterial disease 8%, 42%, previous statin therapy 74%), the cognitive impairment and effects of intensive statin therapy (atorvastatin 80 mg/day) was assessed. Cognitive functions were evaluated by using the Montreal Cognitive Assessment (MoCA) scale before and 6 months after start of aggressive statin therapy. Wilcoxon test and multivariate logistic were performed. P < 0.05 was considered significant.
Results: Atorvastatin 80 mg decreased lipids significantly: total cholesterol from 5.4 ± 1.5 to 4.0 ± 0.8 mmol/l; LDL-C from 3.3 ± 1.3 to 2.2 ± 0.6 mmol/l; non-HDL-C from 4.3 ± 1.4 to 2.9 ± 0.7 mmol/l; triglycerides from 2.1 ± 1.3 to 1.5 ± 0.9 mmol/l, (p < 0.05 for all). Changes of HDL-C were insignificant. Mean MoCA performance was 24.3 ± 2.6. 118 (63%) patients had CD (MoCA score < 26). Patients with vs without stroke (22.4 ± 3.1 vs 24.7 ± 2.7 scores by MoCA, p < 0.05) and older vs less 65 years (21.1 ± 3.3 vs 25.6 ± 1.8 scores by MoCA, p < 0.05) had more severe CD. 87.5% of patients with stroke and 72.9% of patients >65 years had CD. After 6 months of intensive statin therapy mean total MoCA performance was 23.9 ± 3.1. Changes of cognitive function were unsignificant (p = 0.4). In patients with stroke and patients with baseline MoCA score < 26 we observe a trend to decline of cognitive functions: from 21.1 ± 3.3 to 21.6 ± 3.9 (p = 0.08) and from 21.3 ± 3.8 to 20.4 ± 3.8 (p = 0.09), respectively. Severity of CD and changes of MoCA scores were not associated with lipid levels and their dynamics.
Conclusions: 63% of high CV risk patients have CD according to MoCA scale. Patients with stroke and patients ≥65 years had higher prevalence and more

severe CD. No significant association between statin use and cognition was found. Changes of cognitive status were not associated with lipid levels and their dynamics.

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Depressive disorders and peculiarities of cardiohemodynamics in patients with chronic heart failure and comorbidity

G Ganna Tytova[1]; O Liepieieva[2]; N Ryndina[1]; M B Teclebrhan[1]
[1]Kharkiv National Medical University, Kharkiv, Ukraine; *[2]City clinical hospital #27, CCU, Kharkov, Ukraine*

Anemia and kidney dysfunction are considered to be predictors of unfavorable course of chronic heart failure. Numerous studies proved that depressive disorders are a risk factor for re-hospitalization and death in patients with CHF.
Purpose: Study of morpho-functional myocardial changes and estimation of depressive disorders in anemic patients with chronic heart failure and chronic kidney disease.
Material and methods: 145 patients (age 71,42 ± 8,66y.) with CHF II- IVFC as a result of IHD. Main group consisted of 87 patients with anemia and CKD II-III st. on a background of CHF. The comparison group consisted of 58 pts with CHF without anemia and CKD. FC of CHF was estimated by NYHA classification. CKD was defined by USA NKF classification K/DOQ. Anemia – by ICST, 1989 classification. Thus mild anemia was found in 50 pts (Igr), moderate – in 25 pts (II gr) and severe in 12 pts (III gr) of the main group. In order to study the structural and functional myocardium echocardiography was used. Beck depression inventory was used to study depressive disorders.
Results: There was no significant difference in LVESD and LVEDD in mild anemic patients with CHF and CKD. Patients of II gr had tendency for increasing LVESD and LVEDD, pts of III gr had significally increased (p≤ 0,05) comparing to group of pts without anemia and CKD. Patients of the I gr. had significally decreased LVPWd, IVS, EF and increased sizes of RA and RV comparing to group of comparison. Comparing these parameters in pts of I and II groups with comparison group there were no significant differences (p≥ 0,05). There was significant increasing of LVESD, LVEDD, LVESV, LVEDV, sizes of LA and RV, and decreasing of LVPWd, EF in pts of III gr comparing to pts of I and II gr. Due to Beck scale symptoms of depression grew in proportion to severity of anemia with maximum in pts of the III gr. Patients of the Igr mostly had cognitive-affective disorders. Patients of II and III gr, mostly had cognitive-affective disorders as well as somatic manifestation of depression.
Conclusion: : Negative influence of anemic syndrome on myocardium was seen in formation of anemic cardiomyopathy with dilation of heart chambers and decreased EF and also in emotional sphere as development of depressive disorders, which worsen not just a course of CHF but also decrease life quality ruining social and family functioning and behavior in general, aimed at overcoming the disease.

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High prevalence of masked arterial hypertension in patients with rheumatoid arthritis

E Troitskaya[1]; S Velmakin[1]; S Villevalde[1]; Z Kobalava[1]
[1]RUDN University, Moscow, Russian Federation

Background: Patients with rheumatoid arthritis (RA) have increased cardiovascular risk. Arterial hypertension (AH) is highly prevalent, and seems to be under-diagnosed and under-treated among patients with RA. Data on ABPM profile in patients with rheumatoid arthritis are lacking.
The aim of the study was to evaluate ABPM parameters and characterize phenotypes of blood pressure (BP) in patients with RA.
Materials and Methods: 58 patients with RA (EULAR 2010) without known cardio-vascular disease were examined (76% females, age 55,9 ± 15,8 (M ± SD) years, 10% smokers, 56% with AH, 34% with dyslipidemia). Median duration of RA was 8,5 years (IQR 3-16). Seropositive RA was diagnosed in 69% of patients. All patients received disease-modifying antirheumatic drugs (DMARDs), 22 (38%) - biological treatment. Median duration of AH was 4,0 years (IQR 0-12 years). All patients with AH received antihypertensive treatment. 24-h peripheral and central BP monitoring was performed (BPLab Vasotens, 'Petr Telegin'). P < 0.05 was considered significant.
Results: Mean office BP was 126 ± 19/78 ± 11 mmHg (peripheral) and 118 ± 20/80 ± 11 mmHg (central). 10 (17%) patients had elevated office BP (>140/90 mmHg). Mean BP values for peripheral and central BP were as follows: 125 ± 13/73 ± 9 and 116 ± 13/75 ± 9 mmHg for 24-h BP; 127 ± 14/74 ± 9 and 117 ± 13/77 ± 9 mmHg for daytime BP; 119 ± 13/69 ± 10 and 112 ± 14/71 ± 10 mmHg for nighttime BP. AH according to daytime BP was found in 14 (24,1%) pts, nighttime BP – in 28 (48,3%) pts, 24-h BP - in 9 (31,0%) pts. Phenotypes of BP were as follows: sustained normotension – in 36 (62,1%), masked hypertension in 12 (20,7%), sustained AH – in 8 (13,8%), white-coat hypertension in 2 (3,4%) patients. Isolated nocturnal AH was observed in 12 (20,7%) pts. 10 (17%) patients had isolated elevated central BP. 20 (34,5%) pts had elevated central SBP according to individual reference values; all patients with high office BP had elevated central BP.
Conclusions: High prevalence of AH is observed in patients with RA free of CVD and most of patients have satisfactory control of office BP. Relatively high prevalence of masked and isolated nocturnal hypertension despite antihypertensive treatment are observed in this population. These findings may help to optimize hypertension treatment in patients with RA.

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Arterial stiffness elevation is associated with high inflammatory activity in patients with rheumatoid arthritis

VSV Sergey Velmakin[1]
[1]RUDN University, internal disease, Moscow, Russian Federation

Background: Patients with rheumatoid arthritis (RA) are at higher risk of cardiovascular morbidity and mortality. Aortic stiffness is a predictor of CVD. Chronic inflammation plays a role in the development of atherosclerosis in RA. Relationships between inflammation and arterial stiffness in patients with RA are not well understood. The aim of the study was to evaluate parameters of arterial stiffness and their associations with inflammation activity in patients with RA.
Materials and methods: 42 patients with RA (EULAR 2010) were examined (67%female, age 59.7 ± 15.2 years, 14% smokers, 60% with AH, 47% with dyslipidemia. Median duration of RA was 9 years (interquartile range (IQR)3-17). Seropositive RA was diagnosed in 42% of patients. All patients received disease-modifying antirheumatic drugs (DMARDs),20% - biological treatment. hs-CRP and RF were assessed in all patients. Arterial stiffness was measured by applanation tonometry (SphygmoCor, AtCor) and cardio-ankle vascular index (CAVI) was assessed (VaSera1500).p < 0.05 was considered significant.
Results: Median CRP was 13 mg/dl (IQR 3-24mg/dl), median RF was 32 IU/ml (IQR8-165 IU/ml). Median PWV was 9.4 m/s (IQR7-11m/s). PWV increase>10m/s was observed in 16(37.8%) patients. Patients with PWV>10m/s were older (72.0 ± 8.5vs53.3 ± 14.9 years), had higher BMI (30.5 ± 5.9vs24.9 ± 4.5kg/m2) and longer duration of AH (median 14 years [IQR 7.5-18] vs 0 years [IQR 0-4.5]) and higher BP levels (143 ± 21/84 ± 9vs124 ± 13/78 ± 9 mmHg). They also had higher levels of LDL-C (3.0 ± 1.0vs4.1 ± 0.8 mmol/l), plasma glucose (5.6 ± 0.9vs4.9 ± 0.8 mmol/l), hs-CRP (median 9[IQR 2-17.1] vs 22[IQR 13-56.6] mg/dl) and CAVI (9.2 ± 0.5vs7.2 ± 1.2), p < 0.05 for trend. Spearmen analysis revealed positive correlations of PWV with age (r=0.65), BMI (r=0.53), SBP (r=0.62), DBP (r=0.41), LDL-C (r=0.60), glucose (r=0.38), AH duration (r=0.69) and hs-CRP (0.28), < 0.05 for trend. Multiple regression analysis confirmed that age (β=0.3, =0.0012), AH duration (β=0.4, =0.0001), SBP (β=0.42, < 0.0001) and hs-CRP-level (β=0.26, =0.0004) were independent predictors of arterial stiffness increase.
Conclusion: Inflammatory activity as well as other traditional risk factors is a predictor of arterial stiffness increase in patients with RA receiving DMARDs

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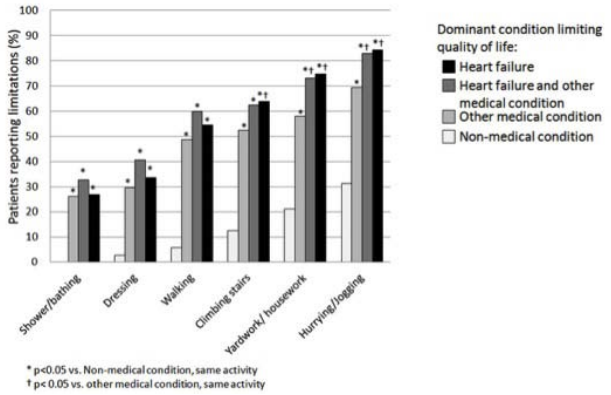
Variable contribution of heart failure to patient-reported limitation of daily activities

R R T Castro[1]; EF Lewis[1]; SR Motiwala[1]; M Bargash[1]; A Nohria[1]; E Joyce[2]; G Stewart[1]; A Desai[1]; LW Stevenson[1]
[1]Brigham and Women's Hospital, Boston, United States of America; *[2]Cleveland Clinic Foundation, Cleveland, United States of America*

Background: While therapy for heart failure (HF) has reduced hospitalization and death, patient-reported outcomes remain a target for further intervention. It is not known how often ambulatory pts report limitation to specific daily activities and how they perceive the effect of HF on their quality of life (QOL).
Objectives: To assess limitation during daily activities as reported by pts, and their perception of the role of HF to decrease their QOL.
Methods: During routine HF clinic visits, 736 ambulatory pts NYHA Class I-III rated limitations during six specific tasks and ascribed the major limitation to their QOL as due to heart failure, or due equally to HF and other medical conditions, more to other medical conditions, or most to non-medical issues.
Results: Limitation was described by 25% of all pts for bathing and 62% for yardwork/housework (Figure). QOL impairment was attributed mostly to HF by 48% of pts, whose limitations were similar to the 19% of pts who perceived equal impairment from HF and other medical conditions, but 33% of pts reported other medical or non-medical conditions to be more important.
Conclusion: Ambulatory pts without Class IV symptoms nonetheless reported substantial limitations to daily activity. However, half of HF patients perceived other medical or non-medical conditions to be equally or more limiting than HF to their QOL. While patient-reported outcomes offer a broad target in the ambulatory population, non-HF conditions may confound the ability to detect the impact of therapy.



Limitations reported by HF patients

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Prevention of contrast-induced acute kidney injury by furosemide with matched hydration in patients undergoing interventional procedures. a systematic review and Meta-Analysis of randomized trials

M Martina Boscolo Berto[1]; A Putzu[1]; A Belletti[2]; E Pasotti[1]; T Cassina[1]; T Moccetti[1]; G Pedrazzini[1]

[1]Cardiocentro Ticino, Cardiology, Lugano, Switzerland; *[2]San Raffaele Hospital of Milan (IRCCS), Intensive care, Milan, Italy*

The objective of this meta-analysis of randomized trials was to evaluate if the administration of furosemide with matched hydration using the RenalGuard System reduces contrast-induced acute kidney injury (CI-AKI) in hight risk patients, undergoing interventional procedures- CI-AKI is a serious complication following angiographic procedures and a powerful predictor of unfavorable early and long-term outcomes.The primary outcome was the incidence of CI-AKI, and the secondary outcomes were need for renal replacement therapy, mortality, stroke, and adverse events. Four trials (698 patients) published between 2011 and 2016 were included in the analysis and included patients undergoing percutaneous coronary procedures and transcatheter aortic valve replacement. RenalGuard therapy was associated with a lower incidence of CI-AKI compared with control treatment (27 of 348 [7.76%] vs. 75 of 350 [21.43%] patients; odds ratio: 0.31; 95% confidence interval: 0.19 to 0.50; I2=4%, $p < 0.00001$) and with a lower need for renal replacement therapy (2 of 346 [0.58%] vs. 12 of 348 [3.45%] patients; odds ratio: 0.19; 95% confidence interval: 0.05 to 0.76; I2=0%, $p = 0.02$). No major adverse events occurred in patients undergoing RenalGuard therapy. The main finding of this meta-analysis is that furosemide with matched hydration by the RenalGuard System may reduce the incidence of CI-AKI in high-risk patients undergoing percutaneous coronary intervention or transcatheter aortic valve replacement. However, further independent high-quality randomized trials should elucidate the effectiveness and safety of this prophylactic intervention in interventional cardiology.

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Predictors and implications of the left atrium volume index in an outpatient clinic.

W Robaeys[1]; HP Brunner-La Rocca[1]

[1]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands

Background: An increased left atrium (LA) is caused by multiple aetiologies and is known to be a risk factor for the development of a cerebrovascular accident and mortality. The LA size has been previously investigated mainly in specific populations (e.g. only hypertension, heart failure (HF), diabetes mellitus, or hypertrophic cardiomyopathy) and/or by inferior echocardiographic techniques (e.g. LA diameter) compared to LA volume index (LAVI), which is the most accurate technique to estimate LA size.
Purpose: Therefore, the objective of the present study was to investigate the predictors and implications of increased LAVI in unselected patients referred by general practitioners for cardiac consultation.
Methods: Investigating an outpatient clinic population of 3441 patients, this study analysed demographics (e.g. medical history), ECG (heart frequency and conduction times), laboratory (e.g. urea and NT pro-BNP), and echocardiography (e.g. E/A and mitral valve regurgitation (MR)) in all patients with a measurement of LAVI during their visit (n = 570). These patients were divided into two groups according to LAVI (LAVI $\geq$ 34 ml/m2, i.e. enlarged LA: n=254; LAVI $<$ 34 ml/m2: n=316). Logistic regression was used to qualify possible predictors and implications of enlarged LAVI.
Results: The present study established increased NT Pro-BNP (enlarged LAVI: 20 (8%), normal LAVI: 3 (1%), odds ratio [OR]:8.9, 95% confidence interval [CI]: 2.6-30.4, $P < 0.001$), prolonged QTc time (enlarged QTc time: 30 (12%), normal LAVI: 9 (3%), OR: 4.6, CI: 2.1-9.8, $P < 0.001$), hyperuricemia (enlarged LAVI: 25 (10%), normal LAVI: 8 (3%), OR: 4.2, CI: 1.9-9.4, $P < 0.001$), history of paroxysmal AFib (atrial fibrillation) (enlarged LAVI: 54 (21%), normal LAVI: 24 (8%), OR: 3.3, CI: 2.0-5.5, $P < 0.001$) and HF (enlarged LAVI: 20 (6%), normal LAVI: 6 (2%), OR: 4.4, CI: 1.7-11.2, P=0.001), history of intake of antiarrhythmics (enlarged LAVI: 55 (22%), normal LAVI: 17 (5%), OR: 4.9, CI: 2.7-8.6, $P < 0.001$), and bradycardia (enlarged LAVI: 59 (23%), normal LAVI: 31 (10%), OR: 2.8, CI: 1.7-4.5, $P < 0.001$) as the most important predictors for increased LAVI in this outpatient clinic. In multivariable analysis, patients with intake of antiarrhythmics are at risk for an enlarged LAVI (OR: 4.9, CI: 2.7-8.6, $P < 0.001$). Implications of enlarged LAVI were newly developed AFib (enlarged LAVI: 20 (8%), normal LAVI: 10 (3%), OR: 2.6, CI: 1.2-5.7, P=0.01) and increased risk for mortality (enlarged LAVI: 48 (19%), normal LAVI: 22 (7%), OR: 3.1, CI: 1.8-5.3, $P < 0.001$).
Conclusion: There are multiple risk factors for an increased LAVI in this low-risk population. Of those antiarrhythmic treatment seems to be the most important one. Patients with an enlarged LAVI are at increased risk to develop AFib or to decease.

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

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Hospital and one year mortality in patients who underwent redo-MVR operation: a 11-year single center experience

A Artan Bajraktari[1]; I Bytyci[2]; E Prifti[1]

[1]University Hospital Center Mother Theresa, Division of Cardiac Surgery, Tirana, Albania; *[2]University Clinical Centre of Kosovo (UCC), Clinic of Cardiology, Pristina, Kosovo Republic of*

Background and Aim: Major advances in mitral valve (MV) surgery, and MV replacement (MVR), improved the survival in these patients, which has inevitably meant that more patients will require redo-MVR during the follow-up. Redo surgery may be associated with significant risk, which must be balanced against the benefits of patients. The aim of this study was to investigate the hospital and one year mortality of patients who underwent the redo-MVR in patients who underwent redo-MVR with previous mitral valve procedures.
Methods: We included in this study 116 patients with age 49 ± 11 years (20-76 years), who underwent redo-MVR operations between 2004 and 2014. We described clinical, pre and postoperative data of the study patients. The hospital and one year follow-up for death were registered for all study patients.
Results: Of study patients, 84% were female, 86% in NYHA III and 12% in NYHA IV class. Re-interventions were done for the first time in 89%, for the second time in 7.8 % and for the third time in 3.5 % of the patients. Mean time of the re-intervention was 11 ± 7.5 years from the previous intervention. Planned operation was done in 68%, whereas in 32% of patients it was an emergency. Previous MVR had 44% of patients, 40% were patients after commisurotomy, 2% after mitral valve reparation and 15% of them had concomitant interventions. Indications for in redo-MVR were: valvular structural degeneration (40%), thrombosis of MV prosthesis (17%), residual MV stenosis (14%), paravalvular fistulas and mitral valve regurgitation (11%, for both). Mechanical MV prosthesis was implanted in 77%, whereas biological MV prosthesis in 12% of patients. Concomitant heart intervention was performed in 40% of operated patients and the duration of hospitalization was 22 ± 13 days.
Patients that underwent redo-MVR had one year overall mortality of 13.7% (13 of116 study patients). The hospital mortality was 8.3%, whereas the mortality at one year follow-up was 5.4%.
Conclusions: Redo mitral valve replacement is safe and can be performed with an acceptable mortality.

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Beneficial effects of percutaneous mitral valve repair (MitraClip): a multiparametric evaluation

C Carlo Vignati[1]; G Damiani[1]; L Fusini[2]; P Gripari[2]; G Tamborini[2]; M Muratori[1]; S Ghulam Ali[2]; M Pepi[2]; P Agostoni[1]

[1]Cardiology Center Monzino IRCCS, Heart Failure Unit, Milan, Italy; *[2]Cardiology Center Monzino IRCCS, Department of Cardiovascular Imaging, Milan, Italy*

Background: MitraClip (MC) therapy is as a secure, feasible treatment option for patients with severe mitral regurgitation (MR) and a high surgical risk. The role of the gold standard surgical repair in patients with functional mitral regurgitation (FMR) is currently under much debate.
Purpose: to evaluate the efficacy of MC therapy in terms of new functional outcomes, comparing data related to degenerative MR and FMR.
Methods: 72 patients with +3 to +4 MR and not eligible for surgical mitral valve repair were enrolled. All patients were assessed before MC implant and after 6 months using echocardiogram, BNP assay, non-invasive measurement of cardiac output (CO) with inert gas rebreathing technique, and cardiopulmonary exercise test (CPET).
Results: MC implant rate was 95%. Immediate success with reduction of MR to ≤2+ was observed in 86.7% of cases. In FMR and DMR, a significant reduction of MR from baseline with was observed ($p < 0.001$). NYHA functional class showed a significant improvement in the functional group (NYHA III-IV from 75% to 34.6% of patients, $p = 0.002$). Significant LV remodeling was observed in both groups (LV End-diastolic Volume in FMR was 211 ± 62 ml at baseline, 190 ± 77 ml at 6 months, $p = 0.003$; in DMR was 123 ± 33 ml at baseline, 103 ± 35 ml at 6 months, $p < 0.001$). LV End-systolic volume (LVESV) also showed a significant reduction at 1 month only in the functional group (LVESV in FMR was 135 ± 55 ml at baseline, 123 ± 67 ml at 1 month, $p = 0.027$). Systolic pulmonary pressure (PAPs) values were significantly reduced from baseline in the population with the functional disease (46 ± 11 mmHg at baseline, 38 ± 8 mmHg at 6 months, $p = 0.005$); in the degenerative group, PAPs showed small variations (42 ± 11 mmHg at baseline and 39 ± 9 mmHg at 6 months, p>.05). CO and cardiac index (CI) increased significantly at rest (3 ± 0.7 l/min at baseline, 3.6 ± 0.9 l/min at 6 months; 1.64 ± 0.42 l/min/m^2 at baseline, 2 ± 0.4 l/min/m^2 at 6 months, respectively, both $p = 0.01$) and at peak of exercise (CO 4.9 ± 1.7 l/min at baseline, 6.3 ± 1.5 l/min at 6 months; CI 2.71 ± 0.98 l/min/m^2, 3.44 ± 0.90 l/min/m^2, both $p = 0.023$) in the functional group. On the other hand, the population with DMR did not present any improvement. Oxygen consumption, anaerobic threshold, and other functional parameters were measured during CPET and showed an improving trend. Heart rate and arteriovenous oxygen difference did not show significant changes both at rest and during exercise.
Conclusions: MC device reduced MR and produced a significant left ventricular reverse remodeling over 6 months in both the populations treated. Functional outcomes, as the implement of CO and CI at rest and during CPET, proved the efficacy of the percutaneous mitral valve repair in patients with FMR. Observing the concurrent absence of significant variation of heart rate and arteriovenous oxygen difference, the improvement of CO could be attributed only to an increase in stroke volume (SV).

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Factors associated with the presence of chronic mitral regurgitation in patients with stable coronary artery disease

A N Alexey Sumin[1]; EV Korok[1]; T YU Sergeeva[1]; LS Barbarash[1]
[1]RAMS Scientific-Research Institute for Complex Studying of Cardiovascular Diseases, Kemerovo, Russian Federation

Background: Mitral regurgitation (MR) of ischemic genesis is an unfavorable prognostic sign. The mechanism of MR development can be various, the cause of its development can be the disorders of regional contractility, left ventricular remodeling and its dyssynchrony. The optimal treatment strategy of ischemic MR (medication, invasive interventions, surgery) depends on the prevailing mechanism of its occurrence.
Purpose: To study the factors, associated with the presence of chronic MR in patients with stable coronary artery disease (CAD).
Material and methods: The study included 874 patients with CAD, who were examined and treated before the planned surgical interventions on coronary arteries, carotid arterial system, abdominal aorta and the arteries of lower limbs. Depending on the presence and severity of MR all the patients were divided into here groups: group 1 – patients without MR (n = 448), group 2– with MR grade I (n = 378), group 3– with MR grade II-IV (n = 48).
Results: It was noted that a clinical presentation of angina pectoris ant the signs of chronic heart failure (CHF) of grade I were observed more often among the patients without MR and with MR grade I (=0.006 and $p < 0.001$). At this the presence of MI history and rhythm disturbances prevailed in the groups of patients with MR grade II-IV (83.3% 29.2%; $p = 0.055$ and $p = 0.059$). According to the results of echocardiography the dimensions and the volumes of left ventricle (LV) cavity, left atrium in the group of patients with MR grade II-IV were significantly higher than the same parameters in other groups, and LV ejection fraction (EF) was the lowest (< 0.001). In this group the presence of chronic LV aneurysm was registered more often (=0.020). The analysis of prevalence and localization of coronary atherosclerosis didn't show any reliable intergroup differences except for the prevalence of significant stenoses of circumflex artery in the group of patients with MR grade I and MR grade II-IV (42.9% and 43.8%; =0.047). Concurrently the risk of perioperative complications by EuroSCORE scale was lower among the patients without MR (< 0.001). According to the results of multivariate analysis the independent predictors of MR grade II-IV detection were: the history of MI (=0.044), LV aneurysm (=0.004), the increase in LV end-systolic volume (ESV) (< 0.001), the increase in risk by EuroSCORE scale (=0.004), as well as the female gender, the presence of the symptoms of CHF and angina pectoris.
Conclusion: When performing the examination of patients with stable CAD a mild ischemic dysfunction of mitral valve was revealed in 43.2% of cases, moderate and severe dysfunction – in 5.5% of patients. The independent factors associated with the presence of moderate and severe MR were the presence of MI history, LV aneurysms, increased LV ESV, symptoms of CHF and angina pectoris, female gender, herewith no connection with the localization of coronary stenoses was noted.

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Right ventricular strain increases early after percutaneous mitral valve repair in patients suffering from severe mitral regurgitation

J Jonas Georg Neuser[1]; HJ Buck[1]; M Hallbaum[1]; F Zauner[1]; JT Sieweke[1]; T Reinke[1]; M Akin[1]; U Bavendiek[1]; J Bauersachs[1]; JD Widder[1]; D Berliner[1]
[1]Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

Introduction: Mitral regurgitation (MR) is the second most common valvular heart disease within the western world. Percutaneous mitral edge-to-edge procedure (PMVR) using the MitraClip system (Abbot Vascular, Santa Clara, CA) is an established therapy for severe MR in patients judged inoperable or at high surgical risk. However, despite of improvement in functional capacity, a notable amount of patients die or are re-hospitalized for heart failure within the first year after PMVR. Right ventricular (RV) function determines exercise capacity, but also has prognostic value in heart failure, as well as after cardiac surgery. We therefore investigated the impact of PMVR on early changes in RV function in patients with severe MR.
Methods: and Results: We analyzed 27 consecutive patients (mean age 79 ± 5y) suffering from severe MR undergoing PMVR using the MitraClip system at our department. Transthoracic echocardiography was performed before and early (2-12d) after PMVR using PHILIPS EPIQ7 ultrasound machines. RV and left ventricular (LV) global longitudinal strain (GLS) as well as 3D determined LV ejection fraction (EF) were assessed using PHILIPS QLAB.
Symptoms of heart failure were apparent in all patients (NYHA class II: 18.5%, III: 77.8%, IV: 3.7%). Most patients (88.9%) presented with reduced LV systolic function (LVEF 36.7 ± 9.8%), caused by ischemic cardiomyopathy in almost half of the study population (44.4%). Acute heart failure had occurred in 44% of all cases. Comorbidities encompassed hypertension (85%), diabetes mellitus (37%), COPD (22%), and atrial fibrillation (85%). Etiology of MR was primary in 34.6% and secondary in 30.8%, while definite discrimination was not possible or combined etiology was apparent in 34.6% of all cases. On average, PMVR significantly improved MR severity (≥2 grades in 22 patients). LVEF did not show any early significant changes ($p = 0.81$) and LV GLS even decreased significantly in patients suffering from ischemic cardiomyopathy (-2.14 ± 2,34%, $p = 0.04$ vs. non-ischemic cardiomyopathy: -0.25 ± 0.30%, $p = 0,75$). However, a significant increase in RV GLS (-1.82 ± 2.42%, $p < 0.01$) and RV free wall longitudinal strain (-0.32 ± 8.31%, $p = 0.02$) early after PMVR was detected.
Conclusion: Our data indicate an early improvement of RV function after PMVR. Further follow-up will show, whether RV function at baseline or an improvement after PMVR is associated with favorable changes in patients' functional capacity, re-hospitalization and survival.

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Effects of atrial fibrillation on mitral valve repair with the mitraclip system in patients with reduced left ventricular ejection fraction.

A M Anna Maria Caggegi[1]; S Scandura[1]; S Mangiafico[1]; G Castania[1]; G Ronsivalle[1]; M Chiaranda'[1]; S Giaquinta[1]; S Farruggio[1]; F Felici[1]; T Salerno[1]; M E Di Salvo[1]; C Grasso[1]; P Capranzano[1]; D Capodanno[1]; C Tamburino[1]
[1]Ferrarotto Hospital - Institute for Cardiology, Department of Cardiovascular, Catania, Italy

Background: Atrial fibrillation (AF) is common in patients with mitral regurgitation (MR) referred for therapy, being often associated with more advanced valvular disease, heart failure and non cardiac comorbidities. However, specific data relating to the impact of this condition on the outcomes after percutaneous mitral valve repair are limited.
Purpose: The aim of this prospective, observational study was to characterize one-year outcomes of MitraClip therapy in high surgical risk patients with moderate-to-severe or severe MR and reduced left ventricular ejection fraction (LV EF) with or without AF.

Methods: Patients enrolled in the prospective Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation (GRASP) with LVEF < 40% who were eligible at one-year follow-up were included in the present analysis. The primary efficacy endpoint was the composite of death, surgery for mitral valve dysfunction and grade 3+/ 4+ MR at one-year follow-up. Secondary endpoints were the components of the primary endpoint, re-hospitalization rates and functional NYHA class. Also echocardiographic parameters at baseline and one-year follow-up were assessed.
Results: A total of 178 patients were included: 106 (59.6%) without AF and 72 (40.4%) with AF. Comparable clinical and echocardiographic baseline characteristics were observed between the two groups except for age, STS score, pace-maker implantation and left atrial (LA) volume (higher in the AF group) and for previous myocardial infarction and percutaneous revascularization (more frequent in the no AF group). A total of 171 (96.4%) patients had a post-procedural residual MR≤2+. At one-year follow-up, no significant differences were reported in terms of primary end-point (21.3% in patients with AF versus 15.9% in patients without AF, p = 0.748). Secondary endpoints rates concerning the two groups are reported in Table 1. At one-year follow-up, a significant reduction in LV volumes was observed regardless of AF; no relevant changes were reported in LA volumes.
Conclusions: The MitraClip procedure was associated with low rates of adverse events in patients with AF and reduced LV EF, reporting one-year outcomes comparable to patients without AF.

Table 1

	no AF	AF	p
Death	15.9%	19.7%	0.522
Surgery for mitral valve	-	-	-
MR grade ≥3+	15.6%	6.6%	0.134
Re-hospitalization	15.6%	22.9%	0.226
NYHA class ≤2	85.1%	79.5%	0.388

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Moderate/severe aortic regurgitation after TAVI with corevalve - anatomically or procedurally determined

S Sara Moura Ferreira[1]; J Almeida[2]; P Fonseca[2]; T Dias[2]; C Guerreiro[2]; R Barbosa[2]; P Teixeira[2]; N Pelicano[1]; N Ferreira[2]; R Faria[2]; P Braga[2]; V Gama[2]
[1]Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal; *[2]Hospital Center of Vila Nova de Gaia/Espinho, Cardiology, Vila Nova de Gaia, Portugal*

AIM: To investigate the determinants of moderate/severe aortic regurgitation (AR) occurring after transcatheter aortic valve implantation (TAVI) with CoreValve.
Methods: Retrospective, observational study including all patients with severe aortic stenosis and submitted to TAVI with CoreValve prosthesis between August 2007 and October 2016. TAVI with CoreValve was performed in 112 patients with severe aortic stenosis (50% male, mean age 79.4 ± 8.8 years old, mean EuroSCOREII 6.3 ± 69) between August 2007 and October 2016. Contrast-enhanced electrocardiogram (ECG)-gated multidetector computed tomography (MDCT) was performed before and after TAVI. Indexed aortic valve (AV), left ventricular outflow tract (LVOT) and device landing zone (DLZ) calcification was quantified by a standard Agatston methodology for all available pre-procedure contrast-enhanced MCDT, with a threshold for calcium detection set at 850 Hounsfield Units. Annular diameter, indexed annular perimeter and area, ellipticity index and transcatheter heart valve (THV) oversizing were determined using post-procedure contrast-enhanced MCDT data, during late systolic phase. Procedure and pre-discharge echocardiographic data were also collected.
Results: TAVI with CoreValve was performed in 112 patients in our centre (50% male, mean age 79.4 ± 8.8 years old, mean EuroSCOREII 6.4 ± 6.8). The incidence of moderate/severe AR after TAVI was 15.1%. Balloon post-dilation was performed in 21.8% of patients. Indexed AV, LVOT and DLZ calcification; annular diameter and indexed annular perimeter and area were significantly different between patients with moderate/severe post-procedure AR and those with milder degrees of AR. The were no significant differences in THV oversizing and ellipticity index between the two groups. After multivariate analysis was performed, only indexed DLZ calcification and indexed annular area remained independent predictors of moderate/severe post-procedure AR.
Conclusion: In the present study, only anatomic parameters assessed by ECG-gated contrast-enhanced MDCT (indexed DLZ calcification and indexed annular area) were independently associated with the development of moderate/severe AR occurring after TAVI with CoreValve. The intraprocedural parameters assessed did not independently predict of the outcome.

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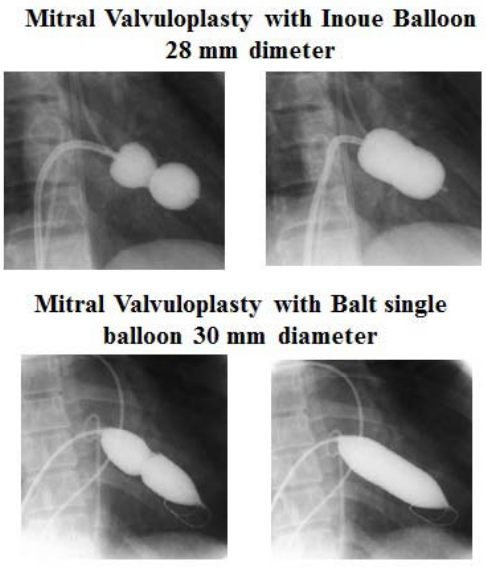
Percutaneous mitral valvuloplasty with inoue versus balt single balloon in mitral stenosis. Survival and event free survival in long-term follow-up

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[2]; AAB Aragao[1]; ILPB Anjos[3]
[1]Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil; *[2]State Institute of Cardiology Aloysio de Castro, Rio de Janeiro, Brazil*; *[3]Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

Background: The single balloon (SB) is the less expensive technique to perform mitral balloon valvuloplasty (MBV) 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 worldwire accepted technique.
Methods: From 1987 to 12/31/2013 a total of 526 procedures were performed, being 313 with a FU, 57 (18.8%) with Inoue balloon (IB), the IB group (IBG) and 256 (82.1%) SB Balt group (SBG). The mean FU in IBG was 33 ± 27 (2 to 118) months and in SBG 55 ± 33 (1 to 198) months (p < 0.0001). Univariate analysis and multivariate Cox analysis were utilized to determine independent predict of survival variables and event free survival (EFS) in both technique groups being major events (ME): death, cardiac surgery and new MBV.
Results: In IBG and SBG there were: female 43 (75.4%) and 222 (86.7%) procedures, (p = 0.0276), 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 ± 0.18 and 0.93 ± 0.21 cm2 (p = 0.2265). Post-MBV mean MVA (Gorlin) were 2.00 ± 0.52 and 2.02 ± 0.37 cm2 (p = 0.9550) and at the end of the FU: echo MVA 1.71 ± 0.41 and 1.54 ± 0.51 cm2 (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%) deaths, (p = 1.000), cardiac deaths 1 (1.8%) and 9 (3.5%), (p = 1.0000), ME 5 (8.9%) and 46 (18.0%), (p = 0.1449). In univariate analysis and in multivariate Cox analysis the SB or IB do not predict survival or event free survival and independent risk factors to survival in multivariate Cox analysis with 2 models with 5 and 6 variables were: age < 50 years (p = 0.016, HR=0.233, CI 95% 0.071-0,764), ES ≤8 (p < 0.001, HR=0.105, CI 95% 0.34-0.327), MBV dilatation area (p < 0.001, HR=16.838, CI 95% 3.353- 84.580) and no mitral valve surgery in the FU (p = 0.001, HR=0.152, CI 95% 0.050-0.459) and to event free survival: no prior commissurotomy (p = 0.012, HR=0.390, CI 95% 0.187-0.813) and post-MBV MVA ≥1.50 cm2 (p < 0.001, HR=7.969, CI 95% 3.413-18.608).
Conclusions: SB and IB MBV had similar survival and event free survival in the FU. Independent predictors of survival were: age, ES, MBV dilatation area and no mitral valve surgery in the FU and event free survival: no prior commissurotomy and post-MBV MVA.



P442

Thrombocytopenia as a predictive marker of heart failure in patients with infective endocarditis

MA Sorokina[1]; NM Povalyaev[1]; AS Pisaruk[2]; EO Kotova[2]
[1]*M.V. Lomonosov Moscow State University, Basic Medicine, Moscow, Russian Federation*; [2]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Purpose: To study the features of thrombocytopenia in patients with infective endocarditis (IE).
Materials and Methods: 156 patients (97 men) with IE (Duke 2015) were included, of which 55 (35%) patients have IE with thrombocytopenia (group 1) and 101 (65%) have IE without thrombocytopenia (group 2). We evaluated the anamnesis, echocardiogram, heart failure (NYHA rates and NT-pro-BNP), inflammation markers (CRP, RF, procalcitonin, presepsin), microbiology tests, CBC (PLT, WBC, HB), embolic complications (EC) and mortality rates. Thrombocytopenia was characterized by total platelet count lower than 180*10^9/l. EC was defined as any embolism at the moment of hospital admission or developed during hospitalization. All EC were verified by instrumental methods of diagnostics (US, CT, MRI). Micro EC as Osler nodes, Janeway lesions, Lukin and Roth spots were not included in this study.
Results: The median age in the group 1 was 42 [34; 66.5], in group 2 60 [36; 72] years, $p > 0.05$. Groups did not differ by gender and comorbidity. cute IE prevailed in both groups [37 (67.3%) in group 1 vs. 53 (52.5%) in group 2, $p > 0.05$], left ventricular EF was mainly preserved [57% (54; 61) vs. 58% (50; 60), respectively, $p > 0.05$]. Mean platelet count in group 1 was 97*10^9/l [71; 152], in group 2 264*10^9/l [214;336], $p < 0.001$. EC (N=68) were found in 29 patients in group 1 (52.7%), in 39 patients in group 2 (38.6%), $p = 0.048$. Also an increase in CRP value of 146.3 mg/l [83.4; 210.5] for group 1 and of 108.9 mg/l [41.8; 190.0] in group 2, $p < 0.001$, was revealed and associated with the severity of thrombocytopenia ($p = 0.011$). Thrombocytopenia in patients with IE is associated with more severe course of heart failure, $p = 0.038$. 55 patients (100%) in group 1 and in 43 patients in group 2 (42.6%), $p < 0.001$ had clinical symptoms of lass III-IV heart failure. Significantly higher incidence of spleen- and hepatomegaly ($p = 0.025$ and $p = 0.004$ respectively) was found in the thrompocytopenia group (1). ongested spleen, in its turn, may be one of the causes of the low platelet count due to the increased platelet uptake. Overall mortality was higher in patients with low total platelet count: in group 1 N = 20 (36.4%), in group 2 N=19 (18,8%), $p = 0.0014$.
Conclusion: IE complicated by thrombocytopenia more frequently occur in younger adults and is associated with more severe course of heart failure and higher activity of the infectious process. Mortality rate, as well as frequency of EC in such patients is also significantly higher.

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Indexed device landing zone calcium volume predicts the need for balloon post-dilation in tavi procedures with self-expandable prosthesis

S Sara Moura Ferreira[1]; J Almeida[2]; P Fonseca[2]; T Dias[2]; C Guerreiro[2]; A Barbosa[2]; P Teixeira[2]; N Pelicano[1]; N Ferreira[2]; R Faria[2]; P Braga[2]; V Gama[2]
[1]*Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal*; [2]*Hospital Center of Vila Nova de Gaia/Espinho, Cardiology, Vila Nova de Gaia, Portugal*

Introduction: Calcification of the device landing zone (DVL) is associated with the need of balloon pos-dilation (BPD) in thranscatheter aortic valve implantation (TAVI) procedures. This study sought to evaluate the relationship of DLZ calcium volume with the need for BPD during TAVI with 1st and 2nd generation self-expandable prosthesis.
Methods and Results: Retrospective, observational study including all patients with severe aortic stenosis and submitted to TAVI with self-expandable prosthesis between August 2007 and October 2016. Calcification of the DLZ was quantified for all available contrast scans, using a dedicated software (3mensioValvesTM), with a threshold for calcium detection set at 850 Hounsfield Units. TAVI with self-expandable prosthesis was performed in 180 patients in our centre (47,8% male, mean age 79.7 ± 7.8 years old). Most of the devices implanted were 1st Generation Self-Expandable Prosthesis (n = 112, 62.2%). BPD was performed in 40 TAVI procedures (22.5%). Body surface area (BSA) indexed DLZ calcium volume was significantly different between patients with and without need for BPD during TAVI procedures: $259{,}1 \pm 45{,}1$ vs. $126{,}6 \pm 9{,}5$ ($p < 0.01$). Area under the curve (AUC) for BSA indexed DLZ calcium volume was 0.70 (95% CI 0.60–0.79 $p < 0{,}01$).
We considered the best cut off point for BSA indexed DLZ calcium volume to be 93.3 (sensitivity 84.2%, specificity 49.6%). In a binary logistic regression model, an BSA indexed DLZ calcium volume equal or above 93.3 was associated with 3 times increase in the probability BPD need during TAVI procedures with self-expandable prosthesis. There were no significant differences in the incidence of moderate/severe AR after TAVI with self-expandable prosthesis, regarding device generation (X2 (1)=007, $p = 0.85$).
Conclusion: Calcification of the DLZ predicts the need for BPD in TAVI Procedures with Self-Expandable Prosthesis, both in 1st and 2nd generation devices.

DEVICES/CRT/ICD/SURGERY

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Comparison of electrophysiological and surgical methods of treatment in patients with heart failure complicated with atrial fibrillation

T Tatyana Troyanova[1]; A Kurlianskaya[1]; D Goncharik[1]; A Chasnoyt[1]; A Kovsh[1]; Y Ostrovsky[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: Cardiac resynchronization therapy (CRT) is an effective method of treatment in patients with severe heart failure, complicated with atrial fibrillation. 100% biventricular pacing is needed to achieve maximum clinical effect, what can be reached by ablation of atrioventricular node (AV-ablation). Valvular surgery with MAZE procedure is also an effective method of treatment.
Purpose: to explore and compare the effectiveness of electrophysiological and surgical methods of treatment in patients with chronic heart failure with NYHA functional class III or IV (III-IV FC CHF), ejection fraction (EF) $< 35\%$, QRS duration ≥ 120 ms and permanent atrial fibrillation (PAF).
Methods: The study involved 30 patients who underwent CRT with AV-ablation (group 1) and 30 patients underwent valvular surgery with MAZE procedure (group 2). Examination was carried out at baseline, in 6 and 12 months after surgery, and included general clinical tests, 24-Hour Holter Monitoring, determination of the level natriuretic peptide (NT-proBNP), myocardial dyssynchrony, transthoracic echocardiography and 6-minute walk test.
Results: After 6 months the improvement in intracardiac hemodynamics was revealed in both groups (table 1, $M \pm SD$, $p<0.05$). However, after 12 months the worsening of global left ventricular contractility was noted in group 1. The effectiveness of surgical treatment was maintained during the year of monitoring in group 2 (table 1, $p<0.05$).
Conclusions: The choice of electrophysiological methods or methods of cardiac surgery in treatment of patients with severe heart failure and atrial fibrillation should be differentiated based on etiology of cardiomyopathy. Electrophysiological methods of treatment are preferably carried out in patients with tachycardia-induced cardiomyopathy. Patients with atrial fibrillation and a heart rate less than 90 beats per minute should be preferably undergone valvular surgery with MAZE procedure.

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Endocardial left ventricle lead implantation for cardiac resynchronisation therapy: an australian experience.

C Caitlin Cheshire[1]; J Alison[1]; S Healy[1]; S Lockwood[1]; J D Cameron[2]; E Kotschet[1]
[1]*Monash Health , Monash Heart , Melbourne, Australia*; [2]*Monash University, Monash Cardiovascular Research Centre , Melbourne, Australia*

Introduction: Cardiac resynchronisation therapy (CRT) is an established therapy for symptomatic patients with advanced heart failure. However, traditional left ventricular lead placement may not always be technically feasible via the coronary sinus approach. Left ventricular (LV) endocardial lead implantation via a transseptal atrial approach may be a potential alternative.
Purpose: We sought to review the feasibility and clinical outcomes in patients undergoing LV lead implantations in a single-centre, tertiary, Australian institution. Endpoints included: technical success, peri-procedural complication rates, percent LV pacing load, change in New York Heart Association (NYHA) class and change in LV ejection fraction (LVEF).
Methods: and Results: Between August 2015 and December 2016, four patients underwent endocardial LV lead implantation (3 males, mean age 71 +/-5 years). All patients had previously failed LV lead placement via the coronary sinus. Mean pre-procedural LVEF was 24 +/-8%, mean QRS duration 161+/- 19ms and baseline NYHA was III (n = 3) and IV (n = 1). All patients had existing indications for therapeutic anticoagulation and were anticoagulated with warfarin (3 for atrial fibrillation, 1 for mechanical aortic valve). Warfarin was withheld for 3 days prior to the procedure. Mean international normalized ratio (INR) at the time of the procedure was 1.6+/-0.3. LV access was via an inferior approach, using femoral transseptal access, with a snare from superior subclavian venous access providing access to the left atrium. The lead was then inserted via the deflectable guiding sheath into the lateral LV endocardial wall. Successful implantation was achieved in all patients. One patient had a thromboembolic complication (non disabling stroke) post procedure, despite an INR of 2.1 at the time. That patient subsequently died from progressive heart failure within a month of the procedure. The 3 remaining patients have a mean follow up of 10 +/-7 months. The mean biventricular pacing volume was 93 +/-5%. %. All 3 patients had an improvement by at least one NYHA class. In the two

P444. Dynamics of echocardiographic parameters

Parameters	At baseline (group 1)	After 6 months (group 1)	After 12 months (group 1)	At baseline (group 2)	After 6 months (group 2)	After 12 months (group 2)
End diastolic dimension, mm	69±8.82	69±7.92•	65.5±11.56•	71.5±15.99	63.5±17.64•	60±18.59•
End systolic dimension, mm	58±8.83	56.5±8.67•	55.5±11.19•	59±13.78	54±15.88•	47.5±16.39•
End diastolic volume, ml (B-mode)	253±76.32	220.5±71.22•	241±74.48•	247±77.76	196±86.56•	171±69.03•
End systolic volume, ml (B-mode)	177±61.72	150±65.13•	166±69.09•	173±54.1	136.5±72.25•	100±51.04•
Ejection fraction, % (B-mode)	29±5.64	54±8.18•	36±8.90•	29.5±6.82	31±12.29•	41.5±13.34•

•p<0.05

patients followed up for more than one year, there was a marked improvement in LVEF (mean 35 + /-7%).
Conclusion: Endocardial LV lead implantation via a transseptal atrial approach is a feasible alternative for CRT in patients with failed lead placement via traditional coronary sinus approach. Thromboembolic complications despite therapeutic anti-coagulation remain the major risk.

P446
Super-response to cardiac resynchronisation therapy

AM Anna Soldatova[1]; VA Kuznetsov[1]; DV Krinochkin[1]; TN Enina[1]
[1]*Tyumen Cardiology Center, Tyumen, Russian Federation*

Background: Data from multicenter studies suggest that left bundle brunch block (LBBB) and wide QRS complex are associated with good response to cardiac resynchronisation therapy (CRT). Other studies evaluated echocardiographic parameters of mechanical dyssynchrony for patient selection to CRT. However, in real clinical practice the usage of these criteria is still debated.
The aim: To evaluate potential clinical, electrocardiographic and echocardiographic parameters related to super-response after CRT.
Methods: 51 CRT patients (mean age 55.6 ± 9.5 years; 72.5% men) with congestive heart failure (CHF) II-IV NYHA functional class were enrolled. At baseline, 1 month, 3 months and each 6 months after implantation clinical, electrocardiographic and echocardiographic parameters were evaluated. Criteria for LBBB were: QRS duration ≥ 130 ms in women or ≤ 140 ms in men, rS or QS morphology in lead V1, mid QRS notching/slurring in at least two of the leads V1, V2, V5, V6, I, aVL (by Strauss). According to the best decrease of left ventricular end-systolic volume (LVESV) (mean follow-up period 29.8 ± 15.4 months) patients were classified as super-responders (SR) (n = 27; reduction in LVESV of ≥30%) and non-SR (n = 24; reduction in LVESV of < 30%).
Results: SR had wider QRS complex (180.3 ± 24.8ms in SR vs 153.9 ± 23.7 ms in non-SR; p < 0,001) and higher incidence of mechanical dyssynchrony (p = 0.032). Percentage of LBBB was equal between groups (96.2% in SR vs 79.2% in non-SR; p = 0.071).
The survival rates in SR and and non-SR were 100% and 79.2% respectively (log-rank test P=0.002). Multiple logistic regression analysis showed that female sex (HR 5.773; 95% CI 1.149–28.998; P = 0.033) and width of QRS complex (HR 1.047; 95% CI 1.017–1.078; P=0.002) were independent predictors for CRT super-response. ROC curve analysis demonstrated sensitivity 75% and specificity 81.5% (AUC=0,824; p < 0.001) of this model in prediction of super-response to CRT in patients with CHF. Conclusion: Super-response to CRT is associated with better survival in long term period. LBBB defined according to Strauss criteria was not associated with CRT super-response. Female sex and width of QRS complex can be used as independent predictors of super-response.

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Typical left bundle branch block is associated with more favorable response to cardiac resynchronization therapy in heart failure patients

J Jaewon Oh[1]; JS Uhm[1]; IC Kim[1]; TH Kim[1]; HN Pak[1]; MH Lee[1]; B Joung[1]; SM Kang[1]
[1]*Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of*

Introduction: Left bundle branch block (LBBB) is a well-known predictor for good response to cardiac resynchronization therapy (CRT). Recently, the presence of typical LBBB was reported to be associated with improved long-term clinical outcomes after CRT.
Methods: We retrospectively analyzed 51 LBBB patients with CRT implantation with follow-up (median 555 days). CRT responders were defined as decreased LV end systolic volume >15%. Typical LBBB was defined as 1) QRS duration of ≥140 ms in men or ≥ 130 ms in women & 2) QS or rS in leads V1 and V2 & 3) mid-QRS complex slowing or notching in ≥ 2 contiguous leads of V1, V2, V5, V6, I, and aVL.
Results: There were 45 (88.2%) typical LBBB patients including notching in V1-2 (5.9%), V5-6 (51.0%), I & aVL (68.6%) leads. The CRT response rate in typical LBBB group was significantly higher (60.0% vs. 0%, p = 0.017) compared to non-typical LBBB group. Especially, mid-QRS notching in V5-6 was significantly related to CRT response (odd ratio: 10.23, 95% confidence interval: 1.91-54.96, p = 0.007) after adjusting other confounders. The LBBB patients with typical LBBB had significantly lower mortality rate (8.9% vs. 66.7%, p = 0.004) and tended to readmit less for HF aggravation (15.6% vs. 33.3%, p = 0.284).
Conclusion: Typical LBBB, especially mid-QRS notching in V5-6 was related to more favorable CRT response and clinical outcomes.

P448
Low EF as a predictor of poor CRT response

R El-Sherif[1]; N Awadh[2]; A Hussein[1]; H El-Aassar[1]
[1]*Cairo University Hospitals, Cairo, Egypt*; [2]*Saudi German Hospitals, Critical Care, Sanaa, Yemen*

Cardiac Resynchronization Therapy (CRT) is a treatment of choice in patients with systolic heart failure and reduced left ventricular ejection fraction (LVEF%) despite optimal medical therapy according to the latest guidelines. Despite the impressive results of CRT, 30% of patients remain non-responders.
Purpose: To assess clinical and echocardiographic response to CRT and to determine whether a low baseline LVEF% (<30%) could be a cause of poor CRT response.
Methods: 25 patients eligible for CRT implantation were included. All patients underwent full history, complete clinical examination, NYHA class, 6MHW distance and echocardiography with measurement of left ventricular end-diastolic and end-systolic diameters and calculation of LVEF%. Echocardiography, NYHA class and 6 MHW were reassessed 6 months after CRT implantation.
Clinical responder was defined as improvement of at least one NYHA class, while echocardiographic responder was defined as absolute increase of LVEF% by ≥ 5% 6 months after CRT
Results: 25 patients (88% males) with mean age of 53 ± 11.7 yrs. 15 patients (60%) had ischemia as a cause of heart failure. Hypertension was present in 48%, diabetes in 44% and chronic pulmonary disease in 20%. The mean 6MHW distance at baseline was 32.1 ± 10.8 m, reaching 37.5 ± 11.9 after 6 months with p 0.001. At baseline, 12% of patients were in NYHA class II, 52% in class III and 36% in class IV.
Thirteen patients (52%) were clinical responders and 9 pts (37%) were echocardiographic responders.
According to the baseline LVEF%, 11 patients had LVEF% ≥30% (all were males with mean age of 52 ± 14 yrs and ischemia as a cause of HF in 73%) and 14 patients had LVEF% <30% (79% males with mean age of 54 ± 9.5 yrs and ischemia as a cause of HF in 50%) When LVEF% was ≥30%, clinical responders were 82% and echocardiographic responders were 55%. The mean 6MHW distance was 41 ± 6 m and reached 47.5 ± 4.9 after CRT. When LVEF% was <30%, clinical responders were 29%, and echocardiographic responders were 22%. The mean 6MHW distance was 24.7 ± 7.4 m and reached 28.8 ± 8.9 after CRT.
Conclusions: Clinical and echocardiographic response to CRT were achieved with a higher incidence in patients with an LVEF% ≥ 30% than those with lower LVEF%. A very low LVEF% is probably a cause for inappropriate CRT response.

P449
Value of cardiac work estimation in the prediction of response to cardiac resynchronization therapy

E Galli[1]; C Leclercq[1]; A Hubert[1]; O Smiseth[2]; A Bernard[3]; E Samset[2]; A Hernandez[4]

[1]University Hospital of Rennes, Cardiology, Rennes, France; [2]University of Oslo, Oslo, Norway; [3]University Hospital of Tours, Tours, France; [4]Laboratory Signal Processing and Image, Rennes, France

Background: Cardiac resynchronization therapy (CRT) in heart failure is limited by still too many non-responders.
Purpose: to evaluate if the estimation of cardiac performance by pressure-strain loops (PSLs) analysis is useful for the selection of CRT candidates.
Methods: 97 patients undergoing CRT (ejection fraction: 27 ± 6%, QRS duration: 164 ± 18 ms) according to current guidelines were studied before and after a median 6-month follow-up (FU). Conventional dyssynchrony parameter were evaluated, and left ventricular (LV) global longitudinal strain (GLS) was used to estimate LV positive work (PosW) and negative work (NegW) by PSLs. Results: At FU, positive response to CRT (CRT+) was defined as ≥15% reduction in LV end-systolic volume and was observed in 63 (65%) patients.
In a multivariate regression model (Basal model, χ^2=27.9) including clinical, electrocardiographic, echocardiographic data and classic dyssynchrony parameters, non-ischemic etiology (OR 3.16, p = 0.036), septal flash (OR 4.20, p = 0.009) and LV end-systolic diameter (OR 0.92, p = 0.016) emerged as significant predictor of CRT+. The addition of both PosW and NegW at the Basal model caused a significant increment in model power (χ^2=47.5, p < 0.0001). After addition of PosW and NegW, SF (OR 8.16, p = 0.002), PosW>1057 mmHg/% (OR 7.9, p = 0.003) and NegW >384 (OR 13.89, p = 0.006) remained the only predictors of CRT+. The combination of PosW >1057 mmHg/% and NegW >384 mmHg/% showed an excellent specificity (100%), positive predictive value (100%) and accuracy (89%) for the identification of CRT +.
Conclusions: the estimation of cardiac work by PSL curves appears to be a novel and very promising tool to identify CRT responders, even when compared with more traditional indexes of cardiac dyssynchrony. Further studies on larger series should be designed to confirm these results.

P450
CRT response, complication-rate and prognosis in elderly patients

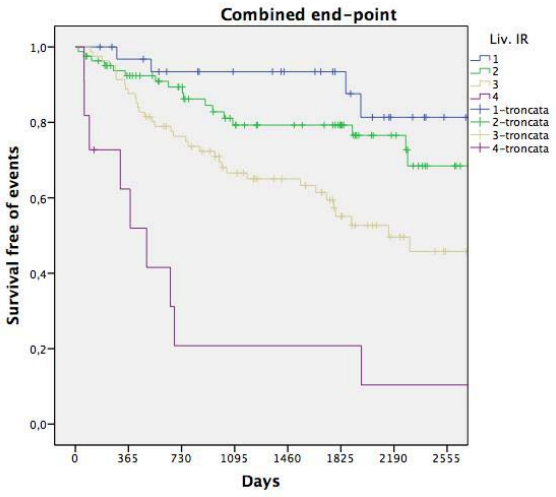
R Baggen Santos[1]; M Trepa[1]; I Silveira[1]; MJ Sousa[1]; C Roque[1]; A Pinheiro Vieira[1]; H Reis[1]; A Albuquerque[1]; S Torres[1]
[1]Hospital Center of Porto, Cardiology, Porto, Portugal

Introduction: The prevalence of congestive heart failure (CHF) increases with advancing age, affecting 10-20% of the elderly population. As such, many patients who receive cardiac resynchronization therapy (CRT) in clinical practice are in fact older than those included in clinical trials. The aim of this study was to evaluate CRT response, complication-rate and prognosis in elderly patients.
Methods: Single-center, retrospective analysis of 316 patients who underwent biventricular device placement, with or without a defibrillator (CRT-P or CRT-D, respectively), between January 2002 and March 2016. Patients were divided into two groups according to age (<75 and ≥75 years old). Baseline characteristics, echocardiographic and clinical response, all cause-mortality and hospitalizations for heart failure were determined. Echocardiographic (echo) responders were defined as those with a ≥5% improvement in left ventricular ejection fraction (LVEF) 6-12 months after CRT. Clinical responders were defined as those with an improvement of at least 1 NYHA functional class 6-12 months after CRT assessed by chart review. Patients were considered global responders if they had both echo and clinical response.
Results: In this study, 34% of patients were ≥ 75 years old (n = 108). These patients had a higher percentage of CRT-P implanted than younger patients (70% vs 33%, p < 0,001).There were no significant differences concerning gender or cardiomyopathy etiology. Surprisingly, cardiovascular comorbidities (hypertension, diabetes, dyslipidemia, tobacco exposure) weren´t significantly different between groups. LVEF before implantation was comparable (28% in older group vs 27% in the younger group; p = 0,6), but older patients had higher NYHA class (90% vs 79% in class III/IV, p = 0,018). As expected, total mortality was higher for the older group (44% vs 27%, p = 0,003), but there was no significant difference between five year survival rates (27% vs 21%, p = 0,3). Hospitalization and complication rates were also not significantly different between older and younger patients (16% vs 19%, p = 0,4 and 14% vs 18%, p = 0,4, respectively). In regard to CRT-response, echo and global response rates were similar for the older and younger groups (58% vs 55%, p = 0,8 and 56% vs 45%, p = 0,1). Clinical response was even considered significantly better for ≥75 year olds (80% vs 68%, p = 0,026). In multivariate analysis (including age, gender, sinus rhythm, QRS length and left bundle branch block), age was not an independent predictor of global response.
Conclusion: In the studied population, patients ≥ 75 years old responded at least as well as younger patients to CRT, without a higher complication rate, confirming the benefit of this therapy to the older group.

P451
Renal function at the moment of cardiac resynchronization therapy (CRT) is a powerful predictor of events during the follow-up.

G Giosue Mascioli[1]; G Coppola[2]; E Lucca[1]; F Michelotti[1]; L Tarantino[1]; A Mignano[2]; R Russo[1]
[1]Cliniche Humanitas Gavazzeni, Bergamo, Italy; [2]University Hospital Paolo Giaccone, Palermo, Italy

Background: Chronic kidney disease (CKD) is significantly related to prognosis in patients affected with heart failure (HF), but data on different stages of CKD in patients treated with CRT are limited.
Aim of the study: Aim of our retrospective study was to analyze the impact of renal function on clinical outcome of patients implanted with a CRT device.
Material and methods: All patients implanted with a CRT device at our Centres were inserted in a custom made database and – for the purpose of this study – data related to CKD stage (eGRF was calculated with CKD-EPI formula) were used to divide pts in four group according to CKD stage (stage 1: eGRF> 90 ml/min/1.73m2; 2: 60 – 90; 3: 30 – 60; 4: 15 – 30; 5: < 15). The end-point was a combined end-point of first hospitalization for acute HF or death: data were evaluated with the log-rank test.
Population: 207 pts (163 men, mean age 70 ± 8 yrs, mean LVEF 28 ± 5%, mean QRS duration 173 ± 27 ms, 108 ischemic, 166 CRT-D) were included in this study. Gr. 1 is constituted by 33 pts, Gr. 2 by 82, Gr. 3 by 81 and Gr. 4 by 11; no pts had a stage 5 CKD. There were no differences between the 4 groups as far as gender, kind of cardiopathy, LVEF and QRS duration, but pts in gr. 3 and 4 were older than pts with in the other 2 groups (gr. 1 66 ± 12 yrs, gr. 2 68 ± 10 yrs, gr. 3 74 ± 6 yrs and gr. 4 72 ± 8 yrs, p < 0.001). There were no significant differences in use of B-blockers and ACE-inhibitors, but less pts with higher stages of CKD were on antialdosteronic drugs and in gr. 3 and 4 the doses of furosemide were higher.
Results: Survival free of events at 1, 3, 5 and 7 yrs were the following: Gr. 1 97%, 93%, 93%, 81%; Gr. 2: 92%, 79%, 79%, 68%; Gr. 3: 87%, 67%, 55%, 46%; Gr. 4: 62%, 10%, 10%, 10% (see Figure). At 7 yrs 88% of Gr. 1 were still alive vs. 81% in Gr. 2, 66% in Gr. 3 and 32% in Gr. 4. Conclusions: Level of renal function at the moment of CRT implant is a powerful predictor of events in the follow-up. Pts with stage 4 CKD have a very negative prognosis both in term of recurrences of acute HF and survival and the use of CRT-D in this group of pts has probably a limited usefulness.



Survival free of combined end-point

P452
Prognostic value of left ventricular ejection fraction after cardiac resynchronization therapy: mid-range ejection fraction also in the echocardiographic response of cardiac resynchronization therapy

B Belen Alvarez[1]; J Garcia Seara[1]; D Iglesias Alvarez[1]; RA Abellas Sequeiros[1]; M Rodriguez Manero[1]; XA Fernandez Lopez[1]; A Varela Roman[1]; A Martinez Monzonis[1]; JL Martinez Sande[1]; JR Gonzalez Juanatey[1]
[1]University Clinical Hospital of Santiago de Compostela, Department of Cardiology, Santiago de Compostela, Spain

Table 1. P452 Baseline Characteristics

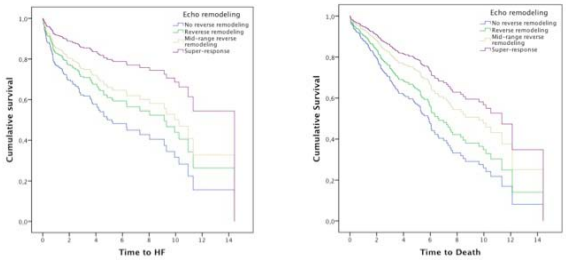
	No reverse remodeling110(33.5%)	Reverse remodeling 71(21.6%)	Mid-range reverse remodeling79(24.1%)	Super-reponders	p-value
Age (y)	70±7	70±10	70±10	70±10	0.831
Sex male, n(%)	88(80.0)	57(80.3)	63(79.7)	45(66.2)	0.119
Ischemic cardiomyopathy, n(%)	42(38.2)	33(46.5)	29(36.7)	15(22.1)	0.025
NYHA class, n(%) II III IV	25(22.7)76(69.1)9(8.2)	17(23.9)49 (69.0)5(7.0)	17(21.5)59(74.7)3(3.8)	20(29.4)46(67.6)2(2.9)	0.650
Atrial fibrillation, n(%)	49(44.5)	17(23.9)	33(41.8)	24(35.3)	0.034
CRT-D, n(%)	57(51.8)	32(45.1)	43(54.4)	40(58.8)	0.424
LBBB, n(%)	67(60.9)	47(66.2)	41(51.9)	43(63.2)	0.305
Glomerular filtration rate	61±26	61±25	61±23	61±24	0.959
Hemoblobine	13±2	13±2	13±2	13±2	0.858
QRS duration prior	160±29	152±26	157±25	147±29	0.166

Introduction: Reverse remodeling response in HF patiens after CRT was defined as ≥5% increased in LVEF, and super-responders have been considered if LVEF ≥50%. We aimed to evaluate the long-term benefit of CRT according the new terminology of HF.

Methods: We investigate the long term outcomes according to ventricular remodeling 1 year after CRT as follows: no reverse remodeling (reduced EF or increased <5%), reverse remodeling (Increase ≥ 5% of LVEF with LVEF <40%), mid-range reverse remodeling (increase ≥ 5% of LVEF with LVEF 40-49%) and super-responders (LVEF ≥ 50%). CRT was implanted in 328 patients between 2002 and 2015 in a single terciary center. Mean follow-up was 4.2 ± 2.9 years.

Results: No echocardiographic response was observed in 110 (33.5%) patients, Reverse remodeling in 71 (21.6%), mid-range reverse remodeling in 79 (24.1%) and super-response in 68 (20.7%). Baseline characteristics were shown in Table1. Mid-range reverse remodeling were not associated with an increased risk of mortality (HR 1.31, IC 95(0.72-2.38), p0.378) or HF (HR 1.83, IC 95% 0.93-3.61, p0.079) than Super-responders. But relative risk was increased when no reverse remodeling (HR 2.34, IC 95% 1.42-4.00, p 0.001 for mortality; and HR 3.06, IC 95% 1.66-5.64, p 0.000 for HF) and with reverse remoding (HR 1.86, IC95% 1.06-3.26, p 0.030 for mortality, HR 1.83, IC 95%0.93-3.61, p 0.079) (Figure 1).

Conclusion: Mild range reverse remodeling has been shown similar outcomes in HF/death events than superresponders. This classification of the echocardiographic response at 1 year of CRT may help best predict long-term prognosis.



Adjusted mortality and Heart Failure

P453

Optimal medical treatment and cardiac resynchronization therapy? Prognostic implications. HF-CardioCHUS Registry

B Alvarez[1]; FJ Garcia Seara[1]; RA Abellas Sequeiros[1]; D Dieguez Alvarez[1]; M Rodriguez Manero[1]; L Gonzalez Melchor[1]; RA Agra Bermejo[1]; MI Gomez Otero[1]; A Varela Roman[1]; XA Fernandez Lopez[1]; A Martinez Monzonis[1]; JL Martinez Sande[1]; JR Gonzalez Juanatey[1]

[1]University Hospital of Santiago de Compostela, Cardiology - CIBERCV, Santiago de Compostela, Spain

Background: Cardiac resynchronization therapy (CRT) is indicated in symptomatic heart failure (HF) patients after achieving optimal medical therapy (OMT). However, many patients may not be under OMT when the CRT device was implanted. We aimed to evaluate the long-term benefit of CRT in symptomatic HF patients according OMT before or after CRT.

Methods: We investigated the effect of being or not under OMT on the clinical outcomes HF/mortality, in 328 consecutive patiens implanted with a CRT device between 2001 and 2015 in a single terciary center. We categorize the patients into three groups: no-basal OMT, OMT at basal and OMT at 1 year follow-up. Multivariate Cox proportional hazards models were used to determinate the effect of OMT on the clinical outcomes.

Results: Patients on basal OMT were 122(37.2%). Baseline characteristics are shown in Table 1. The absence of OMT at baseline was not associated with an increased risk of mortality/HF (HR0.72; 95%CI 0.50-1.02;p0.067) compared with no OMT at basal. 84(40.8%) patients without basal OMT could achieve OMT at 1 year follow-up. Patients without OMT had more risk of mortality or HF than OMT in follow-up (HR1.94, 95%CI 1.25-3.01;p0.003), and the risk of patients with basal OMT and OMT in follow-up was similar (HR0.95, 95%CI 0.59-1.53, p0.826) (Figure)

Conclusion: Basal OMT before CRT implant could not be associated with better outcomes. OMT achieved at 1 year-follow-up was associated with a reduced risk of HF/mortality. Our results suggest that efforts should be made for medical treatment optimization after CRT.

Table. Baseline Characteristics

Clinical Characteristic	no-OMT (n = 130)	Basal OMT (n = 114)	OMT at follow-up (n = 84)	p-value
Sex: male, n(%)	105(80.8)	89(78.1)	59(70.2)	0.192
Age (y)	73.2±8.1	68.4±9.7	76.9±10.0	0.000
Ischemic cardiomyopathy, n(%)	53(40.8)	42(38.6)	22(26.2)	0.078
CRT-ICD, n(%)	70(53.8)	61(53.5)	41(48.8)	0.741
NYHA class, n(%)				0.001
II	19(14.6)	39(34.2)	21(25)	
III	98(75.4)	70(61.4)	62(73.8)	
IV	13(10)	5(4.4)	1(1.2)	
Atrial fibrillation, n(%)	50(38.5)	42(36.8)	31(36.9)	0.958
Glomerular filtration rate (ml/(min x 1.73m^2)	50.1±22.1	65.1±22.6	68.0±24.7	0.000
Hemoglobine level (g/dl)	12.7±1.8	13.6±1.7	13.7±1.5	0.000
Coronary sinus vein,n(%) Anterior	34(26.8)	18(15.9)	17(20.5)	0.085
Lateral	64(50.4)	57(50.4)	49(59.0)	
Posterior	29(22.8)	38(33.6)	17(20.5)	
QRS duration prior (ms)	160.9±25.8	164.9±27.3	161.8±25.6	0.473
LBBB, n(%)	75(57.7)	64(56.1)	59(70.2)	0.097
LVEF prior(%)	27.7±7.1	26.1±6.9	27.2±7.7	0.203

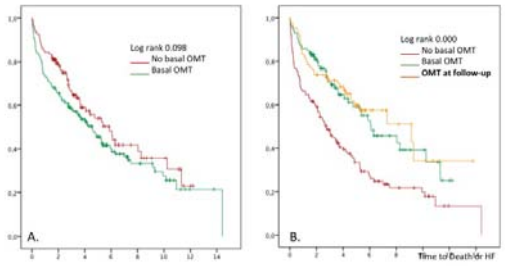


Figure 1. Kaplan-Meier curves of the cum

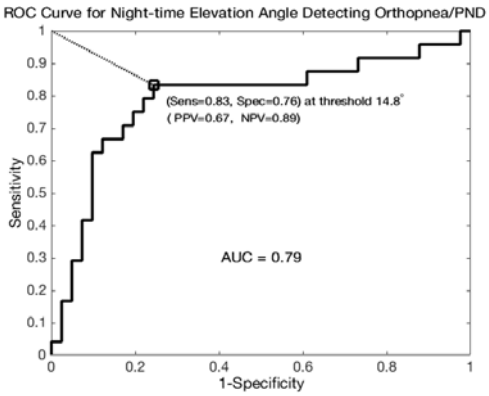
P454

Night-time elevation angle in heart failure patients indicates orthopnea and paroxysmal nocturnal dyspnea

S J Rials[1]; J D Hatlestad[2]; A Smith[3]; D Pubbi[4]; D Slotwiner[5]; J P Boehmer[6]
[1]Grant Medical Center, OhioHealth, Columbus, United States of America; *[2]Boston Scientific CRM, Saint Paul, United States of America*; *[3]Emory University Hospital, Atlanta, United States of America*; *[4]First Coast Heart And Vascular, Jacksonville, United States of America*; *[5]Long Island Jewish Medical Center, New Hyde Park, United States of America*; *[6]Penn State Milton S. Hershey Medical Center, Hershey, United States of America*

Funding Acknowledgements: Boston Scientific Corporation

Background: Orthopnea and paroxysmal nocturnal dyspnea (O-PND) are cardinal signs of worsening heart failure (HF). Guidelines for HF patient management recommend routine assessment of O-PND. These postural symptoms are typically assessed by asking about patients' sleep angle in terms of number of pillows. We evaluated the use of automated posture sensing in assessing O-PND in HF patients.
Methods: 46 HF patients (35 male, 45-83 years of age, NYHA class I-III) in the MultiSENSE study wore an external posture monitoring device for a few days (0.9-14) at a time. At each patient visit, O-PND symptoms were assessed. We compared the device-determined night-time elevation angle (NTEA) for patient visits with & without reported O-PND symptoms.
Results: Patient visits associated with O-PND (n = 24) had an average NTEA of 23.2 ± 2.8 (mean ± standard error), compared to an average NTEA of 10.7 ± 1.7 for those patient visits not associated with O-PND (n = 41, p = 0.0001 using non-paired t-test). A receiver operating characteristic (ROC) curve analysis (see figure) yielded an area under the curve of 0.79 for NTEA detecting O-PND. Selecting an NTEA threshold of 14.8 yielded a sensitivity of 83% and specificity of 76%.
Conclusion: Orthopnea & PND are key symptoms of HF. Night-time elevation angle is indicative of these symptoms, presumably reflecting the tendency of patients to sleep partially elevated to avoid dyspnea. Monitoring posture in future devices may provide valuable insight for the remote management of HF patients.



P455

Acceptance of home telemonitoring in patients with heart failure: the ecare client impact survey in the european funded project smartcare

D Radini[1]; GM Apuzzo[1]; K Stellato[1]; G Sola[1]; N Delli Quadri[2]; E Fragiacomo[2]; A Di Lenarda[1]
[1]Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy; *[2]Ospedale Cattinara, Trieste, Italy*

Objectives: The main goal of this work was to analyze the impact of telemonitoring (TLM) in elderly patients with chronic or post-acute heart failure (HF), and the presence of ≥1 social needs, requiring intensive home monitoring.
Methods: The SmartCare Project was developed as a cohort, prospective, randomized, controlled trial that enrolled from November, 2014 to February, 2016, 201 pts in home care (>50 years, at least 1 severe chronic diseases - HF, COPD or diabetes - and ≥1 missing BADL) to intervention arm (INT - automatic BP monitoring, weight, FC, SO2, ECG: n = 100) or usual care (UC; n = 101). At the end of the program, a culturally adjusted eCare Client Impact Survey (eCCIS) was collected in pts randomized to INT.
Results: General data collected: the patients enrolled were elderly (81 years, 54% males) and with multimorbidities (44% Charlson Index ≥5; 58% ≥7 drugs/day). HF was present in 79% of pts, COPD in 38%, diabetes in 68%. Most pts showed a low level of education (primary school in 58% of end users); 38% were living alone, and 42% were reliant on care. Data eCare Client Impact survey was collected in 45 subjects out of 88 INT users. Reasons for non-responding were: death, hospital admission, not directly involved in self-monitoring activities. Out of a total of 45 respondents, 26 end users experienced a positive increase in motivation; 35 experienced a better emotional wellbeing; 30 experienced a greater ability to perform daily physical activities; 30 had a reduction in anxiety; 29 felt less lonely; 19 experienced an improvement in their relationship with their family carer; 29 experienced an improvement in their relationship with their professionals; 35 felt a general improvement in their ability to manage their health condition; 39 expressed satisfaction with the service, and 39 felt the service was well worth the effort and would continue to use it.
Conclusion: While considering that the questionnaire involved about 50% of patients in the intervention group, the data collected showed good acceptance of TLM system with improved self-care and relationships with relatives and health workers, reduction of anxiety and loneliness. Patients have also expressed a positive opinion about the service and wish to continue with TLM.

P456

How do cardiologists and nurses think about telemonitoring in patients with heart failure? A survey in Lithuania and Norway

E Lycholip[1]; IT Aamodt[2]; I Lie[2]; J Celutkiene[1]; A Stromberg[3]; T Jaarsma[4]
[1]Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania; *[2]University of Oslo, Oslo University Hospital, Department of Cardiothoracic surgery, Oslo, Norway*; *[3]Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*; *[4]Linkoping University, Department of Social- and Welfare studies, Norrkoping, Linkoping, Sweden*

Background: Currently there is still lack of evidence that telemonitoring in heart failure (HF) patients is an effective way to early notice and react to the patient's deterioration when at home, to reduce the frequency of hospitalisations. Meanwhile these systems are implemented in several parts of Europe. Little is known about the opinion of cardiologists and cardiac nurses regarding the suitability and relevance of telemonitrong in Norway and Lithuania.
Purpose: To describe health care professionals' (HCP) perceptions of the feasibility and relevance of telemonitoring in patients with HF in Lithuania and Norway.
Methods: The survey was performed nationwide in two Nordic Baltic countries enrolling cardiologists and cardiac nurses working with HF patients in 47 hospitals in Lithuania and 60 hospitals in Norway. Validated translations from English to Lithuanian and Norwegian of a previously developed validated questionnaire were used. Data were collected between September and December 2016.
Results: Responses from 541 HCP (n = 315 in Lithuania [135 cardiologists, 173 nurses] and n=226 in Norway [62 cardiologists, 157 nurses]) were analysed. Educational degree of respondents included 12% and 9% doctoral, 36% and 11% master and 21% and 67% bachelor in Lithuania and Norway, respectively.
Almost all participants use e-mail and Internet, while 72% and 93% in Lithuania and Norway, respectively, use e-mail in their mobile phones. More than one fifth of respondents in both countries were familiar with TM.
The majority of the cardiologists and nurses in both Nordic Baltic countries consider the outpatient clinic and home visits most often as good ways to follow-up patients after discharge. In total 49% and 58% of the participants in Lithuania and Norway answered that internet-based monitoring was a good way of follow up. Substantial proportion of respondents reported telemonitoring as a relevant (55 and 58%) or very relevant measure (14 and 20%) and frequently named daily feedback to the patient as feasible (22 and 47%).

Conclusion: Modern digital technologies are widely used by health care professionals in Lithuania and Norway. A substantial proportion of cardiologists and nurses are familiar with telemonitoring and believe that daily feedback to the patients is feasible. However, the majority of HC providers in both Lithuania and Norway see a large role for outpatient clinics, GP's and home visits by nurse.

P457

Telemonitoring of vital signs has a minor impact on clinical decision making but well-being improves in patients with chronic heart failure.

FWG Wenzelburger[1]; B Zippel-Schultz[2]; T Luiz[3]; R Erchinger[1]; B Fischer[1]; D Lommel[1]; S Kuerwitz[1]; T Helms[2]; B Schumacher[1]
[1]Westpfalz Klinikum Kaiserslautern, Cardiology, Kaiserslautern, Germany; *[2]Deutsche Stiftung für Chronisch Kranke, Berlin, Germany*; *[3]Fraunhofer Institut - IESE, Kaiserslautern, Germany*

Funding Acknowledgements: Grant of Regional Government of Rhineland Palatinate/Germany

Background: Providing health care for heart failure (HF) patients becomes increasingly difficult because of adverse demographic changes: the number of patients is increasing while the number of physicians, particularly in rural areas, decreases. Telemonitoring (TM) might reduce the symptoms of HF patients and improve their overall well-being. However, how the improvement is achieved remains controversial.
Purpose: The aim of this study was to evaluate the impact of TM of vital signs and weight in a telemedicine program for HF patients.
Method: 68 patients (63.3 ± 11.7 years; 57 male, 11 female) living in a rural area with stable systolic HF (EF < 35%, NYHA II-IV) were included and monitored for 6 months. Patients were equipped with TM systems which sent daily semi-automatically updated data on blood pressure, heart rate, and weight into an integrated electronic health record. An alarm was issued by the software whenever data exceeded a range that was individually defined for each patient. HF nurses of the TM service centre decided whether to wait for a control measurement or to call the patient immediately. During the telephone calls with the patients they discussed symptoms and offered advice regarding further treatment. Every alarm, the following action and a thorough content overview of the telephone calls were documented. Routine telephone calls including questions about the health status and educational elements were performed (every week during the first month, monthly starting from the second month). Symptoms and a depression score (PHQ-9) were evaluated at the inclusion and after 6 months.
Results: During the 6 months 2069 alarms were issued. Every patient had at least one alarm (minimum 3, maximum 132, median 18.5). Most alarms were issued due to blood pressure measurements (86,5%). 10.9% of alarms were sent due to heart rate irregularities, and 2.6% due to an increase in weight. An extra of 116 alarms was registered due to missing transmission of data. 63.1% of blood pressure alarms and 75.1% of heart rate alarms were classified as neglectable within the context of the patient's individual history. After 36.9% of blood pressure alarms and 24.9% of heart rate alarms patients were called and were stable with no further action. 3.6% of all alarms were followed by a clinical decision and a change in therapy or the recommendation to see a physician in due course. The depression score decreased from 8.4 ± 0.8 to 5.5 ± 0.6 ($p < 0.001$). Symptoms improved substantially. This did not correlate with the number of alarms or the number of telephone calls due to alarms.
Conclusion: TM of vital signs and weight had minor impact on clinical decision making in HF patients. However, well being and health related quality of life improved. This may be achieved by the educational effects of taking part in the project and routine telephone calls. Further investigations into the working process of TM are needed to focus on the pivotal techniques in the future.

P458

Heart failure virtual consult: utilising technology to improve heart failure care in the community

SI James[1]; J Gallagher[2]; C Keane[2]; A Fitzgerald[1]; B Travers[1]; M Ledwidge[2]; K Mc Donald[1]
[1]St Vincent's University Hospital, Cardiology, Dublin, Ireland; *[2]Heart Beat Trust, Dublin, Ireland*

Background: One hospital in Ireland had been providing heart failure virtual consult (HFVC) service for primary care physicians (PCPs). HFVC utilises teleconferencing technology to mentor PCPs on management of heart failure (HF). We report on the experience and outcome of HFVC.
Methods: Consecutive 132 consultations from May 2014 till November 2016 were included. The natures of the consultations were categorised as new diagnostic (possible new HF), emerging deterioration (HF with worsening symptoms), or therapeutic (drug therapies query) cases. The demography, comorbidity and medications were recorded. Outcome were measured as final diagnoses in the new diagnostic cases and metric of patient convenience.
Results: In 31 months, there were 73 new diagnostic (49.3% male; median age 78 [72 : 82] years), 35 emerging deterioration (60% male; median age 81.5 [76 : 86] years) and 24 therapeutic (54.2% male; median age 82 [71 : 86] years) cases. High prevalence of hypertension (46.6%; 42.9%; 33.3%) and atrial fibrillation (34.2%; 34.3%; 33.3%). High incidence of IHD in emerging deterioration (42.9%) and therapeutic (45.8%) cases. DM, lipid disorder and CKD were important comorbidity noted. There were high use of ACE-I/ARBs, B-blockers, diuretics and statins. In new diagnostic cases, 34.2% were confirmed HF, 37.0% were confirmed not HF, and 28.8% were still indeterminate HF. The metric of patient convenience is describe in Table 1.
Conclusions: HFVC service is a feasible model in providing specialist care for heart failure patients in the community. This single center early experience proved that HFVC could save time and travel distance for heart failure patients by receiving treatment by their PCPs.

Metric of patient convenience

	New diagnostic case	Emerging deterioration case	Therapeutic case
	n=73	n=35	n=24
Outpatient review (n, %)	0 (0%)	0 (0%)	0 (0%)
Emergency department referral (n, %)	0 (0%)	0 (0%)	0 (0%)
Need follow-up virtual consultation (n, %)	29 (39.7%)	5 (14.3%)	3 (12.5%)
Distance travel saved, kilometer			
Total	4881	1383	1298
Median [IQR]	88.5 [19.2 : 88.5]	12.1 [9.93 : 51.8]	88.5 [10.1 : 89.2]
Time travel saved, minute			
Total	4582	1378	1350
Median [IQR]	88 [37 : 92]	22 [17 : 49.5]	88 [23 : 92]

P459

Post-transplant outcomes in patients bridged with temporary mechanical support.

G Caixal[1]; M Hernandez[1]; E Flores[1]; R San Antonio[1]; G Jimenez[1]; A Garcia[1]; M Farrero[1]; MA Castel[1]; D Pereda[1]; M Castella[1]; R Cartanya[1]; E Santiago[1]; P Sanchez[1]; G Caldentey[1]; F Perez-Villa[1]
[1]Barcelona Clinic Hospital, Barcelona, Spain

Introduction: Heart transplantation is the treatment of choice in several patients with advanced heart failure not responding to medical therapy and cardiac resynchronization. The use of short and mid-term ventricular assist devices (VAD) is increasingly used as a bridge to heart transplantation due the lack of donors.
Objective: To describe our center outcomes in heart transplant patients bridged with ventricular temporary mechanical support.
Methods: We retrospectively reviewed heart transplant patients bridged with temporary VAD from April 2010 to May 2016. We excluded patients died before transplant. We analysed basal characteristics, complications and survival.
Results:A total of 91 patients were transplanted during this period. From them, 18 (19.8%) received VAD as a bridge. Mean age was 53.7 (17-66) years and 67% were male. Pre-existing heart conditions were as follows: ischemic cardiomyopathy 55% (n = 10), dilated non-ischemic cardiomyopathy 33% (n = 6), and postcardiotomy shock 11% (n = 2). Devices used were ECMO in 9 patients, Left Levitronix in 7 (two after ECMO) and biventricular Levitronix in 2. Mean time of support was 11.9 ± 10.9 days. In-hospital complications were infectious with secondary hemodynamic inestability (mediastinis or pneumonia) 61% (n = 11), need of renal replacement therapy (RRT) 50% (n = 9), neurological (ictus or cerebral anoxia) 17% (n = 3), hemorrhage with need of re-intervention 17% (n = 3) and peripheral vascular ischemia 11% (n = 2). Severe right ventricle dysfunction evidenced by echocardiography appeared in 28% (n = 5) and in 4 of them RRT was needed. Only in one case ventricular mechanical support was implanted. Four patients died (4 of 18, 22%) in the immediately post-transplant period, without no new deaths in 1-year follow-up. Mortality was higher in patients with right ventricular dysfunction (3 of 5, 60%). Also, the need of RRT is more frequent among this patients (4 of 5, 80%).
Conclusion: VAD is an effective treatment of terminal heart failure. Post transplant mortality in our series was the same as reported previously. The need of RRT and right ventricular dysfunction were related to a higher mortality.

P460

Improvement in liver and renal biochemistry following left ventricular assist device therapy in advanced heart failure

T A Tarique Al Musa[1]; C D Chue[1]; H S Lim[1]
[1]*University Hospital Birmingham NHS Foundation Trust, Transplant Cardiology, Birmingham, United Kingdom*

Background: Liver and kidney dysfunction are associated with adverse prognosis in patients with advanced heart failure. LVAD therapy effectively bridges patients to heart transplantation but there is little data on the specific effects upon liver and kidney biochemistry.
Purpose: To assess changes in renal and liver biochemistry (and consequent Model in End-stage Liver Disease eXcluding INR, MELD-XI score) at 30 days and 6 months following LVAD.
Methods: A single-centre study of 61 consecutive patients with HeartMate II or III LVADs (bridge to transplant) between January 2011 and October 2016. Renal and liver biochemistry and eGFR were assessed before LVAD, at 30 days and at 6 months. CKD was defined by the Kidney Disease Outcomes Quality Initiative. The MELD-XI score was calculated from bilirubin and creatinine. Data are presented as mean ± standard deviation or median (IQR).
Results: 61 patients (age 53.0 ± 11.1 years, 87% male, 11% diabetic, 84% INTERMACS Profile ≤3, CI 1.78 ± 0.54 L/min/m2) were studied. 6-month follow-up data were available in 42. Baseline urinary albumin: creatinine ratio (UACR) was available in 36 (2.1 (0.0 – 8.9) mg/mmol). No patients required dialysis.
Urea, creatinine and CKD stage improved at 30 days. The improvement in eGFR from baseline persisted at 6 months.15 patients had baseline albuminuria (UACR>3.0) and renal function did not change in these patients. There were significant improvements in serum bilirubin, ALT and albumin, all of which remained normal at 6 months. The MELD-XI score had improved from baseline at 30 days (25.8 ± 5.7 vs. 20.9 ± 5.2, $p < 0.001$) and remained so at 6 months (25.8 ± 5.7 vs. 21.4 ± 4.1, $p < 0.001$).
Conclusions: LVAD therapy is associated with early improvements in liver and renal function which are sustained at 6-month follow-up.

Renal and Hepatic changes post LVAD

	Baseline (n = 61)	30 days (n = 61)	p Value	6 months (n = 42)	p Value (vs. baseline)
Renal Biochemistry					
Urea (mmol/L, NR 3.4-7.8)	8.5±4.6	6.6±5.5	0.029	6.9±2.9	0.200
Creatinine (micromol/L, NR 60-126)	119.7±50.0	85.6±30.0	< 0.001	96.6±27.9	0.017
eGFR (ml/min/1.73m2)	59.9±21.1	75.6±17.3	< 0.001	72.4±17.4	0.004
CKD stage	3.0 (2.0-3.5)	2.0 (1.0-2.0)	< 0.001	2.0 (2.0-2.25)	0.078
Liver Biochemistry					
Bilirubin (micromol/L, NR < 22)	20.9±13.5	15.4±16.8	0.019	10.3±4.9	< 0.001
Alkaline Phosphatase (U/l, NR 40-130)	107.5±65.4	155.3±85.3	< 0.001	105.0±41.6	0.921
Alanine Transferase (U/l, NR 5-41)	48.9±81.9	29.2±29.1	0.085	23.1±12.8	0.023
Albumin (g/L, NR 34-51)	35.4±7.0	35.5±5.1	< 0.001	45.4±3.5	< 0.001

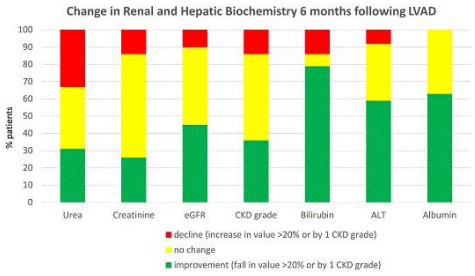


Figure 1

P461

Is the implantation of mechanical circulatory support device a risk factor for immunisation of patients with terminal heart failure ?

I Malek[1]; T Gazdic[2]; M Hegarova[1]; L Hoskova[1]; I Netuka[2]; A Slavcev[3]; L Voska[4]; J Pirk[2]
[1]*Institute for Clinical and Experimental Medicine, Cardiology, Prague, Czech Republic*; [2]*Institute for Clinical and Experimental Medicine, Cardiovascular surgery, Prague, Czech Republic*; [3]*Institute for Clinical and Experimantal Medicine, Laboratory methods, Prague, Czech Republic*; [4]*Institute for Clinical and Experimental Medicine (IKEM), Pathology, Prague, Czech Republic*

Introduction: Program of mechanical circulatory support (MCS) contributed significantly to the treatment of terminal heart failure. As a bridge to transplant MCS led to decreased mortality on waiting lists, in some cases even enables successful cardiac transplantation (CTX). One of possible risks of MCS is the immunisation of patients (pts). This complication was frequent in the era of extracorporal pulsatile systems, in contemporary used implantable non pulsatile systems the data are not consistent.
Aim of the study: To find out whether implantation of contemporary used MCS devices would be a risk factor for anti HLA antibody (HLAabs) development before and during the 1st year after CTX.
Patients and methods. Between 1/2011 and 7/2013 CTX was performed in 119 pts. We studied the group of 91 pts (age 21-73 years,75 men,) who survived at least 12 months after CTX and had complete clinical and immunological data. MCS (Heart-Mate II fi. Thoratec) before CTX was implanted in 31 pts. Follow up was 36-67 months. HLAabs were investigated by single antigen beads (SAB, Luminex) method, cellular rejection (ACR) and antibody mediated rejection (AMR) were assessed from endomyocardial biopsy samples, graft dysfunction (GD) was defined as a decrease of left ventricular ejection fraction below 40 % on echocardiography, coronary vasculopathy (CAV) was evaluated by selective coronary angiography. Examination of HLAabs was performed before and 1, 3, 6 and 12 months after CTX. Clinical end points (EPs) were: treated ACR, AMR, GD, CAV and death from cardiovascular cause. We compared the development of HLAabs and EPs between groups transplanted on / without MCS (chi-square test).
Results: HLAabs developed in 37 (41 %) of pts. EP was reached in 21 (23 %) of pts, in 35 % who developed HLAabs and 11 % without HLA abs ($p = 0.006$). HLAabs developed in 12 from 31 pts (39 %) on MCS and 25 from 60 pts (42 %), without MCS ($p = 0.786$). EP was detected in 8 from 31 pts (26 %) on MCS and 13 from 60 pts (22 %) without MCS ($p = 0.657$).
Conclusion: Non-pulsatile implantable devices for long term circulatory support Heart-Mate II are not a risk factor for HLAabs development before and during the 1st year after CTX as well as for the occurence of immunological complications during middle-term follow up.

P462

Dual antiplatelet therapy use in continuous flow left ventricular assist device patients: a comparison of bleeding and thrombosis outcomes in a single centre

F Njue[1]; K Lam[1]; L Naylor[1]
[1]*Fiona Stanley Hospital, Advanced Heart Failure and Transplant Unit, Perth, Australia*

Background: Left ventricular Assist Device (LVAD) pump thrombosis is a significant complication associated with poor survival. Current guidelines include the use of warfarin and antiplatelet therapy for long-term management. Previous studies found that the highest risk of bleeding was related to higher International Normalised Ratio (INR) levels; consequently, INR of 1.5 to 2.5 is the recommended target range. We implemented dual antiplatelet (aspirin & clopidogrel) with warfarin strategy due to detected "white" thrombus in our LVAD dysfunction cases. We performed minimum weekly INR monitoring on all patients. There is minimal data regarding the risk benefit ratio of this strategy.
Purpose: To assess impact of dual antiplatelet therapy (DAPT) on bleeding or thrombotic events in LVAD patients.
Methods: This is a retrospective observational study of all patients (n = 50) implanted with Heartware and Heartmate II LVADs in Western Australia between 2006 -2016. Data on antiplatelet use, INR level and bleeding/thrombotic events were analysed monthly upto 13 months post implant. Patients were grouped into DAPT + warfarin or Other (nil/warfarin/aspirin/single antiplatelet& warfarin).
Results: 448 months of therapy reviewed. Bleeding occurred in 77 months (17%) and thrombosis in 24 months (5%). INR was within 1.8 to 3.0 in 342 months (76%). DAPT received in 274 months (61%). 21 (42%) patients were on DAPT + warfarin within first month post implant. 34(68%) patients had a bleeding event. Bleeding rates were similar between the groups with 15/24 patients on DAPT + warfarin experiencing a bleed (P=0.31). Time to first bleed was longer in this group compared

to Other (96 vs 43 days, P <0.05) despite similar age and INR levels. 14 patients had a thrombosis event. Of note, 50% of thrombotic events occurred in patients on DAPT + warfarin, despite an average INR >2.

Conclusion: Patients on DAPT plus warfarin therapy receiving regular INR monitoring do not have significantly increased risk of bleeding or thrombotic events whilst on LVAD support. The DAPT plus warfarin strategy at our center is associated with a lower incidence of device thrombosis and comparable bleeding rates to those reported in the literature.

Baseline characteristics of the patients

Bleeding Events	Thrombosis Events			
	DAPT + warfarin	Other	DAPT + warfarin	Other
N (male)	15 (12)	19 (13)	7(5)	7 (6)
Age, years	53 (7)	53 (14)	51 (11)	44 (10)
INR	2.4 (0.6)	2.2 (1.1)	2.3 (0.7)	2.0 (0.9)
Time to event, days	97 (105)	43 (42)	158 (162)	96 (103)

Data expressed as average(SD). * P < 0.05 between groups

P463

HeartWare Continuous flow left ventricular assist device early mortality predictors: Single center experience

E Emre Demir[1]; PÖ Ozturk[2]; ÇE Engin[2]; SN Nalbantgil[1]; MZ Zoghi[1]; TY Yagdi[2]; MÖ Ozbaran[2]
[1]*Ege University, Medicine Faculty Cardiology Department, Izmir, Turkey*; [2]*Ege University, Medicine Faculty Cardiovascular Surgery Department, Izmir, Turkey*

On behalf of: Ege Heart Failure Team

Introduction: Left ventricular assist devices have become standart theraphy for advanced heart failure patients. Aim of this study to investigate in hospital mortality predictors after HVAD (HeartWare International, Framingham, MA) implantation.

Method: From August 2010 to December 2016, 228 patients underwent HVAD implantation. The analysis was performed using a prospectively maintained institutional patient database. The variables evaluated included baseline characteristics, preoperative laboratory, baseline hemodynamics characteristics, echocardiographic data, preoperative clinical data, intraoperative data, and postoperative variables.

Results: Total 228 advanced heart failure patients (mean age: 50.7 ± 12.7, 86% male and 14% female) underwent HVAD implantation. The cause of heart failure was ischemic cardiomyopathy 52.1% (n = 113), dilated cardiomyopathy 44.7% (n = 97) and valvular cardiomyopathy 3.2% (n = 7). In hospital mortality was 17.5% (n = 38)

Subgroup analysis demonstrated preoperative cardiac surgery that was an independent risk factor for hospital mortality. Fifty two (24.1%) patients operated for any cardiac etiology before HVAD implantation who was operated before any cardiac etiology 39.5% (n = 15) died after HVAD implantation (p = 0.014).

The preoperative laboratory parameters were comparable beetween two groups. NT-proBNP was higher in hospital mortality subgroup (6884 ± 8223 vs 16652 ± 17969 pg/ml p = 0.049). In addition to this, higher preoperative blood urea nitrogen was independent predictor hospital mortality (45.4 ± 27.5 vs 68.8 ± 41.0 mg/dl p = 0.002). Moreover serum albumin level was independent predictor hospital mortality (3.92 ± 0.53 vs 3.56 ± 0.58 p = 0.002)

Postoperative major cause of death was early right sided heart failure (RHF), after HVAD implantation 30 patients (13.9%) had diagnosis of RHF and 14 patients (36.8%) died in consequence of RHF. Post operative central venous pressure which reveals RHF was higher in hospital mortality group (14.1 ± 3.2 vs 15.71 ± 3.9 p = 0.024)

Conclusion: Preoperative cardiac surgery and laboratory parameters NT-proBNP, BUN and albumin are predictors of hospital mortality. Post operative major cause of death was RHF and post operative CVP was independent predictor of hospital mortality.

P464

Combining echocardiography with cardiopulmonary exercise stress testing to evaluate recovery of systolic function in patients with left ventricular assist devices

JW Christle[1]; KJ Moneghetti[2]; R Ha[3]; F Haddad[2]; D Banerjee[1]; MT Wheeler[1]
[1]*School of Medicine, Program in Mechanical Circulatory Support, Division of Cardiovascular Medicine, Stanford, United States of America*; [2]*School of Medicine, Biomarker and Phenotypic Core, Cardiovascular Institute, Stanford, United States of America*; [3]*School of Medicine, Department of Cardiothoracic Surgery, Stanford, United States of America*

Background/Introduction: Left ventricular assist devices (LVAD) are increasingly being used for patients with end stage heart failure as a bridge to cardiac transplantation or destination therapy. Some patients with LVAD recover native LV function and exercise capacity, and are considered for explant (bridge to recovery). Pre-explant evaluation involves separate cardiopulmonary exercise testing (CPX) and echocardiographic (echo) examination on full and minimal LVAD support, but CPX with simultaneous echo has not been well studied.

Purpose: We combined CPX with echo to assess native LV and cardiopulmonary function with and without LVAD support in patients being considered for explant.

Methods: Patients with an LVAD of any type and with any indication were recruited for this study. Patients were included if they had CPX to volitional exhaustion within the last six months, were clinically stable and had an INR > 2.0 on the day of examination. Patients were examined on two separate occasions (within 14 days): (a) LVAD at the patient's baseline speed; and (b) LVAD at the lowest speed safely allowed by the device. CPX was performed on upright cycle ergometers with echocardiography performed during rest, exercise, and recovery.

Results: Patients were between 29 and 75 years and 40% female. There were no adverse events during or following testing and adequate image quality was obtained. LVAD speeds were 8400 (Heartmate II) and 2400 (HVAD) rpm at baseline, and 6000 rpm and 1800 rpm on minimal support. Average RER was 1.14 ± 0.09, RPE was 17 ± 1 and resting LVEF was 40%. VO2peak and peak MET were 1.2 ml/kg/min and 1 MET higher for CPX with minimal LVAD support than with full support. Peak LVEDD, SV and SV reserve (% change in SV from resting to peak) were 2 mm, 7.1 ml and 12% higher with minimal LVAD support (see table 1). One patient did not complete a turn-down test due to evidence of ischemia on initial CPX confirmed as a significant coronary artery stenosis. Sixty percent have been successfully explanted.

Conclusion(s): Combining CPX and echo is feasible and effective as part of LVAD pre-explant evaluation. The comprehensive assessment of cardiopulmonary and ventricular function may result in improved clinical decision making for LVAD explantation candidacy.

Selected CPX and Echo parameters

LVAD speed	VO2peak (ml/kg/m)	METs	VE/VCO2 slope	peak LVEDD (mm)	peak SV (ml)	SV Reserve (%)	PA diameter (mm)
High	17.2 ± 4.8	9 ± 3	38.7 ± 11.9	52.5 ± 4.0	61.4 ± 10.4	14	2.13 ± 0.08
Low	18.4± 5.5	10 ± 4	2.4 ±4.5	54.5 ± 7.5	68.5 ± 15.9	26	2.20 ± 0.14

LVAD: Left Ventricular Assist Device, VO2peak: Peak oxygen uptake, MET: Metabolic Equivalent, VE/VCO2: Ventilatory efficiency, LVEDD: Left Ventricular End Diastolic Diameter, SV: Stroke Volume, PA: Pulmonary Artery

P465

The role of BNP longitudinal monitoring as a biomarker of continuous flow pump (Heart Mate II) thrombosis

M Marketa Hegarova[1]; Z Dorazilova[1]; I Malek[1]; T Gazdic[2]; V Melenovsky[1]; J Kautzner[1]; T Marek[2]; J Maly[2]; I Netuka[2]
[1]*Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic*; [2]*Institute for Clinical and Experimental Medicine, Department of cardiovascular surgery, Prague, Czech Republic*

Background: Continuous flow pump malfunction due to the thrombosis in pts with end-stage HF represents life threatening complication. The clot entrapped or developed in the inflow and outflow cannulas or within the rotor entails diminished blood flow with consequent low cardiac output syndrome or thromboembolism. Timely diagnosis of this complication is critical for effectual therapeutic interventions - pump exchange or urgent OHTx in case of a suitable donor.

Purpose: The aim of our study was a retrospective evaluation of BNP dynamics in patients diagnosed with pump thrombosis.

Methods: Longitudinal laboratory measures (BNP levels, Lactate dehydrogenase (LDH) levels , plasma free Hemoglobin (pfHb), echocardiographic parameters alongiside with post pump explant inspection analysis outcomes were correlated.

Results: Between 1.1.2014 till 31.12.2016 4 pump exchanges and 2 urgent OHTx due to pump thrombosis were performed in our institution representing 6 % from 99pts implanted from 18.12.2013. The table 1 depicts laboratory findings in this patient subset. All pts presented with dyspnoea and BNP elevation at a time of

diagnosis. BNP levels ("BNP pump dysf.") increased significantly in contrast to stable status ("BNP on pump") and almost uniformely reached the levels prior to HM II implant (Tab. No. 1). Consequently,LDH levels in 5 pts LDH reached level greater than 3 times upper normal limit and 4 pfHb greater then 40g/l. We have revealed pathological "ramp" test in 5 pts. In 1 patient with restrictive cardiomyopathy, even reappearance of severe pulmonary hypertension has occured. Notably, after the pump exchange, BNP levels decreased to original levels in all patients. All patients but one are still alive and well, the only non-survivor one succumbed 7 months after the pump exchange due to intracerebral haemorrhage.

Conclusion: Abrupt substantial elevation of BNP levels may serve as early and cost-efficient noninvasive tool in suspected pump thrombosis diagnostic algorithm and should prompt further investigations, namely serial recording of LV unloading by means of stepwise pump speed "ramp" test.

Table No.1

Pt. No.	BNP before (ng/l)	BNP on pump (ng/l)	BNP pump dysf. (ng/l)	% BNP pump dysf./ before	BNP after pump exchange (ng/l)	LDH (μkat/l)	free Hb (g/l)
1	767,6	160,3	784,4	102,0	224,7	44,3	1127,3
2	1118,7	642,7	1209	108,0		34,2	688,5
3	1624,3	420,3	1362,3	84,0		24,7	51,0
4	1295,0	99,1	1241,3	96,0	278,1	15,9	84,0
5	1452,8	279,0	622,0	43,0	64,3	5,2	29,0
6	678,3	200,6	708,7	105,0	199,5	26,2	18,0

P466

Analysis of hospital mortality and primary graft dysfunction in urgent heart transplantation according to the type and duration of circulatory/ventricular assistance

R Raquel Lopez Vilella[1]; I Sanchez Lazaro[1]; MP Fuset Cabanes[2]; A Pajares Moncho[3]; L Donate Bertolin[4]; R Gimeno Costa[2]; I Moreno Puigdollers[3]; I Zarragoikoetxea Jauregui[3]; L Martinez Dolz[1]; A Castellanos Ortega[2]; R Vicente Guillen[3]; S Torregrosa Puerta[4]; L Almenar Bonet[1]

[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Intensive Care Unit, Valencia, Spain*; *[3]Hospital Universitario y Politécnico La Fe, Anesthesiology and Reanimation Department, Valencia, Spain*; *[4]Hospital Universitario y Politécnico La Fe, Cardiovascular Surgery Department, Valencia, Spain*

On behalf of: Heart Failure and Transplant Unit. Cardiology Department. La Fe

Introduction and Objetive: In recent years, the percentage of urgent transplantations has increased and short/medium-term mechanical assist devices have been widely used. This study aims at assessing hospital mortality and and primary graft dysfunction in urgent heart transplantation according to the type and duration of circulatory/ventricular mechanical assistance.

Methods: All patients who underwent an urgent heart transplantation with extracorporeal membrane oxygenation (ECMO) and with centrifugal pump were retrospectively and consecutively recruited, from the 21st October 2007 to the 20th December 2016. The sample was divided in 5 groups: group 1 (ECMO assistance for less than 5 days), group 2 (ECMO assistance for 5-10 days), group 3 (ECMO assistance for more than 10 days), group 4 (ECMO assistance and, afterwards, centrifugal pump) and group 5 (centrifugal pump).

Results: 72 patients were included in the study, 52 men (72%) and 20 women (28%), average age 51 ± 13 years. Ischemic dilated cardiomyopathy was the most frequent primary etiology (28 patients, 39%), followed by idiopathic dilated cardiomyopathy (25 patients, 35%). Table I describes the indication, days of stay in the critical care unit, hospital mortality and incidence of primary graft dysfunction in every group. The higher percentage of patients with mechanic ventilation corresponded to those with ECMO assistance up to 10 days (94% in group 1; 100% in group 5; $p < 0.001$). Global hospital mortality of urgent transplantation with circulatory/ventricular assistance was 25% (18 of 72 patients) while it was higher in those with ECMO for more than 10 days (9 patients, 35%), probably related to a higher incidence of primary graft dysfunction in this group (14 patients, 54%, $p < 0.01$).

Conclusions: Hospital mortality is high in urgent heart transplantation with prolonged circulatory/ventricular mechanical assistance, especially at the expense of a higher incidence of a primary graft dysfunction in these patients. The direct implantation of a centrifugal pump as a bridge to urgent trasplantation could identify a subgroup with a better prognosis.

Table I

Group	Number of patients	Primary etiology	Days in the critical care unit	Mechanic ventilation (n, %)	Hospital mortality (n, %)	Primary graft dysfunction
1	16	Idiopathic DCM (50%)	10,5 ± 8	14 (94%)	2 (12.5%)	1 (6,3%)
17(100%)218		Ischemic DCM (40%)	22 ± 15	17(100%)	4 (22%)	9 (80%)
3	26	Ischemic DCM (46%)	18 ± 11	17 (65%)	9 (35%)	14 (54%)
4	3	Ischemic DCM (33%)	15 ± 18	1 (33%)	1 (33%)	1 (33%)
5	9	Idiopathic DCM (67%)	9 ± 8	3 (33%)	2 (22%)	1 (12%)
p			0,001	0,74	0,001	0,42	0,011

MCD: Dilated Myocardiopathy

P467

Successful myocardial recovery of patients with heart failure on long-term left ventricular assist device HeartMate II in IKEM between 12/2006 to 10/2016

Z Dorazilova[1]; M Hegarova[1]; I Netuka[2]; Z Tucanova[2]; J Pirk[2]

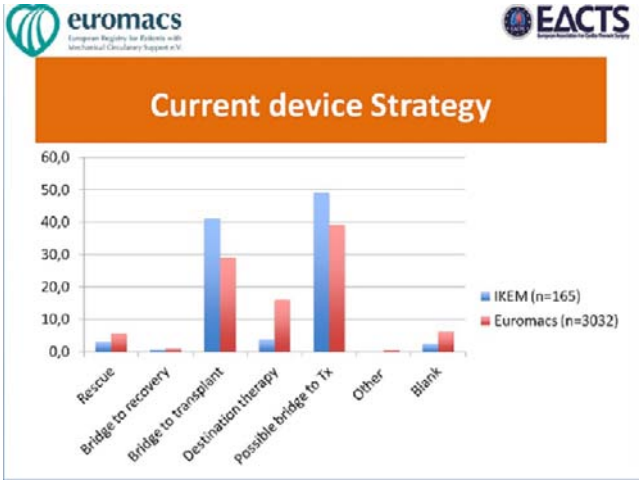
[1]Institute for Clinical and Experimental Medicine (IKEM), Department of cardiology, Prague, Czech Republic; *[2]Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiac surgery, Prague, Czech Republic*

Introduction: LVAD is used in treatment of end-stage heart failure (HF) to assist or completely replace function of failing left ventricle (LV) remain patients alive until heart transplantation. Mechanical circulatory support (MCS) leads in addition to positive effects in the failing heart at the cellular and structural levels. Drug therapy treatment of terminal HF may also contribute with max. titrated doses of drugs (ACEi, BB, spironolactone, AT1-B) known to enhance reverse remodeling of LV. But rarely myocardial recovery allows LVAD explantation, in INTERMACS registry is 1% incidence within a year of support implantation.

File characteristics: Among 208 pts with implantation LVAD HM II between 2006 and 2016 were 40(19%) men and women under 40 years old, with a short history of HF and diagnosis of non-ischemic cardiomyopathy, listed as bridge to transplant (BTT). The unloading of LV in the first year of out-patients follow-up leads to a predictable parameters affecting LV, i. e. regression of end-diastolic diameter (EDD), in isolated cases we also detected increasing of LV ejection fraction (EF), by echocardiographic exam., to value meeting one of the Harfield´s criteria for LVAD explantation.

Results: Six pts(5M) in our cohort of patients with implanted LVAD (2,4%), the average age was 34,8 years, 2 pts with the diagnosis of congenital heart disease, i. e. bicuspidal aortic valve with significant aortic insufficiency and 4 pts with dilated cardiomyopathy, during ambulatory monitoring are observed significant changes not only regression the average LV EDD from 70 ± 8 mm to 51 ± 6 mm, but also to improve the average LV EF from 22 ± 6% to 50 ± 4%. Given the persistence satisfactory parameters despite max. reduction in pump speed, i. e. 8000 RPM for several weeks, some of them testing max. oxygen consumption with exercise (VO2 max) > 18ml/kg/min and improvement of 6 MWDT > 450m (75% predicted value), was approached to explantation system by 2 ways. After 30 min of pump off on the operating room with unchanged echocardiographic measurements were first pts explanted classical technique of total MCS explantation with a patch on the apex of LV, the second way by the minimally invasive technique with an occluder or last time with a special plug on the opening after inflow cannula. The overall mechanical support time was 302 days (between 113 and 755). 5 pts(83%) were successfully discharged from our hospital for ambulatory monitoring, follow-up 7 to 60 months, one patient died one year after explantation due to IE (infection endocarditis) biological aortic valve replacement. One year after explantation the average LV EF was 40 ± 4%, the average LV EDD 54 ± 3 mm.

Conclusion: The results of our single center are consistent with published studies from abroad and international registries, confirmed possibility of reversal end-stage HF secondary to non ischemic cardiomyopathy in a group of young patients using LVAD and special drug therapy.



Strategy of LVAD implantation

P468

Sustained effects of interatrial shunt device on exercise hemodynamics in patients with heart failure with preserved and mid-range ejection fraction: 1-year efficacy data of the REDUCE LAP-HF trial

D Daniel Burkhoff[1]; I Lang[2]; F Gustofsson[3]; D Kaye[4]; J Bartunek[5]; J Van Der Heyden[6]; P Guerin[7]; S Shah[8]; A Kolodziej[9]; M Rosenberg[10]; L Sondergaard[3]
[1]Columbia University Medical Center, New York, United States of America; *[2]Allgemeines Krankenhaus Univesitäts Kliniken, Vienna, Austria*; *[3]Rigshospitalet , Copenhagen, Denmark*; *[4]The Alfred Hospital, Melbourne, Australia*; *[5]Olv Hospital Aalst, Aalst, Belgium*; *[6]St Antonius Hospital, Nieuwegein, Netherlands*; *[7]University Hospital of Nantes, Nantes, France*; *[8]Northwestern University, Chicago, United States of America*; *[9]4th Military Hospital, Wroclaw, Poland*; *[10]University Medical Center of Schleswig-Holstein, Kiel, Germany*

Funding Acknowledgements: Corvia Medical

Introduction: The REDUCE LAP-HF study showed that an interatrial shunt device (IASD) placed in patients with heart failure with preserved or mid-range ejection fraction improved symptoms and exercise (EX) hemodynamics through 6 months (6M) of treatment.
Purpose: We assessed sustainability of IASD effects in patients who underwent repeat EX hemodynamic tests at 12 months (12M).
Methods: 64 patients with heart failure and LV ejection fraction (EF) ≥ 40%, NYHA class II-IV, PCWP ≥15 mmHg at rest or ≥25 during symptom-limited supine bike EX and CVP < 15 mmHg at rest, were implanted with an IASD. All patients were followed for symptoms and EX hemodynamics at 6M. A subset of 18 patients underwent a second, optional repeat EX test at 12M.
Results (Table): Patients averaged 70 ± 8 yrs old with EF 45 ± 6. At baseline Ex markedly increased PCWP, CVP and PCWP-CVP. IASD yielded a shunt with Qp:Qs ˜1.3. Improvements in EX duration, EX intensity and peak cardiac output (CO) were observed at 6M. Following IASD implant, CVP increased, PCWP decreased and the PCWP-CVP gradient was lower at peak EX. Workload-normalized PCWP (PCWP/W/kg) decreased significantly. No changes in pulmonary artery mean pressure (mPAP) or pulmonary vascular resistance (PVR) were noted. All effects noted at 6M were sustained at 12M.
Conclusion: The Corvia IASD remains patent through 12M, with stable inter-atrial shunting. IASD increased exercised duration and reduced PCWP so that PCWP/W/kg decresaed; lower PCWP/W/kg values have been correleated with better outcomes. A randomized, blinded study is underway to further quantify the effects of this IASD. Funding: The study was supported by Corvia Medical.

Rest and Exercise Hemodynamics (n = 18)

	REST	Exercise				
	Baseline	6 Month	12 Month	Baseline	6 Month	12 Month
Qp:Qs	1.09±0.39	1.2±0.2*	1.3±0.3*			
Ex Duration (min)				8.2±3.4	9.7±3.2*	10.4±4.2*
Peak Watts				47.8±18.3	57.8±18*	55±15.5*
CO (L/min)	5.2±1.2	6.3±1.4*	6.8±1.8*	8.7±2.4	10.1±2.3*	11.4±2.9*
CVP (mmHg)	8.4±3.5	10.6±5.9	10.4±3*.	17.7±6.2	20.9±8.8	21.4±8.3*
PAM (mmHg)	24±8	23.3±6.6	26±8	45±11	45±11	45±13
PCWP (mmHg)	18.7±6.1	16.4±7.5	17.4±6	36.3±8.5	33.4±9.1	33.2±10.4
PCWP-CVP (mmHg)	10.4±4.7	5.8±2.4*	7±3.6*	19.3±7.1	12.5±4.8*	11.8±6.4*
PVR (Wood)	1.27±0.74	1.2±0.6	1.3±0.5	1.1±0.9	1.1±0.5	1.2±0.7
PCWP/ (Watts/Kg)				84.3±49.5	59.7±34.6*	62.2±34.4*

*p < 0.05

P469

Propensity matched comparison of two different continuous-flow left ventricular assist devices. A matter of device?

J Jonida Bejko[1]; T Bottio[1]; M Carrozzini[1]; M Comisso[1]; F Toto[1]; V Tarzia[1]; C Lombardi[2]; D Gregori[1]; M Metra[2]; G Gerosa[1]
[1]University Hospital of Padova, Padua, Italy; *[2]Civil Hospital of Brescia, Brescia, Italy*

BACKGROUND: Few comparisons of continuous-flow Left ventricular assist devices (LVADs) have been done. We compared two LVADs implanted at our center: Jarvik-2000 and Heartware-HVAD for early outcomes and further follow-up.
Materials and Methods: Between December 2008 and December 2015, 93 patients were implanted with the Jarvik-2000 (n = 52) or the Heartware-HVAD (n = 41). Outcomes were compared by propensity matching the patients.
Results: After propensity matching, two groups of 73 individuals, were similar for most of the preoperative covariates. The results are presented for original-data (OD) and propensity-adjusted-data (PAD). Similar survival of almost 60% at 2,5 years on Kaplan Meier estimation was recorded (p = 0.088 in OD and p = 0.99 in PAD). Driveline infection incidence was comparable in both groups (p = 0.97 in OD and 1 in PAD). Jarvik-2000 group presented significantly higher incidence of chronic Right-Ventricle-Failure (RVF) (OD p = 0.008; PAD p < 0.001). Higher incidence of VAD-thrombosis (OD p = 0.004, PAD p < 0.001), mortality due to gastrointestinal hemorrhage and hemorrhagic stroke (OD p = 0.2, PAD p = 0.001 and OD p = 0.2, PAD p = 0.001, respectively) was evidenced in HVAD group. The impact of devices on the major outcomes in multivariate analyses is described in Table 1. Different management and accuracy was recorded for the drivelines and the anticoagulation therapy, with much more attention by the HVAD patients and their caregivers. A predictive score for chronic RVF was constructed.
CONCLUSIONS: We believe that due to differences on efforts required for driveline management, antithrombotic therapy, and organ-function-recovery after LVAD implantation, HVAD results more appropriate for BTT support, while Jarvik-2000 for DT.

Impact of device on major outcomes.

Outcome	Original data OR (95% C.I.)	Propensity score adjusted OR (95% C.I.)
Chronic RVF	4.49 (1.37-14.66)	13.19 (2.43-70.71)
Driveline Infections total	0.98 (0.34-2.76)	1.00 (0.23-4.19)
Driveline infections over 6 months	3.03 (0.59-15.46)	2.04 (0.21-19.11)
Driveline infections within 6 months	0.44 (0.09-1.96)	0.47 (0.08-2.60)
Gastrointestinal Complications	1.97 (0.47-8.14)	0.71 (0.12-4.10)
Fatal Cerebral Events	0.37 (0.10-1.38)	0.05 (0.008-0.39)
30-days Mortality	0.67 (0.20-2.17)	0.44 (0.07-2.60)
90-days Mortality	9.21 (1.04-80.94)	5.14 (0.51-51.84)

Estimates are presented both unadjusted and adjusted by propensity score analysis. OR refers on Jarvik-2000 vs HVAD. The table shows Odds ratios and 95% CI. Abbreviations: RVF – right ventricle failure.

P470

Optimising implantable cardiac device prescriptions at the time of generator change

DC Thompson[1]; H Bolam[1]; J Waller[1]; N Andrews[1]; S Kirubakaran[1]; P Kalra[1]; G Morton[1]
[1]*Portsmouth Hospitals NHS Trust, Cardiology Department, Portsmouth, United Kingdom*

Introduction: Implantation of permanent pacemakers (PPM), implantable cardioverter defibrillators (ICD), cardiac resynchronisation therapy with (CRT-D) or without (CRT-P) defibrillators is increasingly common. Follow up, including arranging generator changes, is routinely carried out by cardiac physiologists with minimal physician input. However, many patients' clinical status will change during the lifetime of the device and a planned generator change presents an opportunity to review the original device prescription.
Purpose: To assess the impact of introducing screening pathways to identify patients who may need a change in their device prescription at the time of a generator change.
Methods: Single centre study evaluating the first 11 months after two pathways were implemented in October 2015. A cardiac physiologist led pathway for patients due PPM generator change used a short proforma assessing symptoms, QRS duration and percent of right ventricular (RV) pacing. Those with symptoms suggestive of heart failure, in particular breathlessness, and a prolonged native QRS or >40% RV pacing had an echocardiogram and multidisciplinary team (MDT) discussion within 2 weeks. If device upgrade was indicated the patient was reviewed in clinic to assess suitability. The second pathway aimed to ensure that all patients due an ICD/CRT-D generator change were discussed at MDT. Those with a change in clinical status that may affect the appropriateness of on-going defibrillator therapy were reviewed in clinic.
Results: 189 consecutive patients (145 PPM, 20 CRT-P and 24 CRT-D/ICD), mean age 77 yrs, were included. The pathways resulted in a change in the type of device therapy in 8 patients; 6/145 (4%) of those due PPM and 2/24 (8%) due CRT-D/ICD generator change. All PPM patients were proforma screened. 139/145 PPM patients (96%) went ahead with PPM generator change. 17 patients identified as potential candidates for upgrade to CRT had an echocardiogram. 5 of these had severe LV impairment and MDT/physician review. 4 patients were ultimately upgraded to CRT devices and for 1 patient the upgrade was deemed inappropriate. In 2 patients ongoing device therapy of any kind was felt to be inappropriate and no procedure was undertaken. 10/24 (42%) patients due a CRT-D/ICD generator change were reviewed at MDT. Of these 2 patients went on to have their devices downgraded from CRT-D to CRT-P after discussion.
Conclusions: Physiologist-led follow up can be enhanced with robust and quick screening to ensure that patients get the most appropriate device at the time of generator change. Excellent rates of PPM screening were achieved whereas ICD/CRT-D screening rates need to be improved. Around 1 in 20 of all patients had device prescription changed as a result of these pathways. With the significant morbidity associated with receiving an inappropriate device prescription, implementation of a simple screening process seems to be clinically justifiable.

P471

Hydrostatic pressure gradient implantable ultrafiltration device: a novel approach for extracellular fluids removal

Y Feld[1]
[1]*Sunnybrook Health Sciences Centre, Cardiology, Toronto, Canada*

Funding Acknowledgements: Paragate Medical LTD, Rambam Health Care Campus

Introduction: Diuretic therapies aiming to enhance fluid removal in chronic heart failure are limited due to diuretic resistance in about 30% of the patients. Intravenous diuretics, Dialysis and ultrafiltration as an alternative are associated with side effects, multiple visits of the patient in dedicated centers, and high cost.
Purpose: We suggest a novel approach, in which a permeable absorption chamber is implanted intraperitoneally. A negative hydrostatic pressure is induced in the absorption chamber by a pump, prompting fluids ultrafiltration through the peritoneal membranes into the chamber. The accumulated extracellular fluids are drained to the urinary system. In this work the feasibility of this novel concept is presented and compared to common peritoneal catheters.
Methods: A PTFE disk shaped absorption chamber with 15mm diameter one sided orifice was covered by semi-permeable membrane. The absorption chamber was implanted in the peritoneum cavity of six rats. A micro-catheter that drains the fluids from the chamber was routed to percutaneous port. Drainage and sampling of fluids were conducted for 4 weeks.
Results: Extracellular fluids were drained from the chambers at an average rate of 2.8 ± 0.4 cc/kg/hour during intermittent hydrostatic vacuum induction. The fluids electrolytes and proteins were comparable to the serum content. The average drainage rate remained stable throughout 4 weeks of follow up, ranging between 2 to 3.3 cc/kg/hr. Unlike designated chambers, catheter based designs drained only 0.4 ± 0.2 cc/min per square centimeter, 25 folds less than the membrane based devices.
Conclusions: Implantable absorption chamber enables systemic extracellular fluids removal through the peritoneal membranes, probably due to the direct interface between peritoneal and device's membranes. More broadly, this study suggests that an implantable absorption chamber may be used in fluids overload clinical conditions, providing future novel heart failure therapy.

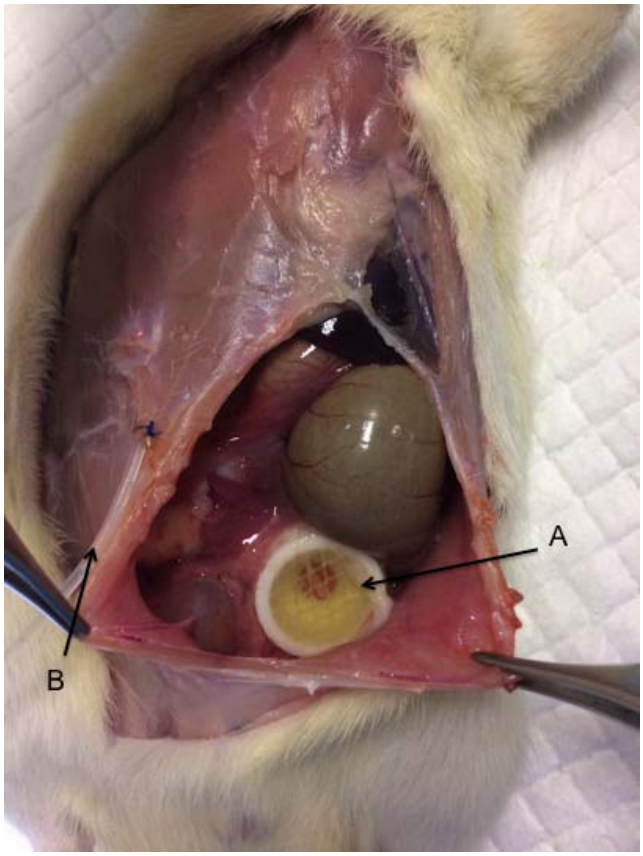


Fig 1: A. Chamber, B. micro-catheter

P472

Baroreflex activation therapy in congestive heart failure: an additional therapeutic option for many of our patients?

H Hazem Omran[1]; KJ Gutleben[1]; D Horstkotte[1]; G Noelker[1]
[1]*Herz- und Diabeteszentrum NRW, Ruhr-Universität Bochum, Clinic for Cardiology, Bad Oeynhausen, Germany*

Background: Baroreflex activation therapy (BAT) is a new promising treatment option for patients (pts) suffering from heart failure with reduced left ventricular ejection fraction (HFrEF) to improve functional status and quality of life. Yet it is unknown how many pts are suitable for this therapy. We aimed to evaluate these pts in a large heart center for eligibility.
Methods: A cross-sectional analysis was performed on all adult pts suffering from cardiomyopathy treated in different departments of our center between April 1st 2015 and March 31th 2016. Pts suffering from hypertrophic cardiomyopathy (HCM) or congenital heart disease (CHD) were excluded from analysis. To evaluate eligibility for BAT, pts were stratified according to the inclusion and exclusion criteria applied in the largest randomized controlled trial of BAT in HFrEF (HOPE4HF). Inclusion criteria mainly consisted of symptomatic HFrEF with New York Heart Association (NYHA) functional class III and left ventricular ejection fraction (LVEF) <35% on stable guideline-directed medical therapy. Pts who recently received ICDs (within 3 months) or CRTs (within 6 months) were excluded.
Results: Screening revealed a total of 1576 pts, after exclusion for HCM or CHD 1504 pts were included in the analysis. Of these, 107 pts (7.1 %) met the above

mentioned criteria and were eligible for BAT. Of those 78.5 % were male, 68 % had an ischemic etiology of HFrEF, and 64.5% had CRT. Other pts characteristics were (mean ± standard deviation) 63.3 ± 10.7 years of age, LVEF 27.6 ± 5%, systolic blood pressure 119.9 ± 15.6 mmHg. Main reasons for exclusion were NYHA < III in 762 pts (50.7%) and LVEF > 35% in 677 pts (45%). In particular, 107 of482 pts in NYHA class III with an LVEF < 35% were eligible for BAT (22.2%).
Conclusion: According to our single center analysis, up to 7.1% of all pts suffering from non-HCM/CHD-cardiomyopathy are suitable for additional device-based BAT. In particular, a high proportion of symptomatic pts with severely impaired LVEF seems to be eligible.

P473

Possibility of renal denervation in patients with chronic heart failure and reduced ejection fraction

A Kurlianskaya[1]; D Goncharik[1]; T Troyanova[1]; T Denisevich[1]; O Zotova[1]; T Osmolovskaya[1]; L Rachok[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background. The problem of the search of new approaches in treatment of chronic heart failure (CHF) still remains relevant because of its high incidence and severity. Catheter denervation of renal arteries (CDRA) is a promising direction in the treatment of patients with CHF and reduced ejection fraction.
Purpose: to explore an effectiveness of CDRA in patients with NYHA functional class III or IV (III-IV FC CHF), ejection fraction (EF) < 40% and sinus rhythm.
Methods: The study involved 30 patients. 15 patients with CHF, EF < 40%, QRS duration < 130ms underwent CDRA (group 1). 15 patients with CHF, EF < 40%, QRS duration ≥130ms underwent cardiac resynchronization therapy (CRT) (group 2). The examination of patients carried out at baseline and at 6 months after surgery; it included transthoracic echocardiography according to a standard methodology, determination of the level natriuretic peptide, 6 minutes walk test and assessment of quality of life using the Minnesota living with heart failure questionnaire.
Results: The study showed a decrease of end systolic and diastolic dimensions (ESD, EDD), end systolic and diastolic volumes (ESV, EDV), an increase in ejection fraction (EF) in both groups (table 1, Me (LQ; UQ)).
We also found an improvement in 6 minute walk test in both groups: from 245 (190-300) meters to 300 (210-380) meters in group 1 ($p < 0.05$) and from 243 (195-290) meters to 317 (215-420) meters in group 2 ($p < 0.05$). A decrease in the severity of CHF FC III to II NYHA was noted in 7 patients after CDRA (46,7%). A significant improvement of quality of life was revealed after surgical treatment in both groups that was confirmed by the median absolute value of the indicator of quality of life. In group 1 this parameter declined by 33%, in the group 2 - 42 %.
Conclusions: Effectiveness of CDRA is comparable to that after CRT in patients with III-IV FC CHF (NYHA), EF < 40% and sinus rhythm. Preliminary results of the study showed the positive dynamics of echocardiographic parameters that was accompanied by improved quality of life. CDRA is might to be considered as a method of treatment in patients with chronic heart failure, reduced ejection fraction and QRS duration < 130ms.

Dynamics of echocardiographic parameters

Parameters	At baseline (group 1)	After 6 months (group 1)	At baseline (group 2)	After 6 months (group 2)
ESD,mm	57,5 (52,0; 62,0)	53,0 (50,0; 59,5)	57,0 (55,0; 66,0)	57,0 (53,0; 64,0)
EDD, mm	70,5 (66,0; 75.0)	67,0 (65,5; 72,5)	70,0 (66,0; 75,0)	69,0 (65,0; 74,0)
ESV, ml (B-mode)	161,5 (123,0; 224,0)	125,0 (103,5; 181,0)	185,0 (177,0; 238,0)	168,0 (126,0; 214,0)•
EDV, ml (B-mode)	237,0 (197,0; 307,0)	218,0 (167,0; 271,5)	268,0 (238,0; 337,0)	252,0 (195,0; 315,0)•
EF, % (B-mode)	31,5 (28,0; 35,0)	39,5 (34,5; 42,0) •	32,0 (26,0; 34,0)	35,0 (32,0 42,0)•

•$p < 0.05$

P474

First steps and experience in cardiac contractility modulation in patients with heart failure with reduced ejection fraction: looking into the near future.

M Trukshina[1]; EA Lyasnikova[1]; VL Galenko[1]; MY Sitnikova[1]; TA Lelyavina[1]; IE Titova[1]; SV Urina[1]; VM Tishkova[1]; ML Abramov[1]; EN Mihaylov[1]; EI Zubarev[1]; MA Vander[1]; DS Lebedev[1]; K Simonova[1]; EV Shlyakhto[1]
[1]*Federal Almazov Medical Research Center , Heart failure, St.Petersburg, Russian Federation*

Purpose: Cardiac contractility modulation (CCM) presented a new promising treatment option in patients with heart failure with reduced ejection fraction (HFrEF) and narrow QRS complex.
Methods: 50 patients were screened and met the inclusion criteria: age > 18 yo, HFrEF, II-III fc NYHA, on OMT, sinus rhythm, QRS<120 ms, signed informed consent. 50 CCM devices (Optimizer IVs) were successfully implanted in the period from 20 Oct 2016 till 22Dec 2016, devices were programmed, patients were educated in device charging, discharged alive and were followed-up (FU) in outpatient HF clinic.
Results: Group of first 20 patients after the operation was analyzed, 15 of them were male, 50 ± 9,7 y.o., CAD- 14, DCM - 6, CHF-2,0 ± 0,5 fc, LV EF 25,0 ± 4,9 (17- 34%), QRS 100 ± 5,3ms (90-110), 6-MWT 375,0 ± 110,2m (92-550), cardiopulmonary exercise test Vo2- 16,7 ± 5,3 m/kg/min (9,1-32,8), NT-proBNP - 1159,0 ± 783,3 pg/ml (241-3453). Among early postoperative complications- 1 patient with device pocket infection lead to device deimplantation, 1 case of unstable angina and hospitalization in FU period, treated conservatively. All patients had 1 month FU with device programming, all patients were stable, no hospitalizations with HF decompensation occurred. HF fc remained unchanged in most patients, decrease in 2 patients, ECG on FU showed no QRS prolongation, arrhythmias or any conduction abnormalities, patients didn't feel uncomfortable during the time periods of stimulation, had good compliance in device charging at home.
Conclusions: Cardiac contractility modulation is newly recommended method of treatment in patients with HFrEF and narrow QRS complex with perspective of improving clinical status and heart contractility. Our first experience in patients with implanted CCM devices confirmed positive trend obtained even after short-time period of follow-up with good patients tolerance of stimulation, absence of arrhythmias and conduction abnormalities on ECG, compliance in therapy and technical aspects of regular device charging.

P475

Efficacy of adipose graft transposition procedure (agtp) in patients with a myocardial scar: rationale and design of the AGTP II trial.

P Paloma Gastelurrutia[1]; C Galvez-Monton[1]; J Nunez[2]; A Bayes-Genis[3]
[1]*Germans Trias i Pujol Health Sciences Research Institute, Badalona, Spain*; [2]*University Hospital Clinic of Valencia, Valencia, Spain*; [3]*Germans Trias i Pujol University Hospital, Badalona, Spain*

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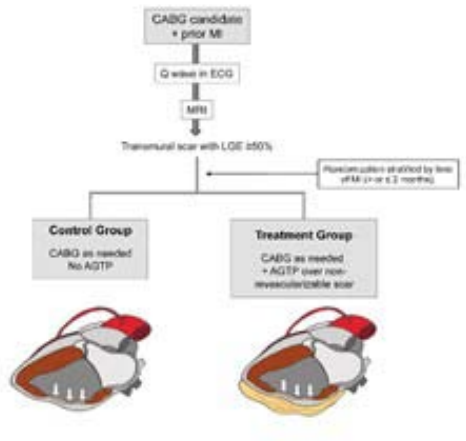
Background: Cardiac adipose tissue is a source of progenitor cells with regenerative capacity. Studies in rodent models have shown that the intramyocardial delivery of cells derived from this tissue improves cardiac function after myocardial infarct (MI). Thus, we have developed a new reparative approach for the damaged myocardium that integrates the regenerative properties of cardiac adipose tissue with tissue engineering. In brief, in our Adipose Graft Transposition Procedure (AGTP) we dissect a vascularized flap of autologous pericardial adipose tissue and position this over the myocardium scarred area. Following encouraging results for the AGTP in both an acute and chronic MI porcine model, we performed the AGTP-I clinical trial (NCT01473433, AdiFLAP Trial) to evaluate safety in patients with chronic MI undergoing coronary artery bypass grafting. There were no differences in safety, and trends in efficacy were detected. This favorable safety profile warranted progression to a larger trial, that we now describe.
Design: The AGTP-II Trial (NCT02798276) is an investigator-initiated, prospective, randomized, controlled, multi-center study to assess the efficacy of AGTP in patients with a non-revascularizable MI. The primary endpoint is change in necrotic mass ratio, with secondary endpoints that include changes in functional parameters and safety outcomes.
Implications: The trial is expected to provide a novel, effective, and technically simple technique for patients that have a non-revascularizable MI with no other therapeutic options.

	Selection and randomization	Surgery	Follow-up		
Visit	1	2	3	4	5
Time	0	0	1week post-discharge	3 months post-discharge	1 year post-discharge
Informed consent &Inclusion/exclusion criteria	x				
Vital signs	x	x	x	x	x
Physical exam	x		x	x	x
Blood test	x		x	x	x
ECG	x		x	x	x
Holter	x			x	x
Cardiac MRI with gadolinium	x			x	x
HF signs and symptoms	x		x	x	x
Adverse events	x	x	x	x	x
Surgical procedure		x			



Flowchart of the clinical trial design.

P476

Preoperative levosimendan is associated with lower mortality in high-risk cardiac surgery patients with systolic left ventricular dysfunction - results of a single-centre retrospective study

M Mihai Stefan[1]; M Luchian[1]; I Marinica[1]; A Paunescu[1]; S Marin[1]; D Filipescu[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Anaesthesia and Intensive Care II, Bucharest, Romania*

Background: Levosimendan was shown to improve cardiac function in various settings. Furthermore, perioperatively, via its pleiotropic effects, it offers a conceptual framework to improving outcomes.
Purpose: We assessed the effects of preoperative administration of levosimendan in patients with left ventricular (LV) dysfunction, scheduled for coronary artery bypass grafting (CABG) and mitral valve repair/replacement (MVR).
Methods: We performed a retrospective analysis of our practice. Patients undergoing elective CABG plus MVR, with LV dysfunction (LV ejection fraction < 50%), between January 2011 and December 2013, were reviewed. Part of the anaesthesia team adhered to preoperative administration of levosimendan in high-risk cases. These patients were admitted in the ICU before surgery and infused levosimendan at a dose of 0.1 μg/kg/min, for 8-12 hours prior to surgical incision. The others received conventional therapy. Retrospective data were collected using written and electronic registries.
Results: Forty-two patients with LV dysfunction underwent elective CABG plus MVR in the two year period. Of these, 2 were excluded due to severe bleeding, 17 received levosimendan and 23 received conventional therapy. Patients treated with levosimendan had a lower in-hospital mortality, despite a pre-operative lower median LVEF (Table 1). The ICU length of stay (LOS), duration of mechanical ventilation, acute kidney injury and new-onset atrial fibrillation rates were not different between the two groups.. A trend toward less need for intra-aortic balloon pump assistance was noted.
Conclusions: Levosimendan shows promise when administered preoperatively in high-risk cardiac surgery. Further research is warranted for establishing whether this translates into better outcomes.

Table 1

Age	59 (55-67.5)	61 (58-67.50	NS
Male sex (%)	12 (70.6)	20 (87)	NS
Preoperative EF (%)	35 (30-40)	45 (40-50)	< 0.001
EUROscore	6.5 (5-8)	5 (3.5-6.5)	0.027
ICU LOS(days)	5 (5-8)	5 (3.5-8)	NS
Hospital LOS(days)	12 (9-14)	11 (8-13)	NS
Need for IABP no/(%)	2 (11.8)	6 (26)	0.088
Duration of ventilation (hours)	18 (13-20)	16 (15-21)	NS
AKI no/(%)	5 (29.4)	9 (39.1)	0.150
New-onset atrial fibrillation no/(%)	7 (41.2)	7(30.4)	0.133
Mortality no/(%)	0 (0)	4 (17.4)	0.040

P477

Incidence and risk factors for cytomegalovirus infection after heart transplantation

E Elizabet Mendez Eirin[1]; E Barge- Caballero[1]; MJ Paniagua-Martin[1]; R Marzoa-Rivas[1]; D Couto-Mallon[1]; G Barge-Caballero[1]; A Canizares[1]; JM Vazquez-Rodriguez[1]; MG Crespo-Leiro[1]
[1]*University Hospital A Coruna, Cardiology, Corunna, Spain*

Background: Cytomegalovirus (CMV) remains the most common viral pathogen in heart transplant (HT) recipients. The prevalence of asymptomatic CMV infection and disease is variable among centers, partially related to immunosuppressive protocols and therapeutic strategies to treat CMV.
Purpose: The purpose of this study was to analyze the incidence of CMV infection and disease during the first year after HT and to identify potential risk factors for CMV infection.
Methods: A retrospective, single-centre study analyzed 222 HT recipients (mean age 54 ± 12 years, 80 % men) who underwent transplantation between February 2001 and December 2011. All patients received universal prophylaxis and were prospectively monitored for CMV infection during the first year after HT. Preemptive treatment was applied to patients with asymptomatic CMV infection. Risk factors for CMV infection were investigated using Cox regression analysis.
Results: The asymptomatic CMV infection incidence rate in the first year post-transplant was 71.9 [95% confidence interval (95% CI), 61.1-84.0] per 100 person-years and the CMV disease incidence rate was 9.6 [95% CI, 5.9-14.7] per 100 person-years. Multivariate analysis showed that donor-recipient CMV discordant serostatus (donor positive and recipient negative [D+/R−]), recipient age, diabetes mellitus, pre-transplant circulatory support and the use of tacrolimus, were independently associated with increased risk of CMV infection (table 1).
Conclusions: In our series, the CMV infection rate was similar to that seen in previous studies, but the progression to overt CMV disease was very low. The donor and recipient CMV serological status, recipient age, diabetes mellitus, pre-transplant circulatory support and the use of tacrolimus, were indentified as independent risk factors for developing CMV infection.

Multivariate Analysis for Risk Factors

Risk factor	HR	CI 95%	p
Recipient age	1.021	1.00-1.039	0.020
Diabetes mellitus	1.862	1.135-3.053	0.014
Risk serology group	1.922	1.196-3.088	0.007
Pre-transplant circulatory support	1.586	1.059-2.376	0.025
Tacrolimus	1.635	1.133-2.360	0.009

P478

Surgical ventricular reconstruction: an alternative therapy in heart failure and coronary artery disease

N Nicolas Lalor[1]; A Acosta[1]; M Vrancic[1]; F Piccinini[1]; M Camporrotondo[1]; L Rodriguez[1]; M Diez[1]; D Navia[1]
[1]*Cardiovascular Institute of Buenos Aires (ICBA), Buenos Aires, Argentina*

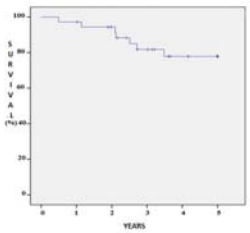
Surgical ventricular reconstruction is a specific procedure for the management of heart failure with left ventricular remodeling caused by coronary artery disease. Heart transplant is an option when nothing else is appropriate. However, limited donors, waiting list may be long, presence of comorbidities or advanced age, restrict this therapy for few patients. In this scenario surgical ventricular reconstruction with CABG is an alternative treatment for patients with coronary anatomy suitable for such surgery, left ventricular ejection fraction of 35% or less, ventricular volumes increase and extended akinesia or dyskinesia.

Objetives: Evaluate hospital mortality, changes in ventricular volumes, ejection fraction and long term follow up of quality of life and survival in those patients who underwent CABG with surgical ventricular reconstruction.

Methods: Between 2001 and 2015, 4503 patients were undergo CABG. Of these patients, 251 had severe left ventricular systolic dysfunction, 45 (1%) underwent CABG with surgical ventricular reconstruction, selecting those with left ventricular ejection fraction of 35% or less, ventricular enlargement (defined by LVESV > 55 ml/m2) and symptoms in NYHA heart failure class III-IV. The follow-up continued through December 31, 2016. The median follow-up for all surviving patients was 60 months. The median age was 58 years, and 43 of the 45 patients were men, 33% diabetic, with body mass index of 27 and 15% had chronic renal insufficiency. The median left ventricular ejection fraction was 25%. The median end-systolic volume index was 92 ml per square meter of body-surface area. Multivessel coronary artery disease was present in all patients.

Results: Perioperative mortality occurred in 5 patients (11%). During the follow up for 5 years, 13 patients died (5 of sudden death and 8 due to non cardiovascular causes). Today out of living 27 patients, 21 have a good and 6 regular quality of life as measured by Duke Index. One patient underwent heart transplant. Table 2 showed changes in ventricular volumes and ejection fraction. The surgical ventricular reconstruction showed an acceptable perioperative mortality with good survival and adequate quality of life in the long run. This strategy should be considered as a potential treatment in heart failure.

	Preoperative	Posoperative	P value
LVESV (ml)	180(146/200)	110 (87/133)	< 0.001
LVEDV (ml)	240(220/290)	150(133/197)	< 0.001
LVESV/m2	92 (76/102)	59 (44/68)	< 0.001
EF(%)	25 (18/31)	37 (30/42)	< 0.001



BETA BLOCKERS

P479

Metoprolol and carvedilol in heart failure - different mechanisms, similar effect?

AD Farcas[1]; AF Cocoi[2]; FP Anton[1]; MA Stoia[1]; CM Goidescu[1]; IL Gavrila[2]; LA Vida-Simiti[1]
[1]*University of Medicine and Pharmacy, Cardiology Department of County Clinical Emergency Hospital, Cluj Napoca, Romania*; [2]*Cardiology Department of County Clinical Emergency Hospital, Cluj Napoca, Romania*

Background: N-terminal pro-brain natriuretic peptide (NT-proBNP), some specific types of white blood cells (WBC) and neutrophil/lymphocyte ratio (NLR) are well-known independent predictors of the worse outcome of HF patients. Plasma cathecolamines induce redistribution of the leukocitary formula [by the activation of lymphocytic β2-adrenoreceptors (AR) and neutrophilic α-AR]. By inhibiting AR (α, β1, β2), beta-blockers (BB) reverse this effect improving the outcome of HF patients.

Purpose: Our goal was to evaluate if BB specificity for different types of AR influences the positive effect on the WBC differential formula (WBC-DF) redistribution in HF patients.

Methods: Our study enrolled 278 patients with HF, NYHA class II-IV (62.7 ± 15.2 yrs), 51.8% male and 48.2% female. After signing an informed consent, all patients were clinically evaluated and blood was drawn to measure: NT-proBNP, total WBC, WBC- differential formula and NLR. The study methodology was approved by the Ethical Committee. Statistical data processing was performed with SPSS.

Results: There were no significant differences regarding gender and age between groups with and without BB treatment. On admission, 61.16% of patients had a BB in their chronic therapy: 44.13% - metoprolol and 26.25% - carvedilol. There was no significant difference in the number of lymphocytes ($p = 0.074$) and granulocytes ($p = 0.910$); our results show that NLR (7.58 ± 13.30 vs 4.58 ± 3.74, $p = 0.045$) and NT- proBNP (2669.01 ± 5923.49 vs 865.82 ± 2476, $p = 0.004$) were significantly higher in patients without BB therapy compared with those with BB at admission. The BB dose on admission was negatively correlated with NT-proBNP plasma level. NT proBNP levels (1079.14 ± 283.48 vs 2328.56 ± 1439.29, $p = 0.005$) were significantly lower in patients treated with metoprolol compared with those treated with carvedilol. In fact, the type and dose of BB used is responsible for 6.1% and 5.9% of the variability in the number of lymphocytes and neutrophiles, respectively. The patients that received treatment with at least 100 mg metoprolol/day had a higher number of lymphocytes (1.74 ± 01.44 vs 1.13 ± 0.63, $p = 0.029$), but not of granulocytes ($p = 0.06$) compared with those treated with lower doses, with a smaller reduction in the values of NLR (4.55 ± 4.77 vs 3.77 ± 2.03, $p = 0.049$). Patients treated with at least 25 mg carvedilol, had a smaller number of lymphocytes (0.73 ± 0.59 vs 0.92 ± 0.76, $p = 0.029$) and a greater number of granulocytes (4.6 ± 3.94 vs 2.29 ± 2.10, $p = 0.026$) respectively, compared with those treated with lower doses, with an increase in the value of NLR (7.10 ± 4.41 vs 2.46 ± 1.09, $p = 0.01$). Although both BB have the same rehospitalisations rate during the 12 months follow-up.

Conclusion: Although their influence on NT-proBNP plasma levels and the NLR was found to be different, both BB improves the outcome of HF patients.

P480

Beta-blockers in chronic heart failure registry FAR NHL and one year follow up

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

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Background: Beta-blockers (BB) decrease morbidity and mortality and are part of the first line treatment of heart failure with reduced ejection fraction (HFrEF).

Purpose: We aimed to compare influence of beta-blocker doses and other factors on hospitalization and mortality in heart failure patients with systolic dysfunction.

Methods: The data come from the FARmacology and NeuroHumoraL activation multicenter registry (FAR NHL). Patients with left ventricle ejection fraction (EF LK) under 50 % who were at least one month stable were included.

Results: 1100 patients were included, mean age 65 years, 80.8 % were male. From those receiving beta blockers 20 % received low dose (LD), 57 % medium dose (MD) and 17 % high dose (HD). 6.2 % of patients were not treated by BB at all (O). The higher the blood pressure (BP; LD 124/77; MD 129/80; HD 132/82 mm Hg, $p < 0.001$), EF LK (LD 29.5; MD 30.5; HD 32.0 %, $p = 0.003$), creatinine clearance rate (CrCl; LD 78.7; MD 87.8; HD 91.1 ml/min, $p = 0.001$) or patients weight (LD 83.2; MD

88.7; HD 93.5 kg, p < 0.001) was, the higher dose of BB they received. The lower NT-proBNP was, the higher dose of BB they got (LD 767; MD 456; HD 314 pg/ml, p < 0.001). At one year follow up 83 patients (7.5 %) died and 436 were hospitalized (39.6 %). The higher was beta-blocker dose, the lower was number of death (O 13.2; LD 10.7; MD 6.3; HD 5.9 %) and hospitalized patients (O 45.6; LD 43.8; MD 38.0; HD 38.0 %). 17 patients underwent orthotopic heart transplant.
Conclusions: According to FAR NHL registry, nearly 94 % of HFrEF patients received BB. But only 17 % received the high dose of BB. The more severe illness was, defined by lower BP, CrCl, EF LK, body weight, or higher NT-proBNP, the lower dose of BB patients got and tolerated. The higher was BB dose the lower was all-cause mortality and hospitalization number.

P481
The reasons of no-prescription of beta blockers in patients with chronic heart failure

K Kaoutar Kharbouche[1]; I Elhaddad[1]; K Kharbouche[1]; L Azouzi[1]; R Habbal[1]
[1]*chu ibn rochd, cardiology, casablanca, Morocco*

Background: Beta-blockers are the cornerstone in the treatment of chronic heart failure (HF), and are actually recommended as first line therapy for systolic HF. However, betablockers (BB) have a low prescription rate comparatively to ACEI and several surveys have documented that many patients are not offered treatment or are not titrated to target doses.
The aim of our study is to analyzed different reasons for no-prescription of b-blockers in CHF and we propose an approach to improve their level of prescription.
Methods: and results: 1600 patients with chronic heart failure and left ventricular dysfunction (mean age: 74 + 11 years) were included into the study between 2009 and December 2014 in our heart failure therapeutics unit, 81 % of patients were being treated with BB. 31% of patients were at the target dose,52% were at ≥50% target dose and 19 % don't received BB, bradycardia and cardiac decompensation were the principal reason of non prescription in 25,6% and 42,1% respectively, then hypotension in 23,8%, and chronic obstructive pulmonary disease in 8,4%.
Conclusion: Given the effectiveness and the potential benefit of beta blockers in terms of mortality, 19% of no-prescription remains high, we need to broaden their prescriptions through some precautions; we propose an approach to improve the level of prescription.

P482
Beta-blockers and lipid profile in heart failure - statins as a dealmakers. Results from CIBIS ELD study.

D Dragana Stanojevic[1]; S Apostolovic[1]; D Kutlesic Kurtovic[1]; R Jankovic-Tomasevic[1]; S Salinger-Martinovic[1]; T Kostic[1]; D Djordjevic-Radojkovic[1]; M Damjanovic[1]; V Mitic[1]; V Atanaskovic[1]; S Dakic[1]; E Tahirovic[2]; HD Dungen[2]
[1]*Clinic for Cardiovascular Diseases, Nis, Serbia*; [2]*Charite - Campus Virchow-Klinikum, Department of Internal Medicine-Cardiology, Berlin, Germany*

On behalf of: CIBIS ELD

Background: Beta-blockers (BB), which decrease sympathetic nervous system activation via β-adrenergic receptor antagonism, are effective in reducing cardiovascular morbidity and mortality in heart failure (HF). Despite these clinical benefits, many physicians are still reluctant to prescribe BB because of perceived negative metabolic effects including dyslipidemia. Numerous studies have established that vasodilating β-blockers (as carvedilol) are associated with more favorable effects on glucose and lipid profiles than nonvasodilating β-blockers (as bisoprolol).
Purpose: The aim of our study was to investigate the influence of BB dosage increase during 12 weeks on lipid profile [total cholesterol (HOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG)].
Methods: In CIBIS ELD study 876 patients with HF were enrolled. The average age was 72.88 ± 5.49 years, 62.4% men. Prior to randomization participants had to be clinically stable and to be BB naive or on ≤25% of the guideline-recommended target or equivalent dose. We up-titrated BB (bisoprolol or carvedilol) up to maximum tolerated dose, over three months.
Results: At the beginning of the study 62.7% of patients had dyslipidemia, however, 52.8% of them had statin in their therapy and 2% fibrates or ezetimibe. We found significant difference in lipid profile before and after increase of BB blocker dose (HOL: 5.35 vs. 5.25 mmol/L, p < 0.01; HDL: 1.32 vs. 1.29 mmol/L, p = n.s.; LDL: 3.32 vs. 4.36 mmol/L, p < 0.05, TG: 1.83 vs. 4.12 mmol/L, p < 0.01). In patients on bisoprolol, there were no significant differences before and after BB titration in HOL, HLD, LDL, TG values (5.27 vs. 5.18 mmol/L; 1.29 vs. 1.27 mmol/L; 3.22 vs. 3.88 mmol/L; 1.85 vs.4.35 mmol/L).
In patients on carvedilol, however, difference was found in HOL, HDL, LDL, TG values (5.43 vs. 5.31 mmol/L, p = 0.02; 1.35 vs. 1.32 mmol/L, p = n.s.; 3.42 vs. 4.82 mmol/L, p = n.s; 1.80 vs. 3.91 mmol/L, p = 0.014).
Conclusions: Our study patients on carvedilol (which has a mild alpha activity that has been shown to exert a beneficial effect on a patient's lipid profile) had significant increase in TG and significant decrease in HOL levels, partially due to fall in HDL fraction, at the end of study. In patients on bisoprolol similar changes were detected in lipid profile, however they were statistically insignificant. Interestingly, only half of our HF patients with dyslipidemia were treated with lipid lowering agents. Although BB interfere with lipoprotein metabolism they should not be withheld/sub-dosed in HF patients. Use of statins and other lipid lowering agents should be also encouraged in HF patients with dyslipidemia.

P483
Acute coronary syndromes without ST-segment elevation and beta-blocker therapy: benefit for preserved or mid-range ejection fraction?

L Reis[1]; A Fernandes[1]; C Lourenco[1]; R Teixeira[1]; M Madeira[1]; P Dinis[1]; J Ribeiro[1]; L Puga[1]; I Almeida[1]; M Costa[1]; J Nascimento[1]; L Goncalves[1]
[1]*University Hospitals of Coimbra, Coimbra, Portugal*

Introduction: According to the guidelines of the European Society of Cardiology, it's suggested to prescribe beta-blockers (BB) after an acute coronary syndrome (ACS) without ST-segment elevation (NSTEMI) in patients (P) with reduced left ventricular ejection fraction (LVEF) to reduce mortality, recurrence of infarction and hospitalization for heart failure (HF). However, there is limited evidence of the role of BB after an NSTEMI ACS with preserved (LVEF≥50%) or mid-range LVEF (40-49%).
Objectives: To evaluate the prognostic impact of BB in P with preserved or mid-range LVEF after an NSTEMI ACS.
Methods: Retrospective and single center study of 533 P (69 ± 13 years, 67% male) admitted to a cardiac intensive care unit over 4 years. All patients underwent transthoracic echocardiography with LVEF assessment and were categorized into 2 groups: Group 1 (G1: LVEF 40-49%, N=131) and Group 2 (G2: LVEF≥50%, N=402). In each group we stratified the P who received BB on discharge and we compared them with P that were discharged without BB in relation to the primary objective (reinfarction and cardiovascular mortality) and secondary objectives (reinfarction, readmission of HF, and total mortality).
Results: The P from G1 and G2 who received BB on discharge were similar to P who were discharged without BB were similar in terms of baseline characteristics, such as demographics, cardiovascular risk factors, history of coronary disease and chronic kidney disease. They also showed similar Killip class, creatinine, troponin I, NT-proBNP and Grace Scores on admission. There were no differences in coronary angiography (acute occlusion, number of lesions or PCI) and in-hospital medical treatment.
We found that P of the G1 treated with BB didn't present statistically significant differences in relation to the primary composite objective (55% vs 56.2%, p = 0.93), re- infarction (17.2% vs 14.3%, p = 0.78) and mortality (36% vs 25%, p = 0.39) compared to those not treated with BB. However, we observed that they had a lower percentage of re-admisson for HF (12.9% vs 35.7%, p = 0.030). In multivariate analysis, BB prescription was an independent predictor for reduced readmission due to HF (OR 0.26, p = 0.035).
With respect to the P of the G2, we observed that the P under BB didn't present significant differences regarding the primary composite objective (77% vs 23%, p = 0.97) and secondary objectives [re-infarction (67% vs 33%, p = 0.089), readmission for HF (89% vs 11%, p = 0.083) and mortality (74% vs 25%, p = 0.63)].
Conclusions: The use of BB in NSTEMI ACS P with preserved LVEF did not show to have a prognostic impact. However, in NSTEMI ACS P with mid-range LVEF, the use of BB was shown to be associated with a reduction in readmission for HF.

METABOLISM – DIABETES MELLITUS – OBESITY

P484
Relationship between cardiac autonomic neuropathy and heart rate variability in young patients with type 1 diabetes mellitus

D Denis Medvedev[1]; VP Efimova[2]; YK Mahamat[1]; AF Safarova[1]; ZHD Kobalava[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*; [2]*City Clinical Hospital No 64, City Clinical Hospital 64, Moscow, Russian Federation*

Background: Type 1 diabetes mellitus (T1DM) is an independent risk factor for the development of various cardiovascular disorders, such as dysrhythmias, sometimes leading to fatal outcomes. Cardiac autonomic neuropathy (CAN) is considered to be the main mechanism responsible for the onset of rhythm disturbances. Assessment of heart rate variability (HRV) is one of the methods applied to determine the predictors of CAN development.
Purpose: To study HRV parameters in young T1DM patients without coronary artery disease (CAD) and history of dysrhythmias.
Material and methods: The study included 71 patients with T1DM [mean age 28.7

years, 41 (57%) male, mean glycated hemoglobin 9,9% (84 mmol/mol), mean body mass index 23,4 kg/m2, mean diabetes duration 6,84 (0,5; 24) years, mean NT-proBNP 62,62 pg/ml, mean EF (modified Simpson method) 61,7%]. All patients underwent stress treadmill testing, 24-hour Holter ECG monitoring (Shiller). We calculated time domain HRV parameters (SDNN, SDNNi, rMSDD, pNN50, circadian index - CI).
Results: Time domain HRV measurements in all studied patients deviated from the lower limit of age-specific reference values (SDNN — 368.82 ± 29.82 ms, SDNNi — 108.51 ± 10.35 ms, rMSDD — 182.17 ± 47.52 ms, and pNN50 — 12.34 ± 10.20 %). Mean 24-hour heart rate was 97.60 beats/min [58; 147]. Time domain HRV parameters were significantly higher in women: SDNN (420.71 ± 85.31 vs 127.40 ± 38.83), SDNNi (139.42 ± 23.49 vs 62.4 ± 22.14), rMSDD (275.43 ± 62.4 vs 51.60 ± 23,11), p < 0,001 for all comparisons. Men had higher pNN50 values than women (15.16 ± 10.08 vs 10.01 ± 38.00, p < 0.05). Mean CI was 1.15 ± 0.94. CI was rigid (< 1.2) in 59.15%, normal (1.24 – 1.42) – in 18.31%, and mildly decreased (1.20-1.23) in 22.53% cases. All participants were in sinus rhythm. Paroxysmal supraventricular tachycardia was detected in 2.8%, incidental ventricular tachycardia in 1.4%, supraventricular premature beats in 22.5%, ventricular premature beats in 8.5%, wandering atrial pacemaker in 11.3%, and second-degree sinoatrial block in 2.8% of patients.
Conclusion: The identified abnormalities in time domain HRV measures and impairment of CI rigidity in young T1DM patients without CAD and history of dysrhythmias indicate the development of CAN.

P486

The relationship between glycemic control and preclinical diastolic dysfunction in patients with type 2 diabetes mellitus or prediabetes

A Albana Doko Banushi[1]; I Refatllari[1]; V Paparisto[1]; N Kuka[2]; S Qirko[1]; A Goda[1]
[1]*University Hospital Center Mother Theresa, Tirana, Albania*; [2]*Polytechnic University, Tirana, Albania*

Background: Type 2 diabetes mellitus (T2DM) is associated with an increased risk of micro and macrovascular complications. The relationship between heart failure and glycemic control is not well established.
Purpose: The aim of this study was to assess relationship between diastolic dysfunction (DD) and glycemic control (HbA1c) in patients (pts) with T2DM or prediabetes (PD) with preserved systolic function (left ventricular ejection fraction ≥ 55%), asymptomatic for heart failure and without overt heart disease.
Methods: 170 diabetics or prediabetic pts (57.8 ± 8.3 years, 52% male) without evident heart disease, and 43 age and sex–matched control subjects were enrolled. Conventional echocardiography, tissue Doppler parameters and HbA1c were measured for all pts.
Results: In pts with good glycemic control (HbA1c 7-7.9%) the risk of DD was 3.6 fold higher (95% CI, 1.03-12.5; p = 0.044) compared to those with tight glycemic control (HbA1c < 7%), in pts with poor glycemic control (HbA1c 8-8.9%) the risk of DD was 5.9 fold higher (95% CI, 1.79-19.57; p = 0.004), and in pts with HbA1c ≥9% this risk was 8.2 fold higher (95% CI, 2.70-25.25; p < 0.001). A logistic regression analysis showed glycemic control as an independent predictor of DD (OR= 1.36; 95% CI, 1.17-1.59; p <0.001).
Conclusion: Our findings support the idea that glycemic control is strongly related with preclinical DD in patients with T2DM or PD.

P487

Weight gain was associated with better prognosis after hospital discharge in patients admitted with heart failure

RM Rosa Maria Agra Bermejo[1]; S Eiras[1]; A Varela Roman[1]; R Gonzalez Ferreiro[1]; I Gomez Otero[1]; A Castro[2]; F F Casanueva[2]; JR Gonzalez Juanatey[1]
[1]*UNIVERSITY CLINICAL HOSPITAL OF SANTIAGO DE COMPOSTELA, DEPARTMENT OF CARDIOLOGY, SANTIAGO DE COMPOSTELA, Spain*; [2]*University Hospital of Santiago de Compostela, Endocrinology, Santiago de Compostela, Spain*

Background: Obesity and overweight were defined as factors associated with higher survival in heart failure (HF) patients. However, the prognostic value of weight gain after hospital discharge in patients admitted with HF is unknown.
Purpose: The aim of our study was to know the consequence of BMI changes in patients after being hospitalized for HF.
Methods: We selected 86 patients consecutively admitted in our hospital for acute HF. Body Mass Index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. BMI was determined during the admission and 6 months after. The mean of follow up was 416 ± 256 days. Cox regression analyses were employed to calculate the estimated hazard ratio (HR) of death or readmission with 95% confidence interval (CI).
Results: During the follow-up 46 patients gained weight, 26 loosed weight and 14 maintained weight. Patients who had gained weight were represented by those with more frequently non-ischemic HF (54.2%). The Kaplan Meir curve showed that patients who gained weight have lower mortality and readmissions during the follow-up compared with the other two groups (p < 0.05). The Cox regression analyses showed that weight gain proved to be a protective factor against death and/or readmission (HR=0.377; CI 95% 0.168-0.847, p = 0.048).
Conclusions: Weight gain after hospital discharge in patients admitted for HF determines a better outcome in terms of death and/or readmission.

P488

Rosuvastatin dose-dependently improves flow-mediated dilation, but reduces adiponectin levels and insulin sensitivity in hypercholesterolemic patients

K Kwang Koh[1]
[1]*Gachon University, Incheon, Korea Republic of*

Background: Increased risk of type 2 diabetes noted with statins is at least partially explained by HMG-coenzyme A reductase inhibition. We investigated vascular and metabolic phenotypes of different dosages of rosuvastatin in hypercholesterolemic patients.
Methods: This was a randomized, single-blind, placebo-controlled, parallel study. Age, sex, and BMI were matched among groups. Forty-eight patients were given placebo, and 47, 48, and 47 patients given rosuvastatin 5,10, and 20 mg, respectively daily during a 2 month treatment period.
Results: Rosuvastatin 5,10, and 20 mg dose-dependently and significantly improved flow-mediated dilation (34, 40, and 46%) after 2 months therapy when compared with baseline (P < 0.001 by paired t-test) or when compared with placebo (P < 0.001 by ANOVA), and increased insulin (median % changes; 16, 20, and 20%, respectively) and glycated hemoglobin levels (mean % changes; 2, 2, and 3%, respectively), and decreased adiponectin levels (mean % changes; 3, 9, and 14%, respectively) and insulin sensitivity (mean % changes; 2, 3, and 4%, respectively) after 2 months therapy when compared with either baseline (all P < 0.05 by paired t-test), or when compared with placebo (P=0.006 for insulin, P=0.012 for glycated hemoglobin, P=0.007 for adiponectin, and P=0.002 for insulin sensitivity by ANOVA).
Conclusions: Rosuvastatin treatment dose-dependently and significantly resulted in decreasing insulin sensitivity and increasing ambient glycemia by reducing adiponectin levels and increasing insulin levels in hypercholesterolemic patients.

P489

Significance of speckle-tracking in identifying subclinical myocardial injury of young patients with Type1 Diabetes mellitus without cardiovascular disease.

Y Makhamat[1]; VP Efimova[1]; DM Medvedev[1]; AF Safarova[1]; ZHD Kobalava[1]
[1]*RUDN University, propaedeutics of internal diseases, Moskow, Russian Federation*

The Aim: to study the importance of speckle-tracking to identify the presence of subclinical myocardial injury of young patients with Type1 Diabetes mellitus without cardiovascular disease and determine the impact of Type1 Diabetes mellitus (DM) on systolic and diastolic function of left ventricle of young patients without clinical of cardiovascular disease.
Methods: Young patients with Type1 DM (N=71) and without cardiovascular disease admitted to the therapy department of Moscow city clinical hospital 64 in the period 2015 till 2016 years were included in the study. Treadmill test was conducted to all patients in order to exclude coronary disease, and also NT-proBNP, glomerul filtration rate (GFR), urine albumin-to-creatinine ratio (uACR). EchoCG examination including analyses of LV EF (modified Simpson method) and global longitudinal systolic deformation (GLS) by speckle-tracking (VIVD 7 Dimencion, GE).
The Results: Mean age was 28,7 years, 57% men, mean glycated hemoglobin 9,9% (84 mmol/mol), mean body mass index 23,4 kg/m2, and mean diabetes duration 6,84 [0,5; 24], mean NT-proBNP 62,62 pg / ml, mean LV EF 61,7%. Subclinical systolic disfunction, that is defined as GLS < 20%, was observed in 63,3%(45/71) cases. Left ventricular mass, left ventricular end-systolic volume and left ventricular end-systolic diameter were higher in patients with GLS < 20% than in patients with GLS>20% (p < 0,05). Furthermore EF, MAPSE; APSE were considerably lower in patients with GLS < 20% than in patients with GLS>20% (p < 0,05). Left atrium volume index(LAVI) was higher in patients with GLS < 20%, but the difference was statistically insignificant(p < 0,01). Left ventricular diastolic disfunction with slow relaxation(grade1) was observed in 5,6 (4/45) patients with insulin-dependent diabetes (Type1) and GLS < 20% as opposed to patients with GLS>20%,who the diastolic disfunction wasn't found. While making the multivariate and regressive analysis it was identified that albuminuria is an independent determining factor of /' (β = 0,22, < 0,001) with the age (β = 0,36, < 0,001) and female(β = 0,24, < 0,004), and also GFR correlate closely with GLS (= 0,28, < 0,006). The strong correlation was found for GFR and GLS (χ2 12,9, < 0,05, r=0,62), and delicate correlation for index albumin/creatinine (χ2 2,47, < 0,05, r=0,26). At the same time the relative risk of GLS decreasing with GFR < 90ml/min/1,73m2 increased in 2,8 (OR 2,8; 95% CI:

1,4;3,2;p < 0,001), with GFR < 60ml/min/1,73m2 increased in 3,4 (OR 3,4; 95% CI: 2,3 ;4,6 ;p < 0,001).
Conclusions: 1) Global longitudinal systolic LV myocardial deformation, identified by speckle-tracking is a sensitive marker of subclinical myocardial injury of young patients with Type1 DM without cardiovascular disease.
2) The correlation was identified: GFR < 90ml/min/1,73m2 with the decreasing global longitudinal systolic LV myocardial deformation (GLS < 20%)

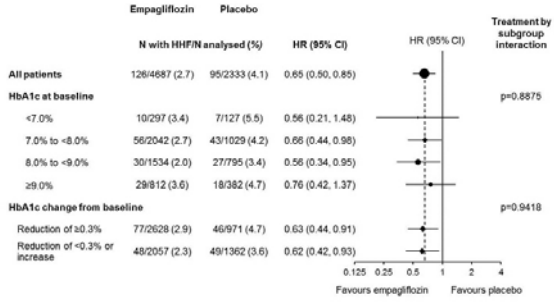
P490

Reduction in hospitalisation for heart failure with empagliflozin is consistent across categories of baseline HbA1c and change in HbA1c: results from the EMPA-REG OUTCOME trial

D Fitchett[1]; SE Inzucchi[2]; C Wanner[3]; M Mattheus[4]; JG George[5]; HJ Woerle[4]; B Zinman[6]
[1]St. Michael's Hospital, Division of Cardiology, University of Toronto, Toronto, Canada; *[2]Section of Endocrinology, Yale University School of Medicine, New Haven, United States of America*; *[3]Department of Medicine, Würzburg University Clinic, Würzburg, Germany*; *[4]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*; *[5]Boehringer Ingelheim Ltd, Bracknell, Berkshire, United Kingdom*; *[6]Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, and Division of Endocrinology, University of Toronto, Toronto, Canada*

Funding Acknowledgements: The EMPA-REG OUTCOME® trial was funded by the Boehringer Ingelheim & Eli Lilly and Company Diabetes Alliance.

Background: In the EMPA-REG OUTCOME trial, EMPA given in addition to standard of care significantly reduced the risk of hospitalisation for heart failure (HHF) vs placebo (PBO) (HR 0.65; 95% CI 0.50, 0.85) in patients with type 2 diabetes (T2DM) and established CV disease. We investigated whether baseline HbA1c or change in HbA1c influenced the effect of EMPA on HHF.
Methods: Patients were randomised to receive EMPA 10 mg, EMPA 25 mg, or PBO. Background glucose-lowering therapy was to remain unchanged for 12 weeks and then be adjusted to achieve glycemic control according to local guidelines. HHF was analysed in the pooled EMPA group vs PBO by categories of (1) baseline HbA1c (< 7.0%; 7.0 to < 8.0%; 8.0 to < 9.0%; ≥9.0%) and (2) change in HbA1c from baseline to the last value in the trial (reduction of ≥0.3%; reduction of < 0.3%). Differences in risk between treatment groups were assessed using a Cox proportional hazards model.
Results: A total of 7020 patients were treated. Median observation time was 3.1 years. The benefit of EMPA vs PBO on HHF was consistent irrespective of baseline HbA1c or change in HbA1c from baseline to the last value before HHF (for patients with HHF) or the last value in the trial (for patients without HHF) (Figure).
Conclusion: In patients with T2DM and established CV disease, the reduction in the risk of HHF with EMPA vs PBO was largely independent of baseline HbA1c and the change in HbA1c from baseline to the last value before HHF or the last value in the trial.



P491

Sacubitril/valsartan and metformin, enemies in the metabolic control of diabetic patients with heart failure?

CN Perez Garcia[1]; D Enriquez[1]; TS Luque[1]; A Travieso[1]; C Olmos[1]; I Vilacosta[1]; D Vivas[1]; J Higueras[1]; M Perez[1]; C Macaya[1]; R Bover[1]; A Esteban[1]
[1]Hospital Clinic San Carlos, Instituto Cardiovascular Clínico San Carlos, Madrid, Spain

Introduction: The combination of sacubitril/valsartan (SV) is a new therapeutic step in patients with heart failure (HF) and reduced ejection fraction, after showing an improvement in functional class, reduced hospital admission due to HF and lower cardiovascular mortality. The increasing commercialization of this drug in the context of a patient with multiple comorbidities and chronically polymedicated, favors the interaction among commonly used drugs, with the possible clinical repercussion that this implies. This phenomenom has already been objectified in pharmacokinetic and pharmacodynamics studies in relation to certain drugs such as omeprazole, ethinylestradiol and metformin.
We report the clinical case of a type 2 diabetic patient on oral treatment with metformin, with introduction of SV in the previous 6 months.
Objective: Through a case report, it is hypothesized that the clinical interaction between metformin and SV has clinical repercussions in terms of a worse metabolic control as well as the role of oral antidiabetic titration in this situation.
Material and Method: We report the case of a type 2 diabetic patient treated with metformin and followed by the HF Unit of a Spanish tertiary hospital for non-ischemic dilated cardiomyopathy since 2013. Because of a LVEF of 32% and persistence of symptoms despite optimized medical treatment with beta-blockers, ARB and eplerenone, SV is introduced at doses of 24/26 mg b.d. In a periodic review at 3 months, the patient reports worse control of capillary glycemia levels after starting the new drug. Pre- and postprandial capillary glycemias are recorded and compared to the previous records in by a non-parametric test (Wilcoxon test for paired data), as well as comparison of glycated haemoglobin (HbA1c) figures. In addition, titration of metformin and new control in 3 months of HbA1c is carried out.
Results: At the moment the patient referred the poor glycemic control, capillary glycemia data were recorded for breakfast, lunch and dinner weekly. So that the preprandial glycemias in breakfast, lunch and dinner before SV were 128.3 ± 4.41, 106.2 ± 13.99 and 122 ± 10.04 mg/dL, respectively. After the onset of SV, these values corresponded to values of 178 ± 14.3, 160 ± 19.4 and 168 ± 19.7 mg/dL with p value < 0.05 in all cases.
As regards postprandial glycemias before SV: 127.8 ± 5.5, 122 ± 8.99 and 116.5 ± 9.7 mg/dL, which increased significantly after SV (193 ± 27.8, 163 ± 20.1 and 161 ± 27 mg/dL, with p < 0.05). Likewise, of a HbA1c of 7% prior to SV, it rises at the third month to 7.9%.
Metformin is tritated (from 850 mg b.d. to 850 mg t.d) reaching three months later a HbA1c of 7.2%.
Conclusions: SV could contribute by pharmacokinetic interaction with metformin to poorer metabolic control of diabetic patients with HF. Metformin dose titration is a suitable option to balance the long term effects of an irregular metabolic control in this subset of patients.

P492

Gender-specific association between metabolic parameters and arterial stiffness in young healthy subjects

E Ekaterina Starostina[1]; I Strazhesko[1]; YA Orlova[1]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation

Early vascular aging (increased arterial stiffness) is associated with cardiovascular diseases, mainly with heart failure. There are some studies demonstrated the association between arterial stiffness, measured as increased pulse wave velocity (PWV), increased central blood pressure (BPao), and metabolic disturbances. Several observational studies suggest that the metabolic syndrome increases the cardiovascular morbidity in women to a greater extent than in men. There are no enough data about gender-specific differences in relationship between increased arterial stiffness and metabolic status.
The objective of this study was to determine the sex-specific association between the metabolic parameters and arterial stiffness in young adults.
Material and methods: We investigated 258 healthy young adults, mean age 18,8 ± 1,6 years, 47% male. PWV and BPao were measured with ambulatory blood pressure monitoring device BPLab Vasotens (BPLab, Russia). Waist circumference (WC), body mass index (BMI), fasting plasma glucose (FG), insulin resistance (HOMA-IR) and lipid profile were measured using routine methods.
Results: Only in women PWV was significantly related to BMI (r=0.34; P < 0.001), WC (r=0.39; P < 0.001), high-density lipoprotein level (r=-0.13; P < 0.01). In both genders PWV was significantly associated with triglycerides, FG, HOMA-IR. All measured metabolic parameters were significantly related to systolic and diastolic BPao in men and women. In women unlike men fasting plasma glucose, HOMA-IR were independent predictors of PWV in a multiple stepwise regression model.
Conclusions: The metabolic parameters are associated with arterial stiffness more severely in women than in men. More importance to women with metabolic disturbances should be given.

P493

Risk of hospitalization for decompensated heart failure in patients with BMI <25 and reduced ejection.

DR Fernando Manzur Jattin[1]; DR Hugo Corrales Santander[1]; DR Rafael Herrera[1]
[1]Centro de Investigaciones Biomédicas - Universidad de Cartagena, Facultad de Medicina, Cartagena, Colombia

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Introduction: obesity is a risk factor for the development of heart failure (HF), however, recet evidence has shown that there is more frequency negative outcomes in hospitalized patients with normal or low body mass index (BMI) than in patient with overweight or obesity, when both groups have decompensated heart failure, a phenomenon called "obesity paradox in HF" (1, 2).
Aim: To estimate the association of BMI in patients with heart failure reduced with ejection fraction (HFrEF) and its impact on hospitalization due to decompensation in a health institution in Colombia.
Methodology: A prospective cohort study was conducted between April 2014 and April 2015, in patients with HFrEF, collected at the outpatient department of Cardiology of a hospital in the city of Cartagena. Patients with BMI <25 kg / m2 and unexposed BMI> 25 kg / m2, without renal impairment, were considered as exposed cohorts. Quarterly follow-up was done by external consultation and telephone follow-up for variables of interest.
Results: 52 patients were included in the present study. 65.4% were male, average age 65.4 ± 13.8. 51.9% (27/52) of patients had BMI greater than or equal to 25kg/m2 and 48.1% (25/52) with BMI <25kg/m2. Of these, 18.5% (5/27) and 20% (5/25) had a smoking habit, 7.4% (2/27) and 4.0% (1/25) alcoholism, 77.7% (21/27) and 92% (23/25) hypertension, 14.8% (4/27) and 24% (6/25) diabetes, 14.8% (4/27) coronary heart disease, 85.1% (23/27) and 68% (17/25) had class Functional NYHA I and II, 14.8% (4/27) and 32.0% (8/25) class III and IV. The incidence rate of hospitalization in exposed patients was 43 x 1,000 person-years and 30.8 x1,000 person years for the non-exposed. The risk of hospitalization for decompensated heart failure in patients with BMI <25 was RR: 1.4 [95% CI 0.7-2.6], and attributable risk was 15%.
Conclusion: Having normal or low weight increased 1.4 [95% CI 0.7-2.6] times the risk of hospitalization for decompensated heart failure. It is suggested to carry out analytical studies with larger sample size.

HEART FAILURE IMAGING

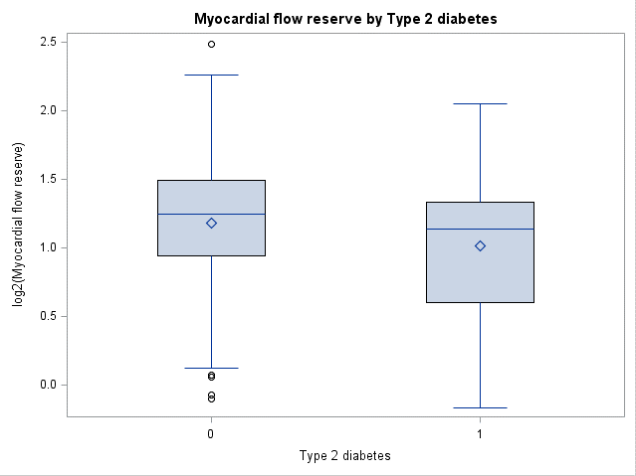
P494

Myocardial perfusion is reduced in patients with type 2 diabetes as comorbidity to non-ischemic systolic heart failure

C Byrne[1]; P Hasbak[2]; A Kjaer[2]; JJ Thune[3]; L Koeber[1]
[1]Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; [2]Rigshospitalet - Copenhagen University Hospital, Department of Clinical Physiology, Nuclear Medicine & PET, Diagnostic Centre, Copenhagen, Denmark; [3]Bispebjerg University Hospital, Department of Cardiology, Copenhagen, Denmark

Funding Acknowledgements: The Danish Heart Foundation

Introduction: Patients with non-ischemic systolic heart failure (HF) often have reduced myocardial blood flow without significant coronary atherosclerosis. However, the mechanism is unknown. Similarly, patients with type 2 diabetes (T2DM) have reduced myocardial perfusion compared with control persons. To our knowledge, no one has previously compared myocardial perfusion in patients with non-ischemic systolic HF with and without T2DM.
Purpose: To investigate whether changes in myocardial perfusion are associated with T2DM in patients with non-ischemic systolic HF.
Methods: In a prospective cross-sectional study, we scanned patients with non-ischemic systolic HF with and without T2DM with 82-Rubidium positron emission tomography (PET)/computed tomography (CT) at rest and adenosine-induced stress, thereby obtaining the myocardial flow reserve (MFR=stress flow/rest flow); 28 patients with T2DM and 123 without T2DM were included. We used a general linear model (GLM) procedure for multiple regression analysis of explanatory variables.
Results: Patients with T2DM had a median age of 68 years (range 60-75 years) and 21.4% were women. The patients without T2DM had a median age of 68 years (range 62-72 years) and 33.3% were women. Patients with T2DM had higher body mass index (BMI) than patients without (29.9 vs. 26.5 kg/m2; P=0.02). Blood glucose measured right before the scan was higher among patients with T2DM (6.2 vs. 5.7 mmol/L; P=0.03) and hypertension was more common in this group (50.0 vs. 26.8%; P=0.02). Also more patients with T2DM were treated with cholesterol lowering medication (60.7 vs. 35.0% P=0.02). Apart from these variables, the two groups were similar. In a multivariable analysis, including sex, age, BMI, T2DM, atrial fibrillation during scan, left bundle branch block, hypertension, N-terminal pro-brain natriuretic peptide and left ventricular mass, MFR was 16 % lower in patients with T2DM compared with patients without (Estimate 0.84; 95% confidence interval [CI] 0.71 to 0.996; P=0.04). In addition MFR was significantly lower in patients with atrial fibrillation during scan (Estimate 0.69; 95% CI 0.57 to 0.82; P < 0.001) and MFR increased with increasing BMI (Estimate 1.02; 95% CI 1.00 to 1.04; P=0.01).
Conclusion: Patients with T2DM and systolic HF had lower myocardial flow reserve compared with HF patients without diabetes. This indicates that T2DM is an independent impairing factor to the coronary microvascular function in patients with non-ischemic systolic HF.



Myocardial flow reserve by diabetes

P495

Right ventricular function and volumes evaluated by cardiac magnetic resonance in dilated cardiomyopathy patients

A Sousa[1]; T Pinho[2]; L Lopes[3]; O Azevedo[4]; S Amorim[2]; M Campelo[2]; A Madureira[2]; F Rocha Goncalves[1]; JC Silva Cardoso[1]; E Martins[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; [2]H. São João, Porto, Portugal; [3]Garcia de Orta Hospital, Lisbon, Portugal; [4]Guimares Hospital, Guimaraes, Portugal

On behalf of: FATIMA investigators
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Introduction: Right ventricular (RV) function assessed by echocardiography has found to have prognostic value in ischemic and idiopathic dilated cardiomyopathy (DCM).
Purpose: We aimed to analyze RV function and volumes, assessed with cardiac magnetic resonance imaging (CMR) in a cohort of patients with genetically characterized DCM and to evaluate their clinical relevance.
Methods: National multicentric study of consecutive patients with idiopathic and familial DCM that underwent a comprehensive CMR study as part of their diagnostic work-up. Ventricular volumes and ejection fraction (EF) were measured using dedicated software. Patients underwent extensive clinical evaluation, ECG, 24h-Holter, echocardiogram and molecular analysis (using next-generation sequencing combined with Sanger sequencing).
Results: 80 patients were included, 52% men, mean age at diagnosis 38 ± 14 years, with 55% of familial cases (44 patients corresponding to 38 families). At least one genetic variant was found in 21%. Mean left ventricular (LV) end-diastolic volume was 127 ± 36 mL/m2 and LVEF 34 ± 12%. Most patients were in NYHA class I (52%). In median follow-up of 41 (IQR 64) months a composite of death/heart transplant/aborted sudden cardiac death was documented in 12% of them.
Mean RVEF, RV end-diastolic and RV end-systolic volumes were 52 ± 11%, 78 ± 22 mL/m2 and 39 ± 21 mL/m2, respectively. Reduced RVEF was found in 45% of patients and enlarged RV end-diastolic and RV end-systolic volumes in 9% and 32%, respectively.
There were no differences in RV parameters between patients with familial or idiopathic DCM or between patients with or without a genetic variant.

Patients with previous hospitalizations presented lower RVEF (48 ± 12% vs 55 ± 10%; p = 0.014) and patients with non-sustained ventricular tachycardia and right bundle brunch block presented higher RV end-diastolic (85 ± 21 mL/m2 vs 72 ± 16 mL/m2, p = 0.015; 112 ± 34 mL/m2 vs 76 ± 21 mL/m2, p = 0.002) and RV end systolic volumes (44 ± 17 mL/m2 vs 33 ± 12 mL/m2, p = 0.014; 68 ± 37 mL/m2 vs 37 ± 19 mL/m2, p = 0.004).
A moderate positive correlation was found between RVEF with LVEF (r=0. 452, p < 0.001) and RV end-systolic volume with left atrium diameter (r=0.414, p = 0.001). There were no differences in RV parameters according to the presence of late gadolinium enhancement or noncompaction criteria.
In univariate analysis RVEF was predictor of the composite outcome (OR 1.066, 95%CI [1.004-1.132], p = 0.036).
Conclusions: RV dysfunction was frequent in DCM patients and was associated with some features of worse clinical outcome. RV functional profile didn't vary between idiopathic or familial DCM or according to molecular results.

P496

A cardiac magnetic resonance-based study on the involvement of the myocardial extracellular matrix in the pathophysiology of hypertensive heart failure

R Eiros Bachiller[1]; A Gonzalez Miqueo[2]; J Pueyo Villoslada[3]; G Bastarrika Aleman[3]; JJ Gavira Gomez[1]; O Beloqui Ruiz[4]; MF Landecho Acha[4]; MU Moreno Zulategui[2]; J Barba Cosials[1]; A Diaz Dorronsoro[1]; I Colina Lorda[4]; B Lopez Salazar[2]; S Ravassa Albeniz[2]; J Diez Martinez[2]
[1]University of Navarra Clinic, Department of Cardiology and Cardiac Surgery, Pamplona, Spain; *[2]CIMA, University of Navarra, Program of Cardiovascular Diseases, Pamplona, Spain*; *[3]University of Navarra Clinic, Department of Radiology, Pamplona, Spain*; *[4]University of Navarra Clinic, Department of Internal Medicine, Pamplona, Spain*

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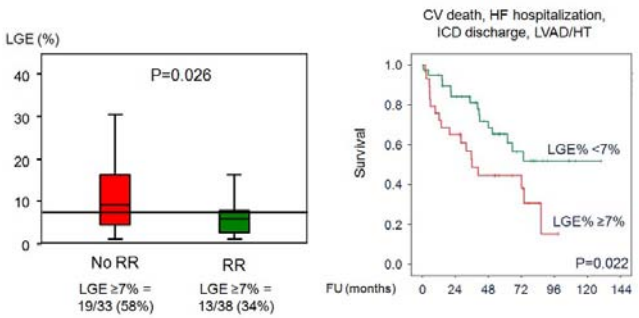
Background: The assessment of alterations in the extracellular matrix (ECM) by cardiac magnetic resonance (CMR) has shown promising results in different cardiomyopathies, mostly in stage of clinical heart failure (HF). However, little is known about its value in patients at earlier stages of the syndrome.
Purpose: To assess alterations of the myocardial ECM by CMR in patients with arterial hypertension with (stage C) or without (stage B) clinical HF and to analyse their associations with parameters of left ventricular (LV) function.
Methods: The study included 37 hypertensive patients without coronary artery disease or suspected cardiac amyloidosis. Eighteen of them presented LV hypertrophy and/or diastolic dysfunction with no clinical symptoms of HF (stage B) and the remaining 19 presented clinically overt HF (stage C). A group of 10 healthy subjects was included as a control group for CMR parameters. In the CMR study the extracellular volume (ECV) was calculated after T1 mapping to assess the presence of diffuse interstitial fibrosis, and the late gadolinium enhancement (LGE) positive mass was quantified using a signal intensity threshold of 5 standard deviations (SD) above the mean remote myocardium to assess the presence of microscars.
Results: ECV was increased in both stage B (24.40 ± 0.47%; P < 0.05) and stage C (28.84 ± 0.68%; P < 0.001) patients compared with control subjects (21.42 ± 0.54%), being higher (P < 0.001) in stage C patients than in stage B patients. LGE was also increased in both groups of patients compared to control subjects (control: 1.18 ± 0.19 g; Stage B: 3.98 ± 0.72 g; stage C: 6.78 ± 1.51 g; P < 0.01 and P < 0.001, respectively), but there were no significant changes between the two groups of patients. Whereas ECV was correlated with the E:E′ ratio (r=0.447; P < 0.05), LGE was correlated with the LV end-diastolic volume (r=0.449; P < 0.05) and LV ejection fraction (r=-0.455; P < 0.05) in all patients. Both ECV (r=0.458; P < 0.05) and LGE (r=0.511; P < 0.01) were correlated with NT-proBNP in all patients. All these associations were independent of age and gender. Conclusions: CMR-assessed alterations in the myocardial ECM of hypertensive patients are present before overt HF develops and are associated differently with LV function (i.e., the increase in ECV is associated with diastolic dysfunction and the increase in LGE is associated with LV remodelling and systolic dysfunction). Therefore, it is suggested that the involvement of myocardial ECM in the pathophysiology of hypertensive HF is variable and depends on the type of alteration considered (i.e., diffuse interstitial fibrosis or microscars).

P497

Late gadolinium enhancement, reverse remodeling and prognosis in patients with non-ischaemic dilated cardiomyopathy and moderate-to-severe systolic dysfunction

A Alberto Aimo[1]; A Barison[2]; A Ortalda[3]; V Castiglione[1]; C Passino[1]; M Emdin[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*; *[3]San Raffaele Hospital of Milan (IRCCS), Milan, Italy*

Background: Reverse remodeling (RR) is defined as the recovery from left ventricular (LV) dilation and systolic dysfunction following guideline-recommended medical treatment for heart failure (HF). The absence of late gadolinium enhancement (LGE) at cardiac magnetic resonance (CMR) has been reported to predict the occurrence of RR in patients with idiopathic dilated cardiomyopathy (DCM).
Purpose: In the broader setting of non-ischaemic DCM (NIDCM), and among patients with moderate-to-severe systolic dysfunction, we explored the relationship among LGE (visually assessed or automatically quantified), RR, and prognosis.
Methods: The inclusion criteria were: diagnoses of NIDCM and stable, chronic HF; two CMR examinations within a maximum interval of 5 years; left ventricular ejection fraction (LVEF) < 45% at baseline CMR. The exclusion criteria were coronary artery disease, recent myocarditis (< 6 months), severe primary valvular disease, untreated hypertension, cardiac amyloidosis, estimated glomerular filtration rate < 30mL/min. RR was defined as a ≥15% reduction of LV end-systolic volume index across the two CMR examinations. The follow-up started at the second CMR examination. The endpoint was a composite of all-cause death, hospitalization for either HF or ventricular arrhythmias, appropriate implantable cardiac defibrillator discharge, ventricular assist device implantation or heart transplant.
Results: Seventy-one patients were enrolled (age 57 ± 14 years, 43 males [61%], LVEF 35% [interquartile range - IQR 27-41%]). NIDCM was idiopathic in 45 patients (63%). Median previous disease duration was 3 month [IQR 1-7 months]. LGE was found in 42 patients (59%). LGE mass was 9 g [IQR 5-18 g], and LGE% was 7% [IQR 3-12%].
Thirty-eight patients (54%) developed RR. The absence of LGE at baseline was univariate predictor of RR (OR 0.338 [95% CI 0.125-0.914]; P=0.033). LGE extent (percentage of LV mass) was significantly lower in the RR subgroup, and emerged as univariate predictor of RR (OR 1.112 [95% CI 1.022-1.210]; P=0.013). At ROC analysis, the best LGE cut-off for RR prediction was 7% (area under the curve - AUC 0.657, sensitivity 65%, specificity 62%).
Over a 42-month [IQR 15-73] follow-up, the endpoint occurred in 36 patients (51%). LGE presence was univariate predictor of the primary endpoint (OR 3.087 [95% CI 1.151-8.284]; P=0.025). Also LGE extent predicted this endpoint (OR 1.109 [95% CI 1.018-1.208]; P=0.018). The optimal LGE cut-off was again 7% (AUC 0.676, sensitivity 65%, specificity 66%). Kaplan-Meier analysis confirmed that patients with LGE < 7% had a significantly better prognosis (Figure).
Conclusions: In patients with NIDCM and moderate-to-severe systolic dysfunction, the absence of LGE at baseline predicts subsequent RR. Among patients with LGE, LGE extent < 7% is a predictor of RR, as well as of better prognosis.



Abbreviations: CV, cardiovascular; HF, heart failure; HT, heart transplant; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVAD, left ventricular assist device; RR, reverse remodeling

P498

Echocardiographic assessments of left atrial mechanic as potentially predictors of worse prognosis during six months follow up in STEMI patients

G Krljanac[1]; D Trifunovic[1]; M Asanin[1]; L Savic[1]; D Matovic[2]; L Jovanovic[2]; G Stankovic[1]; V Vukcevic[1]; I Mrdovic[1]
[1]Clinical Centre of Serbia, Cardiology Clinic, Medical Faculty, Belgrade, Serbia; *[2]Clinical center of Serbia, Cardiology Clinic, Belgrade, Serbia*

Parameters of left atrial mechanic could be substrate of worse prognosis and incidence of major cardiac events (MACE) defined as death, re-infarction, emergency revascularization, ventricular arrhythmias (VT and/or VF) and heart failure which need emergency re-hospitalization in STEMI patients (pts) treated with primary percutaneous interventions (PPCI). Aim: To determine left atrial mechanic parameters as

predictors of MACE during 6 month follow up (FU). We studded conventional echo parameters and parameters of left atrial mechanics: strain (S LA) and strain rate (Sr LA). Method: 99 consecutive STEMI pts treated with PPCI were prospectively included. Echo examination performed on day 4 ± 2 (VIVID 9GE, Echo PAC Ver 113). Results: 12/99 (12.1%) of all pts had MACE during 6 month FU. Parameters of left atrial mechanic: first positive peak (S LAs) and second positive peak (S LAa) LA longitudinal strain, strain rate parameters during systole (Sr LAs), and late diastole (Sr LAa) were significant predictors as well as conventional echo parameters. (table 1). The largest area under the ROC had LA vol index (area 0.724, p = 0.009, 95% CI 0.662-0.938) for cut off 18.43ml/m2, Sn 78%, Sp 60%. LVEF had lower area under the ROC (0.256, p = 0.035, 95% CI 0.088-0.423) and lower Sn 65% and similar Sp 64% for cut off LVEF 46.5%. S LAs (ROC 0.271; p = 0.048, 95% CI 0.066-0.477) had significant Sn 71%, and Sp 72% for cut off 16.45%. Sr LAs (ROC 0.247; p = 0.029, 95% CI 0.073-0.420) had low Sn 57%, but higher Sp 86% for cut off -0.755 s-1. Sr LAa (ROC 0.772, p = 0.019, 95% CI 0.593-0.952), for cut off -1.085 had the better Sn 71% and Sp 80%. Conclusion: During first months after PPCI period the left atrial mechanic parameters could be important to predict of MACE. Still, larger studies are needed to define the best left atrial mechanic parameter of myocardial deformation as predictor of worse prognosis.

Table 1

	Pts without MACE (n = 87)	Pts with MACE (n = 12)	p
LVEF (%)	49.7±10.6	38.4±11.3	0.003
LA vol index (ml/m^2)	18.65±6.21	23.32±6.48	0.039
S LAs (%)	20.54±7.99	14.61±6.57	0.035
S LAa (%)	11.50±6.00	7.82±4.22	0.036
Sr LAs (s^{-1})	1.15±0.44	0.81±0.24	0.023
Sr LAe (s^{-1})	-0.86±0.52	-0.65±0.31	0.253
Sr LAa (s^{-1})	-1.51±0.65	-1.03±0.47	0.034

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Subclinical lv dysfunction detection in hypertensive patients with preserved lv ejection fraction: role of speckle tracking echocardiography

KARIMA Taamallah[1]; IMEN Hamdi[1]; CHADIA Chourabi[1]; HAJER Malek[1]; HOEIDA Mahfoudhi[1]; WAFA Fehri[1]; HABIB Haouala[1]
[1]*Military Hospital of Tunis, cardiology, military hospital, Tunis, Tunisia*

Introduction: Hypertension is a well-recognized risk factor for cardiovascular diseases and causes left ventricular (LV) pressure overload, which results in various geometric changes that progress to diastolic heart failure and/or heart failure, with LV systolic dysfunction. Early detection of subclinical left ventricular (LV) systolic dysfunction in hypertensive patients is important for the prevention of progression of hypertensive heart disease.
The aim of the present study was to detect subclinical LV dysfunction in hypertensive patients with apparently normal LV systolic function, using speckle tracking echocardiography (longitudinal strain pattern).
Patients and methods: Prospective case-control study was carried out on 112 hypertensive patients (61 male/51 female) and 40 age- and sex-matched healthy subjects as a control group. Conventional echocardiographic Doppler study, tissue Doppler imaging, and 2D speckle tracking imaging were performed using Vivid 9 (General Electric Healthcare). Longitudinal strain imaging by 2D-speckle tracking echocardiography (2D-STE) was done with high-quality images from the apical four-chamber, two-chamber, and three-chamber views. The strain values for all the segments were recorded and averaged to obtain the GLS.
Results: In hypertensive patients, The mean age was 60,5 ± 10,53 years. The left ventricular mass index(LVMI) was significantly higher in the hypertensive group. There was no significant difference in the global LV ejection fraction (LVEF) and the tele-diastolic diameter of LV between the two groups. The size of the interventricular septum was higher in the hypertensive group (P < 0.001). E/A ratio and é velocities were significantly lower in the hypertensive patients (p < 0.001). left atrium volume is significantly higher in the hypertensive group (p < 0.001). In comparison with normal controls, GLS was significantly attenuated in patients with systemic hypertension (-22,5 ± 3,19 in the control group vs -17,69 ± 4,06 in the hypertensive group, p < 0.001). this decrease was more marked In the hypertensive group with left ventricular hypertrophy (LVH) (SLG : 13,57 ± 2,045) (p < 0,001).
Conclusion: In hypertensive patients, LV systolic function is commonly considered normal if the global EF and fractional shortening (FS) are normal. However, the EF and FS reflect only the global cardiac contractile function and do not take regional systolic abnormalities into consideration. Our results show that 2D speckle tracking is able to detect subclinical myocardial dysfunction in hypertensive patients, despite normal global systolic parameters by conventional 2D echocardiography. This suggests that earlier intervention in these patients may be beneficial.

P500

Left ventricular diastolic dyssynchrony in patients with in patients with treatment-naive hypertension and the effects of antihypertensive therapy

BJ Kwon[1]
[1]*Hyosung Medical Center, Department of Cardiology, Cheong-ju, Korea Republic of*

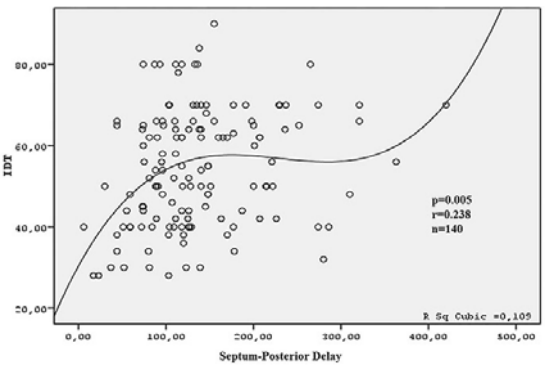
Background: Diastolic dyssynchrony (DD) is an important manifestation in heart failure. We tried to investigate (1) DD in patients with hypertension (2) determinants of DD; (3) the effects of 6-month medical therapy; and (4) the predictors associated with change of DD by performing comprehensive studies.
Methods: and results-DD was more prevalent (15.4% vs. 7.0%, P=0.007) in 325 treatment-naïve hypertensive patients, compared with 172 normal controls. Male (odds ratio [OR], 7.60, 1.69-34.30), magnesium levels (OR per 1 SD, 4.18, 1.54-11.30), nighttime heart rate (HR) (OR per 1 SD, 2.79, 1.19-6.53), and mitral E/A (OR per 1 SD, 0.11, 0.03-0.41) were independent determinants for the DD in hypertensive patients. A follow-up echocardiography was performed in 74 of 275 patients without DD (group 1) and 26 of 50 patients with DD (group 2) at 6 months. Severity and prevalence of DD (Δ=-8.3 ms, -14.6 to -2.1 and 57.7%, P=0.001) improved in group 2 after medical therapy, while those did not in group 1. Baseline daytime HR (P=0.008) and magnesium levels (P=0.029) and changes of the mitral E/A (P=0.003), mean annulus Ea (P = 0.003), mean annulus Ea/Aa (P = 0.020), and mitral peak E (P = 0.042) were independent predictors for changes of DD.
Conclusions: DD is not uncommon in patients with treatment-naïve hypertension. Male, magnesium levels, nighttime HR, and mitral E/A are independent determinants for the DD. Medical therapy reduces the DD, particularly in patients with DD. Moreover, daytime HR, magnesium levels, and indicative of diastolic dysfunction are independent predictors for changes of DD.

P501

Intrinsicoid deflection time predicts ventricular dyssynchrony better than QRS width in patients with indication to cardiac resynchronization therapy

M Koc[1]; O Kaypakli[1]; G Gozubuyuk[1]; DY Sahin[1]
[1]*Adana Numune Training and Research Hospital, Adana, Turkey*

Aim: CRT was shown to improve HF prognosis. But many patients do not benefit from CRT. Patients with LBBB are more likely to benefit from CRT. One of the criteria of LBBB is prolonged time to peak R wave (intrinsicoid deflection) > 60 ms in V5 and V6. In this study, we aimed to investigate the relationship between echocardiographic intraventricular and interventricular dyssynchrony and IDT (Intrinsicoid deflection time).
Methods: We prospectively included 140 patients with HF, QRS≥120 ms, LBBB, NYHA II-IV, LVEF < 35% and scheduled for CRT (84 male, 56 female; mean age 64.9 ± 10.8). Septal-posterior >130 ms delay in M-mode, septal-lateral >60 ms delay for the beginning and >65 ms delay for the peak of systolic velocity in TDI was accepted as intraventricular dyssynchrony. A delay in aortic PSEP > 40 ms was taken as interventricular dyssynchrony. IDT was measured as the time from the beginning of the QRS complex to the peak of the R wave in V5 and V6.
Results: Septum-posterior delay was associated with LDL, LVEF, IDT and QRS width in bivariate analysis. In logistic regression analysis, IDT was only independent parameter for predicting septum-posterior delay (OR= 1.037, p = 0.025). IDT was also associated with septal-lateral delay for beginning, septal-lateral delay for peak of systolic velocity, pulmonary-aortic PSEP delay in bivariate correlations and ROC curve (p < 0.05 for all).
Conclusion: IDT is closely associated with all echocardiographic intraventricular and interventricular dyssynchrony parameters and has a better predictive value than QRS width to detect ventricular dyssynchrony in patients with indication to CRT.



IDT-septum-posterior delay- Scatter plot

P502

Assessment of right and left ventricle function in HIV-infected patients

A Destounis[1]; C Tountas[1]; P Zachos[1]; N Kasinos[1]; C Ioannidis[1]; K Kipourou[1]; M Vassaki[1]; A Theodosis-Georgilas[1]; D Beldekos[1]; G Chrysos[1]; S Foussas[1]
[1]*Tzanio General Hospital, Department of Cardiology, Piraeus, Greece*

Introduction: HIV-infected individuals are at increased risk for pulmonary hypertensionand cardiomyopathy, portending a poor prognosis. Right ventricular (RV) and Left ventricular (LV) diastolic dysfunction isassociated with worse outcomes in these conditions. Therefore early identification of these entities in course disease is crucial for further treatment of these patients.
Purpose: In this study we assessed in relatively newly diagnosed HIV young patients several indices of RV and LV function.
Methods: Echocardiograms were evaluated in 15 HIV-infected adults. Measurements included several indices of LV diastolic function from pulsed Doppler transmitral flow (E, A, DT) and Tissue Doppler Imaging measurements (S, Ea, Aa from the lateral wall and intraventricular septum). In addition, we analyzed indices of RV function such as tricuspid annular plane systolic excursion (TAPSE), RV longitudinal regional and global myocardial strain (RV LMS) and RV fractional area change (RVFAC).
Results: Data from fifteen HIV-infected patients were analyzed (mean age 41,6 ± 11 years, 13 males, body mass index 1,95 ± 0,2 kg/m^2, mean HIV infection 75,1 ± 68).In HIV- infected patients duration of HIV insult was negatively correlated with FAC (r=-0,527, p = 0,053) and had positive correlation with RV systolic area (r=0,56, p < 0,05). Additionally, HIV load was negatively correlated with transmitral E (r=-0,577, p < 0,05). We could not find any correlation with global or regional longitudinal strain of RV and either HIV virus load, duration of infection and CD4 count at time of measurement.
Conclusions: These data suggests that duration of HIV infection affects negatively the RV systolic function. In addition the HIV viral load is also associated with diastolic dysfunction independently of age and duration of HIV infection. In patients of high HIV virulence and increased duration of HIV infection thorough assessment of possible RV and LV diastolic dysfunction should be done.

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Epidemiological and ultrasound characteristics of intracardiac thrombosis

B Bassem Rekik[1]; R Hammami[1]; D Abid[1]; L Abid[1]; M Hentati[1]; S Kammoun[1]
[1]*Hedi Chaker University Hospital, Cardiologie department , Sfax, Tunisia*

Introduction: Our objective is to describe the epidemiological clinical and ultrasound characteristics of intracardiac thrombosis, to underline the interest of the early diagnosis, and the efficiency of the treatment in this pathology.
Methods: It is a descriptive study including cases of patients with intracardiac thrombosis revealed by the echocardiographic examination, during the period from January 01st, 2010 till January 31th, 2013, in our Cardiology department.
Results: Among 13290 echocardiography examinations performed, we diagnosed 43 patients with intracardiac thrombus (0.32%). The sex ratio was 1.3 and the average age was 57.4 years. Topographically we find 20 left ventricule thrombosis (60.5%), 9 left atria thrombosis (20.9%), 6 right atria thrombosis and 2 right ventricles thrombosis.
The mean diameter of thrombus was 19.9 mm and there were 2 cases of multiples thrombi.
The most frequently underlying heart disease were ischemic cardiomyopathy(51.2%), secondary atria fibrillation (18.6%), primitive dilated cardiomyopathy(11.6%) and valvular diseases (one aortic stenosis ,4 mitral stenosis and 4 mitral regurgitation). The thrombus disappeared with only medical treatment (anticoagulant and antiplatelet) in 31 patients after a mean of 3 months, and was treated by surgery in 10 patients. Only 4 patients showed systemic embolization.
Conclusion: Our results suggests that cardiac thrombosis is most frequently localized in the left ventricle and especially in ischemic heart disease , we should ensure an echocardiographic monitoring for these patients so that we can avoid the systemic embolization.

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Two dimensional speckle-tracking echocardiography in comparison to contrast enhanced cardiac magnetic resonance for analysis of myocardial fibrosis in patients with idiopathic dilated cardiomyopathy

L Lupi[1]; E Chiari[1]; A Ravera[1]; D Farina[1]; E Gavazzi[1]; R Maroldi[1]; M Metra[1]; S Nodari[1]
[1]*University of Brescia, Brescia, Italy*

Background: Myocardial deformation analysis by speckle-tracking echocardiography (STE) has been used for analysis of fibrosis, especially in patients with myocardial infarction with preserved left ventricular ejection fraction (LVEF). However there is no data on the use of this method for the identification of regional myocardial fibrosis in patients with idiopathic dilated cardiomyopathy (IDCM) with left ventricular systolic dysfunction.
Purpose: the aim of our study was to evaluate the association between myocardial fibrosis detected by late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) and 2-dimensional (2D) STE.
Methods: We enrolled retrospectively patients suffering from IDCM with LVEF ≤45% followed at our Heart Failure Department from January 2012 to February 2016 underwent CMR with paramagnetic contrast agent administration and STE echocardiography (time range < 90 days between the two tests). LGE CMR was performed to identify the presence of fibrosis in every myocardial segment; the amount of fibrosis was calculated by manual planimetry at each short axis section. Peak systolic longitudinal strains were determined for analysis of regional function (regional longitudinal - RL2D - strain for eachone of the 17 myocardial segments) and global function (global longitudinal - GL2D - strain).
Results: We enrolled 72 patients (76% male, mean age 56 ± 15 years). LGE (found in 60 patients) had midwall and subepicardial distribution in 82% and 8% of patients respectively. There was a positive correlation between the amount of myocardial fibrosis determined by LGE CMR and peak systolic longitudinal strain for the entire left ventricle (rho 0.523, p < 0.0001), basal segments (rho 0.606, p < 0.0001) and midventricular segments (rho 0.497, p < 0.0001), but not for apical segments. A cut-off value of RL2D strain of -7.5% by receiver-operating characteristic (ROC) curves identified LGE segments (sensitivity 91%, sensibility 81%) and a cut-off value of GL2D strain of -10,2% by ROC curves identified LGE presence in left ventricle (sensitivity 76%, specificity 72%).
Conclusions: There is an association between the amount of myocardial fibrosis detected by LGE CMR and myocardial deformation by 2D STE. RL2D and GL2D strain could be helpful for detecting and localizing myocardial fibrosis, especially in patients who cannot perform LGE CMR, and might have a role in prognostication.

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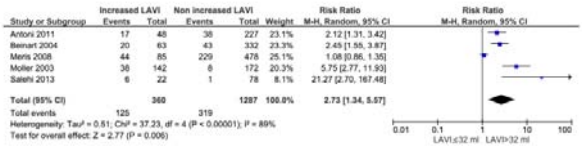
Left atrial volume index as a predictor of outcome in patients with acute myocardial infarction: a systematic review and meta-analysis

I Ibadete Bytyci[1]; G Bajraktari[1]
[1]*University Clinical Centre of Kosova, Clinic of Cardiology, Pristina, Kosovo Republic of*

Introduction: Increased left atrial volume is a marker of diastolic dysfunction and longstanding elevated left ventricle (LV) pressure. The aim of this study was to assess the role of increased baseline left atrial volume in outcome of patients with acute myocardial infarction (AMI).
Methods: We systematically searched PubMed-Medline, EMBASE, Scopus, Google Scholar and the Cochrane Central Registry, up to December 2016 in order to select clinical trials and observational studies, which assessed the predictive role of left atrial volume indexed (LAVI) in outcome in patients with AMI.
We compared clinical outcomes of enlargement LAVI (>32ml/m2) vs. non-enlargement LAVI (≤32ml/m2). Primary end-points were cardiovascular (CV) events: major adverse cardiac events (MACE), and all-cause mortality.
Results: A total of 1647 patients from 5 observational studies with a mean follow-up 25 ± 12 months, were included in the meta-analysis. The increased LAVI correlated with increased risk for MACE (relative risk [RR]=2.73, 95% confidence interval [CI], 1.34 to 5.37, p = 0.006), and all-cause mortality (RR=3.21, 95%CI: 1.48 to 6.97, p = 0.003) in patients with AMI.

In conclusion: Increased LAVI is an independent predictor of outcome in patients with AMI. The assessment of this LA index in these patients in daily practice is important for better risk stratification.



Risk estimates of major adverse cardiac

P506

Correlation between electrocardiography and stress echocardiographic abnormalities and cardiovascular events

P Pedro Von Hafe Leite[1]; T Lopes[1]; F Castro[1]; M Oliveira[1]; B Faria[1]; P Azevedo[1]; M Lourenco[1]; J Portugues[1]; L Calvo[1]; O Azevedo[1]; A Lourenco[1]
[1]Alto Ave Hospital Center, Cardiology, Guimaraes, Portugal

Background: Pharmacological Stress Ecocardiography (SE) has prognostic value in patients with known or suspected coronary artery disease. SE positive for myocardial ischemia and the wall motion score index (WMSI) are associated with a worse outcome. However, the literature is ambiguous regarding the prognostic value of ECG changes during pharmacological SE.
Purpose: To correlate the severity of electrocardiographic and echocardiographic changes during pharmacological SE with the occurrence of cardiovascular (CV) events at follow up.
Methods: Unicentric, retrospective study with 789 patients who underwent pharmacological SE between 2010 and 2015. Demographic, clinical, electrocardiographic and echocardiographic data were collected. CV events were defined as death of cardiac cause, occurrence of AMI and need for revascularization. Statistical analysis to assess whether stress ECG changes and peak WMSI during SE relate to the occurrence of CV events at follow up.
Results: The sample of this study has a higher prevalence of male patients (65%) with a mean age of 64 ± 11 years. From the sample, 55% of the subjects had SE due to suspected ischemic coronary disease (ICD) and 43.9% had SE for the evaluation of already known ICD. SE was performed with dobutamine in 70.6% and dipyridamole in 29.4% of the cases, being positive in 13.6% of the cases. Of the patients studied 13.3% had CV events during the follow up.
ST segment changes during stress ECG were associated with SE positivity ($p < 0.001$) and occurrence of CV events ($p < 0.001$). The value of peak WMSI was statistically different between patients with and without ST elevation during SE (1.67 ± 0.30 vs. 1.2 ± 0.30, $p < 0.001$). There was also a correlation between the dimension of ST-segment elevation and the peak WMSI value ($P = 0.049$). These findings did not occur for patients with ST depression.
Value of peak WMSI was statistically different between patients with and without unsustained ventricular tachycardia during SE (1.55 ± 0.43 vs. 1.2 ± 0.40; $p = 0.002$).
There was a statistically significant difference in peak WMSI between patients with and without CV events (1.58 ± 0.40 vs. 1.27 ± 0.39, $p < 0.001$), a difference that was observed when univariate logistic regression was applied ($p < 0.001$).
Conclusion: Study demonstrated an association between the presence of ST-segment changes in stress ECG and the occurrence of CV events. There was also a statistically significant relationship between the size of ST elevation in SE and peak WMSI, which in turn was associated with the development of CV events.

BIOMARKERS

P507

C-type natriuretic peptide in human blood of adolescent with different degree of endothelial dysfunction: a different trend for plasma levels and mRNA expression.

M Cabiati[1]; V Bianchi[2]; C Caselli[1]; B Marchi[2]; S Marchetti[2]; E Randazzo[2]; G Federico[2]; S Del Ry[1]
[1]Institute of Clinical Physiology of CNR, Pisa, Italy; [2]University of Pisa, Unit of Pediatric Endocrinology and Diabetes, Pisa, Italy

Background: C-type natriuretic peptide (CNP) is a member of natriuretic peptides system and it performs its major functions in an autocrine or paracrine manner through specific binding to the membrane guanylyl cyclase natriuretic peptide receptor B (NPR-B). Recent studies indicated that CNP is an important natural regulator of adipogenesis, possibly involved in obesity pathophysiology, especially in pediatric age. Unfortunately, while CNP plasmatic levels are known in pediatric subjects, no data are available on CNP/NPR-B mRNA expression.
Purpose: Aim of the study was to evaluate both CNP plasma levels and expression of CNP/NPR-B mRNAs in normal-weight (N, n=21) and obese (O, n=15) adolescents (age:13.5 ± 0.4, years).
Methods: Subjects without cardiac dysfunction, referred as outpatients to the Unit of Pediatric Endocrinology and Diabetes, Department of Clinical and Experimental Medicine, Italy, were enrolled. CNP plasma levels were measured with a specific RIA in plasma samples, while expression of CNP and NPR-B mRNAs was assessed in human whole blood samples by Real-Time PCR. Endothelial function was assessed by measuring reactive hyperemia index (RHI)
Results: CNP plasma levels resulted significantly lower in O (6.1 ± 0.8 pg/mL) than in N (15.2 ± 1.3 pg/mL; $p < 0.0001$), while CNP and NPR-B mRNA expression resulted similar in N (4.1 ± 1.7; 5.0 ± 1.6, respectively) and O (4.3 ± 1.6; 3.5 ± 1.1 respectively). Plasma PCR values were significantly ($p < 0.0001$) higher in O (0.3 ± 0.01 mg/dL) than in N (0.01 ± 0.002 mg/dL), while RHI resulted significantly ($p < 0.0001$) lower in O (1.4 ± 0.08) than in N (2.1 ± 0.04) subjects. Surprisingly, dividing all subjects by RHI median (Group 1>1.9, n=18, Group 2 < 1.9, n=18) CNP plasma levels resulted significantly ($p = 0.017$) lower in Group 1 (14.3 ± 1.7) than in Group 2 (8.9 ± 1.2) showing a significant correlation between CNP and RHI (r=0.47, $p = 0.0026$), while CNP mRNA expression was significantly ($p = 0.05$) higher in Group 2 (6.3 ± 2.1) than in Group 1 (1.8 ± 0.4). NPR-B mRNA resulted similar in Group 1 (4.7 ± 1.8) and Group 2 (4.2 ± 1.0). Our data suggest a different trend in CNP plasma levels and in CNP mRNA expression, that were detected for the first time in human peripheral blood mononucleated cells. This discrepancy could reflect changes occurring at CNP transcriptional level in activated leucocytes, due to inflammation, and in blood levels, having CNP paracrine/autocrine activities.
Conclusion: The regulation of CNP/NPR-B transcription constitutes a fruitful area for investigating new therapies targeting CNP/NPR-B production, useful to treat diseases characterized by endothelial dysfunction, such as obesity.

P508

Unexpected age-sex distribution of NP measurements and concentrations : results of Big Data analysis

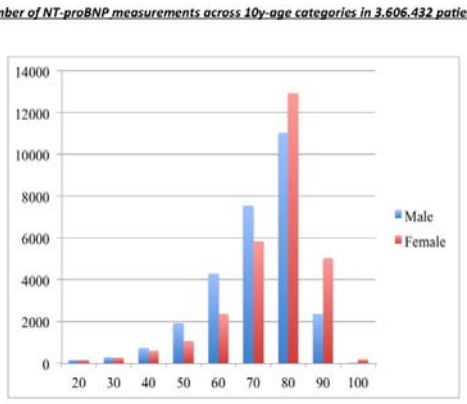
C Meune[1]; FX Goudot[1]; N Garnier[2]; G Copin[3]; A Betraoui[2]; M Schwoerer[2]; A Szosteek[2]; V Bonnivard[2]; M Lescroart[1]; N Charnaux[4]; N Dubois[5]; E Sorbets[1]
[1]Hospital Avicenne of Bobigny, Cardiology, Bobigny, France; [2]ProbaYes, Statitistics, Montbonnot, France; [3]Roche Diagnostics, Medical Care, Meylan, France; [4]Hospital Avicenne of Bobigny, Biochemistry, Bobigny, France; [5]Clinique de la côte d'émeraude, Biorance Laboratory, Saint-Malo, France

Funding Acknowledgements: This study was granted by Roche Diagnostics

Introduction: Since the introduction of routine assay for Natriuretic Peptides (NP), their number of clinical applications has grown. Numerous studies have defined their analytical characteristics in patients presenting with acute or chronic dyspnea. Since the prevalence of chronic heart failure (CHF) increases with age averaging 7.5–10% in patients over the age of 75 years, measurements of NP should increase in a similar way. Plasma concentrations of (NT-pro)BNP are known to be more elevated in women and rise with advancing age in apparently healthy adults almost doubling each age decade. The same age-dependent pattern is also seen in patients with CHF. Our aim was to report the age-distribution of NP measurements and concentrations in a very large population.
Methods: We examined all biological tests performed in two districts from the west part of France, "the French Brittany", covering 13.653km2 and corresponding to a population of 1.723.653 persons. From February 2010 to august 2015, 22 laboratories (including 6 Hospital/clinic laboratories and16 non hospital/clinics laboratories) performed 3.606.432 analysis prescriptions in 3.606.432 adult patients>20y. All laboratories are equipped with Roche diagnostics platform and measure NT-proBNP as the NP.
Results: During the study period, 56.653 (1.6%) measurements of NT-proBNP were performed in 27.527 distinct patients, including 10.1% of measurements in dedicated emergency labs.
NT-proBNP was more often measured in men versus women up to 80 years ($p < 10\text{-}5$), was more frequent in women >80y with overall 28.345 measurements in women and 28.303 in men. NT-proBNP measurements gradually increased by 10y-age categories up 80-90y; 39.828 (70.3%) of measurements have been done in elderly patients ≥ 75y, 31523 (55.6%) in patients ≥ 80y and 7.605 (13.4%) in patients ≥ 90y.
In all 10y-age categories, the number of measurements gradually increased over time ($p < 10\text{-}5$ in all).

As expected, NT-proBNP concentrations increased with advanced age ($p < 10\text{-}5$), with respective mean ± SD and median (IQR) concentrations of 3564 ± 6440 ng/L and 1453 ng/L (468-3778) in patients ≥ 75y and 3642 ± 6730 ng/L and 1825 ng/L (543-4133) in patients ≥ 80y. Opposite to expectations, NT-proBNP concentrations were more elevated in men versus women ($p < 10\text{-}5$).

Conclusion: Among a very large cohort, we report a gradual increase of NP measurements with advances age, averaging 70% of total measurements in patients≥ 75years. NP concentrations also increased with advanced age but unlike expected were overall more elevated in men versus women. Our report suggests that references values should be clearly defined in elderly patients and possibly stratified by sex. Big data analysis may offer a unique opportunity to improve our knowledge in current practices.



Figure

P509

Potential prognostic and clinical role of early measurement of N-terminal pro brain natriuretic peptide (NT-proBNP) in patients of acute coronary syndrome

M Maka Gegenava[1]; T Gegenava[1]

[1]*Tbilisi State Medical Unversity, Tbilisi, Georgia Republic of*

Introduction: The clinical and prognostic role of cardiac natriuretic peptides (NTP) in patients with heart failure is well known; recently, several studies have evaluated the possibility of using N-terminal pro brain natriuretic peptide (NT-proBNP) to evaluate their potential prognostic role in patients with acute coronary syndromes (ACS). Aim of our study was to evaluate the sprognostic value of the early measurement of NT-proBNP in patients with acute coronary syndrome-ACS and compare it' significance with other parameters of systolic dysfunction, for example ejection fraction-EF

Methods: We enrolled n=50 patients admitted to our coronary care units with the diagnose of acute coronary syndrome- ACS. We used diagnostic methods, such as: Resting ECG, determination of cardiacTroponin I level (cTnI), measurements of NT-proBNP, we also measured CK-MB and performed echocardiography measurement of EF. NT-proBNP and echocardiography measurement we performed also during follow up: 1-3 months later after the hospital discharge. Results: According our results totally NT-proBNP was elevated in 36% (n = 18) of hispitalized patients who had not symptoms of heart failure and were hospitalized because of ACS (STEMI and NSTEMI). EF < 54% was seen just in n=8 patients who had elevated level of NT-proBNP. All these patients were investigated after 1-3 months from hospital discharge. In our study group we had not no one case of patient death. From the group with elevated level of NT-proBNP seven patients (38,8%) had recurrent ischemic events (2 subsequent MI, 5 recurrent angina), and 11 (61%) had ymptoms of heart failure (NYHA II-III). We couldn't find correlation between NT-proBNP and decreased EF during hospitalization, but correlation revealed between NT-proBNP elevated level and decreased EF(ejection fraction) $p < 0.005$ in STEMI group during follow up. Such kind of correlation wasn't found in NSTEMI group $p < 0.007$, but during follow up we revealed direct correlation between recurrent episode of ischemia, heart failure symptoms, elevetated NT-Pro BNP level and decreased EF.

Conclusions: Our results suggest that NT-proBNP levels, measured at admission can have much more predictive value for complications, especially for short-term development of heart failure symptoms in patients with ACS, than EF itself in both subgroups-STEMI and NSTEMI. Measurement of this marker at early stage of hospitalization is easy and simple way to predict short-term complications and avoid them

P510

Patterns and prognostic Role of N-terminal pro-B-type natriuretic peptide in heart failure with mid-range vs. preserved vs. reduced ejection fraction

G Savarese[1]; N Orsini[2]; C Hage[1]; U Dahlstrom[3]; GMC Rosano[4]; LH Lund[1]

[1]*Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden*; [2]*Karolinska Institute, Department of Public Health Sciences, Stockholm, Sweden*; [3]*Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*; [4]*St George's University of London, Cardiovascular and Cell Sciences Research Institute, London, United Kingdom*

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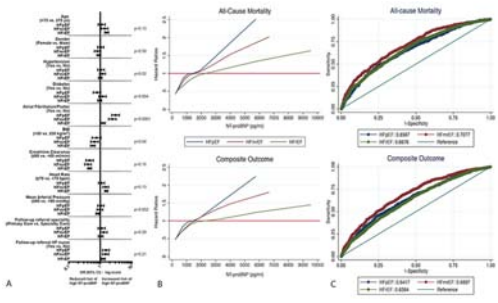
Background: Evidences about the role of N-terminal pro-B-type natriuretic peptide (NT-proBNP) in heart failure (HF) with mid-range ejection fraction (HFmrEF) are still limited. NT-proBNP levels are influenced by demographic and clinical characteristics that may differ in HFmrEF vs. HF with preserved (HFpEF) and reduced (HFrEF) EF.

Purpose: To determine the different determinants and compare the prognostic role and discriminatory power of NT-proBNP levels in HFmrEF vs. HFpEF vs. HFrEF.

Methods: 9,847 out-patients with HFpEF (EF>50%; n=1,811) or HFmrEF (EF 40-49%; n=2,122) or HFrEF (EF < 40%; n=5,914) enrolled in the Swedish Heart Failure Registry were studied. High vs. low NT-proBNP levels were defined according to the median value of peptides. Logistic and linear regression analyses were performed to identify the different predictors of high NT-proBNP levels in HFmrEF vs. HFpEF vs. HFrEF. Survival models were performed to compare high vs. low NT-proBNP levels for prognosis (overall mortality and the composite of mortality and HF hospitalization) across the HF subtypes. ROC curves were fitted to assess the different predictive power of NT-proBNP for each outcome in HFmrEF vs. HFpEF vs. HFrEF.

Results: Median NT-proBNP levels in HFmrEF (1540 pg/ml, IQR: 652-3317) were intermediate between HFpEF (1428 pg/ml, IQR: 623-3000) and HFrEF (2288 pg/ml, IQR: 1022-4835; $p < 0.001$). Among 30 variables analyzed (demographic, clinical, medication use), body mass index (BMI), hypertension, diabetes, dilated cardiomyopathy, atrial fibrillation/flutter (AF), use of angiotensin receptor blockers (ARBs), nitrates, oral anticoagulants and digoxin differently predicted high NT-proBNP levels in HFmrEF vs. HFpEF vs. HFrEF. In particular, in HFmrEF the impact of high BMI (>30 kg/m2) and AF on NT-proBNP was intermediate between that in HFpEF and HFrEF, whereas hypertension, diabetes and use of ARBs and oral anticoagulants were associated with higher NT-proBNP levels in HFmrEF. Digoxin use was associated with higher NT-proBNP in HFmrEF and HFpEF vs. HFrEF, whereas reduced estimated glomerular filtration rate was associated with higher NT-proBNP levels in HFrEF (Fig A). All-cause mortality risk in patients with high NT-proBNP levels vs. those with low values was similarly increased in HFpEF (HR: 2.2), HFmrEF (HR: 1.9) and HFrEF (HR: 1.8), but the risk of the composite outcome was significantly more increased in HFpEF (HR: 2.0) and HFmrEF (HR: 1.9) vs. HFrEF (HR: 1.5)(Fig B). ROC curves showed NT-proBNP having a higher predictive power in HFmrEF vs. HFpEF vs. HFrEF (Fig C). When only the subgroup of patients with AF was analyzed, NT-proBNP predictive power was equivalent across HF subtypes.

Conclusions: HFmrEF, HFpEF and HFrEF show different predictors of high NT-proBNP levels. High NT-proBNP, as compared with lower levels, was associated with higher risk of events in HFpEF and HFmrEF vs. HFrEF NT-proBNP levels had higher predictive power in HFmrEF vs. HFpEF and HFrEF.



P511

Combined hs-cTnT and NT-proBNP plasma levels identify patients with high risk stable coronary artery disease and early LV dysfunction.

C Caselli[1]; C Prontera[2]; V Lorenzoni[3]; R Ragusa[3]; S Del Ry[1]; A Clerico[2]; M Emdin[4]; J Knuuti[5]; SR Underwood[6]; D Neglia[4]
[1]Institute of Clinical Physiology of CNR, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*; *[3]Scuola Superiore Sant'Anna, Pisa, Italy*; *[4]Gabriele Monasterio Foundation, Scuola Superiore Sant'Anna, Pisa, Italy, Pisa, Italy*; *[5]Turku University Hospital, Turku, Finland*; *[6]Imperial College London, London, United Kingdom*

On behalf of: EVINCI

Background: It has been demonstrated that plasma levels of high sensitive-cardiac Troponin T (hs-cTnT) and N terminal-pro brain natriuretic peptide (NT-proBNP) are related with long term prognosis in patients with coronary artery disease (CAD) and heart failure (HF). It is not known whether combined measurements of hs-cTnT and NT-proBNP plasma levels may identify higher risk individuals among patients with stable angina without HF.
Purpose: To correlate plasma levels of hs-cTnT and NT-proBNP with the severity of CAD, the presence of unrecognized myocardial dysfunction and prognosis in patients with stable angina and without HF.
Methods: Clinical, biohumoral and imaging data were collected in 390 patients (237 males, mean age 61 ± 9 years) with stable angina and without known CAD or HF enrolled in the Evaluation of INtegrated Cardiac Imaging (EVINCI) study. All patients underwent baseline echocardiography, circulating hs-cTnT and NT-proBNP measurements, coronary computed tomography angiography (CCTA) to assess the presence of obstructive CAD (>50% stenosis of a major coronary vessel) and stress imaging to detect high risk myocardial ischemia (>10% of LV myocardium). Adverse cardiovascular events (death, hospital admission for non fatal myocardial infarction, heart failure or late >90 days revascularization) were registered in a long term follow-up (average 4.5 yrs).
Results: LVEF was 60 ± 8% (mean ± SD). Circulating hs-cTnT was 7.9 ± 6.2 ng/L and NT-proBNP was 133 ± 217 ng/L. Patients with combined values of hs-cTnT and NT-proBNP above the median values (N=109) had higher prevalence of obstructive CAD at CCTA (44% vs. 23%, $p < 0.001$), of high risk stress induced ischemia (32% vs 14%, $p < 0.001$), of lower systolic function (LVEF<55%) (42% vs. 22%, $p < 0.001$), and of adverse cardiovascular events at follow-up (18% vs. 11%, $p < 0.05$). At multivariate logistic analysis, after correction for age, sex and cardiovascular risk factors, the two combined biomarkers were independent predictors of obstructive CAD (OR 1.72 [1.02-2.91], $p < 0.05$), high risk ischemia (OR: 2.91 [1.62-5.22], $p < 0.001$) and lower LVEF (Coefficient: 2.53 [1.51-4.24], P< 0.001).
Conclusions: Combined hs-cTnT and NT-proBNP levels identify stable angina patients with more severe CAD and early LV dysfunction predisposing to worse prognosis.

P512

Brain natriuretic peptide: a potential modifier of the pharmacodynamic response to antiplatelet agents in acute heart failure

L Malinova[1]; N Furman[1]; P Dolotovskaya[1]; N Puchinyan[1]; T Denisova[2]
[1]Saratov State Medical University, Research institute of cardiology, Saratov, Russian Federation; *[2]Saratov State Medical University, Saratov, Russian Federation*

Expression of natriuretic peptides (NP) receptors in vascular wall and blood cells (including platelets) suggests possibilities of NP involvement in hemostatic balance regulation.
The purpose of the study was to characterize on-treatment platelet aggregation dynamics and to assess influence of brain natriuretic peptide on platelet functions in acute heart failure.
Methods: 80 male patients (54 (47; 60) years old) admitted with STEMI were recruited into the study. According to clinical presentation and baseline level of BNP (cut off level – 100 pg/mL) patients were divided into acute heart failure (AHF) and control groups. Antiplatelet medication consisted of acetylsalicylic acid and ticagrelor in standard doses. Platelet functional testing was performed at admission and on the 7th day. Additionally platelet aggregation was assessed in practically healthy male volunteers (PHV, n = 7) and male patients with AHF (n = 11) with preincubation (37C, 1200 rpm) with BNP solution (37C, 1200 rpm, 1, 3, 5 min, 0 … 1000 pg/mL). Follow-up period was 30 days after admission.
Results: All recruited patients report no previous history of coronary heart disease, prior acute coronary event or heart failure. No one was on antiplatelet therapy before admission. On treatment ADP induced platelet aggregation at base line was significantly higher in patents with BNP level < 100 hg/mL: 2 (1; 8) Ohm vs 0 (0; 2) Ohm, p level 0.019, as well as aggregation slope 2.0 (2.0; 4.0) vs 0.5 (0.0; 1.0), p level 0.013. Patients with AHF showed no significant dynamics of ADP induced platelet aggregation, whereas in patients of control group all studied parameters of platelets aggregation (maximal amplitude, slope and Lag time) decreased (down to 0s) at 7th day of admission (p levels –0.041). Preincubation of blood samples with BNP solution (500 pg/mL and 1000 pg/mL) leaded to significant decrease of both maximal amplitude and slope of aggregation curve in both PHV ($p = 0.041$, 0.036) and patients with AHF ($p = 0.045$, 0.041). Dense granules secretion was not changing in patients with AHF and control group, as well as during preincubation with BNP of blood samples from PHV and AHF patients. Neither bleeding events, nor deaths were observed in recruited patients during 30 days of follow-up period. Early adverse cardiovascular events (stent thrombosis, reinfarction, life-threatening arrhythmias) were observed in 27 patients (33.7%), and these patients had significantly higher level of BNP at 7th day of admittance ($p = 0.040$).
Conclusion: Received data demonstrate potential modifying effect of BNP on pharmacodynamic response to dual antiplatelet therapy in acute heart failure. Dual antiplatelet therapy seems to be more effective in patients with BNP level < 100 pg/mL, whereas further investigation should be performed to assess risk of bleeding events in this group and to increase the statistical power of the study.

P513

Cardiac CD68 and stabilin-1 positive macrophages in wound healing following myocardial infarction

A Aleksandra Gombozhapova[1]; Y Rogovskaya[1]; M Rebenkova[2]; J Kzhyshkowska[3]; V Ryabov[4]
[1]Cardiology Research Institute, Tomsk National Research Medical Centre, Russian Academy of Sciences, Tomsk, Russian Federation; *[2]National Research Tomsk State University , Tomsk, Russian Federation*; *[3]University of Heidelberg, Heidelberg, Germany*; *[4]Siberian State Medical University, Tomsk, Russian Federation*

Introduction: Myocardial infarction (MI) and following heart failure remain the leading cause of mortality and morbidity around the world. The need for better prevention and treatment of heart failure resulted in exploration of new therapeutic strategies to repair the infarct heart. Myocardial regeneration has become one of the most ambitious goals in prevention of adverse cardiac remodeling. Macrophages are key innate immune cells that play a significant role in transition from inflammatory to regenerative phase during wound healing following MI. Scavenger receptor stabilin-1 is proposed as one of the biomarkers for ex vivo diagnostics of M2 macrophages.
Purpose: The purpose of the study is translation of the basic research findings on cardiac macrophage subsets into clinical knowledge in patients with MI.
Methods and Results. The study included 41 patients with fatal MI type 1. All patients were divided into 4 groups depending on the timeline of MI histopathology. Macrophages infiltration was assessed by immunohistochemistry. We used CD68 as a marker for the cells of the macrophage lineage and stabilin-1 as M2 macrophages biomarker. The numbers of CD68+ and stabilin-1+ macrophages in the infarct area increased and peaked in regenerative phase and was not decreased in the late stage. In the peri-infarct area the number of CD68+ macrophages increased in the inflammatory phase, peaked during reparative phase and was not decreased in the late phase. The quantity of stabilin-1+ cells increased in the regenerative phase and further remained unchanged. Numbers of CD68+ and stabilin-1+ macrophages depended on MI phase. The numbers of CD68+ cells correlated with time of MI: strong positive correlation was found in infarct area ($R=0.67$, $p = 0.001$) and moderate positive correlation was found in peri-infarct area ($R=0.55$, $p < 0.001$). Similar relationship was found for stabilin-1+ cells (infarct area: $R=0.6$, $p < 0.001$; peri-infarct area: $R=0.42$, $p = 0.007$). In according to regression analysis, we suggest models which displayed the correlation between macrophage infiltration and clinical scenario of MI. There was relationship between frequency of recurrent MI and following independent variables ($R=0.73$, $p = 0.00013$): day of MI (b=0.46); presence of extensive MI (b=-0.03), chronic kidney disease (b=0.22), postinfarction angina (b=0.42); and quantity of stabilin-1+ macrophages in infarct area (b=-0.36).
Conclusions: Our study translates animal data regarding macrophage subpopulations into human knowledge in clinical settings. There was observed biphasic cardiac macrophage response following MI reminded a murine model. We have noted the increase of stabilin-1+ macrophage infiltration in myocardium during the regenerative phase and strong positive correlation between the number of stabilin-1+ macrophages and timeline of MI. We have supposed the opportunity of usage stabilin-1 as a diagnostic and prognostic M2 macrophage biomarker in wound healing following MI.

P514

Galectin-3 is related to cardiac and vascular function in patients with acute heart failure and preserved left ventricular ejection fraction

A Bechlioulis[1]; S Giannitsi[2]; M Bougiakli[2]; G Chasiotis[3]; K Kontodimou[3]; A Kotsia[1]; I Gkirdis[4]; E Bairaktari[3]; LK Michalis[1]; KK Naka[1]
[1]University of Ioannina, 2nd Department of Cardiology and Michaelidion Cardiac Center, Ioannina, Greece; *[2]University of Ioannina, Michaelidion Cardiac Center, Ioannina, Greece*; *[3]University Hospital of Ioannina, Laboratory of Biochemistry, Ioannina, Greece*; *[4]University of Ioannina, 2nd Department of Cardiology, Ioannina, Greece*

Background: Acute heart failure (AHF) syndromes are related to increased morbidity and mortality. Galectin-3 is released by macrophages in response to inflammation and has been considered to be a marker of myocardial fibrosis but also an independent predictor of cardiovascular and total mortality in heart failure patients. The aim of the study was to investigate the role of Galectin-3 in hospitalized patients with AHF and its association with clinical and biochemical parameters.
Methods: We enrolled 76 consecutive patients admitted in a tertiary cardiology department with a diagnosis of AHF (mean age 71 years, 82% males). All participants were evaluated after clinical stabilization 1-2 days prior to discharge. A complete evaluation of all patients was performed including echocardiogram, vascular function (arterial stiffness) and functional status (6 minute walking test – 6MWT). All patients were followed for 6 months and the occurrence of cardiovascular events (fatal, non-fatal or HF rehospitalization) was investigated.
Results: Galectin-3 levels were positively associated with age (r=0.272, p = 0.018), female gender (r=0.225, p = 0.052), NTproBNP levels (r=0.224, p = 0.053), and inversely with creatinine clearance levels (CrCL) (r=-0.244, p = 0.035) in the total population. In patients with left ventricular ejection fraction (LVEF)>40% (n = 30), increased Galectin-3 was associated with female gender, reduced CrCL, increased aortic pulse wave velocity, E/E′ ratio and systolic pulmonary artery pressures (p < 0.05 for all). In patients with LVEF >45% (n = 13), there was a strong association of Galectin-3 with LVEF (r=-0.575, p = 0.040) and NTproBNP (r=0.768, p = 0.002), while the presence of LVEF >45% was associated with higher Galectin-3 levels (r=0.262, p = 0.025). No relations between Galectin-3 levels and 6MWT or future events were observed . No significant association between Galectin-3 and other parameters was seen in patients with reduced LVEF (i.e. LVEF < 40-45%).
Conclusions: In patients hospitalized with an AHF syndrome, Galectin-3 was shown to differentially relate to clinical and biochemical parameters according to the HF phenotype. In patients with preserved LVEF, Galectin-3 was associated with natriuretic peptides levels, arterial stiffness and echocardiographic indices of heart congestion. No relation of Galectin-3 with cardiovascular events was observed at 6 month follow-up.

P515
Biological markers for the diagnosis of heart failure with preserved left ventricular ejection fraction

E Ekaterina Bazaeva[1]; SA Boytsov[1]; RP Myasnikov[1]
[1]National Research Center for Preventive Medicine, Clinical Cardiology and Molecular Genetics, Moscow, Russian Federation

Purpose: the possibility of using biological markers of myocardial stress and inflammation for the diagnosis of chronic heart failure (CHF) with preserved (over 50%) left ventricle (LV) ejection fraction (EF).
Methods: included 105 patients with stable CHF (65% men) aged 24-84 (mean 58 ± 14) years. Duration CHF ranged from 2 to 96 (mean 24 ± 18) months. The etiology of CHF was as follows: ischemic heart disease - 35 (33%) patients, arterial hypertension - 70 (67%). Distribution of patients with CHF by functional classes according to the NYHA classification was: I - 72%, II - 28%. All CHF patients received drug treatment: ACE inhibitors - 76%, beta-blockers - 72%, diuretics and aspirin - 100%, statins - 80%. The control group consisted of 35 healthy. All subjects identified NT-proBNP, ANP, adiponectin, galectin, pentraxins-3 and growth differentiation factor-15 (GDF-15) by enzyme immunoassay (ELISA) using procedures recommended by the manufacturers of the reagents. Also, all we surveyed performed echocardiography. Results are expressed as median (interquartile range).
Results: The content in NT-proBNP, ANP, galectin, Pentraxin-3 and GDF-15 in patients with CHF was significantly higher than in the control group (p < 0.001 in all cases). In contrast, the level of adiponectin was significantly higher than in healthy individuals - 11.90 (11.39; 12.65) vs 7.73 (3.58; 8.86) ng/ml in patients with chronic heart failure (p < 0.001). The value of LVEF in CHF patients ranged from 30% to 55% and amounted to 45 (38; 51)%. In 35 (33%) of patients with CHF LVEF greater than 50%. Correlation analysis Spearman found significant strong correlation (p < 0.001 for all markers) between the value of LVEF and the content of all biomarkers, in this case between LVEF and the level of adiponectin found a direct correlation (r = 0,862), and between LVEF and the other biomarkers - reverse (from -0.858 to -0.901). Multivariate linear regression analysis found the strongest correlation with the value of LVEF at pentraxins-3 and adiponectin. ROC-analysis confirmed the diagnostic value of adiponectin in patients with CHF with preserved LVEF. Adiponectin values greater than 8.3 ng/ml predicted the presence of CHF in patients with LVEF> 50% with a sensitivity of 94.3% and a specificity of 92.9% (area under the curve 0.977; 95% confidence interval of 0,954-0,999, p < 0.001).
Conclusions: 6 among the studied biological markers of myocardial stress and inflammation only adiponectin has diagnostic significance in patients with CHF with preserved LVEF.

P516
The role of st2 in patients with st segment elevation myocardial infarction

IR Vishnevskaya[1]; OV Petyunina[1]; MP Kopytsya[1]; YV Hilova[1]; LL Peteneva[1]
[1]Government institution'L.T. Malaya Therapy National institute of the National academy of medical sci, Kharkiv, Ukraine

The biomarker ST2 is a member of interleukin family, which is expressed by cardiomyocytes in two forms – membrane — bound (ST2L) and soluble isoform (sST2). sST2 is a "decoy-receptor" for interleukin 33, its level tells us about the left ventricular (LV) remodeling grade and the heart failure's stage.
Purpose: to investigate the role of sST2 in patients with ST segment elevation myocardial infarction (STEMI).
Methods: 65 patients with STEMI were enrolled to the study. Among them are 83,1% male and 16,9% female. Mean age was 57 ± 2,3 years. All patients underwent a baseline investigation which includes: standard electrocardiography, echocardiography, angiography with stenting of the infarct-related artery. In addition, the level of sST2 was determined during the first day of the disease via ELISA test.
Results: Correlation analysis of the studied parameters showed significant negative correlation between the level of sST2 and the ejection fraction of LV (r=-0,5; p = 0,0001), also the rank of correlation coefficient was identified between sST2 and the end diastolic diameter of LV (r=0,31; p = 0,03), and the end systolic diameter of LV (r=0,4; p = 0,007) which is consistent with the role of sST2 in the progression of ventricular remodeling. The level of sST2 was significantly higher in females compared to males, 98,41 ± 36,64 ng/ml and 73,54 ± 29,35 ng/ml, respectively. After comparing the levels of sST2 accordingly to presence or absence of a stable angina before index hospitalization, the patients with a history of stable angina had a significantly lower level of sST2 (p = 0,01). Patients with anterior STEMI had higher concentration of sST2 (88,84 ± 33,66 ng/ml) than those with inferior STEMI - 69,38 ± 23,81 ng/ml, p = 0,003. For patients with two-vessel coronary artery disease (CAD) sST2 level was 118,26 ± 57,67 ng/ml, for those with three-vessel CAD - 61,79 ± 31,98 ng/ml (p = 0,002).
Conclusions: Females are more vulnerable for an early postinfarction remodeling. Higher level of sST2 in patients with anterior STEMI is related to increased infarct zone. Low level of sST2 verifies the patients with a good developing coronary collateral circulation with a history of stable angina. The number of injured coronary artery influences on the heart remodeling – two-vessel injury associated with more expressed remodeling compared with multi-vessel in patients with STEMI.

P517
Biomarkers in long-term prognosis of chronic heart failure formation in patients with acute coronary syndrome

IR Vyshnevska[1]; MP Kopytsya[1]; OV Petyunina[1]; NV Titarenko[1]; YV Hilova[1]
[1]Government institution'L.T. Malaya Therapy National institute of the National academy of medical sci, Kharkiv, Ukraine

The progression of chronic heart failure (CHF) after acute coronary syndrome (ACS) significantly worsens the prognosis for this group of patients. Risk stratification of high risk patient of heart failure formation is very important. 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: to estimate the role of GDF 15 in the formation of CHF during the first year after ACS.
Methods: 73 patients were screened with different forms of ACS (55 male and 18 female), mean age was 61, 8 ± 1, 3 years. Among them, 54% patients with Q-wave myocardial infarction, 20% - with non-Q-wave myocardial infarction, 26% - unstable angina. All patients underwent a baseline investigation. 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. The follow-up period was 1 year. The 6-minute walk test (6MWT) was performed for all patients after 1 year for exercise tolerance estimation. All patients were divided into four groups accordingly to the New York Heart Association (NYHA) guidelines (stages I-IV).
Results: the effect of various variables of clinical, instrumental and laboratory status were assessed on CHF progression. For identification of the main risk factors for adverse outcome, we have used logistic regression (LR) method: NT-pro BNP (area under curve (AUC) 0.54; p < 0.8; 95% confidence interval (CI): 0.31 – 0.72), level of serum creatinine (AUC 0.76; p < 0.0002; 95% CI: 0.62 – 0.90), GDF 15 (AUC 0.87; p < 0.0001; 95% CI: 0.79 – 0.96). NT- pro BNP had no predictive significance. During the statistical analysis the predictive value for estimated parameters was calculated: GDF 15 > 2508 pg/ml (specificity (Spe) 95%, sensitivity (Se) 68%), serum creatinine >118 μmol/l (Spe 86,6 %, Se 56 %). We have developed a LR model (p < 0.0001, X2=14,75) with 88% of Se and 98% of Spe that can predict HF formation in patients during the first year after ACS.

Conclusion: the model can be used for risk stratification in development of CHF in patients after ACS in 1 year prognosis.

P518

PlGF: a putative biomarker in heart failure?

AM Matos[1]; AG Gil[1]; APS Da Silva[1]; T Sequeira[1]; IP Pinheiro[2]; MB Bicho[1]; L F Luiz Filipe De Menezes Falcao[2]; LMF Menezes Falcao[2]
[1]Faculty of Medicine, University of Lisbon, Laboratory of Genetics and Institute of Environmental Health, Lisbon, Portugal; [2]University of Lisbon, Faculty of Medicine, Lisbon, Portugal

Background/Introduction: Placental growth factor (PlGF) was recently associated to heart failure, contributing to atherosclerosis and vascular remodeling. This putative biomarker might modulate clinical parameters, such as haemolytic parameters involved in HF subjects.
Purpose: To determine PlGF levels in patients with HF, as well as its relation with disease severity, cardiac biomarkers and genetic variability.
Methods: In patients with HF and preserved or decreased EF (EF < 40%) were evaluated some possible cardiac biomarkers, PlGF (pg/mL), NT-proBNP (pg/mL), Galectin-3 (ng/mL) and EPO (mIU/ml) determined by ELISA. The genetic polymorphisms of ACE1 and NOS3 were determined by PCR. The sample consisted in 94 patients with HF, aged 78.95 ± 11.9, 52 women (55.3%) and 42 men (44.7%). Statistical methods were the Mann-Whitney test and Spearman´s correlations. Statistical significance were considered for $P < 0.05$.
Results: In HF subjects, PlGF medians were 6.09 (0.2-34.3) and EPO medians were 9.45 (1.1-94.1). In our population PlGF were not associated with severity (EF < 40%), but EPO levels were (P=0.001). Despite the circulating levels of PlGF and EPO were not correlated between them; we found that PlGF levels and Galectin-3 were inversely correlated with hemoglobin (r=-0.287, P=0.041) and EPO levels directly correlated with neutrophils (%) (r=0.300, P=0.022). Relatively to genetic variability, we found that HF subjects with allele A of NOS3 polymorphism (AA + AB genotypes) presented a trend for higher levels of PlGF in relation to subjects with BB genotypes (median: 7.39, IQR: 5.47 vs. median: 5.92, IQR: 6.44; P=0.085).
Conclusions: Although we didn't confirm the role of PlGF in HF, we hypothesized it may be related to inhibition by fms-like tyrosine kinase 1 (Flt-1). Furthermore, the association of higher levels of PlGF to allele A of NOS3 polymorphism (lower activity of endothelial nitric oxide) may reflect a hypoxia status in HF subjects and an increased inflammatory process.

P519

Panel of serum markers of fibrosis does not contribute to prognosis in dilated cardiomyopathy

P Pawel Rubis[1]; S Wisniowska-Smialek[1]; E Dziewiecka[1]; L Khachatryan[1]; P Matusik[1]; A Karabinowska[1]; A Kozanecki[1]; E Wypasek[1]; P Podolec[1]
[1]Department of Cardiac and Vascular Disease, John Paul II Hospital, Institute of Cardiology, Krakow, Poland

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Background: Serum markers of fibrosis are easily accessible parameters that non-invasively provide insight into the dynamics of fibrosis process in heart failure (HF) and dilated cardiomyopathy (DCM). However, their role as predictors of cardiovascular (CV) events in DCM is less clearly defined.
Methods: Since July 2014 till October 2015 we included 70 DCM patients (pts) (48 ± 12.1 years, EF 24.4 ± 7.4). All pts underwent right ventricular endomyocardial biopsy to study the presence and degree of fibrosis. Markers of collagen type I and III synthesis – procollagen type I and III carboxy- and amino-terminal peptides (PICP, PIIICP, PINP, and PIIINP), fibrosis controlling factors – tumor growth factor (TGF1-β) and connective tissue growth factor (CTGF) were measured in serum. Primary outcome of the study was combined with CV death and urgent HF hospitalization. Results: During 12 month of observation, 6 CV deaths and 19 HF hospitalization occurred. Based on logistic regression models, we verified whether serum markers of fibrosis are associated with the primary outcome. Two predictive models were analyzed: unadjusted model and model with the adjustments to the age, disease duration, ejection fraction, collagen volume fraction, and NT-proBNP. None of the analyzed parameters predicted the occurrence of the primary outcome, either in an unadjusted or adjusted model. Conclusions: Serum markers of fibrosis were found not to be useful in predicting cardiovascular events in DCM during 12 months of observation.

P520

Soluble st2 and galectin 3 as potential biomarkers for cardiac fibrosis in peripartum cardiomyopathy

F Feriel Azibani[1]; V Dowling[1]; J Baard[1]; O Briton[1]; T Adam[1]; S Kraus[1]; J Anthony[2]; K Sliwa[1]
[1]University of Cape Town, Medicine, Cape Town, South Africa; [2]University of Cape Town, Obstetrics & Gynaecology , Cape Town, South Africa

Background and objective: Peripartum cardiomyopathy (PPCM) is characterized by new onset of heart failure in late pregnancy and up to the first five months postpartum. The implication of cardiac fibrosis remains controversial in PPCM patients despite clear evidences from animal models. Galectin 3 is a β-galactoside-binding lectin protein that is required for transforming growth factor (TGF)-β pathway-mediated myofibroblast activation leading to cardiac fibrosis. Soluble ST2 (sST2), a truncated soluble receptor of the IL-1 receptor superfamily is highly induced and positively correlated with markers of fibrosis. MicroRNA-21 is implicated in the control of myocardial fibrosis. Galectin-3, sST2 and microRNA-21 were described as prognostic biomarkers in heart failure patients. We aimed to determine the expression levels of these factors and whether they are associated with poor outcome in PPCM patients.
Methods: and results: We recently performed a subgroup biomarker study on 40 consecutive patients with PPCM and 10 age-matched healthy subjects. All patients received ACE inhibitors and beta-adrenergic blocking agents. Plasma NT-proBNP, Galectin 3, microRNA-21 and serum sST2 levels were measured at baseline. Echocardiograms were performed at baseline and six months postpartum. Poor outcome in PPCM patients was defined by NYHA ≥3 or death at 6 month.
At baseline, PPCM patients had significantly higher NT-proBNP, sST2, Galectin 3 and microRNA-21 levels than healthy controls ($p = 0.0005$, $p = 0.0038$, $p = 0.0064$ and $p = 0.01$, respectively). Six months postpartum, three patients did not improve their cardiac function (EF, 26.7 ± 7.4%) and eight died. Baseline NT-proBNP (3973.1 ± 955 vs. 1835.2 ± 268 pmol/l, $p = 0.02$), sST2 (67.01 ± 14.2 vs. 28.5 ± 4.3 ng/ml, $p = 0.011$) and Galectin 3 (15.37 ± 2.8 vs. 8.55 ± 0.66 ng/ml, $p = 0.01$) levels were significantly higher in patients with poor outcome compared to patients that improved their cardiac function (EF, 45.7 ± 11.3%). sST2 and Galectin 3 expression levels were not correlated with baseline ejection fraction. Circulating microRNA-21 levels were not different between recovered and poor outcome patients.
Conclusion: These preliminary results are very promising as for the first time we demonstrated that sST2, Galectin 3 and microRNA-21 are upregulated in PPCM. Galectin 3 and sST2 may be clinically useful biomarkers that identify a subset of PPCM patients at highest risk of myocardial dysfunction due to fibrosis. These findings should be confirmed in a larger cohort.

P521

HYCHeF: A risk score to predict Congestive Heart Failure Incidence in HYpertension. Based on 18795 individual patient data.

H-H Hai-Ha Le[1]; H Ottomani[1]; G Sitruck[1]; F Subtil[1]; F Gueyffier[1]
[1]University Claude Bernard of Lyon, Evaluation and Modeling of Therapeutic Effects, UMR5558, Lyon, France

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Objectives: Patients with hypertension present risk of heart failure development. We aimed to build here a risk score to predict congestive heart failure (CHF) incidence in these patients using data from well-done randomized controlled trials (RCTs) of anti-hypertensive agents.
Method: Data of 18795 hypertensive patients was collected from four trials of INDANA database (Coope, SHEP, STOP and SYST-EUR. The whole population was randomly divided in two subsets: derivation set for model construction and the remaining for model validation with the ratio 2:1 and with similar patient characteristics. We used the Cox proportional hazards model to test the association of each covariable to CHF incidence separately (univariable analysis) and altogether (multivariable analysis) until obtaining the final model where all covariables were significant.
Results: Thirty baseline factors were examined for risk of CHF incidence using a multivariable Cox model, adjusted on trials. Treatment was associated with a significant reduction of 50% of CHF incidence and had no interaction observed with trial or any other covariable. A risk score of CHF incidence in five years was built with 10 significant risk factors: treatment (HR 0.50, CI 95%, 0.36 - 0.69), age (HR 1.52, 1.3 - 1.78 by 5-year increase), serum total cholesterol (HR 0.83, 0.73 - 0.96), cigarette smoking (HR 1.74, 1.10 - 2.75), renal function (HR 0.93, 0.87 - 1.00 by 5 mL/min/1.73 m2 increase of glomerular filtration rate), body mass index (HR 1.05, 1.01 - 1.09 by 1 kg/m2 increase), history of myocardial infarction (HR 3.07,

1.76 - 5.34), history of stroke (HR 3.03, 1.47 - 6.25), diabetes baseline (HR 1.63, 1.01 - 2.63) and ratio of systolic/diastolic blood pressure (HR 1.36, 1.17 - 1.58). This model was then transformed to an integer system, with points added for each factor according to its association with CHF incidence risk.

Conclusion: Our work provides a simple risk scoring system for CHF incidence prediction in hypertension, using individual data from well-established RCTs of antihypertensive treatments. We confirmed the same classical risk factors of CHF development found by other studies on other populations of cardiovascular risk.

Table 1. Final model to predict congestive heart failure incidence in hypertension

Covariables	Hazard Ratio (95% CI)	p-value
Antihypertensive treatment	0.50 (0.36 - 0.69)	<0.0001
Age (by 5 year increase)	1.52 (1.30 - 1.78)	<0.00001
Glomerular filtration rate (by 5 mL/min/1.73 m2 increase)	0.93 (0.87 - 1.00)	0.04
Smoker	1.74 (1.10 - 2.75)	0.018
Body mass index (by 1 kg/m2 increase)	1.05 (1.01 - 1.09)	0.014
Serum total cholesterol (mmol/l increase)	0.83 (0.73 - 0.96)	0.011
History of myocardial infarction	3.07 (1.76 - 5.34)	<0.0001
History of stroke	3.03 (1.47 - 6.25)	0.003
Diabetes baseline	1.63 (1.01 - 2.63)	0.044
Ratio of systolic/diastolic blood pressure	1.36 (1.17 - 1.58)	<0.0001

Multivariable analysis adjusted on trials and performed on the training set.

P522

Exploring risk markers for incident heart failure using a targeted proteomics chip

J Molvin[1]; M Pareek[2]; O Melander[3]; L Rastam[3]; U Lindblad[4]; B Daka[4]; M Leosdottir[1]; PM Nilsson[3]; MH Hecht Olsen[2]; M Magnusson[1]
[1]Lund University, Department of Cardiology, Skåne University Hospital , Malmoe, Sweden; *[2]Odense University Hospital, Department of Endocrinology, Centre for Individualized Medicine in Arterial Diseases (CIMA), Odense, Denmark*; *[3]Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden*; *[4]University of Gothenburg, Institute of Medicine, Department of Public Health and Community Medicine, Sahlgrenska Academy, Gothenburg, Sweden*

Background: The evolving use of multiplex proteomic platforms provides excellent tools for investigating associations between multiple proteins and risk of incident cardiovascular disease (CVD). In this study, we evaluated the impact of 92 proteins, included in a multiplex panel, on incident heart failure (HF).

Methods: All 92 proteins from the OLINK CVD III panel were analyzed in 1,734 participants from a subsample of the population-based Malmö Preventive Project. Only one protein was below detectable limits in >15% samples, i.e., N-terminal pro-brain natriuretic peptide (Nt-proBNP). Therefore, Nt-proBNP was analyzed separately using a competitive enzyme immunosorbent assay. Exclusion of subjects with prevalent HF and missing covariates at baseline examination rendered a final study population of 1,705 subjects. Standardized hazard ratios (HR) for logarithmic values of protein concentrations were reported. A two-sided Bonferroni corrected P-value of 0.05/92=5.4x10-4 was considered statistically significant.

Results: Mean age was 67 years, 29% were women, and 28% had prevalent diabetes. During a mean follow-up time of 8.9 ± 1.5 years, 91 incident HF cases were detected. In age- and sex-adjusted analyses, four proteins were associated with incident HF: Nt-proBNP (hazard ratio (HR): 2.55, 95% CI, 2.07-3.15; P=3.4x10-18), Galectin-4 (GAL-4) (HR 1.60, 1.26-2.01; P=8.4x10-5), Azurocidin (AZU-1) (HR 1.43, 1.17-1.74; P=4.0x10-4) and Growth-differentiation factor 15 (GDF-15) (HR 1.58, 1.27-1.97; 3.8x10-5). When adjusting for traditional risk factors (age, sex, height, systolic blood pressure, anti-hypertensive medication use, diabetes mellitus, prevalent atrial fibrillation and previous myocardial infarction), only Nt-proBNP (HR 2.1, 1.53-2.85; P=4.0x10-6) and GDF-15 (HR 1.37, 1.01-1.84; P=0.042) remained significantly associated with incident HF.

Conclusion: In a community sample of 1,705 elderly individuals without HF, we used an immunoassay designed to analyze 92 proteins with proposed involvement in immunity/inflammation, CVD, and metabolism to explore potential biomarkers for incident HF, and found Nt-proBNP and GDF-15 to be independently associated with future HF development.

Kaplan-Meier curves for cumulative all-heart failure incidence from re-examination (2002-2006) to the end of follow up (31st dec 2014) among 1,705 participants in MPP stratified according to quartiles of log Nt-proBNP.

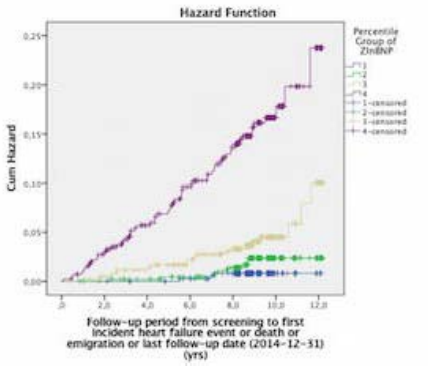


Figure 1.

P523

Morphological alterations of the cardiomyocyte nuclear envelope may preclude the potential for reverse remodelling in patients with non-ischemic cardiomyopathy.

T Katsimichas[1]; T Ohtani[1]; Y Asano[1]; M Kanzaki[1]; Y Tsukamoto[1]; H Kioka[1]; O Yamaguchi[1]; Y Sakata[1]
[1]Osaka University Graduate School of Medicine, Department of Cardiovascular Medicine, Osaka, Japan

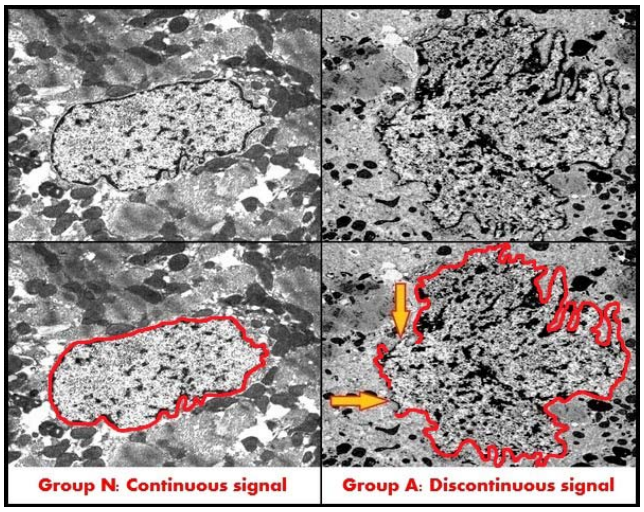
Background: We have previously shown that certain morphological alterations of cardiomyocyte nuclei observed by electron microscopy are associated with worse outcomes in non-ischemic cardiomyopathy (NICM) patients. However, it is unknown whether such characteristics may also preclude a better prognosis, as represented by the process of reverse remodelling (RR). Since no definitive prognostic markers of RR currently exist, research in this field may yield important insights that will improve treatment planning.

Purpose: The purpose of this work was to investigate whether certain alterations of the cardiomyocyte nuclear envelope may preclude reverse remodelling in patients with NICM.

Methods: We conducted a retrospective study of 132 NICM patients with severe heart failure [ejection fraction (EF) < 30%], who were admitted for treatment in our hospital between 2009 and 2015. RR was defined as an increase of EF>10 percentage points, leading to a post-EF>35% after one year, without any occurrence of cardiac events – namely death or left ventricular assist device implantation. Electron microscopy images of all the cardiomyocyte nuclei of samples taken during diagnostic myocardial biopsies were evaluated by a customized computer software. This software measures a signal that corresponds to the thickness and intactness of the nuclear envelope; alterations of the signal, represented by gaps in signal continuity, indicate thinning or breaching of the nuclear envelope. Based on the evaluation, patients were categorized into either Group A (thin or breached nuclear envelope) or Group N (normal nuclear envelope) (Figure).

Results: No group A patients (n = 13) underwent RR (0%), while 45 of 119 group N patients (38%) did (p < 0.01). This difference was significant even after adjustment for age, brain natriuretic peptide, EF, or left ventricular end-diastolic diameter. The EF at baseline was not significantly different between the two groups (20.6 ± 7.7% vs. 20.8 ± 5.3%), and neither was β-blocker dosage.

Conclusion: Our results show that morphological alterations of the cardiomyocyte nuclear envelope in NICM patients might predict the lack of potential for RR. If confirmed in future prospective studies, they may help establish an important prognostic process, accelerating decisions for drastic intervention in patients with NICM.



Group N and Group A nuclei

P524

Plasma glycoproteomics reveals gender-specific activation of distinct pathways linked to heart failure development following myocardial infarction

Y Deleon-Pennell[1]; OK Ero[1]; ER Flynn[1]; I Espinoza[1]; SK Musani[1]; RS Vasan[2]; ME Hall[1]; ER Fox[1]; ML Lindsey[1]
[1]The University of Mississippi Medical Center, Jackson, United States of America; *[2]Boston University, School of Medicine, Boston, United States of America*

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Background and Introduction: Identifying early plasma protein biomarkers that predict the development of heart failure (HF) following myocardial infarction (MI) will help to stratify at risk subjects and provide insight into more effective therapeutic strategies.
Purpose: The goal of this study was to catalogue early post-MI plasma proteins that linked to the development of HF by targeting extracellular proteins using a glycoproteomic approach.
Methods: Plasma samples collected at visit 2 from 60 African American participants in the Jackson Heart Study were analyzed. All participants were diagnosed with MI (but without prevalent HF) prior to collection. The participants were divided into subjects who later presented with adjudicated incident HF after visit 2 (MI + HF; n=15; 3 men/ 12 women) and those who had remained stable through 2012 (MI; n=45; 24 men/ 21 women). N-linked plasma glycopeptides were quantified by solid-phase extraction coupled to mass spectrometry and identified using RefSeq and SwissProt. Proteins were mapped for biological processes and functional pathways using Ingenuity Pathway Analysis (IPA).
Results: A total of 379 glycopeptides corresponding to 88 proteins were identified. Of these, 18 glycopeptides were significantly different between the MI only and MI + HF groups and corresponded to 6 proteins: apolipoprotein F, transthyretin, apolipoprotein C-IV, prostaglandin-D2 synthase, complement C9, and CD59 (p0.05 for all). With the exception of CD59, all other proteins were significantly elevated in MI + HF group. IPA analysis identified 4 canonical pathways enriched in the MI + HF group. Activation of the acute phase response, liver X receptor/retinoid X receptor (LXR/RXR) pathway, and macrophage reactive oxygen species generation were significantly upregulated in the MI + HF group (p0.05 for all). The coagulation pathway was significantly downregulated in the MI + HF group (p0.05). Interestingly, the percentage of women who developed HF after MI was higher (80%) compared to men (47%; p0.05). In the MI group, partial least squares discriminant analysis showed overlapping protein distributions, indicating a lack of gender effect. When comparing patients who developed heart failure post-MI, there was a distinct separation between men and women. By IPA analysis, men who developed HF had upregulation of acute phase response and LXR/RXR pathways, whereas women who developed HF had downregulation of the coagulation pathway. This suggests there are gender-specific pathways responsible for post-MI outcomes.
Conclusion: Our investigation identifies early plasma glycoprotein changes that link to later MI patient outcomes and provides insight into unexplored mechanisms that may explain sex differences in the pathogenesis of post-MI development of HF. Additional studies are warranted to replicate these hypothesis-generating findings in larger samples.

P525

Association of brain natriuretic peptide and adrenomedullin plasma levels with left ventricular filling pressures in end-stage renal disease patients

E Tzatzaki[1]; V Kamperidis[2]; D Konstantinou[2]; G Giannakoulas[2]; P Sarafidis[2]; H Karvounis[2]
[1]Onassis Cardiac Surgery Center, Athens, Greece; *[2]First Cardiology Department, AHEPA Hospital, Aristotle University , thessaloniki, Greece*

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Backgrounds: Adrenomedullin (ADM) and brain natriuretic peptide (BNP) are known to be associated with elevated left ventricular filling pressures. However, little is known about this association in end-stage renal disease (ESRD) patients with preserved left ventricular ejection fraction.
Purpose: The association between E/e′ ratio and plasma levels of BNP and ADM in ESRD patients with preserved left ventricular ejection fraction undergoing chronic hemodialysis.
Methods: The study group enrolled 62 ESRD patients treated with hemodialysis three times weekly. BNP and ADM plasma concentration measurements and echocardiographic investigation were performed 30 minutes after hemodialysis. E/eratio, evaluated by tissue Doppler imaging, measured at the basal septum was used as a surrogate marker for assessing left ventricular filling pressures.
Results: The mean age of patients was 62 ± 25 years, 57% male. The mean BNP and ADM values after hemodialysis were 0.40 ± 6.73pg/ml and 0.06 ± 2.12pg/ml, respectively. Patients of older age, being on hemodialysis for a longer period, with hypertrophied left ventricles and larger left atria displayed higher E/e values. BNP (r=0.324. p = 0.018) and ADM (r=0.319, p = 0.042) plasma levels were positively and significantly associated with E/e. Multivariate regression analysis including BNP, ADM, age, hemodialysis duration, left ventricular end-systolic volume index, ejection fraction, left ventricular mass index and left atrium volume index, revealed that ADM (p value 0,025) but not BNP levels, were independently associated with E/e′ ratio.
Conclusions: ADM, but not BNP, was independently associated with septal E/e in ESRD patients with preserved left ventricular ejection fraction. ADM plasma levels may be helpful to evaluate left ventricular filling pressures in ESRD patients.

P526

Correlation of ceruloplasmin, an acute phase protein, with NT-proBNP and liver function tests in stable HFrEF

F Filip Malek[1]; T Andreasova[2]; D Vondrakova[2]; L Sedlackova[3]; J Dvorak[4]; L Taborsky[3]; P Neuzil[2]
[1]Charles University Prague, 3rd Faculty of Medicine, 1st Clinical Dept of Internal Medicine, Prague, Czech Republic; *[2]Na Homolce Hospital, Department of Cardiology, Prague, Czech Republic*; *[3]Na Homolce Hospital, Clinical biochemistry, hematologa and immunology, Prague, Czech Republic*; *[4]National Institute of Public Health, Prague, Czech Republic*

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Background: ceruloplasmin (Cp) is an acute phase protein produced by liver cells, production is stimulated by circulating cytokines. Liver function test are usualy impaired in CHF patients, mainly increased bilirubin and decreased albumin identify depressed metabolic and synthetic liver function.
Study objective: to assess association of Cp with liver function tests and prognostic parameters in patients with stable HFrEF
Patients and methods: serum Cp, NT-proBNP and liver function tests including total bilirubin, ALT, AST, GMT, ALP and albumin were analyzed in 164 consecutive stable HFrEF patients, mean LV EF was 32 %.
Results: mean Cp level was 0.23 g/l and NT-proBNP 218 pmol/l (1850 pg/ml). Cp correlated significantly with NT-proBNP (r = 0.323, p < 0.001), total bilirubin (r = 0.213, p = 0.0067) and with albumin (inverse correlation r = - 0.273, p = 0.0005), correlation with other liver function tests was not significant. Cp level correlated with NYHA (r = 0.230, p = 0.0034) and LV EF (inverse correlation – 0.237, p = 0.0025) too.
Conclusion: Cp in stable HFrEF correlates with NT-proBNP, total bilirubin and albumin (inverse correlation). Cp might be new potential biomarker reflecting severity of heart failure and hepatic impairment.

P527

Role of uric acid in progression of heart remodeling in patients after myocardial infarction: liaison between metabolic profile and subclinical inflammation

S Sofiya Lypovetska[1]
[1]*Ternopil State Medical University, Ternopil, Ukraine*

Aim: to investigate the potential impact of SUA levels on metabolic profile, subclinical inflammation and heart remodeling in patients after myocardial infarction.
Methods: 147 patients (59,2 ± 0,8 years old) in 6 months after myocardial infarction were included in cross-sectional study. The subjects were divided in two groups with high (0,59 ± 0,06 mmol/l, n=82) and normal (0,32 ± 0,05 mmol/l, n=65) serum uric acid (SUA) levels. Lipid profile and inflammatory biomarkers (high-sensitivity C-reactive protein (hc-CRP), Interleukin -1 (IL-1), tumor necrosis factor (TNF)) identification, echocardiograph assessment were performed.
Results: patients with high SUA had STEMI (61,3% vs 17,1%), mostly anterior (53,8% vs 28,6%), while patients with normal SUA – NSTEMI (82.9% vs. 38.7%). Congestive heart failure often manifested in patients with high SUA (24,5 % vs 4,9 %). Left ventricle aneurysm was formed only in 7 patients with hyperuricemia. Metabolic syndrome was more often found in patients with high SUA than with normal (60.5% vs 7.3%).
Lipid profile of patients with hyperuricemia was characterized by significant increased levels of total cholesterol - 20,9%, triglyceride - by 38,1%, LDL cholesterol - by 31,8% and lower HDL cholesterol - by 32,8% ($p < 0,01$) compared with patients with normouricemia. Combined dyslipidemia (67.9% vs 2.4%) and hypertriglyceridemia (6.6% vs 2.4%) were prevailed in case of hyperuricemia. In patients with high SUA inflammatory biomarkers were increased significantly, including hc-CRP - by 71,4 %, IL-1 - 49,9%, TNF - to 76,2% ($p < 0,01$) compared with patients with normal SUA. The correlation between elevated levels of hc-CRP and SUA ($r = 0,7$, $p < 0,01$), TNF ($r = 0,8$, $p < 0,01$), IL-1 ($r = 0,7$, $p < 0,01$) was found, confirming the direct role of SUA in inflammation.
Patients with high SUA, compared to those with low SUA, had higher left ventricular mass index (220,9 ± 6,9 vs 147,4 ± 8,3, $p < 0,01$) and left atrial dimension (4,0 ± 0,5 vs 3,5 ± 0,8, $p < 0,01$), while did not differ in ejection fraction. Concentric and eccentric hypertrophy were observed in 56,6 % and 40,6 % patients with hyperuricemia, 26,8 % and 31,7% - with normouricemia. Diastolic dysfunction was more frequently investigated in patients with high SUA than with normal (85,8 % vs 36,6 %, $p < 0,01$). SUA levels correlated significantly with mitral A wave velocity ($r=0,61$, $p < 0,01$), E wave decelaration time ($r=0,26$, $p < 0,01$), E/A ratio ($r=0,21$, $p < 0,05$).
Conclusion: Elevated SUA level is associated with heart remodeling progression after myocardial infarction as well as significant inflammatory activation and lipid disorders, reflecting increased cardiovascular risk.

P528

Association of endothelial dysfunction with biomarkers of myocardial fibrosis and left ventricle strain in patients with heart failure

G Gerasimos Siasos[1]; E Dimitropoulos[1]; E Oikonomou[1]; E Kokkou[1]; C Chrysohoou[1]; K Mourouzis[1]; G Vogiatzi[1]; A Antonopoulos[1]; S Tsalamandris[1]; M Vavuranakis[1]; C Stefanadis[1]; D Tousoulis[1]
[1]*National & Kapodistrian University of Athens, Department of Cardiology, Athens, Greece*

Background: Adrenomedullin (ADM) is involved in vascular homeostasis and endothelial function. Atrial natriuretic peptide (ANP) has potent diuretic, and vasodilating actions. Mid-regional epitopes of these peptides (MRproANP and MRproADM) present increased plasma stability. Soluble suppression of tumorigenicity 2 (sST2) has emerged as a novel biomarker for HF, and has been identified as a novel biomarker of cardiac stress, fibrosis and remodeling. We hypothesized that endothelial dysfunction in patients with is associated with markers of myocardial strain and fibrosis.
Methods: In this cohort study we enrolled 75 consecutive patients with stable chronic systolic HF in NYHA class II to IV and 80 matched for age and sex control subjects. Endothelial function was evaluated by flow mediated dilatation (FMD). Serum levels of MRproANP, MR-proADM and sST2 were measured with ELISA. Several other clinical and demographic characteristics were also collected.
Results: There was no difference in age (64 ± 10y vs 65 ± 11y, $p = 0.67$) and male gender (64% vs. 67%, $p = 0.78$) between HF and control subjects. Subjects with HF had significantly impaired FMD compared to control subjects (4.95 ± 2.28% vs. 6.12 ± 3.12%, $p = 0.04$). In HF patients FMD was inversely associated with sST2 levels (rho=0.57, $p < 0.001$) and with MRproADM levels (rho=0.26, $p = 0.02$) while there was no association of MRproANP with FMD (rho=0.09, $p = 0.94$). In HF patients FMD was significantly associated with age ($r=19$, $p = 0.04$), while there was no association of FMD with ejection fraction ($r=0.037$, $p = 0.65$), with NYHA status ($r=0.04$, $p = 0.70$) and with creatinine levels ($r=0.06$, $p = 0.34$). Interestingly, after adjustment for multiple established confounders (age, ejection fraction, NYHA status, smoking status, gender and the use of mineralocorticoid receptor antagonists, angiotensin receptor blockers or angiotensin converting enzyme inhibitors) sST2 was independently associated with FMD in patients with HF [b=0.17 95%CI (0.22, 0.05), $p < 0.05$].
Conclusions: These findings confirm the complex interrelationship between left ventricle strain, myocardial fibrosis and endothelial dysfunction in patients with heart failure.

P529

Creatinine or cystatin-C? Differences in renal function estimates and relation to cardiac parameters in patients with neuromuscular disorders

WC Meijers[1]; J Kootstra[2]; J Doorn[2]; J Nieuwenhuis[3]; HE Meulenbelt[4]; RA De Boer[1]
[1]*University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; [2]*University Medical Center Groningen, Clinical chemistry, Groningen, Netherlands*; [3]*University Medical Center Groningen, Pulmonary Disease, Groningen, Netherlands*; [4]*University Medical Center Groningen, Rehabilitation medicine, Groningen, Netherlands*

Background: Commonly used formulas use creatinine plasma levels to predict kidney function. However, in patients with neuromuscular disorders estimation of kidney function is severely limited due to very low creatinine levels and muscle turnover. Cystatin-C, an emerging marker of kidney function is not influenced by skeletal muscle degradation, and might be of clinical value in these patients. Therefore we studied the association of the CKD-EPI formula using either the cystatin C or creatinine plasma levels with both renal and cardiac function.
Methods: In a tertiary referral academic hospital, we consecutively enrolled 39 patients with neuromuscular disorders that were screened for possible cardiac involvement. In all these patients we measured the plasma levels of creatinine, cystatin-C, NT-proBNP, high sensitivity troponin-T and galectin-3. We performed echocardiography to assess left ventricular function. To directly compare the performance of creatinine and cystatin-C, we used the CKD-EPI formula using either creatinine or cystatin-C.
Results: Mean age of the study patients was 31 (SD ± 11), 82% of the patients were male and 59% were diagnosed with either Duchenne or Becker muscular dystrophy. Median creatinine value was 10 µmol/L (IQR 7-23), and for cystatin-C it was 0.81 mg/L (0.71-0.92). Creatinine and cystatin-C in these patients were not correlated with each other. We calculated creatinine based and cystatin-C based CKD-EPI, and they were markedly different: 252 mL/min per 1.73 m2 and 113 mL/min per 1.73 m2, respectively. NT-proBNP levels were strongly associated with left ventricular ejection fraction (LVEF) (β -0.78 $P < 0.001$). Cystatin-C based eGFR (CKD-EPI) was associated with age and galectin-3 levels (β -0.63 $P < 0.001$; β -0.43 P=0.008), which have established relation to renal function, while creatinine based eGFR (CKD-EPI) was only weakly associated with troponin-T and NT-proBNP (β 0.36 P=0.026; β 0.32 P=0.045).
Conclusions: These data indicate that estimation of renal function cannot reliably be achieved with creatinine, while cystatin-C appears a reasonable alternative. Since the majority of patients with neuromuscular dystrophies develop heart failure, and at some point require heart failure medication, adequate monitoring of renal function is warranted.

P530

Profile of biomarkers of extracellular matrix, inflammation and apoptosis in left ventricular reverse remodeling

S M R Amorim[1]; I Falcao-Pires[2]; M Oliveira[2]; J Rodrigues[1]; M Campelo[1]; B Moura[3]; F Macedo[1]; A Leite-Moreira[2]; J Silva-Cardoso[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Cardiology, Porto, Portugal*; [2]*Faculty of Medicine University of Porto, Cardio-Toracic Surgery, Porto, Portugal*; [3]*Military Hospital, Porto, Portugal*

Introduction: Limited data exists regarding the usefulness and validation of novel biomarkers to predict left ventricular (LV) reverse remodeling (LVRR) in dilated cardiomyopathy (DCM). We aim to evaluate the potential of emerging biomarkers in LVRR, in a cohort of DCM patients, after optimal pharmacological or resynchronization therapy.
Methods: We prospectively included 35 DCM patients with reduced LV ejection fraction (LVEF < 40%, 59.1 ± 9 years-old, 51.4% males) who were referred to our heart failure (HF) outpatient clinic. Clinical and echocardiographic data as well as blood samples were collected before (baseline) and 41.2 ± 23.4 months after to assess LVRR (defined as an increase of LVEF> 10 units) and correlate these parameters to levels of circulatory markers of extracellular matrix (MMP-3, TIMP-2, ST2, Galectin-3) and HF (BNP, GDF-15, sTNF RI, CA 125).

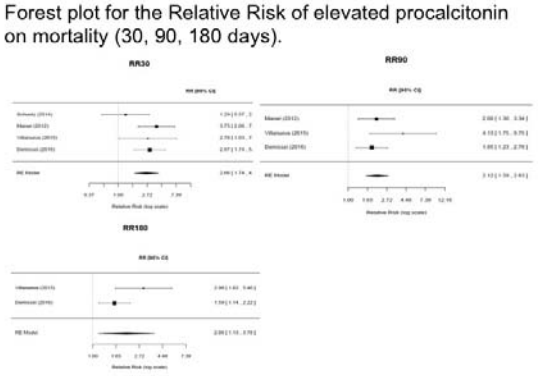
Results: LVRR occurred in 45.7% of patients within 22.6 ± 5.28 months after optimal pharmacological or resynchronization therapy. In this group, LVEF increase 24.6 ± 9.3% and a LV diastolic diameter (LVDD) decrease of 8.8 ± 7.8 mm compared to baseline values (follow-up LVEF of 47.8 ± 7.5% and follow-up LVDD of 53.9 ± 6.9 mm). Concerning the progression of biomarkers plasma levels in the overall population, there was a significant decrease in BNP (35.3 ± 82.2 vs 120.9 ± 266.5 pg/ml, p = 0.01) as well as an increase in GDF-15 (1161.2 ± 826.4vs 935.0 ± 512.6 pg/ml; p = 0.04), MMP-3 (10.1 ± 6.0 vs 6.1 ± 3.0 ng/ml; p < 0.01) at the end of follow-up. A subgroup analysis revealed that BNP and MMP-3 changes occurred both in patients with or without LVRR. GDF-15 increased (marginally) in patients that recovered LVEF (1140.01 ± 928.45 vs 808.35 ± 416.66 pg/ml; p = 0.07). Additionally, patients with pharmacological LVRR had lower baseline values of galectin-3 (5.61 ± 2.98 vs 8.68 ± 4.35ng/ml, p = 0.03).
BNP correlated with LVDDi (r=0.63, p < 0.01), LVDVi (r=0.53, p < 0.01), LVEF (r=-0.43, p < 0.01), LMMi (r=0.42,p < 0.01), LAVi (r=0.36, p = 0.01), E/e´ (r=0.33, p = 0.01). CA 125 correlated with LAVi (r=0.48, p = 0.01), PASP (r=0.62, p < 0.01) and LVDD (r=0.51, p = 0.01). GDF-15 correlated with E/e′ (r=0.32, p = 0.01); TIMP-2 correlated with LVDVi (r=0.31, p = 0.01), LAVi (r=0.28, p = 0.02) and sphericity index (r=-0.29, p = 0.02). MMP-3 had a positive correlation with LVEF (r=0.35, p = 0.01).
Conclusions: Lower baseline values of galectin-3 were associated with LVRR. GDF-15 and MMP-3 increased during follow-up showing important significant correlations between their circulatory levels and echocardiographic parameters of LV remodeling, suggesting there is a multidirectional pathway of activation in HF that involves cytokines, ECM activation and apoptosis. Considering the role that these markers hold at the level of myocardial fibrosis, our data clearly demonstrate the changes at the ECM have an impact on myocardial function and structure recovery in DCM patients.

P531

Diagnostic and prognostic value of elevated serum concentrations of procalcitonin in patients with suspected heart failure and infection - A systematic review and meta-analysis

L Aissou[1]; E Sorbets[1]; E Lallmahomed[1]; FX Goudot[1]; N Pop[1]; L Benouda[1]; C Meune[1]
[1]*Hospital Avicenne of Bobigny, Cardiology, Bobigny, France*

Purpose: The serum concentration of procalcitonin (PCT), a diagnostic tool of bacterial infection, is higher in patients presenting with heart failure (HF) and concomitant infections than in patients with HF alone, and in patients with infection alone. However, its prognostic significance remains uncertain in patients with HF. We reviewed and performed a meta-analysis of studies that measured PCT in patients with acute or chronic HF and suspected infection in order to evaluate the diagnostic robustness and the prognostic impact of PCT concentration in this population.
Methods: Out of 73 published studies, we identify 7 that were eligible for our analysis, including a total of 5,810 patients. We estimate PCT concentration in patients with or without HF and/or infection. We also compared the short-term mortality of patients with versus without elevated serum PCT concentrations. Risk ratios (RR) and confidence intervals (CI) were calculated.
Results: The mean age of the study samples ranged for 58 to 81 years and the proportion of men ranged to 47 to 66%. The analyzed follow-up ranged from 22 to 180 days and the cutoff PCT concentrations ranged from 0.1 to 0.25 ng/l. Patients with HF and concomitant infection tended to have a higher PCT concentration than those with HF alone (respectively 0.26 ng/l [0.06, 0.46] vs 0.10 ng/l [0.08, 0.12]; p = 0.059%).
The mortality rates of patients with elevated PCT concentrations was significantly higher that of patients with PCT concentrations in the normal range at 30, 90 and 180 days (respectively RR 30 days 2.66 [1.74 , 4.05]; RR 90 days 2.12 [1.59 , 2.83]; RR 180 days 2.06 [1.13 , 3.78]).
Conclusions: This review and meta-analysis contribute to strengthen the conclusions of several recent studies of the prognostic role of PCT in patients suffering from HF. The measurements of PCT concentrations enabled their short-term risk stratification. Further studies may investigate outcomes with risk-stratification driven by procalcitonin levels in patients presenting with suspected or confirmed HF.



mortality rates

P532

A novel risk score for prediction of new onset heart failure in patients undergoing coronary or peripheral angiography: Results from the CASABLANCA study

N Ibrahim[1]; A Lyass[2]; HK Gaggin[1]; Y Liu[2]; RRJ Vankimmenade[3]; SR Motiwala[4]; NP Kelly[5]; PU Gandhi[6]; ML Simon[1]; AM Belcher[1]; JE Harisades[1]; JM Massaro[2]; RB D'agostino[2]; JL Januzzi[1]
[1]*Massachusetts General Hospital, Cardiology , Boston, United States of America*; [2]*Baim Institute for Clinical Research, Boston, United States of America*; [3]*Radboud University Medical Centre, Cardiology, Nijmegen, Netherlands*; [4]*Beth Israel Deaconess Medical Center, Cardiology, Boston, United States of America*; [5]*Brigham and Women's Hospital, Boston, United States of America*; [6]*Yale University, New Haven, United States of America*

Background: Heart failure (HF) is a major public health concern with increasing prevalence in the general population. Methods to identify patients at risk for new-onset HF would be welcome as such patients might benefit from earlier interventions. However, clinical risk factors alone are insufficient to identify risk; adding biomarker results to clinical risk factors may improve accuracy. Using the resources of the Catheter Sampled Blood Archive in Cardiovascular Diseases study, we sought to identify clinical and biomarker predictors of the development of new-onset HF in a population undergoing coronary and/or peripheral angiography for various indications as this may have implications on future management.
Methods: The CASABLANCA study is a prospective single-center observational trial of 1251 patients who underwent coronary and peripheral procedures with or without intervention for various indications. Multiple cardiac and renal biomarkers were obtained immediately before the procedure in order to assess their value in predicting short- and long-term events; median follow-up was 3.8 years. Our sample consisted of 991 patients free of prevalent HF at baseline. We used stepwise Cox Proportional Hazard models (using alpha level of 0.05 for both entry and retain) to develop a score to predict an adjudicated diagnosis of new-onset HF using a list of pre-selected covariates. Model discrimination and reclassification (categorical net reclassification and integrated discrimination improvement, NRI/IDI) with and without biomarkers was evaluated.
Results: During follow up, 177 (18%) developed new-onset HF. Patients with incident HF were more likely to be older, and to have history of numerous risk factors for HF such as arrhythmia, hypertension, coronary artery disease, diabetes mellitus or chronic kidney disease; numerous prognostic biomarkers were abnormal in those suffering new-onset HF, including higher concentrations of highly sensitive troponin I, amino-terminal pro-B type natriuretic peptide (NT-proBNP), cystatin C, myeloperoxidase and ST2. Independent predictors of new-onset HF were identified and a scoring system was developed consisting of 5 clinical variables (age, male sex, heart rate, history of atrial fibrillation/flutter, and history of hypertension) and 2 biomarkers (NT-proBNP and ST2). Age and sex were forced into the model. The c-statistic for the model without biomarkers was 0.69; including biomarkers substantially increased the c-statistic to 0.76 (p < 0.0001). Biomarkers also significantly reclassified risk for new-onset HF beyond clinical variables (NRI 0.26; IDI 0.10; both p < 0.0001). When the HF risk score was divided into quintiles, patients in the highest quintile had the highest incidence of development of new-onset HF compared to those with scores in lower quintiles (Figure 1).
Conclusions: We describe an accurate clinical and biomarker score for predicting new-onset HF in an at-risk population.

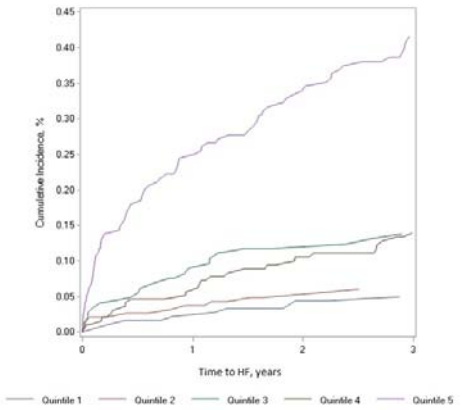


Figure 1

NURSING

P533

The relationship between physical activity and appetite in heart failure - A cross sectional study

C Andreae[1]; K Arestedt[1]; L Evangelista[2]; A Stromberg[1]
[1]*Linkoping University, Department of Medical and Health Sciences, Division of Nursing Science, Linkoping, Sweden*; [2]*University of California at Irvine, Program in Nursing Science, Irvine, United States of America*

Background: Physical activity and appetite are important for maintaining physical health. Yet, sedentary lifestyle and poor appetite are frequently observed in the heart failure (HF) population. However, the relationships between these phenomena are not yet clearly understood.
Purpose: To investigate the relationship between physical activity and appetite in patients with stable HF.
Methods: In this cross sectional study, a consecutive sample of 186 patients with confirmed HF with NYHA class II-IV (median age 72y, 70% men, NYHA class II 61%) participated in the study. Patients were recruited from three HF outpatient clinics in central Sweden. Physical activity measures included total energy expenditure (TEE), active energy expenditure (AEE) above 3 METs, average daily METs and number of steps per day during four days using a validated multi-sensor wearable armband (SenseWear®, Body Monitoring System). Patients also self-reported their physical activity on a ten point numeric rating scale, from extremely low (1) to extremely high (10). Self-reported appetite was measured by Council on Nutrition Appetite Questionnaire (CNAQ), an 8-item instrument (score range 8-40) where CNAQ $\leq$28 indicate poor appetite. Associations between physical activity and appetite were analyzed by Spearman correlation while differences in physical activity between poor vs good appetite were analyzed using Mann Whitney U test.
Results: There was a significant positive relationship between physical activity and appetite assessed by TEE (rs=.184, p = .012), AEE of moderate intensity >3 METs (rs=.262, p = .000), number of steps (rs=.292, p = .000), average METs intensity (rs=.249, p = .001), and self- reported physical activity (rs=.191, p = .009). Levels of physical activity in the low appetite group differed significantly from the group with better appetite, this was seen in all physical dimensions, TEE (U=3225, z=-2.26, p = .024), AEE (U=2902, z=-3.178, p = .001), number of steps (U=2706, z=-3.734, p = .000), average METs intensity (U=3128, z=-2.541, p = .011), levels of self-reported physical activity (U=3185, z=-2.47, p = .013).
Conclusion: This study shows that physical activity is associated with appetite and that levels of physical activity differs between patients with poor and good appetite. These findings has implications for both research and practice and underlines the importance in monitoring both physical activity and appetite. Further research is needed to determine whether interventions targeting physical activity also improve appetite and vice versa in the HF population.

P534

Gender differences in patients-partner dyads affected by heart failure

A Anna Stromberg[1]; M Liljeroos[2]; S Agren[2]; T Jaarsma[3]
[1]*Linkoping University Hospital, Linkoping, Sweden*; [2]*Linkoping University, Department of Medical and Health Sciences, Division of Nursing Science, Linkoping, Sweden*; [3]*Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden*

Background: It is known that women often experience poorer quality of life and more symptoms of depression, both among patients with heart failure and in the norm population. Further it is also known that female caregivers experience more burden and stress in relation to caregiving compared to men.
Aim: The aim of this study was to explore gender differences with regard to quality of life, symptoms of depression, perceived control, emotional support and caregiver burden in patients-partner dyads affected by heart failure.
Method: The study is a secondary analysis of baseline data from a RCT targeting patients with heart failure and their caregiving partners. A total of 155 patient-partner dyads where included. Data were collected using SF-36 , Beck Depression Inventory, Control Attitude Scale, a single item to measure emotional support and the Caregiver Burden Inventory.
Results: There were no significant difference in age, educational level, lifestyle or comorbidities between the genders in either the patient or caregiver group. Mean age of female patients (n = 38) was 70 and male patients (n = 117) 72 years, female caregivers 68 and male caregivers 70 years. Most patients and caregivers stated that they had someone to confine in. Male patients experienced this to a significantly higher extent than female patients (p = 0.01). There were no significant gender differences between the caregivers in perceived emotional support or caregiver burden. There were several gender differences in the eight domains of health-related quality of life measured by SF-36 among the patients. Male patients had significantly better physical function (48 $\pm$ 27 versus 36 $\pm$ 24), social function (67 $\pm$ 28 versus 52 $\pm$ 27) and mental health (70 $\pm$ 22 versus 61 $\pm$ 17). A similar picture was seen among caregiving partners with male partners having significantly better physical function (81 $\pm$ 21 versus 72 $\pm$ 23), less bodily pain (82 $\pm$ 20 versus 67 $\pm$ 2), and better mental health (75 $\pm$ 15 versus 68 $\pm$ 22). Female patients had more symptoms of depression than males (p = 0.048) with 50% of the females having depressive symptoms and 30% of the males. However, there was no gender difference with regard to depressive symptoms in caregivers. No significant gender differences in perceived control over the heart disease neither among the patients, nor among their caregiving partners were found.
Conclusion
In patient and caregiver groups that were equal with regard to age, educational level and comorbidities we found differences between male and female caregivers with regard to health-related quality of life, but no differences in emotional support, perceived control over the heart failure condition, depressive symptoms or caregiver burden. Female patients were found to be more vulnerable than males with poorer quality of life, less emotional support and more depressive symptoms. Interventions targeting to support female patients are warranted, Support programs for caregivers should include both men and women.

P535

Adherence to low sodium diet in heart failure patient-caregiver dyads

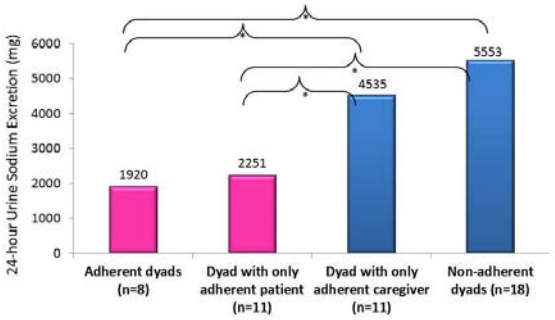
ML Misook Chung[1]; DK Moser[1]; TA Lennie[1]
[1]*University of Kentucky, College of Nursing, Lexington, United States of America*

Funding Acknowledgements: NIH/ National Institute of Nursing Research, USA

Background: Despite the importance of following a low sodium diet (LSD) in improving outcomes of patients with heart failure (HF), adherence to LSD remains. Poor support from family members was identified as a major barrier for patients. However, there is limited knowledge about whether patients increase their adherence to LSD when family caregivers also follow a LSD.
Purpose: To examine the association of adherence to LSD between patients with HF and their family caregivers.
Methods: This was a cross-sectional study in which patients with HF and their primary family caregivers were recruited from a HF clinic in the southern United States. Patients and their caregivers completed 24-hour urine collection for sodium excretion as a measure of sodium intake. Paired t-test was used to compare LSD adherence between patients and caregivers dyad members. One-way ANOVA was used to compare sodium intake among 4-dyad groups stratified by adherence using a cut point of urinary sodium excretion (UNa) less than 3000mg: adherent dyads, non-adherent dyads, dyads with only adherent caregiver, dyads with only adherent patient).
Results: A total of 48 patients (60% male, mean age 59) and 48 caregivers (65% female, mean age 53) provided 24-hour urine samples. The estimated sodium intake of patients was 3957mg ($\pm$2308) which was similar to family caregivers (3621mg $\pm$ 1556, p = .38). There was no difference in adherence rate (UNa < 3000mg) between patients and caregivers (40% vs 40%, p>.05). Half of dyads (54%) had members that were either both adherent (17%) or both non-adherent (38%), and remainder of dyads had only one adherent member. Among 4 dyad groups, patients who were in the non-adherent dyads had highest sodium intake (5553mg), averaging 3300mg higher than those of patients in the adherent dyads (p < .05, Figure 1).
Conclusion: Family support is pivotal in patients' adherence to LSD. In this study, patients and their family caregivers consumed similar amounts of sodium. Sodium

intake was highest in patients whose caregiver also consumed a high sodium diet. These results suggest that interventions aimed at improving LSD adherence should target both patients and family members together.

Figure 1. Comparisons of patients' 24-hours Urinary Sodium Excretion among dyads classified by adherence



ANOVA $P < .001$; * post-hoc test, $p<.05$

P536

Health Care Professionals' compassion rounds

I Ioanna Lakatamitou[1]; E Lambrinou[2]; J Rilley[3]; P Andreou[2]; N Middleton[2]; J Pepper[3]

[1]American Heart Institute, American Heart Institute/American Medical Center, Nicosia, Cyprus; *[2]Cyprus University of Technology, Limassol, Cyprus*; *[3]Imperial College London, London, United Kingdom*

Funding Acknowledgements: HFA nurse training fellowship

Background: "Heath Care Professionals' (HCPs') compassion" rounds are a multidisciplinary forum aiming to help HCPs improve emotional expression, teamwork and communication. The main aim of our study was to explore the views of HCPs about the rounds and assess the impact of these rounds on teamwork and job satisfaction.
Method: A quasi experimental study was conducted in a cardiology/cardiosurgery hospital. Three rounds were established in which a patient case was described and then discussed by a multidisciplinary group. Twenty-five HCPs participated in the study and completed TeamSTEPPS and Minnesota Satisfaction Questionnaires validated in Greek, before and after the rounds. After the rounds, 10 participants were selected (via purposive sampling) to participate to focus groups. Quantitative and qualitative data were analyzed using t-test and content analysis, respectively.
Results: An upward trend on teamwork and job satisfaction was observed after the rounds, with no statistical significance ($p=0.10$, $p=0.18$). Four main themes extracted: exposing emotions; personal impact; inequality of topics; frontiers. Overall, participants reported benefited on sharing concerns and identifying needs in their work environment, teamwork and the management that could be improved.
Conclusions: Findings suggest that "HCPs' compassion rounds'' may contribute to more positive feelings about teamwork, better collaboration and job satisfaction.

POPULATION STUDIES – EPIDEMIOLOGY

P537

The potential use of ivabradine among ambulatory patients with heart failure with reduced ejection fraction in the real world scenario

Zl Zaza Iakobishvili[1]; D Murninkas[2]; A Porter[1]; H Jino[2]; S Birkenfeld[2]; D Hasdai[1]

[1]Rabin Medical Center, Petah Tikva, Israel; *[2]Heart Failure Unit, Clalit Health Services, Tel Aviv, Israel*

Background: Ivabradine, an inhibitor of the If channel, is a relatively new addition to the pharmacological therapeutic regimen for heart failure with reduced ejection fraction (HFrEF). In particular, it is indicated for HFrEF patients in sinus rhythm, NYHA class ≥2, ejection fraction (EF) ≤35%, and heart rate ≥75/min.
Aim: We sought to evaluate the potential use of ivabradine in a large cohort of real-world, ambulatory HFrEF patients.
Methods: We analyzed the electronic records of all 115739 patients 18 years old and insured by our Health Services in the Holon/Bat-Yam District. We identified 550 patients with EF≤40% and age under 85 years. We then further sought the patients who met the criteria for use of ivabradine, as described above.
Results: Of the 550 patients (123 women), with a mean age of 71.4 ± 9.8 years and mean EF of 32.1% + 6.7, 432 patients were in sinus rhythm, 451 patients were in NYHA class≥2, 401 patients had EF≤35%, and 362 patients had heart rate ≥75/min (some patients had more than one exclusion criterion). Altogether, only 154 patients (28.0%) were apparently suitable for consideration of treatment of ivabradine, of whom 138 patients (89.6%) were under treatment with beta blockers (mean 38.6% + 21.6 of maximal dose, and only 2.7% of patients receiving maximal beta blocker dose).
Conclusions: In a large cohort of real-world, ambulatory HFrEF patients, approximately only a quarter of the patients were apparently suitable for consideration of ivabradine treatment. Some patients were not under beta blocker treatment, and the vast majority was receiving submaximal doses. Thus, it seems that there is substantial room for improvement in beta blocker therapy before initiating treatment with ivabradine.

P538

The characteristics of heart failure ambulatory patients with reduced ejection fraction who attend a specialized heart failure clinic compared to those who decline such follow-up

Zl Zaza Iakobishvili[1]; D Murninkas[2]; A Porter[1]; H Jino[2]; S Birkenfeld[2]; D Hasdai[1]

[1]Rabin Medical Center, Petah Tikva, Israel; *[2]Heart Failure Unit, Clalit Health Services, Tel Aviv, Israel*

Background: Specialized heart failure (HF) clinics have been established to ameliorate management. The proportion of HF patients who choose to attend such clinics and their demographic and clinical characteristics remain unknown.
Methods: We analyzed the electronic records of all 115739 patients 18 years old and insured by our Health Services in the Holon/Bat-Yam District. We identified 550 patients with EF≤40% and age under 85 years. In collaboration with the general practitioners in the district and under the auspices of the district management, all suitable patients were actively solicited by a dedicated nurse to attend a specialized HF clinic within their community.The demographic and clinical characteristics of the patients who elected to attend the clinic were compared with those who declined.
Results: Of the patients who were actively solicited, of whom 22.4% were women, 210 (38.1%) elected to attend the clinic, 173 men and 37 women. Men were more likely to attend the clinic (40.5% of men in the cohort vs 30.0% of women, p0.05). Of interest, patients who attended the clinic were less likely to be in NYHA class 1-2 (39.0% vs 65.6% among patients who did not attend, p0.01) and tended to be more likely to have diabetes mellitus (60.4% vs 52.1% among patients who did not attend, $p=0.06$). There were no other differences in baseline characteristics, including the proportion of patients receiving evidence-based medications.
Conclusions: Although a specialized HF clinic was readily available, in our cohort of ambulatory HF patients with reduced election fraction only 38.1% elected to attend. Efforts should be made to to make this service attractive and accessible.

P539

Acute heart failure in the elderly and very old.

L Luis Abreu[1]; H Antunes[1]; L Goncalves[1]; J Gil[1]; I Cunha[1]; B Marmelo[1]; MI Pires[1]; I Almeida[1]; E Correia[1]; C Cabral[1]

[1]Hospital Sao Teotonio, Cardiologia, Viseu, Portugal

Introduction: Heart Failure (HF) is a syndrome with increasing incidence with population aging. However, the guidelines are based on studies in younger populations, and it is not always possible to apply all therapies measures due to comorbidities ande interactions.
Objectives: To evaluate the impact of advanced and very advanced age on comorbidities, therapy and outcomes in a population admitted with HF.
Methods: All consecutive HF admissions in a cardiology department were evaluated for a 6 years (Y) period. Only the first episode of each patient was included. Patients were divided into groups (G) according to age (GA: ≤ 75Y, GB: 76-85Y, GC: ≥86Y). The remaining demographic data, previous co-morbidities, previous medication and the date of discharge, and in-hospital mortality were evaluated. Results: A total of 1006 hospitalizations were performed, corresponding to the same number of patients, with a mean age of 77.5 ± 10.1Y, 50.8% of males. 336 patients were included in GA (36.4%), 417 in GB (41.5%) and 223 in GC (22.2%). The inter-groups comparison is presented in table. In-hospital mortality was 3.8% in GA, 8.4% in GB, and 9.0% in GC ($p=0.041$).
Conclusion: In this population it is evident the negative impact of age on intrainternational mortality. Its also evident a higher prevalence of females and patients with HF with preserved EF (HFpEF) with advancing age, which are underrepresented in clinical studies. Somewhat unexpectedly, there is a lower prevalence of AF, coronary artery disease (CAD) and diabetes mellitus (DM) in the older patient group, which can be explained by the greater pervalence of HFpEF. As expected, its also evident that medical therapies are underused in the elderly.

Group comparison				
	GA (≤ 75Y)	GB (76-85Y)	GC (≥86Y)	
Male	63,7%	45,6%	39,5%	P=0,000
Hipertension	66,8%	68,1%	65,9%	P=n.s.
DM	42,2%	34,1%	27,8%	P=0,000
CAD	19,7%	12,2%	10,3%	P=0,002
Atrial Fibrilation	52,6%	55,9%	48,9%	P=n.s.
Cronic Kidney Desease	20,2%	19,6%	38%	P=0,012
HFpEF	36,7%	49,0%	57,3%	P=0,000
BNP at admission	763±857	880±947	974±1151	P=n.s.
Beta-Blockers at discharge	57,6%	38,0%	33,5%	P=n.s.
ACE inibitor at discharge	76,5%	74,2%	69,3%	P=n.s.
Aldosterone Antagonists	52,1%	39,6%	46,0%	P=0,003

P541

Is there a significant gender bias in treatment among ambulatory patients with heart failure with reduced ejection fraction in the real world scenario?

ZI Zaza Iakobishvili[1]; A Porter[1]; D Murninkas[2]; H Jino[2]; S Birkenfeld[2]; D Hasdai[1]
[1]Rabin Medical Center, Petah Tikva, Israel; *[2]Heart Failure Unit, Clalit Health Services, Tel Aviv, Israel*

Background: Heart failure (HF), in particular with reduced ejection fraction (HFrEF), is associated with considerable morbidity and mortality in both genders. Frequently, women are less likely to receive evidence-based treatments than men, despite similar management recommendations.
Aim: We sought to investigate gender differences in treatment for HFrEF in a large cohort of ambulatory patients.
Methods: We analyzed the electronic records of all 115739 patients 18 years old and insured by our Health Services in the Holon/Bat-Yam District. We identified 550 patients with EF≤40% and age under 85 years.
Results: Women comprised a small minority of the cohort (n = 123, 22.4%), tended to be slightly older (72.7 + 10.2 vs 70.9 + 9.6 years, p = 0.08), and had slightly higher EF values (33.2% + 6.9 vs 31.7% + 6.6 ,p = 0.02), yet were similarly likely to be in NYHA class 1-2 (53.5% vs. 46.6%, p = 0.55). Women had lower eGFR (61.1 + 22.6 vs 66.5 + 24.3 ml/min/1.73m2, p = 0.03) and hemoglobin levels (12.0 + 1.8 vs 13.1 + 1.7 gr/dl, p0.01), and were less likely to have diabetes mellitus (47.9% vs. 57.3%, p = 0.08). Nevertheless, evidence-based treatments were comparable among genders (Table), including the proportion of patients receiving the maximal recommended dosage.
Conclusions: Although there is a strong male preponderance among ambulatory HFrEF patients and subtle differences in demographic and clinical characteristics, we did not identify a gender bias in pharmacological treatment in our cohort.

P542

Characteristics of a group of patients admitted for heart failure presenting intermediate FE

JR Beramendi Calero[1]; I Irene Rilo Miranda[1]; S Garcia Gutierrez[2]; A Anton Ladislao[2]; L Quintas Ovejero[3]; C Goena Vives[3]; M Morillas Bueno[2]; F De La Cuesta Arzamendi[1]
[1]Hospital Donostia, San Sebastian, Spain; *[2]Hospital Galdakao-Usansolo, Bilbao, Spain*; *[3]Hospital Comarcal de Mendaro, Cardiology, Mendaro, Spain*

Objective: Study the characteristics of a group of patients admitted for heart failure who presented FE (49%) and depressed FE (FE < 40%) compared to patients with preserved EF
Methods: A prospective observational cohort study involving a total of 582 patients who come to our hospital for acute decompensated heart failure (acute heart failure and decompensated chronic heart failure).
The following variables were collected: sociodemographic, CV risk factors, comorbidities, history of heart disease (ischemic, cardiomyopathy, valvular, arrhythmia) and analytical and echocardiographic data of the emergency department and hospital admission.
We compared the characteristics of patients with intermediate EF in relation to the patients with preserved EF and depressed EF of 582 patients with a diagnosis of heart failure admitted to 3 hospitals of the Basque Health Service between 2011 and 2013. 188 patients had EF < 40 (Group A), 101 patients FE between 40 - 49% (Group B) and 193 patients FE> 49% (Group C)
Results: 29.26% of patients in group A, 48.51% in Group B and 59.73% in Group C were women (p < 0.0001). The mean age of group A was 73.58 + 12.13, group B 78.33 + 10.73 and group C 80.14 + 9.01 years (p < 0.0001). 77.59% of Group A, 79.17% of Group B and 89.47% of Group C were hypertensive (p 0.0013). 34.57% of patients in group A, 32.67% in Group B and 33.45% in Group C were diabetic (p 0.94). 42.55% of Group A, 31.68% of Group B and 25.94% of Group C had ischemic heart disease (p 0.0007). 43.62% of Group A, 55.00% of Group B and 59.66% of Group C presented atrial fibrillation (p 0.0026). 6.38% of Group A, 2.97% of Group B and 4.78% of Group C had renal failure (p 0.43).
Conclusions: 1. Patients with intermediate EF are older than patients with depressed EF, with no significant difference from the preserved EF group. The presence of women in the intermediate EF group is greater than in the group with depressed EF and lower than in the group with preserved EF.
2. The presence of hypertension in the intermediate EF group is lower than in the group with preserved EF and similar to the group with depressed EF.
3. There is no difference between the intermediate EF group and the other groups regarding the presence of ischemic heart disease and atrial fibrillation, although there is a difference between the group of preserved EF and depressed EF.
3. There are no significant differences regarding the presence of diabetes mellitus and renal failure among the 3 groups.

P543

Clinical characteristics in patients with chronic heart failure who are living in high altitude

S Bolivar[1]; J Lopez[1]; R Lasso[1]; J Torres[1]; L Jumbo[1]; C Segarra[1]; E Izaguirre[1]; J Valiente[1]; J Jativa[1]; E Aguilar[1]; P Segovia[1]; C Saenz[1]
[1]Military Hospital, Cardiology, Quito, Ecuador

Background: Hypoxemia is an adverse atmospheric condition that patients with heart failure (HF) have to face when living in high altitude (HA). It is known that acute ascents generate adverse pathophysiological changes, however little is known about the adaptation of these patients when they are living in HA chronically. Actually, all guidelines have been developed at sea level (SL) and it is not known if these guidelines would be applicable to them.
Methods: We studied 42 patients with compensated HF in the city of Quito that is at 2800 meters and compared to 36 patients living in Guayaquil that is at SL. In both groups patients had to live for at least one year under these conditions. Its clinical characteristics were observed; a six-minute walk test was performed in both groups and they were observed for one year. Mortality, emergencies and hospitalizations were determined in both groups.
Results: The average age was lower in HA (6 8.1 vrs. 77.8 years p 0,0002). The mean left ventricular ejection fraction ih HA was higher (51.1 vrs. 37.7 % p 0.0006). Ischemic disease etiology was more common in SL, while hypertension was mor common in HA. There was a better performence in six minute walk test in patients who are living in HA (370.9 vrs 277.5 meters p 0.004). There were no differences between mortality (20.5% vrs 17.3% p 0.5), hospitalizations (24,3% vrs 34% p 0.7) and cardiac emergencies (29.7% vrs 39.1% p 0.31) in both groups.
Conclusion: In spite of chronic hypoxemia, patients living at high altitude had no significant clinical differences with patients who are living at sea level. Guidelines could be applied to them without significant changes.

P544

Epidemiological, clinical, and etiological study of heart failure on a ten years period (2005 - 2014), in cardiology department of an Hospital

F Fouad Belamri[1]; K Oumokrane[1]; S Lehachi[1]; M Krim[1]
[1]Beni-Messous Hospital, Cardiology, algiers, Algeria

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.
The 5 year survival is 35% in men and 53% in women, significantly lower than the survival of certain cancers. It represents a major public health problem with the highest care cost among all cardiovascular disease. Knowledge about the pathophysiology of heart failure have evolved considerably in recent years ; therefore, its management has also seen a lot of progress where new techniques have emerged and made possible functional improvement and, especially a better survival, to certain category of patients.
Aim: Describe the epidemiological, clinical , etiological and therapeutic characteristics of acute heart failure in patients hospitalized in the cardiology department of the hospital during the period 2005- 2014.
Methods: This descriptive study analyzed retrospectively the records of patients hospitalized for acute heart failure between 2005 and 2014 in the cardiology department.
Results: 550 patients of which 64% are men. The average age was 63 years. The most frequent antecedents were ischemic heart disease (42.36%) hypertensive heart disease (40.36%) and valvular heart disease (27.27%).

Hypertension, diabetes mellitus, and tobacco were the most frequent risk factors.The left heart failure was the most common table.73.45% of patients were in their first acute decompensation.
Regarding the trigger bronchial infection (29.45%) and dietary change (22.72%) were the most common factors.62.91% had impaired FE. The average hospital stay was 17 days.
The mortality rate during hospitalization was 22.36%, with the main cause cardiogenic shock. Finally, the evaluation of drug prescriptions patterns, according to new international recommendations, is quite reassuring to the extent that the new molecules that enabled a significant reduction in morbidity and mortality in heart failure are widely prescribed in our patients.
Conclusion: The results of our study were comparable to data from the literature in particular as regards the epidemiological profile of heart failure patients with a relatively high average age, male predominance, and ischemic etiology that is the main cause of failure heart.

P545

High rates of left ventricular systolic dysfunction in patients with diabetes in Malawi, Africa

CJ Watson[1]; M Chisale[2]; H Lee[3]; J Wu[3]; J O'donoghue[4]; A Cheung[1]; M Ledwidge[5]; K Mcdonald[6]; J Chipolombwe[2]; J Gallagher[5]
[1]Queen's University of Belfast, Belfast, United Kingdom; *[2]Mzuzu Central Hospital, Mzuzu, Malawi*; *[3]Luke International Norway, Mzuzu, Malawi*; *[4]Imperial College London, London, United Kingdom*; *[5]University College Dublin, Dublin, Ireland*; *[6]Heart Failure Unit, St Vincent's University Hospital, Dublin, Ireland*

Background: It is estimated that 415 million people worldwide suffer from diabetes with more than 80% living in low and middle-income countries (LMIC). Sub-Saharan Africa (SSA) will see an 81% rise in incidence of diabetes by 2030, with a predicted 68% increase in hypertension over a similar period. Ventricular dysfunction and heart failure are major complications of diabetes and is involved in the pathogenesis and prognosis of the disease. Limited data is available on heart failure and diabetes in SSA populations. The aim of this project was to investigate the prevalence of left ventricular systolic dysfunction in a cohort of people with diabetes attending a hospital clinic in Malawi, Africa.
Methods: Ninety-five consecutive consenting patients attending a Diabetes Outpatient Clinic were recruited to the MTIMA pilot study. Anthropometric and medication data was collected. Point of care testing for blood glucose, glycated HbA1c, and lipids were conducted. All patients underwent echocardiography.
Results: Echocardiography analysis revealed a high rate of left ventricular systolic dysfunction in patients with diabetes in Malawi, with 35% having an ejection fraction less than 50%. The mean age of the study population was 58 years (range 35-85), and 38% were male. The mean time since initial diagnosis was 6 years (range 0-45 years). Mean BMI was 27, with 24% of the cohort having a BMI >30. Mean HbA1c was 68mmol/mol (range 28-129mmol/mol), with 59% of the patients above IDF HbA1c target for limited care in LMIC. Mean reported lipid data for this cohort was; total cholesterol (4.48mmol/l), LDL (2.71 mmol/l), HDL (0.98 mmol/l), triglycerides (1.79 mmol/l). Blood pressure control was sub-optimal, mean SBP/DBP 147mmHg (96-216) / 86mmHg (54-124), with 79% patients above the IDF blood pressure target for limited care in LMIC.
Discussion: Patient recruitment into this observational study is ongoing with the aim to report of additional heart failure related features in patients with diabetes in Malawi, including profiling of cardiac biomarkers.

P546

Elder heart registry- focus on heart failure: clinical profile and outcome of elderly patients aged above eighty years admitted to a tertiary care center in a developing country.

K Kiran Jacob[1]; S Ahmad[1]; A Bahekar[1]; K Venugopal[1]
[1]Pushpagiri Medical College, Cardiology, Thiruvalla, India

Introduction - Heart failure represents a major public health problem in the elderly. Limited clinical and prognostic data is available in India for development of appropriate prevention and treatment strategies in this subgroup
PURPOSE: - To know the demographics, co morbidities, clinical profile, treatment and outcomes in the 'oldest old'.
Methods: The registry enrolled consecutive admissions of patients with age ≥ 80 yrs in the cardiac care unit from Jan 1st 2014 to Dec 31st 2015. Clinical characteristics at presentation, co morbidities, treatment pattern and in hospital outcomes were collected.A telephonic follow up was done [follow up duration varying from 6 months to 2 years].
Results: - A total of 4199 patients were admitted to CCU in the study period, of which 406 patients were enrolled which constituted 9.67% of the total admissions. The mean age was 84.24(±3.67) years.
The percentage of patients with heart failure was 36.45%. Main etiology for heart failure was ischemia (54.72%). HFpEF was seen in 51.74% of patients. 22.29 % patients had AF. Inhospital mortality among the patients with heart failure was 9.45%.Rehospitalisation rate was 18.9% while mortality on follow up was 8.1%. Among the patients with HFpEF and HFrEF, there was no significant difference in inhospital mortality, rehospitalisation and mortality on follow up.
Conclusion: : The high rates of ACS, HFpEF and AF among the elderly are highlighted, along with the high inhospital mortality, particularly in those who presented with severe LV systolic dysfunction.

Profile of Heart Failure among elderly

	HFpEF(%)	HFrEF(%)	P value
Mean age	84.1	85.27	0.095
Male:female	0.93	1.23	-
Diabetes	58.3	60.34	0.851
Hypertension	63.34	56.89	0.455
Ischemic heart disease	56.67	74.13	0.055
Chronic kidney disease	16.67	22.41	0.490
AF	20	18.96	0.910
Complete heart block	6.67	1.72	0.365
Coronary angiogram	11.66	3.44	0.071
Percutaneous coronary intervention	3.34	1.72	0.420
In hospital mortality	10	12.06	0.775
Rehospitalisation	20	15.52	0.814
Mortality on follow up	8.34	8.62	0.972

P547

Heart failure as the cause of more than 40% of dyspneas in an orthopedic surgery unit

P Losada Mora[1]; A M Alfonso Miguel Garrido Castro[1]; JL Carrillo Linares[1]; M Jimenez[1]; L Morcillo[1]; J M Garcia Pinilla[1]
[1]University Hospital Virgen de la Victoria, Cardiology, Internal Medicine, Malaga, Spain

Introduction: Consultations are a widely used resource between different units in a hospital. In particular, those from Orthopedic Surgery and Traumatology (OST) Unit are some of the most frequent.
Objectives: To analyze the most frequent consultations patients admitted to OST unit asked to a specific team of Cardiology and Internal Medicine physicians, and identify how many of them can be attributed to heart failure.
Material and methods: Descriptive analysis of the reasons for consultation on patients admitted to the OST Service who suffered some kind of medical decompensation that needed to be notified to Cardiology or Internal Medicine.
Results: From June 2008 to November 2014, 1486 consultations were sent from the OST Service to a team assigned to the control of medical pathologies, formed by professionals of Cardiology and Internal Medicine. The most common reason for consultation was "dyspnea" in 371 cases (25%), followed by "pluripathology control" in 163 (11%), "diabetes control" and "blood pressure", both with 124 (8.3% %) and 123 (8.3%) queries. The digestive pathology occupied 10.5% of the consultations, but these were specified according to the disease (diarrhea, nausea-vomiting or abdominal pain). 4% of the consultations were sent because of "analytic alterations". It was remarkable the absence of "fever" as a reason for consultation, which is frequent in other surgical units analyzed; this is because fever is valued in OST by the Infectious Diseases Service.
The team analyzed the meaning of the main reason for consultation, "dyspnea", as a term that was considered too nonspecific. The result was that 46.7% of the dyspneas were of respiratory origin, with the most frequent pneumonia (32%, of which 56% were nosocomial), noncondensing respiratory infection (26%), exacerbation of COPD (18%) and bronchospasm (16%).
41% of dyspnea corresponded to heart failure; 66% of the cases, the main factor inducing dyspnea was not clearly identified (most of the patients presented mixed respiratory and cardiologic episodes), while 13.6% of those with dyspnea presented excessive intravenous fluid therapy, 11.3% anemia secondary to the intervention, and another 11.3% was due to uncontrolled atrial fibrillation. The rest of dyspneas were mainly due to anxiety (4.7%) and pulmonary thromboembolism (2%). In 3,7% of the cases no dyspnea was observed.
Conclusions: One-fourth of the consultations for medical decompensation in patients admitted to OST correspond to dyspnea. Almost half of them correspond to heart failure, induced in a very high percentage by potentially preventable situations such as excessive intravenous therapy or anemia after the surgery. Besides, high

blood pressure and diabetes are cardiovascular risk factors frequently decompensated. We suggest that an early examination of diabetes, blood pressure and factors that could induce to heart failure, performed before the surgery, could be benefitial in terms of morbidity.

P548

Mortality and re-hospitalization in patients with new onset acute heart failure in a region of northern italy

D Pavan[1]; E Clagnan[1]; F Valent[1]; G Lardieri[1]; V Moretti[1]; L Massa[1]; C Fresco[1]; A Di Chiara[1]; P Pierluigi Lesizza[1]; L Zanier[1]; A Di Lenarda[1]
[1]Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy

Background: Our Regional Social and Health Information System (SISSR) provides reliable information on epidemiology, health care pathways and prognosis of cardiovascular diseases (CV). The objective of our analysis was to analyze the survival and the likelihood of short- and medium-term rehospitalization for heart failure (HF) among residents in our region in 2009-10.
Methods: The analyses were made by querying the SISSR using SAS Enterprise Guide 7.1. The new cases of HF in 2009-2010 were identified from the Hospital Discharge Diagnosis Codes of the residents in our region with first ICD-9-CM codes 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0-4 , 428.9. For the survival analysis SISSR was linked with regional Registry of Deaths. The follow-up ended 31/12/2015.
Results: In 2009-2010 there were 5963 admissions for HF (average rate of 2.41 per 1000 patient-years; range in the 5 Regional Health Authorities from 2.14 to 2.72). Hospital admission involved in 86% subjects ≥70 years. 82% of the pts were discharged from Medicine, 11% from Cardiology. Of 5963 pts hospitalized in 2009-10, 506 (8.5%) died during hospitalization. The 5457 discharged alive, 1970 (33%) were re-hospitalized (25% within 76 days from the first admission, 50% within 299 days, 75% within 805 days). At the end of 2015, of 5963 patients from the 2009-10 cohort, 1835 (31%, range 29% -34%) were still alive (25.4% among patients aged ≥ 70 years, 64% of those age <70 years). In the 5 regional Health Authorities survival was similar in pts ≥70 years, while there was a significant difference in pts <70 years. The survival curve of females (significantly older) was significantly worse than males. Conclusions:Our regional data warehouse provides useful information to plan educational activities and improvement of quality of care and clinical pathways. The trend of new admissions for HF is highly variable in the 5 regional Health Authorities, as well as it is clear a lot of room for improvement of post-discharge pathways. Also for this reason re-admissions and mortality are still high especially in older females.

PSYCHOSOCIAL - ETHICAL CONCEPTS - EDUCATION

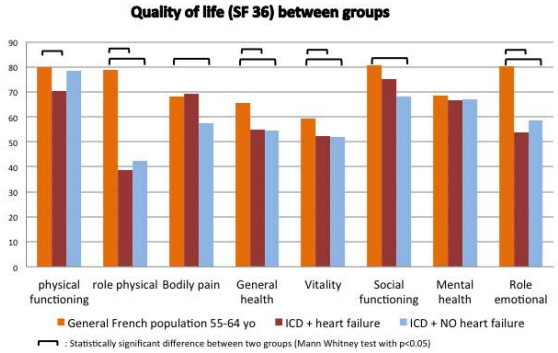
P549

Impact of the implantation of a cardioverter defibrillator on quality of life in heart failure patients: preliminary results of the EDUC-DAI study

CM Maupain[1]; FP Pousset[1]; AHS Abid Saidi[1]; SS Staraci[2]; NB Badenco[1]; XW Waintraub[1]; GD Duthoit[1]; TC Chastre[1]; CH Himbert[1]; YDH Dagher-Hayek[1]; JF Fedida[1]; FHL Hidden-Lucet[1]; EG Gandjbakhch[1]
[1]AP-HP - Hospital Pitie-Salpetriere - Institute of Cardiology, Rhythmology Department, Paris, France; *[2]Centre de référence des maladies cardiaques héréditaires, Paris, France*

Funding Acknowledgements: Fédération Française de Cardiologie

Background: : The implantation of a cardioverter defibrillator (ICD) is associated with an impairment of quality of life. Quality of life in heart failure patients with an ICD is not well documented.
Objectives: To assess quality of life in heart failure patients implanted with ICD (with or without a cardiac resynchronization therapy) in a French tertiary center and involved in our educational therapeutic program.
Materials and Methods: Every patient receiving an ICD from September 2015 to July 2016 at Pitié Salpêtrière university hospital were included. This cohort comes from the EDUC-DAI study which evaluates the impact of an educational therapeutic program for ICD patients. Quality of life was assessed through the Short Form (SF 36) health status questionnaire completed 1 month after ICD implantation and before the first session of the program. Quality of life of ICD heart failure patient was compared to those without heart failure. It was then compared to the general French population aged from 55 to 64 years old.
Results: : Between September 2015 and July 2016, 80 patients completed the SF36 questionnaire. 46/80 (61%) had a clinical heart failure. The mean age of the heart failure patients was 63,4 +/- 10,1 years old. Mean left ventricular ejection fraction in the heart failure group was 29 +/- 8% and 34/46 (74%) benefited from a cardiac resynchronization therapy. Quality of life was significantly impaired in both groups compared to the general French population aged from 55 to 64 years old. Quality of life wasn't different between the heart failure group and the non heart failure group for the 8 domains of the SF 36 (Figure 1).
Conclusion: : In this cohort, ICD recipients have an impaired quality of life compared to the general French population whether or not they experience heart failure. This suggests that ICD implantation has a real impact in quality of life for all patients. Therapeutic education of patients can help them to develop coping skills.



Quality of life between groups

P550

Short term health perception and psychological functioning in heart failure patients undergoing surgical left ventricle restoration and cardiac rehabilitation

E Callus[1]; E Quadri[1]; S Pagliuca[1]; E G Bertoldo[1]; G Frigerio[1]; V Milani[2]; L Maresca[3]; B Girardi[3]; C Tardio[3]; S Lucibello[3]; S Castelvecchio[4]; L Menicanti[4]; R Tramarin[3]
[1]IRCCS, Policlinico San Donato, Clinical Psychology Service , San Donato Milanese, Italy; *[2]IRCCS, Policlinico San Donato, Biostatistics Unit, San Donato Milanese, Italy*; *[3]IRCCS, Policlinico San Donato, Perioperative and Cardiac Rehabilitation Dept. , San Donato Milanese, Italy*; *[4]IRCCS, Policlinico San Donato, Adult Cardiac Surgery Dept., San Donato Milanese, Italy*

Background: Surgical left ventricular restoration (SVR) is a valuable therapeutic option for heart failure (HF) pts with ischemic cardiomyopathy (IC). For these pts health perception, psychological functioning and quality of life (QoL) are relevant outcome indicators.
Purpose: The aims of this study are to evaluate the short-term impact of SVR on health perception, anxiety, depression and QoL and to identify variables that could affect them.
Methods: SF-36 questionnaire and EuroQol for health perception, the Hospital Anxiety and Depression Scale (HADS) and the Minnesota Living with Heart Failure for quality of life, together with biographical data and information about lifestyle were administered to 100 consecutive HF pts with IC (78 males, mean age 65.5 ± 11) who underwent SVR in the last 3 yrs, followed by a comprehensive inpatient cardiac rehabilitation (CR) programme. All questionnaires were administered preoperatively (t0), and the EuroQol and HADS were administered also during admittance (t1) and discharge (t2) from cardiac rehabilitation. The average duration of hospitalization in cardiac surgery is 5-7 days, and 21 days in cardiac rehabilitation. Descriptive data are expressed as means (±1SD) for all continuous variables. Repeated-measures analysis is used to assess trend over time (T0 preoperatively, T1 admission in cardiac rehabilitation and T2 discharge from rehabilitation). Univariate linear regression analysis was performed to identify the variables associated with the variation defined as change from preoperative status to discharge from CR (n = 37) or as change from postoperative status to discharge from CR (n = 85) of the anxiety and depression scales. The analyses included continuous variables (preoperative EuroQol, preoperative NT-proBNP, ejection fraction, age) and categorical variables (sex and NYHA class).
Results: Analyses indicate significant changes in time in health perception and QoL ($p < 0.001$). There is an indication of improvement at discharge from CR in health perception (EuroQol) (Preop mean score 63.2 ± 23.1 and at discharge 81.3 ± 18.9). There is also a significantly decrease in the mean scores of anxiety after discharge from CR (mean score of anxiety 5.1 ± 4.4 to 2.4 ± 3.3 at discharge) ($p < 0.001$). The mean scores of depression was in the normal range at all times. At univariate analysis the variation of the levels of anxiety and depression, during hospitalization in cardiac surgery (t0 to t1) and cardiac rehabilitation (t1 to t2) were not associated to the medical variables and health perception.

Conclusions: These preliminary analyses indicate that HF pts undergoing SVR perceive an improvement in their health status following the SVR procedure. Interestingly, neither the medical variables, nor subjective health perception, were found to be correlated with levels of anxiety and depression. Qualitative data gathered from psychological sessions were used in order to make further inferences.

P551

Comparison of quality of life and perceived self-efficacy between caregivers of heart failure patients and caregivers of heart failure and chronic obstructive pulmonary disease patients.

SC Torres-Montiel[1]; V Pelaez-Hernandez[2]; A Orea-Tejeda[2]; B Robles-Uribe[2]; F Figueroa-Herrera[2]; D Gonzalez-Islas[2]; A Jimenez-Cepeda[2]; A Navarrete-Penaloza[2]; L Verdeja-Vendrell[2]; R Sanchez-Santillan[2]; GK Perez-Cortes[2]
[1]National Autonomous University of Mexico, Mexico City, Mexico; *[2]Instituto Nacional de Enfermedades Resporatorias Ismael Cosio Villegas, Heart Failure and Distress Respiratory Clinic, Mexico City, Mexico*

Introduction: Being a caregiver (CG) of a heart failure (HF) patient affects health negatively. It is thought that this impairment mainly depends on the CGs' characteristics and not on the patients'. However, HF patients often have comorbidities such as chronic obstructive pulmonary disease (COPD), and there are no studies that describe if the CGs' health characteristics differ between CGs of HF patients and CGs of HF + COPD patients. Purpose. To compare the health-related quality of life and the perceived self-efficacy of CGs of HF patients and CGs of HF + COPD patients.
Methods: This study included 18 CGs of HF patients (G1) and 18 CGs of HF + COPD patients (G2), which completed the SF-12 questionnaire and the Perceived Self-efficacy in Caregivers of Chronically Ill Scale. The first includes 8 dimensions: Physical functioning, Social functioning, Role-physical, Role-emotional, Mental health, Energy/vitality, Pain and General health perception. The second classifies perceived self-efficacy as low, moderated and high. Comparisons between groups were made by unpaired Mann-Whitney U test since the data did not have a normal distribution. Results. There were no significant differences in age and sex between the two groups (G1: 55.50 ± 12.22 years, 77.8% women; G2: 55.83 ± 12.90 years, 77.8% women). There were significant differences in the General health perception (XG1=66.39 ± 21.20, XG2=50 ± 27.11; U=96, $p < 0.05$) and Mental health (XG1=77.03 ± 21.62, XG2=64.81 ± 16.41; U=99, $p < 0.05$) SF-12 dimensions, and also in the total score of perceived self-efficacy (XG1=100.44 ± 8.64, XG2=80.39 ± 28.32; U=85, $p < 0.05$). For both tests, a lower score indicates more impairment. Conclusions. CGs of HF + COPD patients have higher impairment in their general and mental health, and they perceive themselves less efficient. For this reason, treatment that offer them caregiving and solving problems skills should be priority, as it could improve their health and self-efficacy.

P552

Comparison of anxiety, depression and psychological stress between heart failure and chronic obstructive pulmonary disease patients with better and poorer performance of the six-minute walk test

SC Torres-Montiel[1]; A Orea-Tejeda[2]; V Pelaez-Hernandez[2]; F Figueroa-Herrera[2]; B Robles-Uribe[2]; D Gonzalez-Islas[2]; GK Perez-Cortes[2]; L Verdeja-Vendrell[2]; A Navarrete-Penaloza[2]; A Jimenez-Cepeda[2]; R Sanchez-Santillan[2]
[1]National Autonomous University of Mexico, Mexico City, Mexico; *[2]Instituto Nacional de Enfermedades Resporatorias Ismael Cosio Villegas, Heart Failure and Distress Respiratory Clinic, Mexico City, Mexico*

Introduction: Psychosocial factors such as anxiety, depression and psychological stress affect the prognosis of patients with heart failure and chronic obstructive pulmonary disease (HF + COPD). Performance of the Six-Minute Walk Test (6MWT) has been used for estimating this prognosis. Literature states that patients who walk less than 300 meters have a worse prognosis. Purpose. To compare the anxiety, depression and psychological stress scores of those patients with HF + COPD who walked less or more than 300 m in the 6MWT.
Methods: This study included 31 patients with HF + COPD, which completed the Hospital Anxiety and Depression Scale (HADS) and the Perceived Stress Scale. The HADS questionnaire is a reliable self-rating scale that classifies anxiety and depression into three ranges: normal, mild-moderate and severe. The Perceived Stress Scale measures the frequency of exposure to stressful situations during the past month. Comparisons between groups were made by unpaired Mann-Whitney U test since the data did not have a normal distribution. Results. The sample was divided into two groups based on the walking distance of the 6MWT: Group 1 (G1) walked less than 300 m (163.19 ± 82.99 m) and Group 2 (G2), more than 300 m (414.13 ± 91.77 m), 51.6% of the patients walked less than 300 m (G1: n=16, G2: n=15). There were no significant differences in age and sex between the two groups (G1: 69.38 ± 14.52 years, 68.8% women; G2: 65.07 ± 13.57 years, 53.3% men). There were significant differences in anxiety scores (XG1=6.19 ± 4.05, XG2=2.53 ± 2.66; U=52, $p < 0.01$). Although there were no significant differences in depression and psychological stress, G1 had higher depression (XG1=6.19 ± 3.97, XG2=4 ± 3.25) and perceived stress scores (XG1=24.75 ± 5.13, XG2=21 ± 5.60).
Conclusions: In this sample, patients that walk less than 300 m in the 6MWT have higher scores of anxiety. For this reason, treating anxiety symptoms is essential, as it could improve the patients' prognosis and quality of life. Although these are preliminary results from a small sample, we will continue working on it.

P553

Factors associated with self-care behaviours in heart failure: a systematic review of european heart failure self-care behaviour scale (EHFScBS) studies

N Natasa Sedlar[1]; M Lainscak[2]; J Martensson[3]; A Stromberg[4]; T Jaarsma[5]; J Farkas[2]
[1]National Institute of Public Health, Ljubljana, Slovenia; *[2]General Hospital Murska Sobota, Department of Internal Medicine, Murska Sobota, Slovenia*; *[3]Jönköping University, School of Health and Welfare, Department of Nursing, Jönköping, Sweden*; *[4]Linköping University, Department of Medical and Health Sciences, Linköping, Sweden*; *[5]Linköping University, Faculty of Health Science, Department of Social and Welfare Studies, Linköping, Sweden*

Funding Acknowledgements: Heart failure epidemiology in Slovenia: prevalence, hospitalizations and mortality (J3-7405) financially supported by the Slovenian Research Agency.

Background: Due to the important role of self-care in the comprehensive management of patients with heart failure (HF), The European Heart Failure Self-care Behaviour Scale (EHFScBS) was developed and tested to measure behaviours that HF patients perform to maintain daily life activities, healthy functioning, and wellbeing. Available evidence shows individual differences in patients' engagement in HF self-care behaviours, but the findings regarding the influence of personal and environmental factors on HF self-care remain inconclusive.
Aims: We reviewed literature to evaluate importance of factors associated with HF self-care behaviours as measured by the EHFScBS.
Methods: Following PRISMA guidelines, PubMed, Scopus and ScienceDirect were searched for studies using EHFScBS. Associating factors of HF self-care, obtained in observational studies were qualitatively synthesised to explore association levels of most commonly addressed factors.
Results: From total of 1357 potentially eligible abstracts screened 74 full-text papers were retrieved and reviewed to include 30 studies in the qualitative synthesis. A diverse range of personal and environmental factors associated with self-care behaviours in HF patients was identified (71 different factors in 18 sub-categories and 6 categories). Association levels between the EHFScBS score and seven factors: age (reported in 11 studies), health-related quality of life (8), gender, education, NYHA class (7), depressive symptoms (6) and LVEF (5), were most often reported, generally indicating negligible or low associations. However, consistent significant association ($p < 0.05$, demonstrated in ≥ 75 % of studies) between HF self-care behaviours and depression was found, while NYHA class and health-related quality of life showed non-significant associations with HF self-care behaviours in most of the studies.
Conclusion: Many factors were analysed for potential associations but only depression was consistently associated with EHFScBS score.

EXERCICE TESTING AND TRAINING

P554

Physical activity of STEMI patients after cardiac rehabilitation.

S Borodzicz[1]; P Balsam[1]; M Peller[1]; R Glowczynska[1]; L Koltowski[1]; P Lodzinski[1]; KJ Filipiak[1]; M Grabowski[1]; G Opolski[1]
[1]Medical University of Warsaw, 1st Chair and Department of Cardiology, Warsaw, Poland

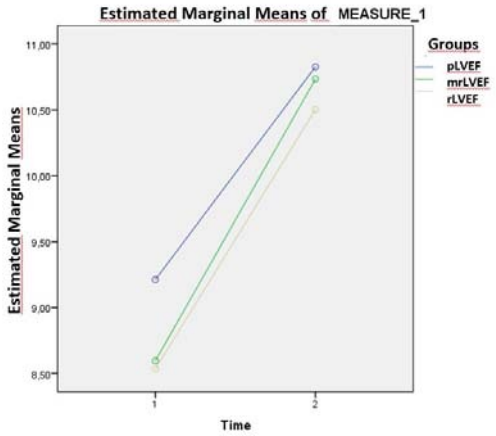
Introduction: While there is a common agreement regarding the efficiency of cardiac rehabilitation (CR) in improving the prognosis of patients after ST-elevated myocardial infarction (STEMI), improving physical activity (PA) after CR is another important goal in STEMI patients.
Purpose: The aim of our study was to estimate the levels of PA in STEMI patients after CR, also known as the third stage of CR and to analyse possible association of both early and late factors of CR and levels of PA in the future.
Methods: It was a retrospective analysis of STEMI patients who underwent invasive coronary angiography and percutaneous coronary intervention (PCI) after STEMI followed by CR in years 2007-2013. The group consisted of 141 patients; the average time of follow-up was 30 ± 14 months (max. 96 months). Information on patients' current activity was assessed with validated International Physical Activity Questionnaire (IPAQ), which takes into consideration time per day and week spent on vigorous (e.g. lifting heavy weights, aerobics) and moderate (riding bike, playing volleyball) activity, walking and sitting. The analysed factors of further physical activity were: gender, age, body mass index (BMI), hypertension, diabetes mellitus

type 2, atrial fibrillation, history of previous MI or stroke, ejection fraction, type of infarction related artery, localization of MI, peak levels of troponin I (TnI), creatine kinase-MB (CK-MB) mass, initial metabolic equivalent of task score (METs), METs after CR, improvement of METs, number of training sessions (12 or 24).
Results: In the analysed group of patients 97.89% of them maintained any form of physical activity. The percentages of patients classified to the high, moderate and low/absent level of activity groups were 20.57% (n = 29), 59.57% (n = 84) and 19.86% (n = 28), respectively. No statistically significant relation between the factors and physical activity was observed.
Conclusions: The physical activity long after CR is maintained by the majority of patients. Most commonly patients maintain the moderate PA.

P555
Response to cardiac rehabilitation: does left ventricle ejection fraction matter?

M Marta Braga[1]; A Rocha[1]; H Nascimento[1]; M Tavares-Silva[1]; R Pinto[1]; G Pestana[1]; P Araujo[1]; A Nunes[1]; V Araujo[1]; F Parada-Pereira[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Introduction: Development of left ventricular systolic dysfunction (LVSD) in acute coronary syndrome (ACS) patients significantly worsens their prognosis. In addition, LVSD is associated with diminished functional capacity (FC). Even though CRP is an essential tool for secondary prevention, some argue against an early cardiac rehabilitation program (CRP) referral of patients with LVSD.
Purpose: The aim of this study was to evaluate baseline clinical characteristics and compare the response to CRP of patients according to left ventricle ejection fraction (LVEF).
Methods: We performed a retrospective analysis of prospectively collected data on a cohort of patients referred to CRP after an ACS. Patients were divided into three groups: Preserved LVEF (pLVEF): LVEF≥50%, mid-range LVEF (mrLVEF): LVEF 40-49% and reduced LVEF (rLVEF): LVEF < 40%. FC was assessed using metabolic equivalents (METs) achieved at a standard exercise test using Bruce protocol before and after CRP. We used ANOVA analysis and a mixed between-within analysis of variance.
Results: Of a total 586 patients, 370 (63.1%) had pLVEF, 115 (19.6%) had mrLVEF and 101 (17.3%) had rLVEF. Mean age was no different between groups (pLVEF: 53.9 ± 10.0, mrLVEF: 53.8 ± 9.6, rLVEF: 54.9 ± 10.5, p = 0.601) and most patients were males in all groups. Prevalence of diabetes, hypertension, active smoking, and dyslipidaemia were no different between groups. The main diagnosis in pLVEF patients was acute myocardial infarction (AMI) without ST elevation (51.4%) while in mrLVEF and rLVEF patients was AMI with ST elevation (73.0% and 76.2%, respectively). Coronarography showed obstructive disease of one coronary artery in majority of patients in all groups and percutaneous coronary intervention was the treatment of choice in pLVEF, mrLVEF and rLVEF groups. Baseline FC was better in pLVEF patients (9.2 ± 2.3 METs), followed by mrLVEF (8.6 ± 2.3 METs) and rLVEF patients (8.5 ± 2.3 METs). After CRP, all groups significantly improved their FC (pLVEF: 10.8 ± 2.1 METs, mrLVEF: 10.7 ± 2.0 METs, rLVEF: 10.5 ± 2.1 METs, within-groups partial Eta square 0.28, p < 0.001). Comparing between-groups, improvement of FC was associated with LVEF, being mrLVEF patients the group that showed the best response to CRP (p = 0.041).
Conclusion: FC ameliorated after CRP in all groups of patients despite different LVEF. Patients with mrLVEF were those who presented a better responder to CRP. Other studies are needed to further confirm this data in order to reinforce the referral of patients to CRP in spite of LVEF.

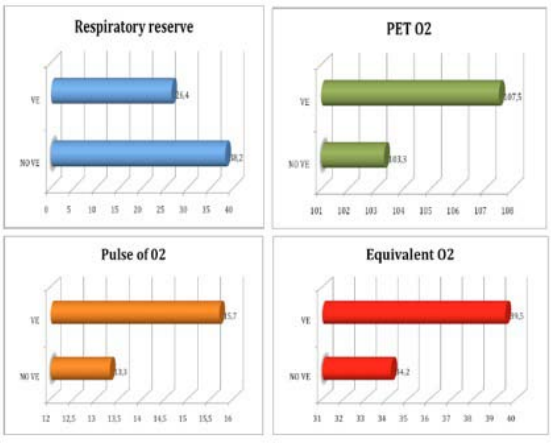


Response to CRP according to LVEF

P556
Determinants of frequent ventricular extrasistole during ergometry with oxygen consumption in patients with coronary disease

N G Uribe Heredia[1]; J Balaguer Recena[2]; H Alvaro Fernandez[1]; L Gil Fraguas[1]; LG Piccone Saponara[3]; R Arroyo Espliguero[2]; S Moreno Reviriego[2]; E Novo Garcia[2]; S Garcia Ortego[2]; E Diaz Carballo[2]; I Rodriguez Guinea[2]; JL Garcia Gonzalez[2]; ME Jimenez Martinez[2]; B Tarancon Zubimendi[2]; MA San Martin Gomez[2]
[1]*Guadalajara University Hospital, Cardiac Rehabilitation Unit, Guadalajara, Spain*; [2]*Guadalajara University General Hospital, Cardiology Department, Guadalajara, Spain*; [3]*Hospital General de Ciudad Real, Nefrology, Ciudad Real, Spain*

Introduction: In patients with coronary artery disease, ventricular arrhythmias during exercise may indicate a two to eightfold increase in the probability of cardiac death. However, factors related to ventricular extrasystoles (VE) other than ischemia are not known.
Material and Methods: Cross-sectional study. 63 patients undergoing ergometry with oxygen consumption, with ischemic heart disease who were discharged from an acute coronary event who underwent cardiac catheterization and coronary revascularization between 2 and 3 months before the test were included, being excluded those with a positive result for myocardial ischemia. Frequent VE were considered in those that were at rest not observed in the VE and during any stage of the exercise test (based on previous work by Schweikert RA). manifested a frequency of seven or more VE/minute, isolated, in pairs, bigeminism or ventricular trigeminism. Demographic variables, blood analysis, characteristics coronary and angioplasty, electrocardiographic, echocardiographic, cardiovascular risk factors and other comorbidities were evaluated. Statistical analysis SPSS 20. Qualitative variables were evaluated by X^2. The quantitative are expressed as means +/-SD, evaluated with student T and the non-parametric with U Mann-W. Statistical significance p < 0.05.
Results: 63 patients analyzed; 14(22.2%) presented exercise-induced VE. Mean age 57.8years; 90.5%men, 6.3%bronchopathy moderate, 49.2%hypertension, 20.6%diabetics, 63.5%dyslipemic, 50.8%smokers, mean ejection fraction 56.3%. There were significant differences between the two groups; In the thickness of the interventricular septum, a mean 10.4mm in the group that did not present VE (group1) and 12mm in the patients Induced the VE (group2), p = 0.01. Maximum heart rate reached during the exercise test, group1 a mean 133.3bpm, while in group2 120.4bpm, p = 0.03. Pulse of oxygen was lower in group1 a mean 13.3ml/beat was obtained and in group2 15.7ml/beat, p = 0.03. RER achieved, group1 reached an RER 1.04, while group2 1.1, p = 0.03. The respiratory reserve, being higher in group1 with an average 38.2% and in group2 26.4%, p < 0.01. The pressure of O2 at maximum load is lower in group1 with a mean 103.3mmHg and in group2 107.5mmHg, p = 0.02. The equivalent O2 is lower in group1 with a mean 34.2mmHg and in group2 39.5mmHg, p < 0.01. HDL cholesterol, in group1 38.7mg/dl and in group2 32.4mg/dl, P=0.02. The creatinine levels were lower in group1 with 0.96mg/dl and in group2 1.1mg/dl, p = 0,02.
Conclusions: In our study, the group of patients who had frequent VE induced during the exercise test had interventricular Septum thickness, reached a lower cardiac frequency at maximum load, a lower maximum pulse O2 rate, RER on higher maximal load, higher respiratory reserve consumption, higher oxygen pressure at maximal load, higher oxygen equivalent, lower HDL cholesterol levels and higher creatinine levels than the group of patients who did not present VE during the exercise test.



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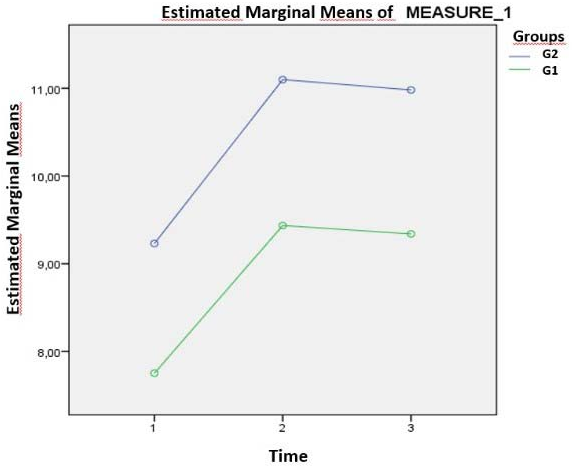
Cardiac rehabilitation in older patients: long-term effects

M Marta Braga[1]; A Rocha[1]; H Nascimento[1]; R Pinto[1]; G Pestana[1]; M Tavares-Silva[1]; P Araujo[1]; A Nunes[1]; V Araujo[1]; F Parada-Pereira[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Introduction: It has been acknowledged that elderly may also benefit from cardiac rehabilitation programmes (CRP). However, the long-term impact of controlled exercise training in older patients is not completely clear.
Purpose: To compare patients aged ≥65 years with those < 65 years concerning baseline clinical profile, functional capacity (FC) and the long-term response to CRP.
Methods: We performed a retrospective analysis of prospectively collected data on a cohort of patients referred to CRP after an acute coronary syndrome (ACS). Patients were divided into two groups, G1: age≥65 years and G2: age < 65years. FC was assessed using metabolic equivalents (METs) achieved in standard exercise test performed in 3 moments, T1: baseline; T2: at the end of CRP; T3: after 12 months of follow-up. A mixed between-within analysis of variance was used to allow comparison between groups and at different time periods.
Results: Of a total 469 patients, 73 patients were aged ≥65 years. Mean age was 69.1 ± 3.9 years in G1 and 51.3 ± 7.9 years in G2. In both groups, most patients were male. Diabetes was more prevalent in G1 (37.3% vs 13.5%, p < 0.001) while active smoking was more frequent in G2 (58.0% vs 29.3%, p < 0.001). Mean LDL-cholesterol was higher in G2 (125.0 ± 37.7 mg/dl vs 105 ± 32.8 mg/dl, p < 0.001). The main diagnosis in G1 was acute myocardial infarction (AMI) without ST elevation (50.9%) and in G2 was AMI with ST elevation. In both G1 e G2, obstructive disease of one coronary artery was the most prevalent finding at coronarography and percutaneous coronary intervention was the treatment of choice. Patients from the 2 groups improved their FC between T1 and T2, and showed a nonsignificant decrease between T2 and T3 (T1: G1: 7.8 ± 1.9 METs vs G2: 9.2 ± 2.2 METs; T2: G1 9.4 ± 1.8 METs vs. G2: 11.1 ± 2.0 METs; T3: G1: 9.3 ± 1.8 METs vs G2 11.0 ± 2.2 METs, within-groups partial Eta square 0.28, p < 0.001). Comparing between-groups, FC of G2 was better than G1 at all 3 moments (partial Eta square 0.09, p < 0.001).
Conclusion: Although FC of older patients was inferior to younger patients, we demonstrated that the benefit of CRP in elderly is sustained one year after ACS. This data reinforces the need for more referral of this group of patients for a structured CRP.



Response to CRP in older patients

P558

Exercised-based cardiac rehabilitation in heart failure patients with mid-range ejection fraction after myocardial infarction

I Burazor[1]; P Seferovic[2]; S Dodic[3]; Y Adler[4]; Z Cosic[5]; R Babic[6]; M Moraca[5]; A Kovacevic[5]; B Milovanovic[5]
[1]*Institute for rehabilitation, Medical Faculty, Cardiology, Belgrade, Serbia*; [2]*Medical Faculty, University of Belgrade, Clinical Center of Serbia, Belgrade, Serbia*; [3]*Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia*; [4]*Sheba Medical Center, Tel Aviv, Israel*; [5]*Institute for rehabilitation, Belgrade, Serbia*; [6]*Institute for Cardiovascular Diseases Dedinje, Belgrade, Serbia*

Heart failure is a major cause of morbidity, mortality and re- hospitalizations and is highly prevalent in myocardial infarction survivors. Cardiac rehabilitation based on exercise training and heart failure self-care counseling have each been shown to improve clinical status and clinical outcomes. We aimed to evaluate the usefulness of exercise based in house cardiac rehabilitation in patients with heart failure with mid-range ejection fraction (HFmrEF) after myocardial infarction.
Patients and methods: Out of 1654 patients who were admitted to our three weeks in- hospital secondary prevention program – exercised based cardiac rehabilitation, we analyze a total of 89 patients who were admitted early after coronary revascularization (percutaneus coronary interventions or coronary bypass surgery) with HFmrEF. The majority of patients were males (66%).We noted risk factors and co morbidities. Patients were selected for exercise training after six minute walking testor exercise stress test (cardiopulmonary dominantly to evaluate unexpected exertional dyspnea). After 3 weeks in hospital cardiac rehabilitation the patients were re-tested.
Results: The major comorbidities in our patient population were as follows: hypertension, diabetes and dyslipidemia. Six minutes walking test was performed and the total distance walked ranged from 120 to 440 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 ˜39%. 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). Also we noted silent ischemia in 2% after CABG with ST segment depression detected by telemetry. None had acutisation of heart failure (with peripheral edema and congestion). All patients fulfilled cardiac rehabilitation program.
Conclusions: Supervised multidisciplinary cardiac rehabilitation program, including an individualized exercise component is safe and can improve functional status and exercise tolerance in patient with HFmrEF after myocardial infarction.

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Linear correlation between cardiac output and oxygen uptake at peak exercise at different heart failure stages.

A Del Torto[1]; N Corrieri[1]; P Gentile[2]; C Vignati[3]; G Cattadori[4]; S Paolillo[3]; P Agostoni[3]
[1]*University of Milan, Milan, Italy*; [2]*University of Trieste, Trieste, Italy*; [3]*Cardiology Center Monzino IRCCS, Milan, Italy*; [4]*IRCCS Multimedica of Milan, Milan, Italy*

Introduction: In heart failure (HF) patients, alterations in central haemodynamics, peripheral vasodilatory capacity, intrinsic skeletal muscle changes, pulmonary factors, iron deficiency, anaemia and overall conditioning status can all impair effective oxygen delivery and utilization. A reduced cardiac output (CO) response during exercise is an early and major limiting factor to exercise performance in HF patients. According to Fick's law, CO is directly proportional to oxygen consumption (VO2) and inversely proportional to arteriovenous oxygen difference (Δ(a-v)O2). However in HF patients Δ(a-v)O2 shows a relevant interpatient variability and the role of the different peripheral mechanisms in determining exercise performance may vary at different stages of the disease.
Purpose: To analyze the correlation between peak exercise VO2, CO and Δ(a-v)O2 at different stages of HF.
Methods: We retrospectively analyzed data of 278 consecutive stable ambulatory HF patients (NYHA II-III) who performed a maximal cardiopulmonary exercise test with simultaneous CO measurement by inert gas rebreathing technique. We evaluated resting hemoglobin of all patients and in a subset of them also biomarkers of iron metabolism. Iron deficiency was defined as serum ferritin concentration < 100 μg/L or between 100 and 300 μg/L with transferrin saturation < 20%.
Results: A linear regression model demonstrated the following equation: CO = 5.3 x VO2 + 1.13 (r^2=0.705, p < 0.001). We analyzed the correlations between peak CO and peak VO2 grouping patients according to exercise limitation (% achieved of predicted peak exercise VO2): Group 1 consisted of 101 patients with peak VO2 < 50% of predicted; Group 2 of 89 patients with peak VO2 ≥50% < 65% of predicted peak VO2; Group 3 of 88 patients with peak VO2 ≥65% of predicted. Group 1 patients had the lowest peak exercise CO and Δ(a-v)O2. Group 2 patients achieved a significantly lower peak exercise CO when compared to Group 3. We observed a linear relationship between VO2 and CO at peak exercise in Group 1 (r^2=0.381, p < 0.001), the strongest in Group 2 (r^2=0.756, p < 0.001) and Group 3 (r^2=0.744, p < 0.001). Several reasons may be responsible for the lower Δ(a-v)O2 observed in Group 1. Hemoglobin was on the average lower in Group 1 than in Group 2 and 3, but, it cannot be considered the only cause; in a small subset of patients, we finally observed a non-statistically significant trend (p = 0.059) toward a greater prevalence of iron deficiency in Group 1 (86%) compared to Group 2 (57%) and Group 3 (53%). Other reasons could be impaired peripheral vasodilatory capacity and intrinsic skeletal muscle changes.
Conclusions: The peripheral component of peak VO2 seems to be multifactorial and more determinant in patients with more severe HF, while the haemodynamic

component seems to be the major determinant of peak VO2 in patients with less severe HF.

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Effect of pedometer-based walking intervention on functional capacity and neurohumoral modulation in patients with chronic heart failure: study protocol for a multicentre randomized controlled trial

M Michal Siranec[1]; T Vetrovsky[2]; V Bunc[2]; A Linhart[1]; J Belohlavek[1]
[1]First Faculty of Medicine and General Teaching Hospital, Second Internal Clinic – Clinic of Cardiology and Angiology, Prague, Czech Republic; *[2]Charles University of Prague , Faculty of Physical Education and Sport, Prague, Czech Republic*

Background: Regular physical activity is recommended in patients with chronic heart failure to improve their functional capacity. Walking is a popular, effective and safe form of physical activity and pedometers have shown potential to increase walking across a range of chronic diseases. It is not known whether a pedometer-based intervention improves functional capacity and neurohumoral modulation in heart failure patients.
Methods: The project is designed as a multicentre randomized controlled trial, with follow-up at 6 and 12 months. Physically inactive participants (n = 200) with chronic heart failure (with both reduced and preserved ejection fraction) will be randomly assigned to intervention or control arms.
The six-month intervention will consist of an individualized pedometer-based walking program with weekly step goals, monthly face-to-face sessions with the physician, and monthly telephone calls with the research nurse. The intervention will be based on effective behavioural principles (goal setting, self-monitoring, personalized feedback).
The primary outcome is the change in a 6-minute walk distance at 6 months. The secondary outcomes include changes in serum biomarker levels, pulmonary congestion assessed by lung ultrasound, average daily step count measured by accelerometry, anthropometric measures, depression symptoms, health-related quality of life, self-efficacy, and MAGGIC Risk Score.
Discussion: To our knowledge, this is the first study to evaluate a pedometer-based walking intervention in patients with chronic heart failure. The study will contribute to a better understanding of physical activity promotion in heart failure patients as well as to informing future physical activity recommendations and heart failure guidelines.

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Influence of a physical exercise program over functional capacity of patients with artificial pacemakers

LEONARDO Lopes Do Nascimento[1]; TSV Jardim[1]; LAB Sa[1]; IPM Garcia[2]; AS Oliveira[3]; AMC Lima[4]; PCBV Jardim[1]
[1]Federal University of Goias, Hypertension League, Goiania, Brazil; *[2]State University of Goias, Physical Therapy, Goiania, Brazil*; *[3]Salgado de Oliveira University , Physical Therapy, Goiania, Brazil*; *[4]Santa Casa Hospital, Goiania, Brazil*

Patients with pacemakers are prone to functional capacity limitations despite the disease that lead to the device implantation. Cardiac Rehabilitation programs addressed to improve functional capacity of this group are rare. The aim of the present study was assess functional capacity of subjects with pacemakers after 12 weeks of physical exercise program. The sample included patients with pacemakers that were divided in two groups with 10 subjects each: control group (CG) and exercise group (EG). The patients performed an exercise test (ET) to plan the exercises and a six-minute walk test (6MWT) to evaluate initial and final functional capacity. The EG program frequency was 3 times a week and included: 5′ warming up, 40′ conditioning in treadmill (moderate intensity) and 5′ of cooling down; the CG remained in its usual activities. The CG sample was mainly female (70%), with mean age of 62,7 (±8,32) years while the EG was predominantly male (70%), mean age 64,20 (± 6,25). The groups were similar in the beginning regarding to functional capacity (table 1). The covered distance in the 6MWT (D6MWT) from the CG was 506,90m ± 67,08 in the first evaluation and 532,80m ± 89,89 in the second (p = 0,14). The D6MWT from the EG was 536,10m ± 100,54 e 590,40m ± 67,97, respectively (p = 0,007). The EG increased the covered distance in 54,30m ± 49,14. During the training period no complications prevented the protocol completion. In conclusion a supervised exercise program is safe and promotes improvements in the D6MWT performance and functional capacity in patients with cardiac pacemakers.

Comparison between the D6MWT			
Variables	1ª Evaluation	2ª Evaluation	p*
Control	506,90 ± 67,08	532,80 ± 89,89	0,14
Exercise	536,10 ± 100,54	590,40 ± 67,97	0,007
p**	0,35	0,09	

*Wilcoxon Test **Mann-Whitney Test

P562

Real-time monitoring of hemodynamic response during resistance exercise in cardiac surgery patient

J-H Jung-Hyun Choi[1]; B-J Lee[1]; M-J Shin[1]
[1]Busan National University Hospital, Busan, Korea Republic of

Object: Coronary artery bypass grafting (CABG) is a surgery that improves blood flow to the heart for the patient who have severe coronary artery disease. After that surgery, the patient should be treated in intensive care unit (ICU). During that period, physical functioning will be impaired. Physical therapy interventions delivered in the ICU can reduce these impairments, but the safety is not still established especially to the patient who received CABG. We monitored the patients using a software during exercise and this is the first attempt in Korea.
Method: 4 patients who received CABG, were extubated, had hemodynamic stability and proper awareness to cooperate were enrolled to exercise. A low-intensity resistance exercise was comprise of 3 sets of isokinetic knee extension, 10 times per each set, with 2-Kg sandbag at the patient's ankle. We use the software named Datex-Ohmeda S/5 Collect to collect records of vital signs from B650 monitoring system. (Fig 1)
Result: All four patients had the low intensity resistance exercise safely in ICU at post-operative day 3. In the patient 1, vital signs during exercise were as follow: at the resting period, blood pressure (BP) was 137.93 ± 1.02/84.98 ± 0.62 mmHg (mean BP : 103.39 ± 0.75 mmHg). At the 1st, 2nd and 3rd exercise period, BP were slightly increased to 142.35 ± 0.67/87.96 ± 0.30 mmHg, 142.42 ± 0.91/88.76 ± 0.33 mmHg, 144.73 ± 0.90/82.29 ± 0.56 mmHg, respectively. The BP was decreased to 140.15 ± 0.77/85.21 ± 0.44 mmHg at recovery period. Baseline heart rate (HR) was 78.83 ± 0.55 beats/minute, increased to 80.38 ± 1.15 beats/minute at exercise period and decreased to 77.15 ± 0.63 beats/minute at recovery. The blood oxygen saturation level (SpO2) was maintained, between 97.95 ± 0.13% and 98.51 ± 0.02%. The patient did not complained of chest pain, dyspnea, excessive fatigue, and other symptoms during the entire period.
Discussion: Exercise for critically ill patients in ICU is important and necessary, but physicians were passive to prescribe exercise because of safety issue by this time. But using this type of monitoring system, we can monitor real-time vital signs during interventions. In future, well-designed randomized study involving more participants may be necessary to confirm the safety and effectiveness of exercise during ICU hospitalization and early post-operative days.

P563

Cardiac rehabilitation after sudden cardiac arrest in patients with left ventricular systolic dysfunction

V Veronica Angela Rial Baston[1]; R Dalmau Gonzalez-Gallarza[1]; FJ Irazusta Cordoba[1]; P Meras Colunga[1]; O Gonzalez Fernandez[1]; SO Rosillo Rodriguez[1]; AM Iniesta Manjavacas[1]; RA Mori Junco[1]; CA Alvarez Ortega[1]; L Rodriguez Sotelo[1]; JM Garcia De Veas[1]; A Rivas Perez[1]; A Velez Salas[1]; A Castro Conde[1]; JL Lopez Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain

Background and objectives: Patients (P.) with left ventricular systolic dysfunction (LVSD) benefit from close monitoring, which can be provided in cardiac rehabilitation programs (CRP). However, information is still missing regarding its effectiveness and safety in special features such as sudden cardiac arrest (SCA). We aimed to describe the impact of CRP on these patients (P.).
Methods: We studied 29 P. with low ejection fraction (EF) (defined as EF<51 %) who were resuscitated from cardiac arrest and then referred to a CRP between May 2006 and October 2014. An echocardiogram and a treadmill test were performed at the beginning and at the end of the program (Pr.) to evaluate respectively the EF and the exercise capacity (EC). The Pr. included supervised exercise training and comprehensive disease-related self-care counseling. Results: 86.2% were male with a mean age of 53.9 ± 11.3 years. The most frequent reason for their inclusion in the CRP was an ST-elevation acute myocardial infarction (AMI) in 24 P. (88.9%), followed by non-ST elevation AMI in 2 P. (7.4%) and chronic ischaemic heart disease in 1 P. (3.7%). 10.3% needed inotropes or an intra-aortic balloon pump during

hospitalization and 3 P. were implanted with an ICD before starting the Pr. The initial mean EF was 39.5% and EC measured in METs was 7.0 ± 2.7. There were no complications in any of the P. and only one of them left the Pr. prematurely. Eighteen P. (75%) experienced an improvement in functional capacity of at least 2 METS (mean EC increase in absolute terms: 2.7 ± 1.1 METs), 2 P. (11.1%) normalized their ventricular function and the percentage of P. with severe LVSD was reduced from 13.8% to 5.6% (p = 0.02). The results of the Pr. are shown in table 1.
Conclusion: Cardiac rehabilitation can be safely implemented in P. with LVSD after SCA. Therefore, we should not be hesitant to refer these P. to a CRP as they can benefit from exercise capacity improvement and lifestyle correction, which in turn will help to improve their cardiovascular outcomes.

Results of the program

	At the beginning of the Pr.	At the end of the Pr.	p
Smoking	22 patients (75.9%)	3 patients (14.3%)	p = 0.05
HbA1c	8.1	7.3	p = 0.3
LDL cholesterol	96 mg/dL	77.5 mg/dL	p = 0.06
Triglycerides	132.5 mg/dL	92 mg/dL	P=0.03
Abdominal perimeter	91.5 cm	91 cm	p = 0.10
Ejection fraction	39.5%	47%	p < 0.01
Exercise capacity	7.0 METs	10.1 METs	p < 0.01

P564
The role of diastolic function in the quality of life and functional capacity of patients with heart failure undergoing a combined exercise program

MG Roscani[1]; T Fabri[2]; AM Catai[3]; FHO Ribeiro[2]; JA Araujo Junior[2]; JM Mattos[3]; DAA Rossi[2]; RC Borra[4]; SGZ Bazan[2]; MTS Peracoli[5]; JC Hueb[2]; BB Matsubara[2]
[1]Federal University of Sao Carlos, Medical Department, Sao Carlos, Brazil; *[2]Sao Paulo State University, Botucatu Medical School, Department of Internal Medicine, Botucatu, Brazil*; *[3]Federal University of Sao Carlos, Physiotherapy, Sao Carlos, Brazil*; *[4]Federal University of Sao Carlos, Biosciences, Sao Carlos, Brazil*; *[5]Univ. Estadual Paulista (UNESP), Biosciences Institute, Botucatu, Brazil*

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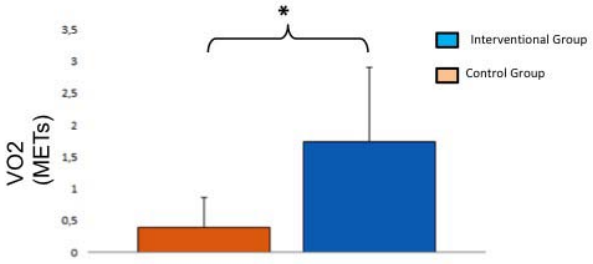
Background: The favorable effects of a combined exercise program (CEP) in patients with heart failure (HF) are established in the literature. There are controversies if these beneficial effects are due to the improvement in left ventricle diastolic function (LVDF) with the exercise. The aim of this study was to evaluate the effect of CEP on LVDF assessed by echocardiogram and verifies if the LVDF is associated with improvement in the quality of life (QOL) and functional capacity (FC) of these patients.
Methods: Randomized clinical trial that included 42 patients with HF and reduced ejection fraction (< 50%), older than 18 years divided into two groups matched for age and sex: Control group n = 20: not subjected to the practice of EFC. Intervention group n = 22: underwent supervised CEP, composed of aerobic exercise supplemented by resistance exercise 3 times a week for 12 weeks. The two groups underwent initially and after 12 weeks for clinical evaluation, 12-minute walk test to assess the FC, transthoracic echocardiography and assessment of QOL by the SF-36 questionnaire. The diastolic function was assessed by mitral annulus velocities on tissue Doppler, mitral inflow patterns and indexed atrium volume in the absence of significant mitral reflow. Statistical analysis was performed using test "t" of the results of the differences between the pre and post moments of the protocol comparing the two groups, or Mann Whitney test for data with non-normal distribution. Correlation test was used for variable associations of the same group. Results: There was no difference in diastolic function variables between the groups and no correlation with QOL and CF. The Intervention Group, compared to Control Group, showed significant improvement at the end of research in the dyspnea (p = 0.01) and chest pain (p = 0.02) symptoms, improvement in the FC (p < 0.001) and in four of the eight dimensions of QOL questionnaire: functional capacity (p < 0.001), physical limitation (p = < 0.001), general health (p < 0.001) and vitality (p < 0.001).
Conclusion: Supervised CEP of 12 weeks was able to promote favorable impact on symptoms, CF and QOL in patients with HF and reduced ejection fraction. These effects did not depend on LVDF.



Comparison of VO2 between Groups

P565
CPET-based "rule out" tool for pulmonary vascular resistance > 3 WU

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

Aims: We aimed to elucidate potential relationships between cardiopulmonary exercise test (CPET) variables and invasive measures of right ventricular afterload and translate those findings into a clinical "rule out tool" for pulmonary vascular resistance (PVR) > 3 WU, in end stage heart failure patients awaiting cardiac transplantation.
Methods: Retrospective study that included stable end-stage heart failure patients who underwent a scheduled in-hospital evaluation for heart transplantation and performed CPET and invasive hemodynamic assessment ≤ 7 days apart.
Results: 52 patients were included. PVR was positively correlated with VE/VCO2 slope (r=0,41, p = 0,013) and negatively correlated with PETCO2 at AT and peak O2 pulse (r=-0,42, p = 0,013 and r=-0,38, p = 0,005, respectively). Pulmonary arterial compliance was negatively correlated with VE/VCO2 slope (r=-0,34, p = 0,046) positively correlated with PETCO2 at AT and O2 pulse at AT (r=0,47, p = 0,005 and r=0,46, p = 0,007, respectively). A "rule out" tool for PVR>3 WU including peak O2 pulse and VE/VCO2 slope showed a sensitivity of 91%, specificity of 48%, positive likelihood ratio of 1,75 and negative likelihood ratio of 0,19, being particularly useful in the identification of low risk patients for high PVR. For an estimated pre-test prevalence of 42%, a low risk classification decreases the probability of high PVR to 12%. Conclusion: CPET predicts invasive measures of right ventricular afterload in end stage HF patients. A low risk CPET reduces the probability of PVR>3 WU from 42% to 12%. A potential clinical application of these findings is the periodicity guidance of invasive hemodynamic assessment in patients listed for cardiac transplantation

PULMONARY HYPERTENSION

P566
Platelet reactivity in advanced chronic left heart failure with secondary pulmonary artery hypertension - A hidden potential tool in patient management?

M Pasalic[1]; J Samardzic[1]; B Skoric[1]; H Jurin[1]; J Ljubas Macek[1]; M Cikes[1]; D Milicic[1]
[1]University Hospital Centre Zagreb, Department of Cardiovascular Diseases, Zagreb, Croatia

Background: Pulmonary artery hypertension (PAH) caused by chronic heart failure (HF) has a large impact on patient outcomes. Both systolic and diastolic HF cause an increased left atrial filling pressure and a postcapillary PAH which, if left untreated, eventually induces irreversible structural changes in pulmonary arteries. Pathogenetic pathway leading towards elevated pulmonary vascular resistance (PVR) in idiopathic PAH is based on vasoconstriction, inflammation, thrombosis and vascular proliferation. Platelets are known mediators in each of these processes and have been shown to have an important role in the development of idiopathic PAH. However, the extent to which platelets are involved in the pathogenesis of secondary PAH, especially due to HF, remains unclear and insufficiently explored.
Purpose: We investigated whether platelet reactivity (PR) correlates to the level of PAH and/or the reversibility of pulmonary artery haemodynamics in patients with advanced HF.
Methods: Platelet reactivity was tested using Multiplate function analyzer (ASPI, ADP, COL, TRAP tests) in patients with advanced chronic HF undergoing diagnostic evaluation at our department. Blood samples were taken directly from Swan-Ganz catheter during the right heart catheterization before and immediately after PVR reversibility tests was performed using intravenous prostaglandins.

Results: Herein, we report analyzed data collected on 75 patients (84% male, mean age 57.1 ± 11.5 y), most of which suffer from either dilated or ischemic cardiomyopathy. Arachidonic acid mediated PR (ASPI test) showed statistically significant correlation with changes in transpulmonary pressure gradient during reversibility test (R=-0.348, P=0.037), while changes in ASPI, ADP and COL tests correlated significantly to changes in PAPm (R=0.589, P=0.000; R=0.406, P=0.021; R=0.607, P=0.004, respectively).
Conclusion: Although the present sample size is insufficient to confirm our hypotheses, current results suggest that PR has a significant role in pulmonary vasculature changes in patients with PAH (WHO II). Results warrant further research to determine whether platelet function testing might have a potential role in routine management of these patients.

P567

Exercise pulmonary artery pressure change as a prognostic parameter in heart failure

I Sari[1]; R Darvishova[1]; M Sunbul[1]; N Sayar[1]; K Tigen[1]; B Ozben[1]; Y Basaran[1]
[1]*Marmara University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey*

Background: Although increased resting systolic pulmonary artery pressure (sPAP) is associated with adverse outcome in patients with heart failure and previous myocardial infarction, the significance of exercise sPAP is less clear. Furthermore, pulmonary artery pressure normally increases with exercise but clinical significance of change in sPAP from rest to peak exercise (ΔsPAP) is not known.
Purpose: We aimed to investigate the role of resting and peak exercise sPAP and ΔsPAP to predict cardiovascular (CV) outcome.
Methods: A total of 50 patients (mean age 61.6 ± 11.3 years, 40 % female) with heart failure and a history of myocardial infarction were included into the study. Demographic, laboratory and resting echocardiographic parameters of the patients were collected. Additionally all patients underwent bicycle stress echocardiograph and resting sPAP, peak exercise sPAP and ΔsPAP were recorded. Primary end point was development of any CV event (hospitalization for a cardiovascular event including heart failure, recurrent acute myocardial infarction, coronary revascularization or CV death).
Results: During median follow-up of 12 months CV events occurred in 26 of 50 patients (52%). The incidence of CV events was higher in females (p: 0.01) when compared with males. In addition those who experienced CV events were older (64.7 ± 12.2 years vs 58.3 ± 9.6 years, p:0.042), had lower 6 minutes walking distance (321.9 ± 111.5 m vs 411.4 ± 84.5 m, p:0.002), higher log-NT-proBNP level (3.19 ± 0.6 vs 2.6 ± 0.6, p: 0.001), worse NYHA class (2.3 ± 0.6 vs 1.6 ± 0.5, p: 0.001), higher peak exercise sPAP (57.5 ± 13.6 mmHg vs 47.6 ± 10.7 mmHg, p:0.006) and higher ΔsPAP (18.1 ± 9.4 mmHg vs 11.1 ± 6.1 mmHg, p < 0.001). In univariate analyses peak exercise sPAP, ΔsPAP, log-NT-proBNP level, 6 minutes walking distance, gender and NYHA class were among predictors of CV event development. In multivariate analyses, only female gender (p: 0.038, odds ratio: 5.316, 95 % confidence interval: 1.100 - 25.683) and ΔsPAP (p: 0.022, odds ratio: 1.125, 95% confidence interval: 1.017 - 1.243) were independent predictors of CV event development. In Receiver-Operating Curves analysis a ΔsPAP of 15 mmHg or higher predicted CV event development with a sensitivity of 73 % and specificity of 75 % (area under curve: 0.747) (Figure 1). Sensitivity was 69% and specificity 71% for peak exercise sPAP (area under curve: 0.730) and sensitivity and specificity were both 50% for rest sPAP (area under curve: 0.599).
Conclusions: Our study is the first to investigate and demonstrate the clinical significance of ΔsPAP. According to our findings ΔsPAP has a potential to be used in diagnosis, classification, staging and management of various disease states which needs and warrants to be tested with large scale prospective studies.

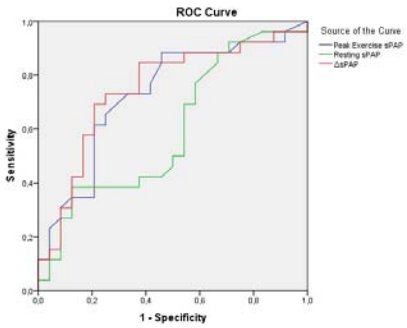


Figure 1

P568

Early diagnosis of severe right ventricular dysfunction in pulmonary arterial hypertension through clinical evaluation. Insights from Argentine RECOPILAR Registry

E R Eduardo Perna[1]; A Lescano[2]; A Echazarreta[3]; G Cursack[4]; M Coronel[1]; L Lema[5]; S Pereiro[6]; J Caneva[7]; L Favaloro[7]; D Echazarreta[3]; M Diez[8]
[1]*J.F. Cabral Cardiology Institute, Corrientes, Argentina*; [2]*Finochietto Clinic, Buenos Aires, Argentina*; [3]*Hospital San Juan de Dios, La Plata, Argentina*; [4]*Sanatorio Esperanza, Esperanza, Argentina*; [5]*Model Institute of Cardiology, Cordoba, Argentina*; [6]*Hospital Argerich, Buenos Aires, Argentina*; [7]*Favaloro Foundation University Hospital, Buenos Aires, Argentina*; [8]*Cardiovascular Institute of Buenos Aires (ICBA), Buenos Aires, Argentina*

On behalf of: RECOPILAR Investigators

Severe right ventricular dysfunction (SRVD) is commonly diagnosed by echocardiogram (ECHO) and it is considered an important marker of poor prognosis in patients with pulmonary arterial hypertension (PAH). We sought to evaluate the prevalence of SRVD in PAH in Argentinean RECOPILAR Registry, and to identify simple clinical and biochemical variables associated with the diagnosis of SRVD.
Material and methods: From Jul-14 to Jul-15, 144 incident and prevalent patients with PAH were prospectively included by 60 investigators from 20 provinces of Argentina. The inclusion criteria were: 1-patients over three months of age; 2 -mean pulmonary arterial pressure (mPAP) at rest ≥ 25 mmHg by right heart catheterization and 3 - clinical stability in the absence of hospitalization in last month. SRVD was defined by tricuspid annular plane systolic excursion (TAPSE) < 16 mm.
Results: Mean age was 49 ± 19 years (SD) and 74% were females. SRVD was identified in 54 cases (35,5%). Patients with and without SRVD were different in terms of history of heart failure (HF) (37 vs 15.6%, p = 0.007), Dressler sign (48 vs 30%, p = 0.045), hepatomegaly (HEP) (45.7 vs 16.3%, p = < 0.01), positive hepatojugular reflux (RHY)(28 vs 10%, p = 0.008), right third sound (S3), peripheral edema ≥ 2 + (29.6 vs 13.3%, p = 0.017), elevated jugular venous pressure ≥ 2/3 (JVP) (50 vs 23.3%, p = 0.001), systolic blood pressure < 115 mmHg (lowSBP) (76 vs 49%, p = 0.003), urea > 30 mg/dl (79,2 vs 61,1%, p = 0.037), and creatinine > 0.90 mg/dl (68 vs 48%, p = 0.027). Classification and regression tree (CART) analysis was carried out to categorize the best predictors of SRVD (Figure 1). Three group of risk were identified: High (22%) (HEP + JVP + urea > 30 mg/dl; or absence of HEP + HF + lowSBP), intermediate (15,3%)(HEP + no JVP; or absence of HEP + HF + no lowSBP) and low (62,7%)(all the others), with an incidence of SRVD of 76.9, 44.4 and 21.6%, respectively (p < 0.0001).
Conclusions: One out of three patients with PAH had SRVD. Simple and widely available clinical variables allow the early diagnosis of this condition, thus helping in decision making for early initiation of specific treatment

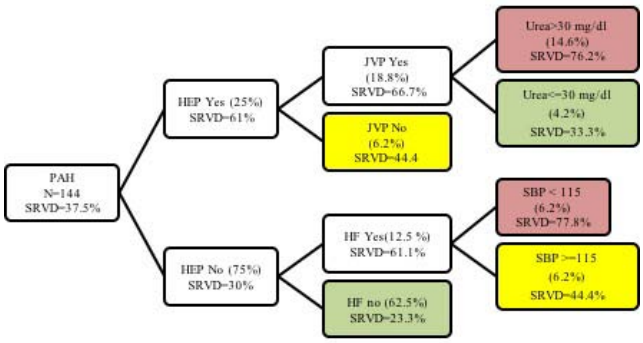


Figure 1

P569

Gender differences in functional capacity, quality of life, anxiety, depression and common symptoms in pulmonary arterial hypertension patients

M S Serdar Kucukoglu[1]; R Demir[1]; R Ceylan[1]; Ü Y Sinan[1]
[1]*Istanbul University Institute of Cardiology, Department of Cardiology, Istanbul, Turkey*

Pulmonary Arterial Hypertension (PAH) negatively affects patients' exercise capacity, quality of life (QOL), psychological mood. Although PAH is known to be more common in women, little is known about the effect of gender on symptoms and

functional capacity (FC). We aimed to investigate the difference between men and women in terms of FC, QoL, anxiety (A), depression (D) and common symptoms in PAH.
Methods: Data were retrieved from 41 (10 males, mean age 35.5 and 30 females mean age 42.4) stable PAH patients in NYHA classes I- III. All patients were assessed by measurement of dyspnea levels with UCSD-Shortness Of Breath Questionnaire, Baseline Dyspnea Index, Modified Medical Research Council, Oxygen-Cost Diagram and Modified Borg Dyspnea scale, fatigue levels with Fatigue Severity Scale, Modified Borg Fatigue scale, sleep quality with Pittsburg Sleep Quality Index and PAHSS-Sleep Disturbance Subscale, QoL with Nottingham Health Profile and SF-36 questionnaires,A-D levels with Hospital A and D Scale and functional capacity with six-minute walk test.
Results: None of the parameters were significantly different between men and women).
Conclusion: There was no difference between men and women in terms of FC, QoL, anxiety, depression and common symptoms in patients with PAH.

P570

Morbidity and mortality in patients with pulmonary hypertension treated with iloprost

L C Liz Carolina Casafuz Martinez[1]; FNG Fernandez Chamorro[1]
[1]*Social Security Institute , Cardiology, Asuncion, Paraguay*

Introduction: Pulmonary hypertension (PH), has a difficult diagnosis and poor prognosis, can be primary or secondary and has a high mortality rate.
Objective: To determine the morbidity and mortality in PH in patients under treatment with Iloprost during the period of August, 2013 to August, 2016.
Methods: Observational, cross-sectional, retrospective study in patients with PH treated with iloprost in functional class III or IV of the World Health Organization (WHO) upon admission.
Results: Study population 33 patients. Deaths from August 2013 to August 2016: 8/33 (24%), mortality was as follows: first year 4/33 (9%), second year 6/33 (18%) and third year 8/33 (24%). Distribution by sex: female 26/33 (79%). Deaths by sex: female 4/26 (15%), male 4/7 (57%). Mean age 51± 13 years. Labor occupation: teacher 30%, administrative 27%, household chores 24%. High-risk PH factors that were associated with increased hospitalization: 6-minute walk test (PC6min) <300m (79%), time of onset of symptoms> 1 year (79%), Pro-BNP> 300pg/ml (39%), right ventricular failure (30%). Reasons for hospitalization: Acquired community pneumonia 21%, Congestive Heart Failure (13%), Arrhythmias (12%), Haemorrhages (12%). Connective tissue diseases (CTE) (39%) were the most frequent and the highest percentage of deaths were: 6 of 8 deaths (75%), 4 with Scleroderma and 2 with lupus. The most frequent cardiovascular risk factors (CVRF) were: Hypertension (45%), obesity (24%), overweight (21%).
Conclusion: A mortality rate was observed according to the international literature. The female-male sex ratio was 3.7 / 1. There was a higher mortality rate among men. The high risk factor for PH that was related to a higher percentage of hospitalization was PC6min <300m. The reason for major hospitalization in these patients was Acquired community pneumonia. Patients with CTE predominated, with a high mortality rate. The most frequent CVRF was Hypertesion.

P571

Right ventricular 18F-FDG uptake in PET/MRI hybrid and hemodynamics in patients with pulmonary arterial hypertension.

K Karol Kaminski[1]; R Kazimierczyk[1]; M Jasiewicz[2]; P Blaszczak[3]; L Malek[4]; B Milosz-Wieczorek[5]; J Misko[5]; P Szumowski[6]; D Jurgilewicz[7]; M Hladunski[7]; B Sobkowicz[2]; R Grzywna[3]; J Mysliwiec[6]; WJ Musial[2]
[1]*Medical University of Bialystok, Bialystok, Poland*; [2]*Medical University of Bialystok, Department of Cardiology, Bialystok, Poland*; [3]*Cardinal Wyszynski Hospital, Cardiology, Lublin, Poland*; [4]*Collegium Masoviense, Zyrardow, Poland*; [5]*Institute of Cardiology, Cardiac Magnetic Resonance Unit, Warsaw, Poland*; [6]*Medical University of Bialystok, Department of Nuclear Medicine, Bialystok, Poland*; [7]*Medical University of Bialystok, Laboratory of Molecular Imaging, Bialystok, Poland*

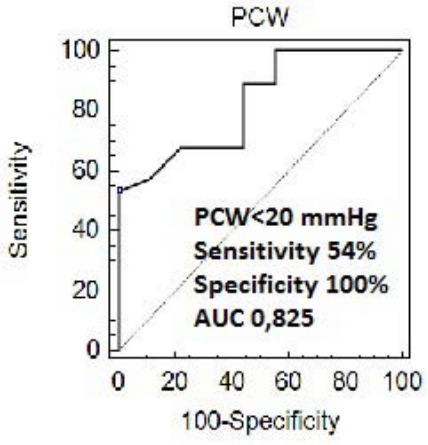
Right ventricular (RV) function is a major determinant of survival in patients with pulmonary arterial hypertension (PAH). RV 18F-fluoro-2-deoxyglucose (FDG) accumulation in positron emission tomography (PET) was recently connected with progressive RV dysfunction in PAH patients. In our pilot study we compared hemodynamic parameters obtained during right heart catheterization (RHC) and RV function assessed in magnetic resonance imaging (MRI) with PET-derived glucose uptake values.
Methods: Twenty stable PAH patients (mean age 50.1 ± 16.5 years, diagnosis confirmed in RHC according to current ESC criteria, I-III WHO class, all prevalent cases, treated with specific PAH therapies) had cardiac PET/MRI scans with FDG as a tracer. FDG uptake was presented as a standardized uptake value (SUV) of both left (LV) and right ventricle. A ratio of SUVRV/SUVLV was then calculated. RVEF was assessed in MRI scans performed simultaneously with PET, whereas hemodynamic measurements were obtained from right heart catheterisation performed within two months from the PET/MRI scanning.
Results: Subjects presented wide range of pulmonary vascular resistance (PVR) (2.1 to 18.9 WU), mean pulmonary artery pressure (mPAP) (24 to 90 mmHg) and RV ejection fraction (RVEF) (27% to 58%). SUVRV directly correlated with mPAP (r=0.85, $p < 0.0001$), PVR (r=0.76, $p < 0.0001$), right atrial pressure (RAP) (r=0.48, $p = 0.03$) and inversely with RVEF (r=-0.52, $p = 0.04$). Mean SUVRV/SUVLV ratio was 0.97 ± 0.63. SUVRV/SUVLV ratio also correlated with mPAP (r=0.84, $p < 0.0001$), PVR (r=0.75, $p < 0.0001$) and RVEF (r=-0.7, $p = 0.02$). Patients with mPAP higher than 40 mmHg presented abnormally high SUVRV/SUVLV ratio (1.28 vs 0.38, $p < 0.0001$).
Conclusions: Increased glucose uptake in RV myocytes as assessed by FDG PET is associated with worse hemodynamics indicating more advanced PAH. Similarly, worse RV function evaluated in MRI was associated with increased FDG uptake in RV. PET/MRI hybrid could provide insights into right ventricle function and metabolism in PAH patients, however its usefulness in diagnostic process requires further investigations.

P572

Predictors of irreversible pulmonary hypertension reduction with Sildenafil therapy in heart transplant candidates

A Agata Duszanska[1]; M Zakliczynski[1]; M Zembala[1]
[1]*Medical University of Silesia, Silesian Centre for Heart Diseases, Zabrze, Poland*

Objective: Increased transpulmonary gradient (TPG) and pulmonary vascular resistance (PVR) without reversibility with vasodilators(irreversible pulmonary hypertension-IPHT), are considered as contraindications to orthotropic heart transplantation (OHT) in advanced heart failure (HF) patients. We sought to determine predictors of reduction of IPHT secondary to Sildenafil therapy in patients with advanced HF disqualified from OHT due to increased TPG and PVR.
Methods: 50 patients (46 M, mean age 54,3 ± 8,9 years, NYHA 3 ± 0,4, ischaemic etiology n=19) with indications for OHT based on clinical assessment, N-terminal pro-brain natriuretic peptide (NT-proBNP), ECG, echocardiography, cardiopulmonary test (VO2) were disqualified from OHT following right heart catheterization with nitropruside (NPS) study confirming IPHT (TPG>12 mmHg, PVR>2,5 Wood units). In all patients Sildenafil was introduced and uptitrated to a maximal tolerated dose following optimal medical therapy according to ESC guidelines. Patients were assessed at 3-month intervals. Results: During 10,9 ± 4,2 months observation reduction of TPG(16 ± 5,9 to 9 ± 3, with NPS: 11,5 ± 4,5 to 7,7 ± 3,3 mmHg) and PVR (4,2 ± 1,3 to 2,2 ± 1,0, with NPS:2,8 ± 1,1 to 1,6 ± 0,8 W) enabling qualification for OHT was observed in 37 pts. On univariate analysis pulmonary capillary wedge pressure (PCW) [[OR 0,79; 95% CI (0,67-0,94) $p = 0.008$], mean pulmonary arterial pressure (mPAP) [OR 0.79, 95% CI (0.67-0,93) $p = 0.005$]; PVR at baseline [OR 0,55, 95% CI (0,31-0,99) $p = 0.05$] were defined as markers of IPHT reduction with Sildenafil. On multivariate analysis PCW ($p = 0.03$) was identified as an independent predictor of of successful reduction of TPG and PVR with Sildenafil enabling patient qualification for OHT (PCW < 20 mmHg, sensivity 54%, specificity 100%). Conclusions: Sildenafil can support pulmonary hypertension reduction in advanced heart failure patients ineligible for orthotropic heart transplantation due to increased transpulmonary gradient and pulmonary vascular resistance. Pulmonary capillary wedge pressure prior to Sildenafil therapy was identified as an independent predictor of successful reversibility of pulmonary hypertension.



Independent predictor of IPHT reduction

P573

Physiological insights of exercise hyperventilation in pulmonary hypertension

N Bruno[1]; S Farina[1]; C Agalbato[1]; M Contini[1]; S Harari[2]; P Agostoni[1]
[1]Cardiology Center Monzino IRCCS, cardiology , Milan, Italy; *[2]San Giuseppe Hospital, Pneumology , Milan, Italy*

Background: Pulmonary hypertension (PH) patients show, during exercise, an excessive increase in pulmonary ventilation (VE) compared to carbon dioxide output (VCO2), determining a high VE/VCO2 slope. There are several possible causes, including an elevated dead space ventilation (VEDS), VE/perfusion (Q) mismatch and/or an enhanced peripheral or central chemoreceptor activity. We evaluated the causes of exercise hyperventilation in PH patients.
Methods: Eighteen class I and IV PH patients underwent cardiopulmonary exercise test with hemogasanalysis at every minute. VE, alveolar ventilation (VEALV) and VEDS vs. VCO2 relationship were calculated. Resting chemoreceptor sensitivity was analyzed through hypoxia/hypercapnia tests.
Results: PeakVO2 and VE/VCO2 slopes were 1.06 ± 0.24L/min and 39.1 ± 9.0, respectively. Throughout the exercise, 30% of VE was due to VEDS. VE/VCO2 slope significantly correlated with VEDS/VCO2 slope (r=0.82, $p < 0.001$) but not with VEALV/VCO2 slope (r=0.3, p=ns). Peak exercise end-tidal CO2 (PetCO2) correlated with VEDS/VCO2 slope (r=-0.79, $p < 0.001$) and VE/VCO2 slope (r=-0.91, $p < 0.001$). DS/tidal volume and P(arterial-et)CO2 were elevated without arterial hypoxemia suggesting an high VE/Q mismatch. Peripheral responses to hypoxia and hypercapnia were 0.416 ± 0.402 L/min/O2Sat and 0.076 ± 0.047 L/min/mmHg, respectively; central hypercapnic chemosensitivity was 4.475 ± 3.99 L/min/mmHg. Chemoreceptor peripheral response was unrelated with exercise. Vice versa, a positive correlation was found between central CO2 response and VEALV/VCO2 slope (r=0.65, $p = 0.013$).
Conclusions: Increased DS and VE/Q mismatch are among the main mechanisms involved in exercise hyperventilation in PH. Central CO2 chemoreceptor seems to play a role, since it positively correlates with VEALV.

P574

Simple parameters predict combined post- and pre-capillary pulmonary hypertension in patients with severe heart failure

P Peter Lesny[1]; M Luknar[1]; V Simovicova[1]; M Kovacova[1]; M Dankova[1]; S Wimmerova[2]; E Goncalvesova[1]
[1]National Institute for Cardiovascular Diseases, Bratislava, Slovak Republic; *[2]Slovak Medical University, Bratislava, Slovak Republic*

Background: Pulmonary hypertension (PH) is a negative prognostic factor in patients (pts) with left-sided heart failure (HF). Particularly, pts with combined post-capillary and pre-capillary PH are at risk.
Purpose: To determine simple predictors of combined PH (defined as mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg, pulmonary arterial wedge pressure > 15 mmHg, pulmonary vascular resistance > 3 W.U. and/or diastolic pressure gradient ≥ 7 mmHg) in pts with severe HF.
Patients and methods: Three hundred and eighty five heart transplant candidates were retrospectively evaluated. Mean age was 48.3 ± 10.1 years, left ventricular ejection fraction 23.9 ± 7.9 %. Eighty nine % of pts were in NYHA classes III or IV. Main etiologies of HF were dilated cardiomyopathy in 53% and coronary artery disease in 32% of pts. Right heart catheterization using Swan-Ganz catheter was performed. Presence and type of PH, as well as one-year mortality for each PH type were determined. Twenty simply available clinical and laboratory parameters were included in multivariate stepwise logistic regression analysis to determine independent predictors of combined PH.
Results: Prevalence of pts without PH, with isolated post-capillary PH and with combined post- and pre-capillary PH was 21%, 38% and 41%, respectively. One-year mortality was 13.5%, 18.1% and 27.2% in pts without PH, isolated post-capillary PH, and combined PH, respectively ($p < 0.05$, for combined PH group vs two other groups of pts). Right ventricular diameter >35 mm, and daily furosemide dose > 160 mg were identified as only independent predictors of combined post- and pre-capillary PH.
Conclusion: Right ventricular dilation and high daily furosemide dose are independent predictors of combined post-capillary and pre-capillary PH in pts with severe HF. Due to their worse prognosis, these pts should be referred to an HF center earlier.

P575

Clinical efficiency of macitentan in patients with pulmonary hypertension. our experience in argentina

H Gomez Santa Maria[1]; A Ferro[1]; G Bortman[2]; V Gregorietti[3]; N Atamanuk[4]; N Carusso[2]; A Adrian Lescano[1]
[1]Finochietto Clinic, Buenos Aires, Argentina; *[2]Sanatorium Mitre, Buenos Aires, Argentina*; *[3]Hospital El Cruce, Florencio Varela, Buenos Aires, Argentina*; *[4]Hospital Fernandez, Buenos Aires, Argentina*

Introduction: Pulmonary Hypertension (PH) is a disease characterized by an increase in pulmonary resistances that leads to right heart disfunction, heart failure and death. There are multiple associated pathophysiological mechanisms that are used as therapeutic targets. Macitentan (M) is a non-selective inhibitor of endothelin receptors, which has demonstrated clinical benefits in morbidity and mortality in a Phase III study. (Macitentan and Morbidity and Mortality in Pulmonary Arterial Hypertension SERAPHIN trial).
Objective: To describe the clinical efficacy in our population of Macitentan in PH patients.
Material and methods: A prospective, consecutive, open, phase IV registry of patients with PH who started treatment with M (Opsumit MR) in Argentina, from March 2015 to November 16, was performed. We included those p who received M for at least 6 months or presented an event. Baseline characteristics, functional class (FC), 6-minute gait test (TM6M), adverse effects and survival were determined according to the recommendations of the national and international guidelines, at baseline and at 6 month. Clinical efficacy was determined by the improvement in FC from III-IV (advanced) to FC I-II (not advanced), and improvement in 6MWT> 15%. The data was loaded into an Excel database and evaluated with the Bioestat 5.0 program. The normality of the sample was analyzed by the D'Agostino-Pearson test. In relation to the distribution, the t test was used for quantitative variables, Chi^2 for qualitative and McNemar test for paired variables. A p value of < 0.05 was defined as a significant difference between baseline and 6 months.
Results: We included 151 p, 74% women, the average of age was 46 years (28-63) and 98.4% had HP group 1. 98.6% received M 10 mg and 1.4% 5 mg. At baseline, functional class evaluation presented the following distribution: FC I 2.4%, II 19.4%, III 65.3% and IV 12.9% (advanced FC 78.2%). The mean baseline TM6M was 321 m (250-400). At 6 months FC I was 13.5%, II 62.2% and III 24.3% (advanced FC 24.3%), with significant statistical benefit ($p < 0.001$). The mean TC6M reached 397.2 m (320-467), an increase of 24%, with a significant difference ($p < 0.0001$, 95% IC-533-51.6).
Conclusion: In our PH registry, administration of Macitentan was associated with a significant benefit in achieving the objectives of functional class improvement and the distance reached in the 6MWT (76 meters), at 6 months. These data are in agreement with those obtained in the randomized study SERAPHIN.

RIGHT VENTRICULAR FUNCTION

P576

Right ventricular dilatation in coronary artery disease patients without myocardial infarction

El Yaroslavskaya[1]; VA Kuznetsov[1]; DV Krinochkin[1]; GS Pushkarev[1]; EA Gorbatenko[1]
[1]Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Tyumen, Russian Federation

Background: Detection of right ventricular (RV) dilatation in patients with coronary artery disease (CAD) is very important to identify subjects at high risk for adverse cardiovascular events. Data about factors associated with RV dilatation in CAD patients without myocardial infarction (MI) are insufficient.
Purpose: To reveal factors associated with RV dilatation in CAD patients without MI.
Methods: Out of 16.839 patients from coronary angiography database we selected patients without acute or prior MI, congenital or acquired valvular heart disease with stenosis ≥75% of at least one coronary artery: 1.134 patients without RV dilatation (end-diastolic RV outflow tract diameter measured by echocardiography ≤26 mm) and 75 patients with RV dilatation (RV outflow tract diameter ≥30 mm). Patients with RV diameter >26 mm and < 30 mm were not included to have higher discrimination between groups.
Results: There were more male patients in the group with RV dilatation (92.0% vs 80.2%, $p = 0.012$). Mean body mass index (BMI) was higher in this group (31.7 ± 5.2 kg/m2 vs 30.1 ± 4.7 kg/m2, $p = 0.010$). Patients with RV dilatation more often had a higher NYHA functional class (III – 22.2% vs 12.5%, $p = 0.002$), arrhythmias (45.5% vs 17.8%, $p < 0.001$), reduced LV systolic function (LV ejection fraction < 50% - 24.3% vs 2.9%, $p < 0.001$) and significant mitral regurgitation (MR) (29.4 % vs 4.0 %, $p < 0.001$). There were no differences in lipid profile and coronary angiographic parameters between the groups. The prevalence of high CCS angina class (III/IV) was lower in the group with RV dilatation (30.3% vs 52.8%, $p = 0.007$). According to the multivariate analysis, RV dilatation was independently associated with reduced LV systolic function (OR 4.22; 95% CI 1.73-10.30; $p = 0.002$), male gender (OR 4.03; 95% CI 1.47-11.04; $p = 0.007$), arrhythmias (OR 2.98; 95% CI 1.62-5.49; $p < 0.001$), significant MR (OR 2.34; 95% CI 1.44-3.81; $p = 0.001$), higher NYHA functional class (OR 1.87; 95% CI 1.05-3.32; $p = 0.034$), higher BMI (OR 1.08; 95% CI 1.02-1.15; $p = 0.010$), and lower CCS angina class (OR 0.42; 95% CI 0.25-0.71; $p = 0.001$).
Conclusions: RV dilatation in patients without MI was predominantly associated with male gender, parameters describing severity of LV dysfunction and higher BMI.

P577

Right ventricular systolic dysfunction in patients with coronary artery disease: gender-related differences

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

Background: Right ventricular (RV) dysfunction is one of the most significant independent predictors of prognosis in patients with coronary artery disease (CAD) who were presented with myocardial infarction (MI) and without it. However, gender-related differences in RV function of CAD patients are still poorly understood.
Aim: To evaluate gender-related differences in echocardiographic parameters of the right chambers of the heart in CAD patients.
Material and Methods: 719 patients with coronary artery disease undergoing medical examination on an outpatient basis in the Federal Budgetary Institution Rehabilitation Center "Topaz" of the RF Social Insurance Fund were included in the study. All patients were assigned to two groups according to the gender: Group 1 – men (n = 432, 61 [55; 67] years), Group 2 - women (n = 287, 62 [56; 67] years).
Results: The analysis of the structure and systolic function of the RV showed that RV and right atrium (RA) end-diastolic dimension, diastolic RV wall thickness, and RA area were significantly higher in men than in women ($p < 0.001$). Thus, the prevalence of RV systolic dysfunction (SD) was similar in both groups of patients: 17.6% in men and 15% in women ($p = 0.356$). The independent predictors of LV SD in both groups were as follows: prior coronary artery bypass grafting (CABG), decreased early mitral flow propagation velocity ($p < 0.05$). However, reduced left ventricular ejection fraction (LVEF; $p < 0.001$) was found only in men.
Conclusion: The prevalence rate of right ventricular systolic dysfunction in patients with coronary artery disease was similar in both men and women. Men demonstrated lower values of systolic and diastolic LV function. The factors associated with RV systolic dysfunction in both groups were as follows: prior CABG and diastolic LV dysfunction. Reduced LVEF was found only in men. The results of this study should be used to assess gender-related differences in RV dysfunction in CAD patients.

P578

echocardiographic predictors of acute right ventricular dysfunction in postoperative state of congenital heart surgery

LA Cota Apodaca[1]; E Garcia Cruz[1]; F Baranda Tovar[1]; C Salgado Solorio[1]; E Bucio Reta[1]; N Garcia Cruz[1]
[1]*National Institute of Cardiology Ignacio Chavez, Cardiac Intensive Care Unit, Mexico City, Mexico*

Background: Congenital cardiac diseases have become more prevalent in adult population.. We can now say that in most of the western civilization it is possible for the 85% of the new born with congenital cardiac disease to survive to adult age. Congenital defects are classified as simple and complex, in the study we now present we included complex congenital cardiopathies and patients with two or more common defects.
Purpose: This study suggests that the patient who will present chronic heart failure tends to show less acute heart failure signs during the immediate post surgical time, because of a preconditioning effect.
Methods: We analyzed the files of the intensive care unit from January 2015 to December 2016. Inclussion criteria: complex congenital heart disease who went through a surgical correction of their defect, age greater than 18 years, cardiothoracic post surgical status. We excluded patients with: unique ventricle, incompletepatient's file, one congenital common defect. To determine if the patient with right heart hypertrophy or chronic right heart failure shows a minor probability of acute heart failure, all of the variables were obtained from the echocardiographic evaluation: chronic right heart failure was define as decreases in fractional area shortening, tricuspid annular plane systolic excursion (TAPSE), Doppler S′ velocity or increases in the right heart dimensions. Acute right heart failure was define as an decrease in the fractional area shortening less than 25% or paradoxical septal movement plus inotropic administration for more than 24 hours. We determined the echocardiographic variables before and after the surgical event.
Results: 16 patients met the inclusion criteria: 9 with right ventricular hypertrophy (right free wall thickening >5 mm), 6 met chronic right heart failure criteria, 8 patients showed acute right heart failure, and 8 did not. We did a bivariate analysis obtaining an OR 0.3, Fisher's test 0.34. Right free wall hypertrophy in relation to acute heart failure, obtaining an OR of 0.2 , Fisher's test of 0. 15. In the same way, the right ventricular free wall strain was analyzed and severe dysfunction was defined as less than -6%.This latter parameter was related to acute right heart failure with an OR 1.3, Fisher's test of 0.68.
Conclusions: The free wall strain was only calculated after cardiac surgery, obtaining an OR of 1.3, and it showed relation to acute right ventricular dysfunction. Free wall thickening measure reflects preconditioning that can bear greater intracavitary pressure and this can be a protection factor against acute heart failure during the postsurgical process and also chronic right heart failure. Nevertheless the exact Fisher's test for both parameters showed no statistical significance maybe restricted by the amount of the sample, which was one of the most important limitations of our study.

P579

Acute adaptation of the right ventricle to pressure and volume overload. Preliminary analysis in human model

R Raquel Lopez Vilella[1]; S Benlloch Perez[2]; E Marques-Sule[3]; F Perez Esteban[4]; M Lloret Larrea[5]; I Sanchez Lazaro[1]; S Martinez Penades[6]; J Melero Ferrer[1]; J Sanz Sanchez[1]; D Plaza Lopez[1]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]*Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain*; [2]*Hospital Universitario y Politécnico La Fe, Gastroenterology and hepatology Department, Valencia, Spain*; [3]*University of Valencia, Physiotherapy Department, Valencia, Spain*; [4]*Hospital Universitario y Politécnico La Fe, Intensive Care Unit, Valencia, Spain*; [5]*Hospital Universitario y Politécnico La Fe, Radiology Department, Valencia, Spain*; [6]*Instituto de Investigación Sanitaria La Fe, Valencia, Spain*

On behalf of: Heart Failure and Transplant Unit. Cardiology Department. La Fe
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Background/Introduction: Acute overload of the RV produce a remodeling that, if it is not reversible, can condition an adverse prognosis. Thus we did a comparative and descriptive analysis of the response of the RV to acute overload, including volume and pressure overload, and its short-term evolution. PURPOSE. To assess structural and functional changes of RV when there is acute pressure and volume overload, and its potential reversibility.
Methods: Prospective study including 30 consecutive patients recruited between June 2014 and June 2016. Severe pulmonary embolism (PE) was the selected model for the study of acute pressure overload, whilst implantation of a transjugular intrahepatic portosystemic shunt (TIPS) was selected for the acute volume overload. Electrocardiogram (ECG), determination of biomarkers and echocardiographic study were serially performed to all patients.

Table I P579

	Pressure overload, n 13 Basal	Pressure overload, n 13 Early (4 h)	Pressure overload, n 13 3 m	p	Volume overload, n 17 Basal	Volume overload, n 17 Early (48 h)	Volume overload, n 17 3 m	p
hs-cTnT	205±154	87±80	13±8	0,01	17±10	16±13	21±17	0,80
NT-ProBNP	3410±3000	1650±1000	159±130	0,05	183±155	833±800	1083±1066	0,09
RV diameter	45±3	39±3	37±2,80	0,01	37±2,60	41±2,7	40±1,8	0,03
PASP	62±20	45±5	30±5	0,16	25±3	30±5	38±2,7	0,01
TAPSE	14±5	19,6±3,6	19±7	0,07	21,60±4	24±8	17±11	0,80
S′	9±2,5	13±2,6	15±3	0,02	15±2	14±3,50	15±2	0,60

ABBREVIATIONS: hs-cTnT: Ultrasensitive Troponin t; RV: Right ventricle; PASP: Pulmonary artery systolic pressure, estimated by transthoracic echocardiography; TAPSE: Tricuspid annular plane systolic excursion (mm); S´: Systolic velocity of the tricuspid ring (cm/seg); m: Months

Results: 13 patients with acute pressure overload were evaluated. Table I shows the main analytical and echocardiographic results, both basal and evolutive. At baseline, 10 patients (77%) had a depressed function of the RV and 11 (85%) presented RV dilatation. At 3 months all patients normalized the function of the RV. 17 patients with acute volume overload were assessed, 14 men (84%), average age 57 ± 8 years. At the first moment after overload, no patient presented RV dysfunction; however, 6 patients (35%) presented a slight RV dilatation which did not implied related clinical events. At 3 months, 2 patients had a slight RV dilatation without dysfunction.
Conclusions: Ventricular dilatation and dysfunction with short-term reversibility is frequent in RV acute pressure overload. Dilatation without dysfunction is produced in the RV acute volume overload, but dilatation tends to persist.

LEFT VENTRICULAR FUNCTION

P580
Predictors of diastolic function and adverse diastolic remodeling after ST-elevated myocardial infarction

L Lawien Al Ali[1]; JK Prins[1]; S Assa[1]; CHP Lexis[1]; YM Hummel[1]; E Lipsic[1]; DJ Van Velduisen[1]; CS Lam[1]; ICC Van Der Horst[1]; P Van Der Harst[1]
[1]*University Medical Center Groningen, Cardiology, Groningen, Netherlands*

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Background: Pathologic cardiac remodeling as a result of acute myocardial infaction (AMI) can deteriorate systolic and/or diastolic function and ultimately cause heart failure. Previous research in the post-AMI setting has mainly focused on systolic function. This one-sided focus has left gaps in our knowledge on how remodeling affects diastolic function.
Purpose: We aimed to determine the risk factors associated with diastolic function and diastolic remodeling after AMI.
Methods: This is a sub-study of the GIPS-IIII trial, a single center, randomized, double blind, placebo-controlled study. Non-diabetic ST-elevated myocardial infarction (STEMI) patients were randomized to metformin or placebo initiated directly after PCI.The primary endpoint was left ventricular ejection fraction at 4 months measured by MRI. Trans-thoracic echocardiography was performed during hospitalization and after 4 months to evaluate diastolic function as a predetermined secondary endpoint. As previously reported, both endpoints were unaffected by metformin treatment. The ratio of E/e′, signifying cardiac filling pressure, was used as a marker of diastolic functioning status for the current study.
Results: 267 (70%) patients from the GIPS-III cohort had E/e' available at both time points. Mean age was 58.0 (± 11.3) years and 23.2% were females. Linear regression analyses of the baseline variables found a multivariabel model with age, gender, hypertension, multi vessel disease, glucose, and peak CK-total be predictive for E/e′ (R^2:0.20). After correction for E/e' during hospitalization female gender (β: 0.26), multi vessel disease (β: 0.26), and higher glucose (β: 0.26) were found to be associated with adverse diastolic function.
Conclusions: Age, female gender, history of hypertension, multi vessel disease, glucose and peak CK-total are independently associated with worse diastolic function at 4 months after STEMI. Furthermore, female gender, multi vessel disease and higher glucose are independently associated with adverse diastolic remodeling.

Table: Multivariate prediction models

Predictor	Multivariate model		multivariate model adjusted for E/e′ in hospital			
Coeff.[a]	SE[b]	P-value	Coeff.[a]	SE[b]	P-value	
Age	0.03	0.01	0.01	0.01	0.01	0.56
Female gender	1.38	0.32	< 0.01	0.77	0.28	0.01
Hypertension	0.76	0.31	0.01	0.39	0.27	0.16
Multi vessel disease	1.11	0.29	< 0.01	0.75	0.26	< 0.01
Glucose, mmol/L	0.17	0.06	0.01	0.13	0.06	0.03
Peak CK-total[c], U/L per 1000	0.21	0.08	0.01	0.04	0.07	0.56

a. Coefficient b. Standard error c. Total creatine kinase

P581
Mid-range ejection fraction as a continuum of poor prognosis - a national STEMI patients analysis

C Catarina Ruivo[1]; F Montenegro Sa[1]; L Graca Santos[1]; J Correia[1]; J Morais[1]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*

On behalf of: Portuguese National Registry of Acute Coronary Syndromes

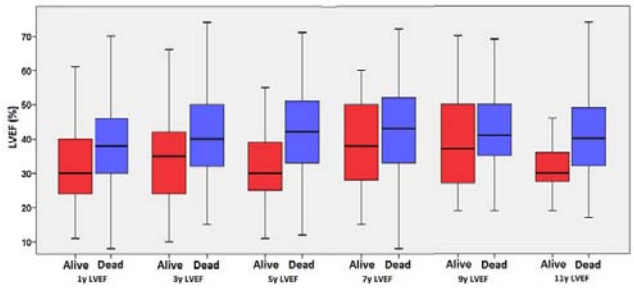
Background: Heart failure with mid-range ejection fraction (mrEF – ejection fraction 40-49%) is a newly defined entity that certainly will be considered in future ST segment elevation myocardial infarction (STEMI) patients approaches. We aim to characterize these patients and analyze in-hospital adverse events according to their EF.
Methods: A retrospective analysis of data from consecutive STEMI patients enrolled in a multicenter national registry from October 2010 to September 2016 was conducted among 3914 patients. Patients without echocardiographic (Echo) EF evaluation or without reperfusion strategies were excluded. The clinical characteristics and coronary angiographic findings were evaluated and compared between patients with EF>50% (n = 2236, 57.1%), EF 40-49% (n = 929, 23.7%) and EF < 40% (n = 749, 19.1%) on Echo. Different components of delay were considered and compared: time from symptom onset (SO) to first medical contact (FMC) (SO-FMC), from SO to reperfusion therapy [(SO-RT) both fibrinolysis and percutaneous coronary intervention] and FMC to RT (FMC-RT). In-hospital adverse events (death, sustained arrhythmias or mechanical complications) were considered as endpoints.
Results: Comparative analyses between patients with EF>50%, EF 40-49% and EF < 40% found a continuum in: increase age (61 ± 13 vs. 63 ± 14 vs. 64 ± 14, p = 0.008), longer delays [SO-FMC: median time of 110 (interquartile range: 60-205) minutes vs. 120 (66-128) vs. 123 (60-247), p = 0.02; SO-RT: 227 (162-360) vs. 255 (174-414) vs. 275 (183-455), p < 0.001; FMC-RT: 105 (65-165) vs. 115 (70-178) vs. 125 (83-200), p < 0.001], more severe acute event [Killip-Kimball class > I (6.0% vs. 12.1% vs. 29.0, p < 0.001)] and multivessel coronary artery disease in an increase proportion of patients (40.6% vs. 41.0% vs. 45.4%, p = 0.08). Analyzing the endpoints, we observed increasing in-hospital mortality rates (0.7% vs. 2.4% vs. 9.2%, p < 0.001), sustained arrhythmias (1.3% vs. 3.0% vs. 6.3%, p < 0.001) or mechanical complications (0.5% vs. 1.1% vs. 2.3%, p < 0.001). Conclusion: Patients with mrEF are particularly important stratum of patients to identify because they have significant rates of in-hospital adverse events. They represent a continuum of higher baseline risk profile and higher hemodynamic instability, in whom the tendency to delay their treatment can lead to higher myocardial damage, with reduction of EF.

P582
Very long-term LVEF dynamics and prognosis in HFrEF and HFmrEF

M De Antonio[1]; J Lupon[1]; J Lopez-Ayerbe[1]; P Moliner[1]; M Domingo[1]; E Ferrer[1]; E Zamora[1]; N Vallejo[1]; F Gual[1]; A Teis[1]; G Junca[1]; MI Troya[1]; M Rodriguez[1]; B Gonzalez[1]; A Bayes-Genis[1]
[1]*Germans Trias i Pujol University Hospital, Badalona, Spain*

Background: Advances in heart failure (HF) treatment are responsible for systolic function improvement in patients with reduced (HFrEF) and mid-range (HFmrEF) ejection fraction. Left ventricular ejection fraction (LVEF) dynamics and associated survival is not completely elucidated.
Purpose: To prospectively assess very long-term (up to 13 years) LVEF dynamics and prognosis in consecutive HFrEF and HFmrEF patients.
Methods: Ambulatory patients admitted to a multidisciplinary HF Unit were prospectively evaluated by 2D-echocardiography at baseline and at 1,3,5,7,9,11, and 13 years of follow-up. Out of 1912 patients, 1097 patients with LVEF < 50% and at least 2 determinations of LVEF were included in the study. Patients with CRT previous two the second echocardiography were excluded. Two patients were censored at the moment of heart transplantation and 59 at the moment of CRT.
Results: LVEF measurements were obtained from 1097, 995, 610, 393, 239, 148, 112, and 62 patients at the predefined time-points, accounting for 100%, 91%, 72%, 65%, 61%, 57%, 64%, and 63% of the alive patients at every time. Mean number of echocardiography measurements performed were 3.3 ± 1.6 per patient. Mean LVEF at each study time-points were: 30% ± 9, 38% ± 12, 40% ± 12, 41% ± 12, 42% ± 13, 42% ± 11, 42% ± 12, and 41% ± 11. Paired data comparisons showed statistical significance between baseline and 1 year (p < 0.001) and between 1 and 3 years (p < 0.001). HFmrEF patients showed significantly lower improvement than HFrEF at 1 year (3 ± 9 vs. 9 ± 12 points respectively, p < 0.001) but maintained better LVEF than HFrEF patients up to 7 years (p = 0.01). At the end of follow-up survivors of both groups has similar LVEF. LVEF at each study time-points in HFmrEF: 43% ± 3, 46% ± 9, 46% ± 11, 45% ± 10, 46% ± 12, 44% ± 10, 43% ± 12, and 41% ± 11. LVEF at each study time-points in HFrEF: 28% ± 7, 37% ± 12, 39% ± 12, 40% ± 13, 41% ± 13, 41% ± 12, 41% ± 12, and 41% ± 11. Non-ischemic patients, despite slightly lower baseline LVEF, showed higher numbers during follow-up vs. ischemic HF patients (around 7-10 points, all p < 0.01). Remarkably, patients who

died in the following period after each of the predefined time-points of follow-up, had always lower previous LVEF (figure). Also during the first 5 years patients who died had significantly worse LVEF dynamics in the precedent period.
Conclusions: LVEF in patients with depressed systolic function significantly improves up to 3 years, and remains steady afterwards. HFrEF showed higher LVEF rise during follow-up relative to HFmrEF, yet at the end of follow-up survivors of both groups had similar LVEF. Non-ischemic aetiologies showed higher improvement and maintain higher LVEF values along follow-up. Decedents always had lower LVEF and also tended to have worse dynamics in the precedent study period.



Vital status at 3, 5, 7, 9, 11 and 13 y

P583
Development and validation of sex-specific diagnostic models to detect diastolic dysfunction in primary care

A Aisha Gohar[1]; H Den Ruijter[1]; R Kievet[2]; A Hoes[2]; G Pasterkamp[1]; M Bots[2]; F Rutten[2]
[1]*University Medical Center Utrecht, Experimental Cardiology, Utrecht, Netherlands*; [2]*Julius Health Center - Julius Gezondheidscentra, Utrecht, Netherlands*

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Background: The prevalence of undetected left ventricular diastolic dysfunction (DD) is high in the general population particularly in the elderly population. This is mainly due to the asymptomatic nature of the disorder making it difficult to diagnose in primary care. Identifying people at high risk of DD is important as DD is a prognostic indicator of heart failure and future cardiovascular and all-cause mortality.
Purpose: The purpose of this study was to develop diagnostic models that can be implemented in primary care to assess who is at risk of DD and therefore requires referral for echocardiography. Given that diastolic dysfunction impacts men and women differently, sex-specific models were developed.
Methods: Individual patient data from four primary care HF-screening studies were analysed (1477 participants, 732 men). 11 candidate predictors were entered into sex-specific logistic regression models to predict the presence of DD. Internal-external cross-validation was performed to develop, validate and calibrate the models by omitting a different cohort each time for use as the validation cohort.
Only age and pulse pressure remained as clinical predictors in women. In men, the model consisted of age, body mass index, pulse pressure, AF and use of beta-blockers. The model performed poorly in women with the c-statistic ranging from 0.55 to 0.65. The model performed better in men with a c-statistic ranging from 0.59 to 0.75
Conclusions: Clinical predictors of DD differ between men and women highlighting importing sex differences in the underlying mechanisms of DD. We present a diagnostic model for DD that performs better in men than for women indicating the need to investigate DD in a sex-specific manner.

Discrimination and calibration					
Developed in	Validated in	c-statistic clinical model (95% CI)	c-statistic clinical model & NTproBNP	Observed/ Expected (OE) ratio clinical model	Observed/ Expected (OE) ratio clinical model & NTproBNP
Women					
TREE, DM and COPD	STRETCH	0.65 (0.56-0.73)	0.64 (0.56-0.73)	2.65	2.67
STRETCH, DM and COPD	TREE	0.55 (0.56-0.73)	0.56 (0.43-0.66)	3.26	3.26
STRETCH, TREE and COPD	DM	0.67 (0.60-0.73)	0.72 (0.66-0.78)	2	2.06
STRETCH, TREE and DM	COPD	0.56 (0.43 -0.70)	0.63 (0.50-0.76)	2.66	2.58
Men					
TREE, DM and COPD	STRETCH	0.75 (0.68-0.83)	0.78 (0.71-0.86)	3	1.56
STRETCH, DM and COPD	TREE	0.59 (0.49-0.693)	0.61 (0.51-0.71)	2.38	2.78
STRETCH, TREE and COPD	DM	0.7 (0.63-0.77)	0.69 (0.62-0.76)	1.87	1.85
STRETCH, TREE and DM	COPD	0.66 (0.54 -0.78)	0.65 (0.53-0.76)	4.34	4

Discrimination and calibration of the sex-specific models at cross-validation

P584
Heart failure with mid-range ejection fraction: prognostic impact of left bundle branch block

H Hugo Antunes[1]; L Abreu[1]; J Pereira[1]; ML Goncalves[1]; B Marmelo[1]; I Pires[1]; D Moreira[1]; I Almeida[1]; M Correia[1]; C Cabral[1]
[1]*Hospital Sao Teotonio, Cardiology, Viseu, Portugal*

Introduction: Left Bundle Branch Block (LBBB) is associated with poorer prognosis in patients (P) with heart failure (HF) with reduced ejection fraction (rEF). In the new classification of HF, a new group of P with mid-range ejection fraction (mrEF) appears. Clinical characteristics and therapeutic approach still remain uncertain in this group of P.
Objectives: To evaluate the prognostic impact of LBBB in P with HF and mrEF.
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. Only the P with mrEF (40-49%) were selected. We considered 2 groups: group with presence of LBBB (gLBBB) and a control group without LBBB (gCONTR). We compared in-hospital mortality (IHM), the combined endpoint (death / hospitalization for HF) at 6 and 18 months (M) and the survival curves of each group.
Results: Of a total of 1006 P admitted, 191 cases were included: 59.7% male and mean age 75.72 ± 10.33 years. IHM was 2.6%. The combined endpoint at 6M was 29.7% and 52.2% at 18M. gLBBB represents 17.8% of the P. In this group, there was predominance of females (64.7% vs 35.0%, $p < 0.001$) and of P diabetics (50.0% vs 29.5% $p = 0.021$) compared to gCONTR. There were no differences in age, other cardiovascular risk factors, history of ischemic heart disease, chronic kidney disease or atrial fibrillation.
Analytically, there was no difference in hemoglobin, creatinine or BNP on admission. gLBBB evolved more frequently with acute renal injury (32.4% vs 16.2%, $p = 0.031$). There were no statistically significant differences in IHM (gLBBB 2.9% vs 2.5%). There was a greater number of events (combined end-point) at 6M and 18M in gLBBB (45.5% vs 26.3%, $p = 0.029$ and 68.8% vs 48.6%, $p = 0.039$). Survival curves showed that the gLBBB has a worse outcome at 6M and at 18M ($p = 0.036$ and $p = 0.034$ respectively - Figure 1).
Conclusion: In this study, the LBBB showed to have a prognostic impact on P with mrEF heart failure compared to P without LBBB and was associated with a greater number of events in the medium and long term follow-up. These results may have an impact on future research, particularly with regard to the benefit of early cardiac resynchronization therapy.

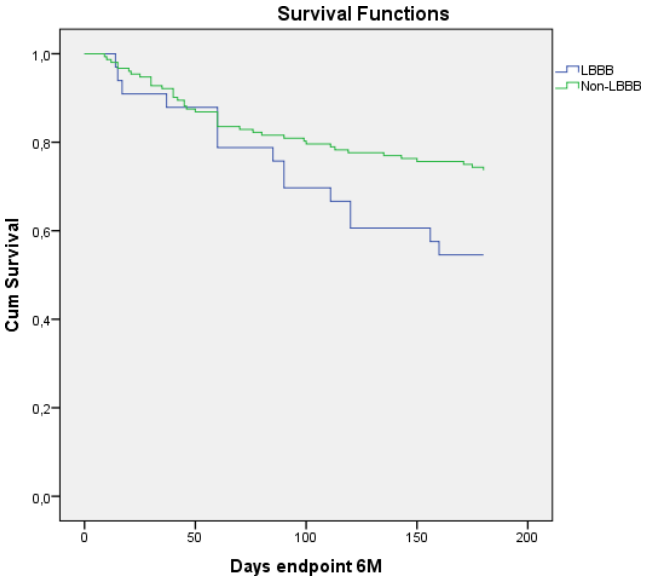


Figure 1

HFpEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

P585

Prevalence and correlates of left ventricular diastolic dysfunction in hypertensive community residents with preserved ejection fraction. Insights from survey-SEPHAR III

A Scafa Udriste[1]; OF Tautu[1]; RO Darobant[1]; D Dimulescu[1]; D Pitic[2]; G Tamasescu[2]; M Stoian[2]; S Onciul[2]; M Dorobantu[1]
[1]*University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*; [2]*Emergency Hospital Bucharest, Bucharest, Romania*

Introduction: Left ventricular diastolic dysfunction (LVDD) is present in half of patients with hypertension and has been associated with increased cardiovascular morbidity, as well as the development of heart failure with preserved ejection fraction (HFpEF). Without proper medical treatment the progression continue tword systolic LV disfunction an clinical overt heart failure
Purpose: We aimed to evaluate the presence and predictors of distolic dusfunction in hypertensive adults from an national representative survey SEPHAR III survey.
Methods: Adult subjects enrolled in SEPHAR III survey were evaluated throughout two study visits by: anthropometric measurements, 3 sitting BP measurements per visit according to ESC-ESH guidelines, arterial stiffness measurements (with an oscillometric device), laboratory workup (lipids, fasting plasma glucose, HbA1c) and standard echocardiography. Normotensive state was defined as BP below 140/90 mmHg and lack of HT history or treatment. LVH was defined as indexed left ventricular mass (ILVM) > 95g/m2 in females and > 115 g/m2 in males. HT prevalence and control was defined by current ESC-ESH Guidelines. Diastolic dysfunction was defined by E/A < 1 or ≥2 on Doppler mitral inflow.
Results: From the total 889 adult hypertensive subjects identifies in SEPHAR III survey (mean age 55.79 ± 15.68, 51% males, 72,2% treated hypertensives out of which 30.8% with controlled BP values), diastolic dysfunction was recorded in 46.9%. Diastolic dysfunction was similar in treated vs. non-treated hypertensive (46.3% vs. 48.6%), and significantly less frequent among controlled vs. uncontrolled hypertensives (39.9% vs. 48.9%). Adjusting for MAP, treatment and treatment controll, regression analysis confirmed as predictors of diastolic dysfunction: PWVao (OR 1.11; 95% CI for OR: 1.01-1.12), LVH (OR 1.04; 95% CI for OR: 1.03-1.05), AF (OR 1.76; 95% CI for OR: 1.72-1.81), BP control (OR 0.85; 95% CI for OR: 0.82-0.89), antihypertensive treatment with RAAS blockers (OR 0.74; 95% CI for OR: 0.71-0.76), aortic SBP (OR 1.10; 95% CI for OR: 1.01-1.25).
Conclusions: Our study reveals that beyond well recognized determinants of diastolic dysfunction (LV, AF, BP values, RASS blockade), parameters of arterial stiffness and central BP values independently contributes to diastolic dysfunction adult hypertensive subjects, stressing the need specific treatment strategies, preventing the progression to overt heart failure.

P586

Hemodynamic correlates of right ventricular dilation in pulmonary hypertension due to HFpEF

E Berthelot[1]; MT Bailly[1]; S El Hatimi[1]; I Robard[1]; D Montani[2]; D Chemla[3]; P Assayag[3]
[1]*Hopital Bicetre, AP-HP - Service de Cardiologie, Université Paris-Sud, Le Kremlin-Bicetre, France*; [2]*Hopital Bicetre, AP-HP - Service de Pneumologie et Soins Intensifs, Université Paris-Sud, Le Kremlin-Bicetre, France*; [3]*AP-HP - Hospital Bicetre, University Paris Sud 11, Le Kremlin-Bicetre, France*

Background: Right ventricular (RV) remodelling and pulmonary hypertension (PH) are increasingly recognized in heart failure with preserved ejection fraction (HFpEF), with high prevalence and poor outcome. Factors leading to RV dilation in PH-HFpEF patients are unknown.
Purpose: We thought to determine the hemodynamic correlates of RV dilation (indexed end- diastolic right ventricular area EDRVA) in HFpEF patients with PH.
Methods: Right heart catheterization and echocardiography were performed in 93 PH-HFpEF patients (60 women) enrolled prospectively in our center. PH-HFpEF was defined by a resting mean pulmonary artery pressure (mPAP) ≥25 mmHg and a resting pulmonary artery wedge pressure (PAWP) >15 mmHg.
Results: Mean age (± SD) was 69 ± 12 years, mPAP was 40 ± 10 mmHg, PAWP was 21 ± 4 mmHg. 30 PH-HFpEF patients (31%) had RV dilation. The Pearson correlation coefficient between EDRVA (9.6 ± 3.1 cm^2/m^2) and hemodynamic variables was 0.39 for right atrial pressure (RAP) and 0.36 for the diastolic pressure gradient (each $p < 0.001$), and 0.27 for mPAP ($p = 0.01$). There was no correlation between EDRVA and PAWP, pulmonary vascular resistance or pulmonary arterial stiffness.
Conclusion: In PH-HFpEF patients, we documented a significant relationship between RV remodeling and RAP, mPAP and the diastolic pressure gradient. The classic variables quantifying pulmonary arterial load (resistance, stiffness) did not contribute.

P587

Left ventricular diastolic dysfunction and cardiovascular mortality in dialysis patients with preserved ejection fraction.

M Cafka[1]; M Rroji[2]; J Djamandi[3]; J Seiti[1]; G Burazeri[4]; A Goda[1]
[1]*University Hospital Center Mother Theresa, Department of Cardiology & Cardiac Surgery, Tirana, Albania*; [2]*University Hospital Center, Nefrology-Dialysis-Transplant Department, Tirana, Albania*; [3]*Hygeia Hospital, cardiology department, Tirana, Albania*; [4]*Institute of Public Health, Tirana, Albania*

Introduction: Cardiovascular disease is the major cause of death in dialysis patients. Diastolic dysfunction (DD) is common among dialysis patients. The aim of the study was to evaluate diastolic dysfunction, using TDI, in hemodialysis (HD) or peritoneal dialysis (PD) with preserved ejection fraction, and to identify its correlation with cardiovascular mortality.
Methods: A case control study was conducted, enrolling all patients on chronic dialysis (HD and PD) older than 18 years, who had more than 3 months in therapy. The echocardiography was performed 2-24 h after the dialysis session. LV diastolic dysfunction was defined as E/E′average (septal and lateral wall) ≥ 14. All patients had been followed up for 2 years. The end point was cardiovascular mortality.
Results: :Our population consisted in 122 pts, 78 pts (61%) on hemodialysis, mean age 53.4 ± 14.5 years, mean time on therapy 40.4 ± 14.4 months, 56% of patients were male, 27.8% with diabetes melitus,31.8% with hypertension; EF 0.60 ± 0.07. 30% of the patients have E/E′averaged >14. 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 ; 19.7 % in the group of patients with E/E′averaged >14) vs 10.1% in the group with E/E′averaged <14 ($p = 0.023$). Binary logistic regression analysis showed that E/E′averaged >14 [OR= 1.06 (1.01-1.21) $p = 0.011$], was independent risk factor for cardiovascular mortality
IN CONCLUSION: Diastolic dysfunction is independent predictor of cardiovascular mortality in dialysis patients with preserved ejection fraction.

P588

Left atrial volume index progresses significantly over time in diabetic and non-diabetic at risk populations

G O' Carroll[1]; E Tallon[1]; S Zhou[1]; C Watson[1]; M Ledwidge[1]; J Gallagher[1]; V Harkins[1]; K Mc Donald[1]
[1]*St Vincent's University Hospital, Dublin, Ireland*

Purpose: Left atrial volume index (LAVI) elevation is a significant predictor of cardiovascular disease. Progression of LAVI has also been shown to predict cardiovascular outcomes in the general population but little data exists in the diabetic population. LAVI progression may contribute to heightened cardiovascular risk in diabetic patients. The aim of this study is to describe LAVI progression in a community diabetic population compared with a non diabetic at risk cohort.
Methods: Patients attending the STOP-HF service between January 2011 and December 2013 were included in this study. Using transthoracic echocardiography, we measured LAVI in all participants in addition to standard Doppler-echocardiographic parameters. Echocardiography was performed at baseline and at a predefined follow up visit (2 – 5 years post baseline). Based on previous reported observations from our unit, significant change in LAVI ('LAVI progression') was defined as a change in baseline LAVI > 3.5 ml/m2.
Results: There were 1253 patients enrolled in the service. Four hundred and fifty four (36.2%) of these were diabetic (median age 65.3, 57.7% male). There was no difference in baseline cardiovascular risk factor between the groups except hypertension which was higher in the diabetic population (74% vs 66.8% p = 0.01). LAVI progression was seen in almost one third of patients (44.3% male, median age 67.9) (Table one).
Diabetics with LAVI progression were more often male (60.3% vs 34.8%, p < 0.001) with hyperlipidaemia (86% vs 71.6% p = 0.05). Both groups had similar rates of hypertension (78.5% vs 72.1% p = 0.24) There was no significant difference between the progressor groups in left ventricular ejection fraction (baseline median 67% vs 67%, follow up median 66.2% vs 66%, p = 0.97), left ventricular mass index (baseline median 91.1g/m2 vs 98.9g/m2, follow up median 93.6g/m2 vs 97g/m2, p = 0.004) or E/E′ (baseline median 8.4 vs 8.9, follow up median 8.5 vs 9.2, p = 0.02). Use of RAAS modifying therapy was similar in both progressor groups (48.1% vs 48.7% p = 0.25).
Conclusion: LAVI progression was similar in the diabetic and non diabetic groups, occurring in almost one third of patients. These at risk groups need further attention given the increased cardiovascular risk associated with diastolic dysfunction.

comparison of LAVI progression

	DM group	Non DM group	p value
Mean baseline LAVI	26.1 ml/m2	26.8 ml/m2	0.0766
Mean change in LAVI at follow up	2.18 ml/m2	2.20 ml/m2	0.54
LAVI change > 3.5 ml/m2	121 (30.9%)	204 (28.7%)	0.49

P589

Heart rate variability in heart failure patients with mid-range versus preserved ejection fraction and premature ventricular complexes

G Gheorghe[1]; A Ciobanu[2]; I Hartan[2]; ACD Gheorghe[2]; G Stanciu[2]; IT Nanea[2]
[1]University of Bucharest Carol Davila, cardiology, Bucharest, Romania; *[2]"Th. Burghele" Hospital, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania*

Background: Heart failure (HF) with reduced left ventricular ejection fraction (LVEF) has a high ventricular arrhythmic risk but there is few information about the arrhythmic risk in patients (pts) with heart failure and mid-range LVEF (HFmrEF) or preserved LVEF (HFpEF).
Purpose: To evaluate the heart rate variability (HRV) in the time and frequency domains as marker of myocardial electrical instability in sinus rhythm pts with HFmrEF versus pts with HFpEF.
Method: We included consecutive pts in sinus rhythm with HFmrEF (EF 40-49%) and HFpEF (EF≥50%) and premature ventricular complexes (PVC) during 24 hours ECG Holter monitoring. Pts with HF and reduced LVEF, atrial fibrillation or autonomic neuropathy were excluded. Demographic data, NYHA class and medical history were noted. The severity of PVC was evaluated according to the Lown classification. HRV was determined in the time domain (standard deviation of normal to normal (NN) R-R intervals - SDNN; standard deviation of the average NN intervals calculated over 5 minutes periods - SDANN; mean of the 5-min standard deviation of the NN interval calculated over 24 h - SDNN index; root mean square of successive differences - rMMSD; proportion of pairs of successive NNs that differ by more than 50 ms divided by total number of NNs - pNN50) and in the frequency domains (total power - TP; very low frequency – VLF; low frequency – LF; high frequency – HF, LF/HF ratio). Statistical analysis was performed with Epi Info 8.
Results: 70 pts were included, 73 ± 9 years old, 57.1% men. 88.6% pts had hypertension, 65.7% coronary artery disease, 40% old myocardial infarction, 8.6 % peripheral artery disease, 40% diabetes, 40% chronic kidney disease. 48.6% pts had HFpEF and 51.4% HFmrEF. 62.9% pts were in NYHA class II, 28.6% in NYHA class III and 8.6% in NYHA class IV. There were statistical significant more Lown IV PVC (couplets and ventricular tachycardia) in HFmrEF than in HFpEF pts (94.4% vs 52.9%, p < 0.001). There were no statistical differences between the two groups regarding SDNN, SDANN, SDNNI, rMMSD, pNN50. LF/HF ratio was augmented in HFmrEF comparing to HFpEF (p = 0.08).
Conclusions: The majority of HFmrEF pts had Lown IV PVC, with a statistical significant greater prevalence than in HFpEF pts. HRV parameters were similar in HFmrEF and HFpEF pts except LF/HF which was augmented in HFmrEF compared to HFpEF, reflecting a more important sympathetic nervous stimulation

P590

Does RAAS modifying therapy attenuate the cardiomyopathic effect of diabetes?

G O' Carroll[1]; E Tallon[1]; S Zhou[1]; C Watson[1]; M Ledwidge[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Dublin, Ireland

Purpose: In the general population, the presence of left ventricular diastolic dysfunction (LVDD) is an independent risk factor for cardiovascular disease including heart failure. We hypothesise that LVDD is more prevalent in diabetic populations than in a general at risk cohort resulting in worse cardiovascular outcomes. The aim of this study is to describe the prevalence of diastolic dysfunction in a community diabetic population and an at risk nondiabetic population and to characterise those with diastolic dysfunction.
Methods: Patients enrolled in the STOP-HF service between January 2011 and December 2013 were included in this study. Using transthoracic echocardiography, we measured LAVI in addition to standard Doppler- echocardiographic parameters. (LAVI < 28ml/m2 = normal, 28 – 32ml/m2 = indeterminate and > 32 ml/m2 = increased). Echocardiography was performed at baseline and at a predefined follow up visit (2 – 5 years post baseline).
Results: There were 1253 patients in this cohort. Four hundred and fifty four (36.2%) of these were diabetic (median age 65.3, 57.7% male). Baseline cardiovascular conditions were similar in both groups except hypertension which was higher in the diabetic population (74% vs 66.8% p = 0.01). The median BNP level at baseline was lower in the diabetic group (15.9 pg/ml vs 21.9 pg/ml, p < 0.001). The mean LAVI was 26.1 ml/m2 in the diabetic group and 26.8 ml/m2 in the non diabetic group (p = 0.0766). E/E′ was similar in both groups (baseline median 8.8 vs 8.1 p = 0.0669). Use of RAAS modifying therapy was higher in the diabetic group (59.7% vs 44%, p < 0.001).
Conclusion: Despite the higher rate of hypertension in the diabetic group, prevalence of LVDD was similar in both groups. This may reflect the fact that both groups are managed in a heart failure prevention service where emphasis on RAAS modifying therapies and other cardioprotective medications is standard.

comparison of diastolic parameters

	DM Population Baseline	Non DM Population Baseline
LAVI < 28 ml/m2	288 (63.4%)	492 (61.5%)
LAVI 28 - 32 ml/m2	50 (11%)	112 (14%)
LAVI > 32 ml/m2	67 (14.7%)	120 (15%)
E/E' < 8	197 (43.3%)	403 (50.4%)
E/E' 8 - 15	224 (49.3%)	340 (42.5%)
E/E' > 15	16 (0.2%)	33 (4.1%)

P591

Significant diastolic dysfunction is associated with cardioembolic stroke independent of history

I Indranill Basu Ray[1]; G Schwing[2]; T Middour[2]; D Monlezun[2]; K Katikitala[1]; K Korrane[1]; S Martin - Schild[3]; W Lam[1]; H Afsar[1]; I Giorgberidze[4]; J Cheng[1]; M Saeed[1]
[1]Texas Heart Institute, Cardiac Electrophysiology, Houston, United States of America; *[2]Tulane University, Cardiology , New Orleans, United States of America*; *[3]Tulane University, neurology , New Orleans, United States of America*; *[4]Michael E. DeBakey VA Medical Center , Cardiac electrophysiology , houston, United States of America*

Hypothesis: Diastolic dysfunction (DD) is an independent risk factor for Cardioembolic Stroke (CES) in patients both with and without atrial fibrillation (AF).
Background: DD may be associated with a thrombotic milieu, even in the absence of AF. Present guidelines are ambiguous whether risk stratification for AF should include DD. It is also unknown if DD is a risk factor for stroke without AF.
Methods: All patients admitted with diastolic dysfunction grade <4 and recorded stroke based on TOAST classification between 6/2008-5/2014 were identified.

Transthoracic echocardiogram was used to diagnose and grade DD. Multivariable logistic regression was used to investigate the possible independent association between stroke type and DD, adjusting for age, race, sex, and history of CHF, HTN, DM, stroke, mitral regurgitation (MR) >1 and AF. (Table)
Results: 388 patients met study criteria, 97(25.00 %) had DD grade > 1, the mean (SD) age was 62.46 (11.67), 154 (39.79%) were female, 17 (4.44%) had AF, and 77 (27.80%) had CES. In fully adjusted multivariable regression, DD grade >1 significantly increased the odds of CES (OR 3.96; 95%CI 1.02-15.36; p = 0.047).
Conclusion: DD (grade > 1) is an independent risk factor for patients with CES irrespective of AF. Larger studies are essential to delineate the complex relationship of DD and CES, both with and without AF, to determine appropriate anticoagulation strategy. This is particularly so as DD itself has been incriminated in the pathogenesis of AF.

Multivariable analysis of DD and Stroke

Covariate	OR(95% CI ; p - value)
DD grade> 1	3.95(95% CI1.02-15.36; p = 0.047)
Age	1.02(95% CI0.97-1.07; p = 0.461)
Black	0.50(95% CI0.15-1.62; p = 0.245)
Female	0.39(95% CI0.13-1.21; p = 0.102)
CHF History	2.56(95% CI0.63-10.50; p = 0.191)
Hypertension History	0.39(95% CI0.07-2.30; p = 0.300)
Diabetes History	0.41(95% CI0.13-1.30; p = 0.130)
Atrial Fibrillation History	3.01(95% CI0.17-54.83; p = 0.456)
Mitral Regurgitation	1.66(95% CI0.55-5.04; p = 0.370)

P592
A single blind, randomised, cross over trial of short term oxygen use during cycle ergometry in ambulatory patients with heart failure with normal ejection fraction

P Shah[1]; P Pellicori[1]; S Rimer[1]; A Bennett[1]; A Clark[1]
[1]*Castle Hill Hospital, Academic Cardiology, Hull, United Kingdom*

Introduction: Diuretics are the only treatment that improves exercise tolerance in patients with heart failure with normal ejection fraction (HFnEF). We investigated whether increased concentrations of inspired oxygen (FiO2) affects exercise tolerance in patients with HFnEF.
Methods: This is a single centre, randomised, single blind, crossover trial. HFnEF was defined as signs and symptoms of heart failure requiring treatment with diuretics, with a left ventricular ejection fraction of more than 45% and N-terminal pro brain natriuretic peptide (NTproBNP) >220 ng/l. 30 patients with HFnEF undertook three maximal incremental exercise tests with different FiO2 (room air, 28% and 40%) in random order. Patient blinding was maintained by using the same Venturi mask for all visits and FiO2 was controlled by investigator.
Results: Mean age was 74 years (73% male) and median NTproBNP of 1289 (IQR: 566-2243) ng/l. The results of the outcome variables measured are shown in the table:
Conclusion: Increasing FiO2 during exertion does not improve exercise capacity in patients with HFnEF.

P593
Diagnostic score for the detection of cardiac amyloidosis in patients with left ventricular hypertrophy

E Eve Cariou[1]; GM Galinier[1]; CD Carrie[1]; RJ Roncalli[1]; FP Fournier[1]; RD Ribes[1]; LO Lairez[1]
[1]*Toulouse Rangueil University Hospital (CHU), Toulouse, France*

Background: Cardiac amyloidosis (CA) is a disease with poor prognosis. Early non-invasive identification is of growing clinical importance. The objective of our study was to integrate clinical, electrocardiographic and echocardiographic parameters to build a diagnostic score in patients with left ventricular hypertrophy (LVH).
Methods and Results: 114 patients with LVH underwent a cardiac magnetic resonance and a 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid scintigraphy allowing to discriminate 3 groups of diagnosis: CA (n = 50), hypertrophic cardiomyopathy (n = 19) and unspecific cardiomyopathy (n = 45). Seven continuous variables associated with CA (systolic arterial pressure < 130 mmHg; PR duration > 200 ms ; Sokolow index < 12 mV; diastolic left ventricular posterior thickness > 13 mm ; E/Ea ratio > 10 ; global longitudinal strain > -12% and sum of basal longitudinal strain > -47%) were selected according to the best cut-off value. The area under the ROC curve for the diagnosis of CA using the score was 0.933 (95%CI 0.889-0.978). The best cut off value for the score was 3 leading to a sensitivity of 90% and specificity of 81%.
Conclusion: – An integrated evaluation of 7 diagnostic factors to build a diagnostic score is an easily method to discriminate CA in patients with LVH.

variables associated with CA

	AUC	IC95%	P-value	Best cut-off value
Systolic arterial pressure	0.789	0.619-0.919	0.001	< 130 mmHg
Troponin	0.667	0.515-0.819	0.061	
NT pro-BNP	0.667	0.515-0.817	0.063	
PR duration	0.740	0.600-0.881	0.007	> 200 ms
Sokolow index	0.793	0.669-0.917	0.001	< 12 mV
DI + DII + DIII	0.758	0.594-0.921	0.004	
Diastolic LV posterior thickness	0.758	0.624-0.891	0.004	> 13 mm
Transmitral flow peak E velocity	0.751	0.612-0.890	0.005	
E wave deceleration time	0.756	0.608-0.904	0.004	
Transmitral flow E/A ratio	0.741	0.587-0.895	0.007	
E/Ea ratio	0.808	0.688-0.928	0.001	> 10
Global longitudinal strain	0.775	0.644-0.907	0.002	> -12%
Sum of basal longitudinal strain	0.776	0.647-0.906	0.002	> -47%

AUC, area under the curve; LV, left ventricle; NT-ProBNP, N-terminal prohormone of brain natriuretic peptide

P592 Effect of increased oxygen on exercise

Variable	21% oxygen	28% oxygen	40% oxygen	P value (between 21% and 28%)	P value (between 21% and 40%)	P value (between 28% and 40%)
Mean exercise time (minutes)	9.07 (3.24)	9.46 (3.15)	9.15 (3.21)	0.06	0.11	0.44
Peak workload (watts)	61 (27)	64 (27)	62 (27)	0.16	0.14	0.14
Metabolic equivalent	2.5 (1.1)	2.6 (1.1)	2.6 (1.2)	0.10	0.10	0.74
BORG score	4.7 (1.7)	4.5 (1.5)	4.8 (2.0)	0.32	0.65	0.19
Heart rate at peak exercise (bpm)	111 (26)	109 (22)	108 (24)	0.87	0.44	0.42
Oxygen saturations at peak exercise (%)	95 (6)	97 (3)	97 (4)	0.20	0.09	0.55

bpm: beats per minute

P594

Diastolic dysfunction in patients with primary antiphospholipid syndrome

A Djokovic[1]; L Stojanovich[1]; S Radovanovic[1]; B Todic[1]; DV Simic[2]; M Zdravkovic[1]
[1]University Hospital Medical Center Bezanijska Kosa, Belgrade, Serbia; *[2]University Clinical Center of Serbia, Clinic of cardiology, Belgrade, Serbia*

INntroduction: The traditional view of atherosclerosis as a lipid storage disease crumbles in the face of extensive and growing evidence that inflammation participates centrally in all stages of this disease. Systemic inflammation in autoimmune diseases exhibits proatherogenic effects by induction of dyslipidemia, insulin resistance, hypercoagulation, endothelial dysfunction and oxidative stress. Patients with antiphospholipd syndrome (APS) are facing the higher risk of development of cardiovascular disease not only due to thrombophilia mediated by antiphospholipid antibodies (aPL) but accelerated atherosclerosis as well.
Objectives: To evaluate left ventricular (LV) diastolic function and presence in APS patients.
Methods: We analyzed 101 APS patients, 16 men (16.0%) and 85 women (84.0%) average age 47.70 ± 13.14. aPL analysis included detection of aCL(IgG/IgM), beta2GPI(IgG/IgM) and lupus anticoagulans (LA). According to the recent guidelines, we considered LV diastolic function normal if none or one available parameter met cut-off values (septal e' velocity >7cm/s, average E/e' >14, tricuspid regurgitation velocity >2.8 m/s, and left atrial indexed volume (LAVI) >34mL/m2). LV diastolic dysfunction was considered intermediate in cases meeting 2 cut-off values. If more than 2 parameters met cut-off values, a diagnosis of LV diastolic dysfunction was made. Results were compared to 32 healthy age and sex matched controls.
Results: Mean values of peak A wave, DT, IVRT as well as septal and lateral E/e' ratio and LAVI were significantly higher in APS patients compared to healthy subjects (p = 0.001, p = 0.0001, p = 0.008, p = 0.018, p = 0.012, p = 0.038 respectively) whereas E/A ratio was significantly lower (p = 0.046). Presence of diastolic dysfunction was significantly higher in APS patients (p = 0.001). aCL IgG positive APS patients had significantly higher values of peak A wave and IVRT (p = 0.008, p = 0.027 respectively), b2GPI IgG positive significantly higher values of peak A wave, IVRT and septal e' velocity (p = 0.011, p = 0.008, p = 0.008 respectively), beta2 IgM positive had significantly higher values of IVRT (p = 0.024), LA positive had significantly lower values of E/A ratio (p = 0.032).
Conclusion: Autoimmune diseases are associated with presence of LV diastolic dysfunction as a main determinant of heart failure with preserved EF (HFpEF). More aggressive education and prevention considering standard risk factors as well as timely cardiac evaluation in this group of patients seems to be of high importance.

P595

Left atrial volume index predicts cardiovascular events in diabetic and general at risk populations

G O' Carroll[1]; E Tallon[1]; S Zhou[1]; L Mc Donald[1]; C Watson[1]; M Ledwidge[1]; V Harkins[1]; J Gallagher[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Dublin, Ireland

Purpose: Left ventricular diastolic dysfunction (LVDD) is a significant predictor of cardiovascular disease. Left atrial volume index (LAVI) in the absence of atrial fibrillation and significant mitral valve disease is an excellent measure of diastolic function. We hypothesise that LAVI may be more predictive of cardiovascular outcomes in the diabetic population compared with the general at risk population. The aim of this study is to investigate the predictive value of LAVI in determining cardiovascular hospital admissions.
Methods: Patients enrolled in the STOP-HF service between January 2011 and December 2013 were included in this study. Using transthoracic echocardiography, we measured LAVI in all participants in addition to standard Doppler-echocardiographic parameters. Echocardiography was performed at baseline and at a predefined follow up visit (2 – 5 years post baseline). Hospitalisation for major adverse cardiovascular events (MACE) was determined using the hospital inpatient enquiry (HIPE) database. Hospitalisation for MACE was determined at least 2 years after the baseline visit. A significant change in LAVI ('LAVI progression') was defined as a change in LAVI > 3.5 ml/m2.
Results: There were 1253 patients enrolled in the service. Four hundred and fifty four (36.2%) of these were diabetic (median age 65.3, 57.7% male). At baseline, the mean LAVI was 26.1 ml/m2 in the diabetic group and 26.8 ml/m2 in the non diabetic group (p = 0.0766). MACE occurred in 7.01% of the diabetic population and 3.13% of the non diabetic population. Stroke/TIA (1.36%) was the commonest cardiovascular hospitalisation followed by arrhythmia (1.20%), myocardial infarction (0.72%) and heart failure (0.72%). A LAVI > 32 ml/m2 was most predictive of cardiovascular hospitalisation. MACE occurred in 6.47% of those with LAVI progression and in 3.59% of those without LAVI progression.
Conclusion: Cardiovascular admissions were twice as common in the diabetic population. Cardiovascular admissions were also more common in patients with LAVI progression. Elevated LAVI was most predictive of cardiovascular hospitalisation in both groups.

MACE Hospitalisations

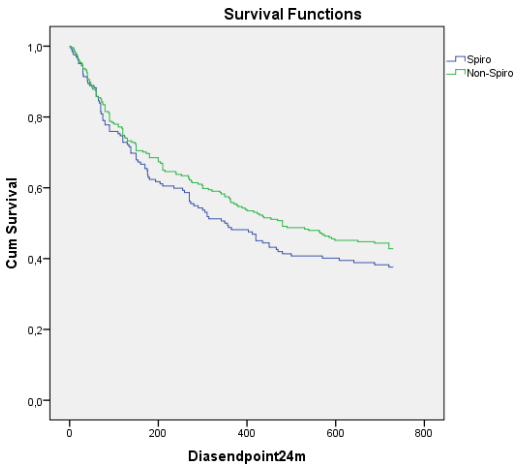
MACE hospitalisation	LAVI < 28 ml/m2	LAVI 28 - 32 ml/m2	LAVI > 32 ml/m2	LAVI change > 3.5 ml/m2	LAVI change < 3.5 ml/m2			
	DM	Non DM	DM	Non DM	DM	Non DM	n = 325	n = 778
Heart Failure	0.69%	0.41%	0.00%	0.89%	1.49%	0.83%	0.31%	0.51%
Myocardial Infarction	1.04%	0.00%	0.00%	0.00%	5.97%	1.67%	1.23%	0.64%
Arrhythmia	0.69%	0.61%	0.00%	0.00%	7.46%	1.67%	2.77%	0.51%
Stroke/TIA	2.78%	0.61%	2.00%	1.79%	2.99%	0.00%	1.54%	1.29%
DVT/ Pulmonary Embolism	0.35%	0.41%	2.00%	1.79%	0.00%	0.83%	0.62%	0.64%

P596

Prognostic impact of spironolactone in patients with heart failure with preserved ejection fraction

H Hugo Antunes[1]; J Gil[1]; ML Goncalves[1]; L Abreu[1]; B Marmelo[1]; I Pires[1]; D Moreira[1]; I Almeida[1]; M Correia[1]; C Cabral[1]
[1]Hospital Sao Teotonio, Cardiology, Viseu, Portugal

Introduction: Therapy for heart failure with reduced ejection fraction (HFrEF) is well established, with a prognostic impact in this group of patients (P). On the other hand, no treatment showed convincingly to reduce the morbi-mortality in P with heart failure with preserved ejection fraction (HFpEF).
Objectives: To evaluate the prognostic impact of spironolactone therapy in P with HFpEF.
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. Only the P with HFpEF were selected. We considered 2 groups, according to therapy instituted at the time of discharge: Group with Spironolactone (gSpiro) and group without spironolactone (gCONT).
We compared the combined endpoint (death / hospitalization for HF) at 12 and 24 months (M) and the survival curves of each group.
Results: Of a total of 1006 P admitted, 435 cases were included: 61.2% female and mean age 79.4 ± 8.3 years.
In-hospital mortality was 3.2%. The combined endpoint at 12M was 45.7% and 56.9% at 24M.
The gSpiro represented 38.4% of the P. There was a predominance of females in both groups (56.9vs 61.7% in gCONT, p> 0.05), mean age 79.6 ± 8.5 (vs 79.2 ± 8.3, p> 0.05).
The two groups were similar in terms of co-morbidities (Arterial hypertension in the gSpiro 66.2% vs 75.7%; Diabetes 29.6% vs 38.0%; History of ischemic heart disease 13.8% vs 9, 6%; History of stroke 9.2% vs 6.1%; p> 0.05).
Analytically, the sodium value was 139 ± 5 (vs 140 ± 5, p = 0.033), potassium of 4.5 ± 0.71 (vs 4.63 ± 0.66, p = 0.053), urea 60.4 ± 29.7 (vs. 70.47 ± 36.08, p = 0.002) and creatinine of 1.1 ± 0.4 (vs 1.3 ± 0.60, p < 0.001).
There was a greater number of events in the combined endpoint at 12 and 24M in gSpiro (63.5% vs 42.0%, p = 0.006 and 74.6% vs 57.4%, p = 0.024). Survival curves did not show statistically significant differences between the two groups at 12 or at 24M (p> 0.05)
Conclusion: This study showed that spironolactone therapy is associated with a greater number of adverse events at both 12 and 24M, although this difference was not evident when the survival curves of both groups were evaluated.
Thus, in this study, there was no benefit in the introduction of spironolactone in patients with HFpEF.



P597

Economic impact of heart failure with preserved ejection fraction: Insights from the prospective, randomized placebo-controlled ALDO-DHF trial

D Djawid Hashemi[1]; L Dettmann[2]; TD Trippel[1]; A Bobenko[1]; G Gelbrich[3]; R Lindhorst[1]; HD Duengen[1]; R Wachter[2]; G Hasenfuss[2]; B Pieske[1]; F Edelmann[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; *[2]University Medical Center Gottingen (UMG), Gottingen, Germany*; *[3]University of Wuerzburg, Wurzburg, Germany*

Background: Heart failure accounts to the main diseases in the developed countries and persists as the leading cause of hospitalization among adults >65 years of age in the United States and in the European countries. 50% of these patients are characterized with heart failure with preserved ejection fraction (HFpEF). Despite the increasing prevalence of this syndrome the health care related costs and its implications –in contrast to heart failure with reduced ejection fraction (HFrEF)– remain unclear.
Methods: In this analysis we explore the costs of the clinically stable ALDO-DHF cohort and the effect of spironolactone. This cohort included 422 ambulatory patients (mean age, 67 [SD, 8] years; 52% female) with chronic New York Heart Association class II or III heart failure, preserved left ventricular ejection fraction of 50% or greater, and evidence of diastolic dysfunction. Patients were randomly assigned to receive 25 mg of spironolactone once daily (n = 213) or matching placebo (n = 209) with 12 months of follow-up. We used a single-patient approach to explore the resulting general cost structure and included medication, number of general practitioner and cardiologist visits, and hospitalization in both acute and rehabilitative care facilities.
Results: The average annual costs per patient in this cohort came up to $ 1,300, the median costs were $ 360. We confirmed the main factor was hospitalization and have to conclude that spironolactone did not affect the overall costs. We identified being male, a low hemoglobin level, high oxygen uptake (VO2max), coronary artery disease, hyperlipidemia and especially atrial fibrillation as independent predictors for higher costs.
Conclusion: The costs are far below expected and compared to the HFrEF population. Regarding the ALDO-DHF cohort we have to allow for the relatively young, oligosymptomatic patient selection. The strict protocol excluded patients with major, e.g. pulmonary, co-morbidities leading to a lower limit of the costs. Further investigation is needed regarding the impact of co-morbidities and their effect over a longer period of time. Simultaneously, this analysis shows that early diagnosis and prevention of co-morbidities are necessary to reduce costs in the health care system.

P598

The occurence of interatrial dyssynchrony in heart failure across the spectrum of ejection fraction

M Cikes[1]; D Fabijanovic[1]; I Planinc[1]; B Skoric[1]; D Lovric[1]; J Ljubas Macek[1]; N Jakus[1]; H Jurin[1]; J Samardzic[1]; B Bijnens[2]; D Milicic[1]
[1]University of Zagreb School of Medicine, Department of Cardiovascular Diseases, Zagreb, Croatia; *[2]Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain*

Purpose: Heart failure with preserved EF (HFpEF) is characterized by phenotypic heterogeneity. Loss of atrial function is of relevance in HFpEF, and interatrial dyssynchrony (IAD) appears to be one of its aspects. The prevalence of IAD has not been compared between patients with HF and various categories of LVEF.
Methods: Data from 51 patients (24 HFpEF, 6 HFmrEF, 21 HFrEF) diagnosed with HF per current guidelines were analyzed retrospectively. IAD was measured from echo Doppler traces as the difference between the time of transmitral and transtricuspid A wave onsets.
Results: IAD>60 ms was present in 8 HFpEF pts. (33.3%), 1 HFrEF (4.8%) and 1 HFmrEF patient (16.7%) (p = 0.039). Compared to pts. with LVEF<50%, those with HFpEF were older, had higher SBP, heart rate, LVEF, LVmass, smaller LVIDd and lower sPAP; there was no difference in incidence of diabetes, NYHA class, NT-proBNP or eGFR , E/e' or atrial volumes. Higher IAD was associated with a higher proportion of HFpEF, lower heart rate, and higher LVEF (Table 1).
Conclusion: IAD is more prevalent in HFpEF compared to patients with LVEF<50% and does not appear associated with standard clinical parameters, NT-proBNP, LV mass, E/e' or atrial size.

Table 1

	1. Quartile n=13 IAD < -9 ms	2. Quartile n=13 IAD -9 - 24 ms	3. Quartile n=15 IAD 24 - 49 ms	4. Quartile n=10 IAD >49 ms	P value for trend
HFrEF (n, %)	9 (69.2%)	5 (38.5%)	6 (40%)	1 (10%)	0.02
HFmrEF (n, %)	3 (23.1%)	0 (0%)	2 (13.3%)	1 (10%)	
HFpEF (n, %)	1 (7.7%)	8 (61.5%)	7 (46.7%)	8 (80%)	
Age (years)	61.7 ± 11.3	63.3 ± 17.5	68.7 ± 11.8	68.9 ± 10.5	0.4
Male sex (n,%)	8 (61.5%)	6 (46.2%)	5 (33.3%)	2 (20%)	0.2
History of AF (n, %)	5 (38.5%)	5 (38.5%)	5 (33.3%)	6 (60%)	0.59
SBP (mmHg)	116.4±19.0	130.6±19.1	122.6±21.3	138±17.9	0.06
Heart rate (BPM)	76.6±13.1	75.9±13.3	64±10.7	66.7±14.7	0.028
eGFR (ml/min/1.73 m2)	55.1±26.6	67.8±17.9	53.3±16.3	58.7±21.9	0.31
NT-proBNP (pg/mL)	3597.5± 3661.5	2396.5± 2765.7	2262.8± 3262.9	955.1± 665.1	0.22
NYHA II/III/IV	6 (46.2%)/ 6 (46.2%)/ 1 (7.7%)	9 (69.2%)/ 3 (23.1%)/ 1 (7.7%)	9 (60%)/ 6 (40%)/ 0 (0%)	7 (70%)/ 3 (30%)/ 0 (0%)	0.7 (between groups)
LAVI (ml/m2)	43.6±18.5	39.1±10.5	39.9±13.4	50.5±19.7	0.31
RAVI (ml/m2)	31.5±16.6	24.4±10.7	30.3±21.5	24.7±19.8	0.65
EF (%)	32.2±12.6	47±18.9	44.7±16.6	54.8±16.3	0.014
LVIDd (cm)	6.2±1.0	5.6±0.8	5.5±0.6	5.5±1	0.17
sPAP (mmHg)	47.2±18.3	36.9±10.5	44.5±20.2	36.9± 8.4	0.41
E/e'	15.9±10.8	14.5±7.8	13.7±4.8	19.4±6.1	0.38

Values are given as mean +/- standard deviation.

P599

Is there an association between hidden HFpEF and markers of preclinical atherosclerosis?

AM Jakstaite[1]; J Celutkiene[2]; J Badariene[2]; E Rinkuniene[2]; A Cypiene[2]; I Slyvovskaja[3]; M Miglinas[4]; R Navickas[2]; L Ryliskyte[2]; A Laucevicius[2]
[1]Vilnius University, Medical faculty, Vilnius, Lithuania; *[2]University Hospital Santariskiu Klinikos, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; *[3]University Hospital Santariskiu Klinikos, Department of Rehabilitation, Physical and Sports Medicine, Vilnius, Lithuania*; *[4]University Hospital Santariskiu Klinikos, Clinic of Gastroenterology, Nephrourology and Surgery, Vilnius, Lithuania*

Background: In 2020 the prevalence of HFpEF is projected to exceed 8% of persons older than 65 years. However, there is a lack of knowledge on early detection of HFpEF and its' relation to cardiovascular risk markers.
Purpose: To investigate the association between early heart failure with preserved ejection fraction (HFpEF) and arterial markers of preclinical atherosclerosis.
Methods: We performed a prospective study and evaluated 148 high cardiovascular risk patients. Inclusion criteria were: metabolic syndrome (MetS), availability of brain natriuretic peptide (BNP) test, cardiopulmonary stress test, echocardiography and arterial markers (pulse wave velocity (PWV), augmentation index (AI), common carotid artery intima media thickness (IMT), common carotid artery stiffness (CAS),

ankle brachial index (ABI), reactive hyperemia index (RHI). We considered patients as having initial HFpEF if peak VO2 value was lower than 90% and/or BNP≥35 pmol/l. All patients were divided into 5 groups: (1) without HFpEF, with normal values of peak VO2 and BNP, (2) with at least one abnormal finding, either VO2 or BNP, (3) with elevated BNP, (4) with decreased peak VO2, (5) with both abnormal findings.
Results: 46 men and 102 women were analysed, mean age 56.41 ± 6.57 years. Group 1 was composed of 52 healthy individuals (35.14%), group 2 – of 96 (64.86%), group 3 – of 43 (29.05%), group 4 - 80 (54.05%), group 5 - of 28 (18.92%) patients. Significant differences were found between group 1 and remaining four groups in values of BNP – in group 2, 3, 4 and 5 (16.22 ± 6.60 vs 31.71 ± 23.15, 50.69 ± 21.90, 27.39 ± 20.93 and 48.59 ± 21.80, respectively; $p < 0.000$), for peak VO2 – in group 2, 3, 4 and 5 (103.11 ± 7.64 vs 82.69 ± 14.03, 87.42 ± 17.40, 78.40 ± 9.25 and 77.89 ± 9.83, respectively, $p < 0.000$). After comparison of arterial markers significant differences were found between groups 1 and 2, 1 and 3. Mean AI values were found as follows: 31.20 ± 9.87 vs. 27.33 ± 7.44; $p = 0.016$ and 31.60 ± 10.16 vs. 27.33 ± 7.44; $p = 0.020$. Average correlation was found between peak VO2 and left ABI (r=0.421; $p = 0.036$), right ABI (r=0.433; $p = 0.040$) in group 3 and weak relation between BNP and right CAS (r=0.300; $p = 0.032$) in group 1.
Conclusions: Two thirds of studied MetS patients had at least one pathological finding indicative of occult HFpEF. A significant relationship between heart failure markers and markers of preclinical atherosclerosis was found.

ISCHEMIA - REPERFUSION - PRECONDITIONING - POSTCONDITIONING

P600
ST-elevation myocardial infarction: risk factors at admission associated with a prolonged in hospital stay

MJ Maria Joao Vieira[1]; M Madeira[2]; L Reis[2]; P Dinis[2]; J Ribeiro[2]; A Fernandes[2]; F Caetano[3]; M Alves[1]; C Lourenco[2]; R Teixeira[2]; L Goncalves[2]
[1]Hospital Santarém, Cardiology, Santarém, Portugal; *[2]University Hospitals of Coimbra, Hospital Geral, Cardiology, Coimbra, Portugal*; *[3]King's College Hospital, NHS Foundation , London, United Kingdom*

Introduction: The length of hospital stay is an important measure of efficiency in the use of hospital resources as health care costs increase with prolonged hospitalization. Several predictors of length of hospitalization have been described in patients with ST-elevation myocardial infarction (STEMI), but little is known about the risk factors at admission for a prolonged in hospital stay (IHS).
Aim: Determine the risk factors at admission associated with a prolonged IHS in patients (Pts) undergoing percutaneous coronary intervention (PCI) for STEMI.
Methods: We performed a retrospective study of 313 consecutive patients (Pts) presented with STEMI (mean age: 64 ± 13.8, 72.8% male) who undergone PCI. Patients were divided in two groups based on mean in-hospital stay ≤ 5 days (short IHS) and > 6 days (long IHS). Demographic, clinical, laboratory and echocardiographic parameters at admission were evaluated. Statistical analysis was performed using Stata software version 14.1.
Results: Of the population, 229 Pts (73%) were included in the short stay group and 84 Pts (27%) were included in the long stay group. Male gender is associated with a shorter IHS (76,4% short IHS vs 63.1% long stay, P=0.019). Patients with long IHS were older (62 vs 69 years old; $p < 0.001$), were more likely to have prior arterial hypertension (75 vs 61%; P=0.023), prior history of chronic kidney disease (23.8 vs 7.0%, P=0<001). Also, the long HIS group presented at admission higher creatinine levels (118.3 ± 125.1 vs 87.3 ± 34.4 μmol/L; P=0.027), potassium levels (4.47 ± 0.7 vs 4.28 ± 0.4 mmol/l; P=0.007), glucose levels (9.71 ± 5.2 vs 8.1 ± 9.7 nmol/L; P=0.005), NTproBNP levels (6028.1 ± 8232 vs 1854.8 ± 2674.7 pg/ml; $p < 0.001$), troponin I levels (78.6 ± 138.7 vs 38.6 ± 93 ng/ml; $p < 0.004$), C-reactive protein (4.3 ± 6.6 vs 1.2 ± 2.33 mg/dl; $p < 0.001$), white blood cell count (12240.8 ± 3984 vs 10870.3 ± 3377 cells/μL; P=0.003); but lower hemoglobin concentration (13.49 ± 1.97 vs 14.18 ± 1.7 g/dl; P=0.004) and lower left ventricular ejection fraction (42.2 ± 11.4 vs 48.4 ± 9.9%; P=0.001), when compared to short IHS group. In the multivariate analysis, male gender (OR 0.26: 95%CI 0.07-0.96; P=0,043), creatinine level at admission (OR 1.02: 95%CI 1.0-1.05; P= 0.05), and C-reactive protein at admission (OR 1.23: 95%CI 1.004-1.51; P= 0.045) were found to be independently associated with prolonged IHS for patients with STEMI following PCI.
Conclusion: According to our data, in hospital length stay is strongly influenced by baseline characteristics of Pts, namely creatinine level, C-reactive protein and gender. These findings suggest that the assessment of several baseline variables together may represented a better clinical risk profile for in hospital length stay and its evaluation at admission may play an important role in the risk stratification of this Pts.

P601
The severity of myocardial dysfunction following ST-elevation myocardial infarction in patients undergoing acute percutaneous coronary intervention: time delays impact

L Malinova[1]; N Furman[1]; P Dolotovskaya[1]
[1]Saratov State Medical University, Research institute of cardiology, Saratov, Russian Federation

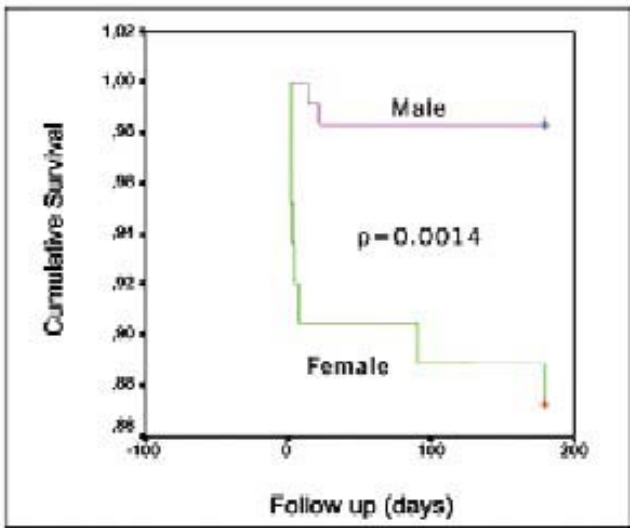
Despite the obvious fact that increased delay from myocardial infarction (MI) symptom onset to reperfusion is associated with worsening of the prognosis, and because of that have been introduced as performance indicator of MI care quality, intimate mechanisms underlying poor outcomes associated with time delays remain discussable.
Purpose of the study was to assess the impact of time delays on severity of myocardial dysfunction following STEMI.
Methods: 80 male patients (54 (47; 60) y.o.) admitted with STEMI were recruited into the study. Patient delay, health care systems delay and total ischemic time were estimated. BNP levels were measured on admission (BNP 1), at ~24 hours from reperfusion (BNP 2), at 7th day of admission (BNP 3, on discharge). The follow-up period was 12 months. Clinical signs and symptoms of heart failure were checked at 1, 6 and 12 months points. Primary endpoint was defined as the new-onset of heart failure according to 2016 ESC guidelines diagnostic algorithm.
Results: All recruited patients report no previous history of coronary heart disease, prior acute coronary event or heart failure. Symptom onset to first medical contact (FMC) time (patient delay), was 120 (40; 240) min. Symptom onset to arrival at hospital time (patient delay + health care system delay #1) was 175 (125; 230) min. Symptom to PCI delay in all recruited patients never exceeded 500 min. All studied time delays revealed moderate to high positive correlations with BNP levels measured at 24 hours from reperfusion and at 7th day of admission, but not BNP level at admission: i.e. patient delay + health care system delay #1 and BNP 2 – Spearman R = 0.63 ($p = 0.006$), patient delay + health care system delay #1 and BNP 3 – Spearman R = 0.72 ($p = 0.024$). Measured STEMI delays negatively correlated with left ventricular ejection fraction (Spearman R -0.57 … -0.791, $p < 0.05$) There were no associations between age, troponin I level, myocardial infarct size or culprit artery and BNP 2 and BNP3 levels as well as between severity of clinical signs of heart failure during follow up and time delays. On admission BNP level was 74.0 (18.1; 275.0) pg/mL. 9 patients (11.25%) reached primary end point within follow up period. Delays in FMC to PCI were associated with increased risk of new-onset of heart failure (HR 2.5 CI 1.5; 4.7, $p < 0.05$) at delays of more than 60 min.
Conclusion: Received data demonstrate significant impact of time delays on severity of myocardial dysfunction and risk of new-onset heart failure following STEMI. FMC to PCI time was associated with increased risk of new onset of heart failure) at delays of more than 60 min.

P602
Primary percutaneous coronary intervention in women. independent risk factors for death and major events after immediate and medium-term follow-up

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[1]; ILPB Anjos[2]; AAB Aragao[1]; VF Marcolla[1]
[1]Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil; *[2]Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

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 other to set out whether there are gender differences in a real-world comtemporary 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 independente

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



P603

In-hospital mortality in STEMI and NSTEMI: are they so different?

MJ Maria Joao Vieira[1]; P Dinis[2]; L Reis[2]; M Madeira[2]; J Ribeiro[2]; A Fernandes[2]; F Caetano[3]; M Alves[1]; C Lourenco[2]; R Teixeira[2]; L Goncalves[2]
[1]Hospital Santarém, Cardiology, Santarém, Portugal; *[2]University Hospitals of Coimbra, Hospital Geral, Cardiology, Coimbra, Portugal*; *[3]King's College Hospital, NHS Foundation , London, United Kingdom*

Introduction: Many studies have been published on outcomes in acute myocardial infarction (AMI). Most of these studies have shown a higher unadjusted in-hospital mortality rate (IHM) in ST elevation myocardial infarction. However, the impact of age, gender, co-morbidities, clinical findings at presentation and treatment in IHM still needs clarification.
Aim: Compare the in-hospital mortality in a population of patients (P) undergoing percutaneous coronary intervention (PCI) for an AMI according to the presence (STEMI) or absence of ST segment elevation (NSTEMI).
Methods: We performed a retrospective analysis of 580 consecutive P (72% male, 66 ± 13.9 years of age) hospitalized for AMI and submitted to PCI in a tertiary center. P were divided into two groups according to the presence (STEMI group) or absence (NSTEMI group) of ST segment elevation. Demographic, clinical, laboratory and echocardiographic parameters were evaluated. The primary endpoint was IHM and a univariate analysis and multivariate analysis were used to estimate the relationship between baseline variables and the outcome. Statistical analysis was performed using Stata software version 14.1.
Results: Of the sample, 338 P (58%) were included in the STEMI group (72% male) and 242 P were included in the NSTEMI group (72% male). Patients with STEMI were younger (65 ± 14 vs 68 ± 13 years old; P= 0.005) and less likely to have prior arterial hypertension (66 vs 83%; $p < 0.001$), prior history of heart failure (4.7 vs 16.1%; $p < 0.001$) and prior history of chronic kidney disease (13.9 vs 21.5%, P=0.017). At admission the STEMI group had lower systolic blood pressure (129.9 ± 3.0 vs 135 ± 2.6 mmHg; P=0.034), lower creatinine levels (99.1 ± 75 vs 117.2 ± 90 µmol/L P=0.027), lower NTproBNP levels (3745.1 ± 803 vs 7848 ± 2153 pg/ml; P=0.002) and lower left ventricular ejection fraction (46.1 ± 10.9 vs 50.7 ± 12.1%; P=0.004), but higher troponin I levels (48.8 ± 107 vs 8.3 ± 30 ng/ml;$p < 0.001$), glucose levels (8.8 ± 4.8 vs 7.7 ± 3.7 mmol/L; P=0.002), C-reactive protein (1.7 ± 2.4 vs 2.4 ± 4.6 mg/dl; P=0.026) and white blood cell count (11502.7 ± 3965 vs 9521.5 ± 3524 cells/µL; $p < 0.001$) when compared to the NSTEMI group. A total of 32 patients (5.5%) died before discharge. In the STEMI group a higher in hospital mortality crude rate was observed (7.4 vs 2.9%; P=0,019), but this difference was lost (OR: 2.0; 95% CI 0.09-45.1; P= 0.65) after adjusting for age, history of hypertension, prior history of heart failure, prior chronic kidney disease, systolic blood pressure at admission, Killip class at admission, left ventricular ejection fraction, and blood parameters at admission (creatinine, NTproBNP, troponin I, glucose, C-reactive protein and white cell count).
Conclusion: According to our data, there were no differences regarding in-hospital mortality associated with the presence or absence of ST segment elevation in AMI patients. NSTEMI are older and have a higher prevalence of comorbidities that may influence these findings.

P604

Cardiogenic shock in acute myocardial infarction

R Rim Ben Said[1]; B Jedaida[2]; M Mimouni[2]; M Gommidh[2]; N Ben Mansour[2]; R Dahmani[2]; C Chourabi[2]; H Mahfoudhi[2]; N Hajlaoui[2]; A Haggui[2]; D Lahidheb[2]; W Fehri[2]; H Haouala[2]
[1]La Rabta hospital, cardiology, Tunis, Tunisia; *[2]Military Hospital of Tunis, Tunis, Tunisia*

Introduction: Cardiogenic shock (CS) remains the leading cause of death in the acute phase of myocardial infarction (MI). Mortality from CS remains high despite marked advances in the treatment of MI. The aim of our study was to investigate the epidemiological clinical and echocardiographic characteristics of a serie of patients hospitalized for MI complicated by CS as well as the predictive factors of intra-hospital mortality.
Methods: We retrospectively analysed 70 patients affected by AMI complicated by CS admitted to cardiology department of the military hospital between October 2005 and April 2015
Results: A total of 70 patients were included in the study: 56 (80%) patients were male.The mean age was 63 ± 10 years.
Thirty-nine percent were admitted before the 6th hour from the onset of the chest pain, 12% were admitted between the 6th and the 12th hour and 45% were admitted beyond the 12th hour. On admission, 41% of patients were in left ventricular failure and 59% in shock.
The majority of myocardial infarction (45%) were anterior followed by inferior infarction with extension to the right ventricle (34%).
The mean LVEF was 49 ± 14.4%: mean LVEF was 37.8% in anterior MI and 57.6% in inferior MI. Mean LV end-diastolic diameter was 53.17 ± 7.8 mm and the mean LV end-systolic diameter was 36.5 ± 5.1 mm. Two patients had intraventricular thrombus. Ischemic myocardial regurgitation grade I, II was found in 4 patients. 22 patients had right ventricular dysfunction. Mean systolic pulmonary pressure was 37 mm Hg ± 10. Six patients had pericardial effusion.
Thrombolysis was performed in 51% of patients, 57% of them had thrombolysis before the 6th hour.
Seventy-two (72%) of patients underwent angiography and 56.6% had percutaneous coronary intervention (PCI). Of these, 27% were taken for primary PCI and 73 % had rescue PCI. Angiography had identified a single-vessel disease in 28% of cases, double-vessel disease in 44% of cases and multi-vessel disease in 28 % of cases. Revascularization was complete in 37% of cases. The success rate of PCI was 85%. The average of hospital stay was 7 ± 8 days. In-hospital outcome of the study, patients revealed a mortality rate of 47%, occurring on average in the 6th day of hospitalization. We found that renal failure ($p = 0.014$), late onset of shock ($p = 0.031$), hyperglycemia ($p = 0.014$), leukocytosis ($p = 0.02$), use of vasopressors ($p = 0.003$), LVEF ($p = 0.004$) and the anterior territory of MI ($p = 0.003$) were significantly predictive of hospital mortality.
Conclusion: Despite significant advances in the treatment of myocardial infarction, particularly techniques of reperfusion, therapeutic drug, and the advent of several circulatory support techniques, mortality of cardiogenic shock in acute phase of myocardial infarction remains high.

MOLECULAR BIOLOGY - GENETICS

P606

Genome wide association study reveals novel genetic loci associated with renal function in heart transplant recipients receiving calcineurin inhibitor therapy

D David Snipelisky[1]; M Hathcock[1]; W Kremers[1]; A Batzler[1]; G Jenkins[1]; S Kushwaha[1]; N Pereira[1]
[1]Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America

Introduction: Certain genetic variants are associated with a predisposition to developing renal dysfunction in the general population. There have been no genome-wide studies (GWAS) performed that assess the association of common genetic variation with renal function in heart transplant (HTx) recipients receiving calcineurin inhibitors (CNI).
Methods: Clinical and demographic data of patients that underwent HTx between January 1998 and December 2014 and were receiving CNI therapy was assessed.

Genotyping was performed using Illumina Infinium HumanCoreExome v1.0 analysis kit. A GWAS utilizing linear regression models were performed with estimated glomerular filtration rate (eGFR). When eGFR was unavailable, the Modification of Diet in Renal Disease (MDRD) formula was used to estimate it at 1 year as the phenotype after adjusting for baseline eGFR and change to sirolimus therapy.
Results: A total of 287 patients were included, and 314,903 single-nucleotide polymorphisms (SNP) were analyzed. The average age was 50 years (standard deviation, 12.5), most were of European descent (n = 278, 96.9%) and male sex (n = 179, 71%). Significant variants in HMHB1 (rs918378, p = 2.27e-6), C12orf75 (rs1230081, p = 2.76e-6), LOC339894 (rs35649103, p = 2.93e-6), LOC10042392 (rs4617520, p = 6.07e-6), and MMP12 (rs652438, p = 7.05e-6) genes were associated with renal function as assessed by eGFR (Figure 1 and Table 1).
Conclusions: Our first of its kind GWAS demonstrates that genetic variation in five individual genes are associated with renal function in HTx recipients receiving CNI therapy. Larger studies are needed to replicate these findings and aid in the development of a genetics-based risk model for CNI nephrotoxicity.

Table 1

Chromosome	Gene	Reference number	Minor allele frequency	Beta (SE)	p-value
3	LOC339894	rs35649103	0.11	12.61 (2.63)	$2.93e^{-6}$
5	HMHB1	rs918378	0.08	14.18 (2.93)	$2.27e^{-6}$
10	LOC10042392	rs4617520	0.12	11.95 (2.52)	$6.07e^{-6}$
11	MMP12	rs652438	0.05	16.70 (3.64)	$7.05e^{-6}$
12	C12orf75	rs1230081	0.07	14.55 (3.03)	$2.76e^{-}$

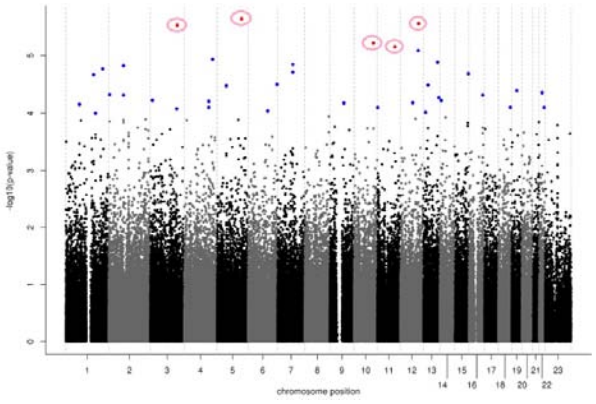


Figure 1.

P607

Coronary heart disease and genetic polymorphisms. clinical, angiographic, procedure technique and long-term follow-up evaluation post percutaneous coronary intervention. major events and restenosis

LLB Bandeira[1]; IP Borges[1]; ECS Peixoto[2]; RTS Andrade[3]; ILPB Anjos[1]; RTS Peixoto[2]; RTS Peixoto[2]; SA Simoes[3]
[1]Medical School of Severino Sombra University, Vassouras, Brazil; *[2]Fluminense Federal University, Niteroi, Brazil*; *[3]Rio de Janeiro State Government, Rio de Janeiro, Brazil*

Background: There are clinic and genetic polymorphism differences in coronary artery disease (CAD). Percutaneous coronary intervention (PCI), clinic, angiographic, procedure technique may influence the evolution, major events (death, AMI, revascularization) and clinical restenosis.
Objective: This study aims to evaluate if genetic polymorphism have some influence in long-term follow-up after PCI.
Methods: A total of 182 patients, the coronary disease group (CDG) with CAD of a closed health system were submitted to PCI from 2001 and 2007 and to genetic follow-up evaluation until 12/31/2008. The control group (CG), with 36 patients, were angiographically normal but they were submitted to genetic evaluation. The polymorphisms evaluated were the ACE I/D and A166C (AT1R). In this period 221 procedures were perfomed in 182 patients. Restenosis was considered as symptoms and/or as a ischemic tests with angiographic restenosis. Qui square, Fisher exact and Student t test were used. Cox multivariate regression analysis were not used because only three clinical characteristics and A166C had P < 0.10.
Results: The CG and CDG patients were: female 20 (55.6%) and 49 (26.9%), (P=0.0007); age 55.9 ± 11.1 and 60.8 ± 10.5(P=0.0100); tabaco smokers 5 (13.9%) and 67 (36.8%), (P=0.0132); diabetes 4 (11.1%) and 48 (26.4%), (P=0.0802); hypertension 29 (80.6%) and 146 (80.2%), (P=0.9631); dyslipidemia 14 (38.9%) and 112 (61.5%), (P=0.0119); family history 12 (33.3%) and 60 (33.0%), (P=0.9659); obesity 9 (25.0%) and 60 (33.0%), (P=0.3476); ACE polymorphism DD 16 (44.5%), DI 17 (47.2%), II 3 (8.3%) and DD 81 (44.5%), DI 70 (38.5%), II 31 (17.0%), (P=0.3612); A166C polymorphism AA 36 (100.0), AC 0 (0.0%), CC 0 (0.0%) and AA 135 (74.2%), 42 (23.1%), 5 (2.7%), (P=0.0026).
Conclusion: In CDG with 221 procedures, there were no difference: between ACE and A166C polymorphism at one, two or three vessel disease; between majors events, deaths, AMI and revascularization; and between restenosis and the mean vessel diameter, lesion extension and bare metal or drug eluting stents (DES), although were implanted in 27 (12.2%) patients, being 15 (55.5%) patients with in stent restenosis and the others with small vessel diameter and long lesions.
In CDG there were more males, older people, more smokers, dislipidemia and they were genetically A166C polymorphism different from CG, the latter did not have CC or AC. There were no differences between the variables studied and illness extension, major events and restenosis in the CDG, even in relation to bare stens and DES, maybe because DES were used to the less favorable lesions and in stent restenosis.

	NORMAL GROUP (N=36)	CORONARY ARTERY DISEASE GROUP (N=182)	P
Female (n,%) Male (n,%)	20 (55.6) 16 (44.4)	49 (26.9) 133 (73.1)	0.0007
Age (year)	55.9±11.1 (38-81)	60.8±10.5 (39-85)	0.0026
AT1R (n,%)	AA 36 (100.0) AC 0 (0.0) CC 0 (0.0)	AA 135 (74.2) AC 42 (23.1) CC 5 (2.7)	0.0026
ECA (n,%)	DD 16 (44.5) DI 17 (47.2) II 3 (8.3)	DD 81 (44.5) DI 70 (38.5) II 31 (17.0)	0.3612

P608

Impact of glutathione S-transferase M1 gene polymorphisms on the chronic heart failure

N Natasa Jankovic[1]; DV Simic[1]; O Gudelj[2]; S Radovanovic[3]; D Djikic[1]; S Suvakov[4]; V Coric[4]; T Djukic[4]; T Simic[4]
[1]Clinical Center of Serbia, Clinic for Cardiology, Belgrade, Serbia; *[2]Military Medical Academy of Belgrade, Belgrade, Serbia*; *[3]Department of Cardiology, Medical Center Bezanijska Kosa, Belgrade, Serbia*; *[4]Institute for Medical Biochemistry, Belgrade, Serbia*

Background: Chronic heart failure (CHF) secondary to ischemic heart disease belongs to oxidative disease. Glutathion S-transferas M1 (GSTM1) is a gene family of phase II metabolic enzymes that detoxify free radicals, particulary in tobacco smoke. Smoking is a potent source od free radicals and well known risk factor for coronary disease. Inactive form of GSTM1 (null genotype) causes lower detoxification, which may be a risk factor for coronary disease.
Aim: To examine influence of different risk factors and GSTM1 polymorphism on the risk of development CHF.
Material and method: The study population consisted of 120 patients with CHF and 69 patients without heart failure in the control group matched for sex and age. The criterion for admission was left ventricular ejection fraction (LVEF) < 45%. Age, sex, smoking history, hypertension, dyslipidemia, diabetes mellitus and obesity were evaluated as risk factors. The genetic polymorphism analyses for the GSTM1 gene were determined by multiplex polymerase chain reaction (PCR). Both patients and controls were dichotomized into GSTM1 null and GSTM1 active genotype. Independent factors on CHF risk were evaluated by multiple logistic regression model.
Results: Frequency of GSTM1 null genotype was higher in CHF patients in comparison to controls (55.8 vs. 49.3%, respectively). GSTM1 null individuals exhibited a higher risk of CHF when compared to carriers of at least one active GSTM1 allele with un-significant of 1.30 (CI:0.72-2.36; p>0.05). Hypertension (OR=7.08; CI:2.89-17.33; p < 0.05), diabetes (OR=8.73; CI:1.79-42.66; p < 0.05), old age (more than 50 year) (OR=6.21; CI:1.45-26.50; p < 0.05) and obesity (OR=2.56; CI:1.16-5.65; p < 0.05) were independent risk factors for CHF. Smoking wasn't independent risk factor for

CHF (OR=1.59; CI:0.77-3.29; p>0.05). GSTM1 null genotype alone wasn't independent risk factor for CHF (OR=1.30; CI:0.72-2.36; p>0.05), but GSTM1 null genotype in smokers was independent risk factor (OR=3.99; CI:1.47-10.85; p < 0.05).
Conclusion: The frequency of GSTM1 null genotype in present study was similar to what was published previously. The presence of GSTM1 null genotype increases the risk of CHF among smokers.

P609
Mutational screening of PKP2 and DSG2 genes in Russian patients with arrhythmogenic right ventricular cardiomyopathy

A G Anna Shestak[1]; O V Blagova[2]; YU A Lutokhina[2]; YU V Frolova[3]; S L Dzemeshkevich[3]; E V Zaklyazminskaya[1]
[1]Russian Research Center of Surgery, Laboratory of Medical Genetics, Moscow, Russian Federation; *[2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*; *[3]Russian Research Center of Surgery, Moscow, Russian Federation*

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Background: Arrhythmogenic right ventricular cardiomyopathy (ARV) is an inherited disease characterized by progressive fibro-fatty replacement of right ventricle or both ventricles and leading to electrical instability and sudden cardiac death (SCD). Mutations in five desmosomal genes and seven non-desmosomal genes account about 65% of all ARVC cases. The most common forms of disease are caused by mutations in PKP2 gene and in DSG2 gene which account 25-40% and 12-40% of all genotype-positive cases, respectively. Identification of mutations in ARVC-related genes is one of a major diagnostic criterion (Marcus, 2010).
Methods: Instrumental examination and genetic counseling were performed for 38 Russian patients from 35 unrelated families with definite, borderline or possible diagnosis of ARVC (Task Force Criteria, 2010). Clinical examination had included standard and 24-hours ECG monitoring, Echo-CG, cardiac MRI, myocardial biopsy. Genetic study: PCR-based direct Sanger sequencing of coding exons and adjacent intronic areas of PKP2 and DSG2. Potential role of all genetic variants was evaluated in silico by PolyPhen2, SIFT or NetGen2, BDGP tools. The cascade screening for family members of genotype-positive probands was provided upon request. Results: Screening for mutations in the PKP2 and DSG2 in 35 DNA samples was performed. We found four rare genetic variants in PKP2: two truncating mutations .W538X, .1523_1538del, missense variant p.L582P, and splice-site mutation c.IVS2 + 1G>T. Patients carrying these genetic variants in PKP2 had clinical manifestation at the third/fourth decade of life with high-grade VA; ICDs were implanted in 2 cases. We found four rare genetic variants in DSG2: p.S194L, p.V533I, p.N245H, and p.R49H. Patients carrying these genetic variants in DSG2 also have had clinical appearence at the third decade of life with VT and RV hypertrophy. All variants have not been detected in a healthy cohort (100 samples). Thus, mutations in two genes responsible for most common forms of ARVC were identified in 22.9% of patients. Identification of mutation in DSG2 in male proband of 22 y.o. had led to increase the reliability of the diagnosis from 'possible' to 'definite'. We have analyzed the mutation detection rate in the groups with definite, borderline and possible diagnoses of ARVC and the total contribution of genetic data in the disease diagnosis. Mutational screening for the DSP, DSC2, JUP genes and in non-desmosomal genes for patients with no mutations in PKP2 and DSG2 is in process now. Conclusion: We found 8 genetic variants in 35 Russian ARVC index patients (22,9%). Our findings in Russian patients are consistent with the representation data of two common genetic forms of ARVC in other ethnic groups. DNA diagnostics results were used for verification of diagnosis in probands and their families, even on pre-clinical stages of the disease. Positive results were used for SCD risk stratification and decision on ICD implantation.

P610
(-75)G allele of APOA1 gene is associated with non-attainment of target lipid levels in very high cardiovascular risk patients

M Vorobyeva[1]; O Gigani[1]; M Azova[1]; S Villevalde[1]; Z Kobalava[1]
[1]RUDN University, Moscow, Russian Federation

Objective: Dyslipidemia is recognized as a prominent risk factor for cardiovascular diseases. The recent cholesterol guideline recommends aggressive statin therapy in patients with very high cardiovascular risk. The aim of the study was to investigate genetic predictors of its efficacy in very high cardiovascular risk patients.
Methods: In 58 patients with history of clinically evident cardiovascular diseases and fasting low-density lipoprotein cholesterol (LDL-C) >1.8 mmol/l or non-high-density lipoprotein cholesterol (non-HDL-C) >2.6 mmol/l (62.1% male, 61.9 ± 8.6 (M ± SD) years, arterial hypertension 82.8%, myocardial infarction 69.0%, non-hemorrhagic stroke 34.5%, diabetes mellitus 27.6%, total cholesterol (TC) 5.3 ± 1.5 mmol/l, HDL-C 1.1 ± 0.4 mmol/l, LDL-C 3.3 ± 1.3 mmol/l, triglycerides (TG) 1.9 ± 0.7 mmol/l, very LDL-C (VLDL-C) 0.8 ± 0.3 mmol/l, non-HDL-C 4.2 ± 1.5 mmol/l, previous statin therapy 82.8%) polymorphisms of gene CYP3A4 (encoding a member of the cytochrome P450 superfamily of enzymes) and gene APOA1 (encoding apolipoprotein A1) and efficacy of 1 month of high-intensity statin therapy (atorvastatin 80 mg/day) were assessed. The APOA1 genotypes were determined at two polymorphic sites (G/A at -75 bp, and C/T at + 83 bp). Statistical analysis was performed with SPSS Version 8.0 statistic software package. A value of p < 0.05 was considered statistically significant.
Results: 16 patients (27.6%) attained target LDL-C level < 1.8 mmol/l and 21 (37.6%) patients attained target non-HDL-C level < 1.8 mmol/l after 1 month of therapy. CYP3A4 *1 genotype was identified in all the patients. The allele frequencies for the (-75)G, (-75)A, + 83C and + 83T of gene APOA1 were found to be 0.53, 0.47, 0.94 and 0.06, respectively. No association was found between APOA1 + 83 C/T polymorphisms and response to intensive lipid-lowering therapy. We did not found any impact of (-75) G/A APOA1 polymorphisms on attainment of target LDL-C level. (-75)G allele of APOA1 gene was significantly associated with non-attainment of target non-HDL-C (Fisher's exact test result: p < 0.05(two-tailed), p < 0.01 (one-tailed)). Patients who attained vs did not attained target level of non-HDL-C were more often APOA1 (-75) G allele carriers (73.9 vs 25%, p < 0.001). 26% of APOA1 (-75) G allele carriers and 38.1% of APOA1 (-75) A allele carriers attained target non-HDL-C.
Conclusion: (-75)G allele of APOA1 gene is associated with non-attainment of target non-HDL-C and may be a predictor of resistance to statin therapy in very high cardiovascular risk patients.

BASIC SCIENCE - CELLULAR BIOLOGY

P612
Effects of chronic ACE inhibitor treatment on a translational model of heart failure with preserved ejection fraction

NAJAH Harouki[1]
[1]Sanofi R&D, Cardiovasculaire et métabolisme, pharmacologie, Chilly-mazarin, France

Background/Introduction: Heart failure (HF) with preserved ejection fraction (HFpEF) is a major epidemiological clinical issue, which parallels the prevalence of risk factors in the elderly (e.g. diabetes). In contrast to HF with reduced EF, clinical trials targeting neurohormonal activation with RAAS inhibitors or b-blockers have all failed in HFpEF. This failure has been attributed to patient heterogeneity and poor matching of therapeutic mechanisms and primary pathophysiological processes. Moreover part of the challenge relies also on the lack of relevant animal models recapitulating the contribution of cardiovascular and non-cardiovascular co-morbidities in the etiology of the syndrome. ZDF rats have been recently reported to develop an HFpEF phenotype.
Purpose: The objectives of this study were to further characterize cardiac and renal dysfunctions of the ZDF rats and determine whether improving renal function with an ACE inhibitor has a beneficial impact on HFpEF.
Methods: The cardiac function of Zucker Diabetic Fatty (ZDF) and lean animals was assessed after 8 weeks of daily treatment with ramipril (1 mg/kg per os) both in vivo, using echocardiography and PV-loop methodologies, and in vitro, using myocyte calcium contractility recording system after primary cardiomyocytes isolation. Renal and cardiometabolic biomarkers were monitored along the time course of the study and renal as cardiac histological analyses were performed at the end.
Results: We demonstrated that, at the age of 16 weeks, ZDF rats were overtly diabetic and displayed a significant decrease in cardiac output despite a normal ejection fraction and an increased fractional shortening. Moreover, in comparison to lean controls, ZDF rats showed an impairment of left ventricular (LV) diastolic function as documented by alterations of LV filling (decrease in E/A ratio), LV relaxation (increase in isovolumic relaxation time both in vivo and in vitro) and increase in end-diastolic volume and pressure. This diastolic dysfunction was associated with LV hypertrophy and fibrosis. Plasma biomarkers of HFpEF (ANP, BNP and Galectin-3) were also significantly increased in ZDF animals compared to lean littermates.
After 8 weeks of treatment ramipril decreased LV hypertrophy and fractional shortening, increased end diastolic volume and tended to restore cardiac output in ZDF rats. This beneficial effect on cardiac remodeling was not associated with a reduction in plasma ANP, BNP or galectin-3 levels.
Conclusions: In summary, this study confirmed the ZDF model as a promising and reproducible model of HFpEF which displays most of the features of this syndrome. Despite a positive effect on cardiac remodeling, ramipril at 1 mg/kg/d partially improved the cardiac function in this HFpEF model.

P613

Epigenetic therapy reduces angiotensin-II induced cardiac hypertrophy and fibrosis

A Adam Russell-Hallinan[1]; L Shiels[1]; E Mcnamara[1]; C Watson[2]; J Baugh[1]
[1]*University College Dublin, Conway Institute, Dublin, Ireland*; [2]*Queen's University of Belfast, Wellcome-Wolfson Institute for Experimental Medicine, Belfast, United Kingdom*

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Background: Heart failure with preserved ejection fraction (HFpEF) is one of the leading causes of global morbidity and mortality. HFpEF is driven by pathological remodelling in the heart where there is hypertrophy of cardiomyocytes (cardiac hypertrophy) and an increased accumulation of extracellular matrix proteins in the interstitium (fibrosis). Recent evidence suggests that epigenetic processes such as DNA methylation are involved in the pathogenesis of cardiac remodelling. Inhibition of DNA methylation may yield a novel therapeutic avenue for the treatment of HFpEF.
Purpose: This study investigated the therapeutic potential of the DNA methyltransferase inhibitor, 5-azacytidine (5aza) to inhibit pathological hypertrophy and fibrosis in the Angiotensin-II (AngII) infusion model, a preclinical model of HFpEF.
Methods: Wild type C57BL6/J mice were implanted with subcutaneous micro-osmotic pumps infusing 1000 ng/kg/min AngII to induce cardiac injury. Saline infusion was used as a negative control and blood pressure was measured weekly in conscious mice via tail-cuff method. Infused mice were treated every four days after pump implantation with intraperitoneal administration of either placebo or 5aza. Cardiac structure and function was examined in vivo using non-invasive echocardiography followed by post mortem histological analysis.
Results: Echocardiographic analysis revealed that AngII infused mice treated with 5aza displayed a significant reduction in the left ventricular (LV) mass, interventricular septal wall and LV posterior wall thickness compared to mice which received placebo treatment. Positive pixel analysis of picrosiris red stained cardiac tissue demonstrated reduced levels of moderate and strong positive staining for collagen in the hearts of 5aza treated mice. 5aza was found to have no effect on blood pressure levels.
Conclusion: Therapeutic options for HFpEF patients are limited. The DNA methylation inhibitor, 5aza, shows therapeutic potential by reducing hypertension-induced cardiac hypertrophy and fibrosis independently of an effect on blood pressure.

P614

Increased plasma clusterin levels in patients with left ventricular remodeling after myocardial infarction has cardiac origin and is due to a defect in proteasome activity

A Annie Turkieh[1]; S Porouchani[1]; P Mulder[2]; M Fertin[3]; O Besemes[1]; M Chwastyniak[1]; P Amouyel[1]; V Richard[2]; C Bauters[3]; F Pinet[1]
[1]*Institute Pasteur of Lille, Risk Factors and Molecular Determinants of Aging-Related Diseases, Lille, France*; [2]*INSERM U1096, ROUEN, France*; [3]*Cardiology Hospital of Lille, Lille, France*

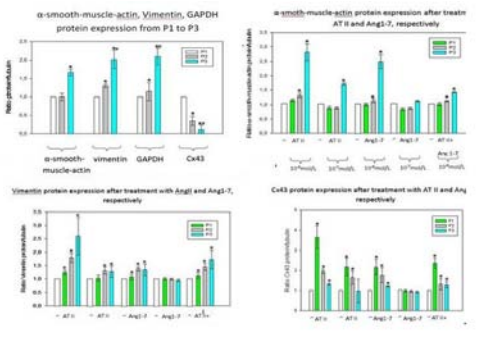
Heart failure (HF) following myocardial infarction (MI) is characterized by alterations of left ventricle (LV) structure and function, named LV remodelling (LVR). Proteomic analysis of plasma of patients from our REVE-2 cohort identified increased plasmatic levels of clusterin (Clu) in patients who have developed high LVR one year after MI. Our aim was to determine if increased clusterin in plasma has a cardiac origin and to analyze the mechanisms of Clu regulation in the heart.
For these purposes, we used a MI rat model induced by ligation of the left coronary artery to analyze Clu expression in the LV of rats at different time post-MI. Clu mRNA level was increased in the LV of rat at 7 days (1.9 fold, $p = 0.001$) and 2 months (1.4 fold, $p = 0.010$) post-MI. Clu precursor form (p-Clu) was only increased at 7 days post-MI (2.2 fold, $p = 0.001$). Clu mature form (m-Clu) was increased at 7 days (2.0 fold, $p = 0.001$) and 2 months post-MI (1.3 fold, $p = 0.035$). Also we observed that Clu mRNA level was positively correlated with ANP and BNP expression at 7 days ($r = 0.93$, $p < 0.001$/ $r = 0.91$, $p < 0.001$ respectively) and 2 months ($r = 0.56$, $p = 0.020$/ $r = 0.60$, $p = 0.011$ respectively) post-MI. p-Clu and m-Clu levels were positively correlated with plasmatic BNP level ($r = 0.73$, $p = 0.001$/ $r = 0.60$, $p = 0.015$ respectively) at 7 days post-MI. m-Clu level was positively correlated with LV end diastolic diameters (0.67, $p < 0.001$) and LV weight/body weight ratio ($r = 0.76$, $p < 0.001$) at 2 months post-MI
Then, we used primary cultures of rat neonate cardiomyocytes (NCM) that we treated with different modulators of protein degradation (PDG) systems in order to estimate their role in Clu expression and secretion in post-MI. Proteasome inhibition (MG132 treatment) of NCM was validated by increased levels of ubiquitinylated proteins. We found increased Clu mRNA (2.2 fold, $p < 0.001$), p-Clu (2.5 fold, $p < 0.001$), m-Clu (1.6 fold, $p = 0.003$) and its secreted form (s-Clu; 4.9 fold, $p < 0.001$) in the treated cells compared to control cells. We have detected another form of clusterin demonstrated by co-immunoprecipitation as ubiquitinylated clusterin only in the MG132 treated cells. We observed a cross-talk between the different PDG systems in the treated NCM with increased LC3II/LC3I ratio corresponding to activation of macroautophagy. To decipher which PDG systems or both are involved in increased Clu, NCM were co-treated with MG132 and 3-MA, an inhibitor of macroautophagy, and we observed increased mRNA Clu (1,7 fold, $p = 0;010$) and m-Clu (1,3 fold, $p = 0.031$) with no difference on p-Clu and s-Clu levels compared to MG132 treated cells.
Our data suggest that the increased plasma levels of Clu in patients with high LVR post-MI has cardiac origin and is mainly due to a defect in proteasome activity in heart. More informations are need to understand the cross-talk between the PDG (proteasome and macroautophagy) systems on the behavior of Clu in heart.

P615

Angiotensin 1-7 might be a new solution in the treatment of chronic heart failure

A Alena Kazak[1]; A Kurlianskaya[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Heart Failure Laboratory, Minsk, Belarus*

Introduction: Cardiac fibroblasts (CF) are the major non-contractile cells present in the myocardium. Proliferation and differentiation of cardiac fibroblasts play a pivotal role in adverse cardiac remodelling. During cardiac remodeling cardiac fibroblasts undergo phenotypic changes: they acquire a myofibroblast character, proliferate and produce extracellular matrix (ECM) proteins. Interactions between cardiac fibroblasts (CF) and cardiomyocytes (CM) are still not fully understood.
Purpose: The first aim of our study was to get more information concerning the specific phenotype of cardiac myofibroblasts. The second aim was to learn changes of properties of CF and CM in co-cultures by the 24-hours stimulation of AngiotensinII (AngII) and Angiotensin 1-7 (Ang1-7).
Methods: We have studied the properties of CF and CM ($n = 24$ experiments) isolated from the hearts of Sprague-Dawley rats with chronic heart failure. With Immunhisto and Western Blot methods we studied the changes of structural proteins such as vimentin, α-smooth muscle actin (α-sma), myosin heavy chain and desmin, and also gap-junctional protein such as Cx43 in P1, P2, P3 of CF and CM co-cultures. At the same time we investigated the quantitative change of these proteins after the 24-hours stimulation of AngII and Ang 1-7 in 10-6 mol / L and 10-7 mol / L concentrations as well as co-stimulation of these therapeutic agents in 10-6 mol / L concentration.
Results: Our study has shown that the quantity of structural proteins such as vimentin, α-sma and myosin heavy chain increases in co-culture of CF and CM from P1 to P3, conversely decreases the quantity of Cx43. Desmin was not detected in all passages. Thus already in P3 the CF transform in myofibroblasts The 24-hours stimulation of Ang1-7 increases the quantity of proteins, but less than angII. It was detected that in co-stimulation of AngII + Ang1-7actin in 10-6 mol / L concentration angiotensin 1-7 has shown the antagonistic property to angiotensinII, which was manifested in less increase of strucrural proteins quantity compared to angII alone stimulation.
Conclusion: Our study has shown that already in P3 the fibroblasts transform in myofibroblasts. Angiotensin 1-7 shows the antagonistic property to angiotensin II. The proof of the positive effect of angiotensin 1-7 might have therapeutic potential. The effects mediated by the action of angiotensin 1-7 could be a new solution in the treatment of chronic heart failure.



Phenotype transformation

P616

SIRT1 protects the heart from endoplasmic reticulum stress-induced apoptosis through eIF2a deacetylation

J Pires Da Silva[1]
[1]*University of Paris-Sud 11, 92296, Chatenay-Malabry, France*

Over the past decade, endoplasmic reticulum (ER) stress has emerged as an important mechanism involved in the pathogenesis of cardiovascular diseases including heart failure. Cardiac therapy based on ER stress modulation is viewed as a promising avenue towards effective therapies for the diseased heart. Here, we tested whether sirtuin 1 (SIRT1), a NAD+-dependent deacetylase, participates in modulating ER stress response in the heart. Using cardiomyocytes and adult inducible SIRT1 knockout mice, we demonstrate that SIRT1 inhibition or deficiency increases ER stress-induced cardiac injury, whereas activation of SIRT1 by the sirtuin-1-activating compound STAC-3 is protective. Analysis of the expression of markers of the three main branches of the unfolded protein response (i.e. PERK/eIF2α, ATF6 and IRE1) showed that SIRT1 protects cardiomyocytes from ER stress-induced apoptosis by attenuating PERK/eIF2α pathway activation. We also present evidence that SIRT1 physically interacts with and deacetylates eIF2α. Mass spectrometry analysis identified lysines K141 and K143 as the acetylation sites on eIF2α targeted by SIRT1. Furthermore, mutation of K143 to arginine to mimic eIF2α deacetylation confers protection against ER stress-induced apoptosis. Collectively, our findings indicate that eIF2α deacetylation on lysine K143 by SIRT1 is a novel regulatory mechanism for protecting cardiac cells from ER stress and suggest that activation of SIRT1 has potential as a therapeutic approach to protect the heart against ER stress-induced injury.

P617

Influence of iron availability in the normoxic versus hypoxic conditions on the morphology and atrophy of skeletal myocytes.

K A Kamil Aleksander Kobak[1]; M Kasztura[1]; M Dziegala[1]; J Bania[2]; A Orlowska[2]; V Kapusniak[3]; L Kiczak[4]; K Josiak[5]; W Banasiak[6]; P Ponikowski[5]; E A Jankowska[1]
[1]*Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland*; [2]*Wroclaw University of Environmental and Life Sciences, Department of Food Hygiene and Consumer Health, Wroclaw, Poland*; [3]*Wroclaw University of Environmental and Life Sciences, Department of Histology and Embryology, Wroclaw, Poland*; [4]*Wroclaw University of Environmental and Life Sciences, Department of Biochemistry, Pharmacology and Toxicology, Wroclaw, Poland*; [5]*Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; [6]*Military Hospital of Wroclaw, Centre for Heart Diseases, Wroclaw, Poland*

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Background: Muscle atrophy reflects a systemic response to various chronic diseases, including heart failure (HF). Disease-associated decrease in muscle tissue mass can occur as a result of various pathologies and one of the reported causative factors is hypoxia. Iron deficiency (ID) is one of the potential pathomechanisms contributing to increased skeletal muscle fatigability and impaired exercise tolerance in HF. It is worthy of mentioning that beneficial effects of iron supplementation on the improvement of muscle function in patients with heart failure with ID have already been reported. However, the mechanisms responsible for this phenomenon remain unknown.
Purpose: It is expected that skeletal muscle cell line subjected to different iron availability and/or hypoxic conditions will demonstrate changes in cell morphology and in the expression of atrophy markers.
Methods: L6G8C5 rat skeletal myocytes were cultured in normoxia or hypoxia at the optimal versus reduced versus increased iron concentration. We analysed cell morphology and expression of Atrogin1, MuRF1 [specific markers of muscle atrophy], SMAD4 [gene involved in the maintenance of balance between muscle atrophy and hypertrophy] and Desmin [muscle class-III intermediate filament protein] at the mRNA and protein level using qPCR, Western Blotting and immunocytochemistry.
Results: Hypoxic treatment caused, as compared to normoxic conditions, an increase in expression of Atrogin1($p < 0.01$) and Desmin ($p < 0.001$) and did not affect the expression of MuRF1 and SMAD4 in the cells. Iron-deficient cells displayed morphological abnormalities and demonstrated an increased expression of Atrogin1 ($p < 0.01$), MuRF1 ($p < 0.05$) both in normoxia and hypoxia, indicating activation of the ubiquitin proteasome pathway involved in protein degradation during muscle atrophy. ID combined with hypoxia also causes a decrease in SMAD4 expression ($p < 0.05$) suggesting modifications leading to atrophy. In contrast, cells cultured in a medium enriched with iron during hypoxia exhibited reverse changes in the expression of atrophy markers (all $p < 0.05$) along with increased SMAD4 expression ($p < 0.05$). Desmin was upregulated in the cells subjected to both ID and iron excess in normoxia ($p < 0.01$) and hypoxia ($p < 0.05$), but the greatest augmentation occurred when ID was combined with hypoxia. Notably, in hypoxia an increased expression of Atrogin1 and MuRF1 was associated with an increased expression of transferrin receptor 1, reflecting intracellular iron demand (R=0.76, $p < 0.01$; R=0.86, $p < 0.01$). Further, the expression of desmin during hypoxia was associated with an increased apoptotic activity (estimated by Bax/BCl2 ratio) of skeletal myocytes (R=0.94, $p < 0.001$).
Conclusions: Hypoxia and iron deficiency when combined has the most detrimental impact on skeletal myocytes, especially in the context of muscle atrophy markers. Inversely, iron supplementation in in vitro conditions might act in the protective manner on these cells.

P618

Alterations in natriuretic peptides system in adult stem cells in heart failure

N Khromova[1]; V Galenko[2]; D Smirnov[3]; P Tikanova[1]; T Lelyavina[2]; R Dmitrieva[1]
[1]*Federal Almazov North-West Medical Research Centre, Institute of Molecular Biology and Genetics, Saint Petersburg, Russian Federation*; [2] *Federal Almazov Medical Research Centre , Research Department for Heart Failure, St Petersburg, Russian Federation*; [3]*Peter the Great St. Petersburg Polytechnic University , Saint Petersburg, Russian Federation*

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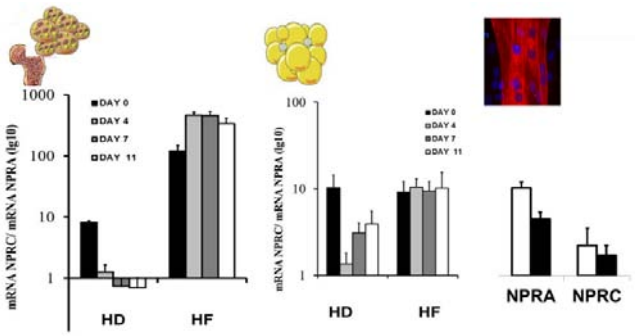
Background and aim: Heart failure (HF) is associated with an increase of myocardial and systemic insulin resistance, mitochondrial disfunction, altered levels of circulating adipocytokines, decrease of metabolism of fatty acids (FA) and a shift toward glucose for ATP generation. Metabolic alterations in HF were demonstrated not only for myocardium, but also for other organs including adipose tissue, skeletal muscles, and bone tissue. Our study was aimed to test the hypothesis that systemic metabolic abnormalities in HF could be related to alterations in signaling pathways known to be important in regulation of metabolism, and regulated by natriuretic peptide (NP) system in adult stem cells derived from skeletal muscle (SC) bone marrow (BMMSC) and subcutenious (ADMSC) adipose tissue from HF patients related to chronic activation of natriuretic peptides system.
Methods: 7 patients with HF and 6 healthy donors were involved in this study. All patients were diagnosed as having HF based on clinical signs of heart failure and echocardiographic or angiographic evidence of impaired left ventricular systolic function, and have a disease history of at least 12 months. To study the dynamics of gene expression, RNA samples were collected at different time points during adipose and muscle in vitro differentiation course.
Results: The dynamics of expression of NPRA/NPRC differ significantly between HF and HD in all tested stem cell samples (SC, BMMSC, ADMSC), as well as in course of in vitro adipose differentiation. Data are summarized in Figure 1: the regulation of natriuretic peptides system in adult stem cells of different origin is altered significantly in HF patients.
Conclusion: the observed low ratio of NPRA to NPRC expression in HF samples could indicate the "switch" in NP-cGMP signaling in adipose and muscle tissue in heart failure patients.



NPRA/NPRC expression in BMMSC, ADMSC, SC

P619

Mechanisms of action of sacubitril/valsartan on cardiac remodeling: a systems biology approach

O Oriol Iborra Egea[1]; C Galvez Monton[1]; S Roura[1]; I Perea Gil[1]; C Prat Vidal[1]; C Soler Botija[1]; A Bayes Genis[1]
[1]*Health Sciences Research Institute Germans Trias i Pujol (IGTP), ICREC (Heart Failure and Cardiac Regeneration) Research Programme, Badalona, Spain*

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Sacubitril/Valsartan, proved superiority over other conventional heart failure (HF) management treatments, but its mechanisms of action remains obscure.
In this study, we sought to explore the mechanistic details for Sacubitril/Valsartan in HF and post-myocardial infarction (MI) remodeling, using an in silico, systems biology approach.
Myocardial transcriptome obtained in response to MI in swine was analyzed to address post-infarction ventricular remodeling. Swine transcriptome hits were mapped to their human equivalents using Reciprocal Best (blast) Hits, Gene Name Correspondence, and InParanoid database. HF remodeling was studied using public data available in GEO (accession GSE57345, subseries GSE57338), processed using the GEO2R tool. Using the Therapeutic Performance Mapping System (TPMS) thecnology, dedicated mathematical models trained to fit a set of molecular criteria, defining both pathologies and including all the information available on Sacubitril/Valsartan, were generated. All relationships incorporated into the biological network were drawn from public resources.
An artificial neural network analysis revealed that Sacubitril/Valsartan acts synergistically against cardiomyocyte cell death and left ventricular extracellular matrix remodeling via 8 principal synergistic nodes. When studying each pathway independently, Valsartan was found to improve cardiac remodeling by inhibiting members of the guanine nucleotide-binding protein family, while Sacubitril attenuated cardiomyocyte cell death, hypertrophy, and impaired myocyte contractility by inhibiting PTEN.
The complex molecular mechanisms of action of Sacubitril/Valsartan upon post-MI and HF cardiac remodeling were delineated using a systems biology approach. Further, this dataset provides pathophysiological rationale for the use of Sacubitril/Valsartan to prevent post-infarct remodeling.

P620

Vegf and hgf realized postinfarction cardiac repair by control cardiac stem cell mobilization, angiogenesis and inflammation

K Konstantin Dergilev[1]; PI Makarevich[2]; E Shevchenko[1]; Z Tsokolaeva[1]; I Beloglazova[1]; E Zubkova[1]; M Menshikov[1]; YE Parfyonova[1]
[1]Cardiology Research Center , Moscow, Russian Federation; *[2]M.V. Lomonosov Moscow State University, Faculty of Basic Medicine, Moscow, Russian Federation*

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Chronic heart failure (HF) continues the most important problem of modern medicine. Despite many advances in the management of HF, treatment options for many patients remain limited and new treatment strategies are clearly needed. Gene therapy and therapeutic vascular growth may provide a new treatment option for these patients.
The aim of the present study is to analyse the potential of combined HGF and VEGF gene therapy for stimulation of endogenous mechanisms of cardiac repair after myocardial infarction.
As a proof-of concept we have tried to evaluate VEGF, HGF and HGF + VEGF plasmid based gene delivery to rat ischemic myocardium. We have found that within 14 days post injection combination of VEGF + HGF plasmids was superior to single VEGF or HGF in terms of vascular density increase (both capillary and arteriole), but was unable to significantly reduce post-infarction fibrosis, yet certain trend was observed. HGF and HGF + VEGF injections significantly stimulate accumulation of c-kit + resident cardiac stem cells in border zone and WT1 + epicardial cell activation in compare to VEGF plasmid injections. We have also found the reduction of inflammatory cellular infiltration of border zone in VEGF + HGF group compared to VEGF group, which might indicate decrement of inflammatory response in myocardium. In further in vitro studies using HUVEC and TIME endothelial cells we found that production of pro-inflammatory chemokines MCP-1 and IL-6 is increased by recombinant VEGF and reduced after addition of HGF. Combination of both factors resulted in medium levels of MCP-1 and IL-6 production, thus HGF seems to counteract the pro-inflammatory action of VEGF. As for pro-angiogenic IL-8, both factors had stimulating effect on its production and their combination yielded maximum amount of IL-8 expression and secretion by endothelial cell cultures, which suggests an alternative way for IL-8 regulation involved.
As a result of the study we can conclude that combination of VEGF and HGF has good translational promise for myocardial repair and regeneration. Deeper in-sights into their mechanism of action might show non-canonical properties and modes of action of that combination that may drive its way into practice.

P621

Cardiac progenitor cells isolated from duchenne muscular dystrophy patients with heart failure have impaired intracellular calcium signaling and electrophysiological properties

D Domenico D'amario[1]; F La Neve[1]; A Siracusano[1]; G Perri[1]; A Amodeo[2]; M Massetti[2]; R Piacentini[1]; C Grassi[1]; F Crea[1]
[1]Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy; *[2]Bambino Gesu Children's Hospital, Rome, Italy*

Background: Duchenne Muscular Dystrophy (DMD) is an X linked recessive disorder due to mutations of the Dystrophin gene. Heart failure (HF) is emerging as the most relevant clinical challenge. Cardiac progenitor cells (CPCs) appear early during development and are responsible for cardiomyogenesis in fetal life and affect myocardial homeostasis.
Aims: 1. to test whether is possible to isolate and characterize CPCs from patients with DMD and HF
2. to investigate the functional characteristics of the CPCs isolated from DMD patients with HF in terms of intracellular Ca2 + signaling and electrophysiological features.
Methods: 4 consecutive patients with DMD undergoing LVAD implantation were enrolled; the LV core was used for CPCs isolation and characterization. To evaluate the differentiation potential, Confocal Ca2 imaging was performed in human differentiatied CPCs from DMD patients with HF and HF alone (i.e. controls). Intracellular Ca2 + transients were recorded and quantified for each cell. Parameters such as the time-to- peak, the mean peak amplitude and the area underneath the curves were analyzed. The contribution of L- (Cav1.2 subunit) and T-subtypes VGCCs to transient changes in [Ca2 +] were evaluated using a channel blockers (e.g. nifedipine).
Results: CPCs expressed markers of mesenchymal origin. CPCs population doubling time averaged 26.5 hours. Telomere length averaged 7.1 kbp. Telomerase activity was present in all cell lines. Extracellular application of KCl, induced intracellular Ca2 + transients in the 83% of studied differentiated cells at P10 in both groups. No significant transients were observed in undifferentiated cells. CPCs from DMD patients with HF or with HF alone (i.e. control) were analyzed and compared. In control CPCs, these transients, likely due to depolarization-induced activation of voltage-gated Ca 2 + channels had mean peak amplitude, expressed as ΔF/F ratio, equal to 5.9 ± 0.5, and the mean time-to- peak was of 18 ± 1 s. These values were significantly altered in CPCs isolated from DMD patients: the amplitude of Ca 2 + transients was significantly smaller (3.2 ± 0.4; $P < 0.001$) and the response was slower (26 ± 1 s). Nifedipine significantly reduced the mean amplitude of KCl-evoked Ca2 + transients from 5.81 ± 0.54 to 2.16 ± - 0.48 in controls. There was an even higher reduction in DMD-CPCs from 3.40 ± 0.31 to a 0.5 ± 0.2. In order to evaluate the Ca 2 + homeostasis and the contribution of the endoplasmic reticulum, we performed experiments adding caffeine (20nM). Data showed that Ca2 + is reduced in DMD CPCs compared to controls (-0.376 ± 0.33 VS -0.288 ± 0.25 $P < 0.000125$).
Conclusions: CPCs from DMD patients retain significant growth reserve in vitro and have impaired calcium signaling and electrophysiological properties. Moreover, generating personalized functionally competent cardiomyogenic cells from DMD patients may be used as an in vitro cell model for functional studies and drug testing in heart failure.

BASIC SCIENCE - ANIMAL EXPERIMENTATION

P622

Inflammation inhibition effects in diabetes induced heart failure

V Cobet[1]; M Popovici[2]; L Ciobanu[2]; L Tacu[1]; V Ivanov[2]; I Popovici[2]; I Moraru[2]; E Cobet[3]; M Ivanov[1]; E Panfile[2]; V Rotaru[1]
[1]State University of Medicine and Pharmacy, Chisinau, Moldova Republic of; *[2]Institute of cardiology , Chisinau, Moldova Republic of*; *[3]State University of Moldova , Biopharmaceutical chemistry , Chisinau, Moldova Republic of*

Background: Inflammation is appreciated as a leading factor regarding cardiovascular disorders triggering and exacerbation. Nevertheless a promising antinflammatory treatment concerning cardiac mismatch improvement is not yet consolidated.
Aim: The in vitro evaluation of cardiac effects of the TNF-alpha antagonist administration during diabetes-induced heart failure (DHF).
Material and methods: DHF was classically reproduced in rats by i/p administration of streprozotocin (50 mg/kg, 5 days) – series 1 (of reference). TNF-alpha antagonist, TNF-McAb (TNF monoclonal antibody, analog of infliximab) has been administered i/p during DHF modeling and 5 days after – series 2. After 10 days animals of both series have been euthanized, and isolated heart was perfused in isovolumic regimen (Langendorff model) or exterior working (Neely-Rovetto model). Cardiac reactivity was assayed in: (1) hemodynamic effort due to pre- and afterload

increase; (2) neuroendocrine activation modulated by action in diverse concentrations of norepinephrine, angiotensin II and endothelin-1 (ET-1); (3) in ischemia (30 min) followed by reperfusion (45 min) syndrome.
Results: TNF-alpha inhibition led to significant increase of cardiac output (CO) in effort with volume and resistance respectively by 23,7 and 26,2% comparatively to reference indices. Systolic pressure of left ventricle (LV) was in series 1 higher in all induced hemodynamic stress levels, but on aortic pressure of 100 and 120 cm H20 the increment was significant and averagely represented 18-19%. DHF was characterized by LV lusitropic function impairment, whose principal parameters, telediastolic pressure (LVTDP) and index of diastolic myocardial rigidity significantly decreased during TNF-alpha inhibition by 26-28%. The norepinephrine action led in DHF to inotrop-chronotropic effect dissociation, but endothelin-1 (ET-1) induced a negative inotropic effect, associated by CO reducing by 10,3%. TNF-alpha inhibition led to appearance of positive inotropic effect to ET-1 action and cardiac output increase by 11%. Myocardial ischemic contracture assayed after 30 min of ischemia thereby of LVTDP is doubly more in DHF vs control pattern (56,3 ± 3,6 vs 28,4 ± 1,9 mm Hg) and remains above on 45th min of reperfusion (39,2 ± 2,5 vs 18,8 ± 1,2 mm Hg). TNF-McAb notably attenuated consequences of ischemia-reperfusion syndrome, leading to LVTDP drop by 29,3% at finish of ischemia and by 26,8% at finish of reperfusion.
Conclusions: 1. TNF-alpha inhibition during diabetes-induced heart failure improved cardiac functionality, confirming the pathogenical role of inflammation and, on the other hand, the therapeutic relevance of TNF-McAb regarding outworn heart functioning in hemodynamic and neuroendocrine efforts.
2. Most conspicuous TNF-McAb benefit has referred to appearance of positive inotropic effect to ET-1 action and significant decrease of LV telediastolic pressure by around 29% in ischemia-reperfusion syndrome.

P623

Atrial and ventricular cellular Ca signaling at different stages in a rat model of heart failure with preserved ejection fraction

F Felix Hohendanner[1]; D Bode[1]; U Primessnig[1]; T Guthof[1]; S Jeuthe[1]; V Adams[2]; N Rolim[3]; U Wisloff[3]; P Burkert[1]; F Heinzel[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; *[2]University of Leipzig, Leipzig, Germany*; *[3]Norwegian University of Science and Technology, Trondheim, Norway*

Funding Acknowledgements: BIH (Clinical Scientist); OptimEx

HF with preserved ejection fraction (HFPEF) constitutes about 50% of HF patients who present symptoms for HF, but normal or near-normal systolic function. No standardized treatment has shown to improve prognosis, and the underlying pathomechanisms are not resolved and may differ with etiology. We postulated that alterations in atrial and ventricular function in vivo are associated with phenotype and disease stage-dependent alterations in cardiomyocyte Ca signaling.
We examined in vivo function and cardiomyocyte Ca transients (Fluo4-AM, field stim) in a clinically relevant rat model of metabolic risk factors and HFPEF. ZSF-1 +/- (lean, hypertension; Ln) and ZSF-1 +/+ (metabolic syndrome, HFPEF; Ob) rats fed with high fat diet at 21 weeks were compared to another series examined at 28 weeks and to wildtype (CTRL).
Results: At 21 weeks, in vivo measurements showed unaltered ejection fraction, LV mass and relaxation in Ln. In Ob ventricular ejection fraction was also preserved, but ventricular relaxation was impaired and LV mass and E/e′ increased, as in HFpEF. This was paralleled by an unchanged cytosolic Ca2+ transient (CaT) peak amplitude (Fpeak), and unchanged SR Ca2+ content in cardiomyocytes isolated from the left ventricle. Diastolic decay of the cytosolic CaT was unchanged in Ln, but significantly slowed in Ob. At 28 weeks, even though in vivo data indicated an HFPEF phenotype in Ob, cardiomyocyte CaT showed significantly reduced Fpeak and SR Ca2+ content indicating that cellular changes in obesity-related HFPEF are highly stage-dependent.
Left atrial size was increased and atrial emptying fraction was reduced vs. CTRL already at 21 weeks in Ob but not in Ln. Interestingly, CaT amplitude in isolated atrial myocytes was increased in both Ln and Ob (2.3 ± 0.2 vs 2.9 ± 0.2 and 2.8 ± 0.2; n=22, 22 and 26 cells; $p < 0.05$). Moreover, time to 50% of maximal Ca release (TF50) was significantly increased in atrial Ln but not in Ob, suggesting a lower number of recruited Ca release sites in Ln. Sodium Calcium exchanger (NCX) and SR Ca ATPase (SERCA) activity, as assessed by application of caffeine were not significantly altered in Ln or Ob. Ca spark frequency after 3 Hz stimulation was significantly increased in Ln (to 1.9 ± 0.4 vs. 1.0 ± 0.2 and 0.7 ± 0.2 Sparks/100µm/sec in ZSF-obese and WT in n=7, 18 and 11 cells resp.; $p < 0.05$) but unchanged in Ob. Tetracaine-dependent SR Ca leak, however, was significantly increased in Ln and Ob suggesting increased spark-independent SR Ca leak in Ob.
Summary: Ventricular diastolic dysfunction in obesity-related HFPEF is associated with altered Ca signaling during excitation-contraction coupling with a time-dependent worsening of the CaT. However, in vivo atrial function deteriorates at early states of remodeling despite increased cardiomyocyte CaT amplitudes. In addition, our data suggest underlying altered local control of Ca in atrial cardiomyocytes from obesity-related HFPEF vs lean rats with metabolic risk factors.

P624

Development of a prototype for remote monitoring of patients with heart failure by short message service in middle-income country: study protocol

LL Pedraza[1]; JRW Moraes[2]; GB Aliti[3]; E Eneida Rejane Rabelo-Silva[4]
[1]Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; *[2]Federal University of Rio Grande do Sul, Porto Alegre, Brazil*; *[3]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil*; *[4]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil*

Background/Introduction: Despite advances in the care of patients with heart failure (HF), results after hospitalization are still below expectations, especially in developing countries. Strategies and new approaches are necessary in the current scenario and worldwide panorama of HF epidemiology, in order to prevent both hospital readmissions and morbidities caused by this clinical syndrome. The monitoring program through Short Message Service (SMS) has been successful for HF in developed countries, reducing the number of hospital readmissions. There is currently no knowledge of this strategy being developed with HF patients and recent hospitalization in developing countries. In order to fill this gap, this study will use this SMS approach for the remote monitoring of HF patients.
Purpose: To develop a remote monitoring system that includes information on HF, self-care and adherence to medications for HF patients that can be used in developing countries.
Methods: Clinical variables such as weight, presence of signs and symptoms of decompensation, management of self-care and adherence to regular use of medications will be monitored through SMS. The system features will be divided into two groups: executed automatically by the system and executed through commands from an operator. This monitoring system will be tested with 10 patients through a pilot study.
Results: It is expected that this prototype of SMS remote monitoring can contribute to improve patients' abilities to/in self-care and health management. The attainment of these outcomes may contribute to the reduction of crises of decompensation and unplanned hospitalizations.
Conclusions: There is an opportunity to drive the increasing accessibility of mobile technologies to empower patients to monitor and manage their own health after discharge. If the results are favorable, other countries with a similar profile may benefit from this technology.

P625

Characterization of a porcine model of heart failure with preserved ejection fraction

W Winston Shim[1]; KPMM Ja[1]; CH Lua[1]; SQ Li[1]; P Wong[1]
[1]National Heart Centre Singapore (NHCS), Singapore, Singapore

Funding Acknowledgements: National Medical Research Council Singapore (Industry Alignment Fund)

Background: Heart failure patients with preserved ejection fraction (HFpEF) are increasingly being recognized as a distinct subtype from heart failure patients presenting with reduced left ventricular (LV) ejection fraction. Lack of suitable preclinical large animal HFpEF models is hampering better understanding of this important clinical subgroup of heart failure. We aim to establish and to characterize a porcine model with relevant characteristics of clinical HFpEF.
Methods: and Results: Yorkshire pigs (n = 9) were subjected to aortic banding to achieve defined trans-stenotic pressure gradient and were fed with high salt diet for up to 20 weeks. Baseline and follow-up transthoracic echocardiography showed LV remodeling with end-diastolic diameter remodeled from baseline of 4.0 ± 0.3 cm to 3.8 ± 0.2 cm, 4.0 ± 0.5 cm and 4.8 ± 0.2 cm ($p < 0.005$) at 4-week (n = 3), 12-week (n = 3) and 20-week (n = 3) respectively. There was an increase in LV mass index (LVMI) from 2.5 ± 0.5 to 3.8 ± 0.6, 2.8 ± 0.7 and 3.7 ± 1.0 ($p < 0.05$) respectively during the corresponding follow-up time points. The animals maintained a relatively stable LVEF from 61.8 ± 7.3% to 70.7 ± 7.2%, 65.4 ± 13.8% and 65.0 ± 8.5% during the three follow-up time points, indicating a hypertrophic LV remodeling with preserved systolic function. Compared to diastolic function at baseline, there was a decrease in early (E) and late (A) ventricular filling ratio whereby a reduction in E/A ratio was observed at 20-week follow-up (1.25 ± 0.09 vs. 0.97 ± 0.05, $p < 0.001$), suggesting a restrictive LV filling. This was supported by observation of an increase in LV stiffness constant (β) from 0.02 ± 0.01/ml at rest to 0.04 ± 0.04/ml in response to dobutamine stress at 20-week follow-up as determined by pressure-volume loop

assessment. Myocardial hypertrophy with enlarged myofibers and increased interstitial fibrosis was observed in the LV and left atrium (LA) during follow-up. Consistent with heart failure presentation, histopathological examination revealed pulmonary and hepatic congestion in the HFpEF pig model starting from 12-week follow-up.
Conclusion: We characterized myocardial hypertrophy, fibrotic remodeling, restrictive filling and peripheral congestion in a novel porcine model with characteristics of LV diastolic dysfunction with preserved ejection fraction that are consistent with HFpEF. This may represent a useful tool to study pathophysiological presentation of clinical HFpEF.

P626

Right ventricular histological and molecular alterations in a rat model of HFpEF: effects of exercisetraining

L Rosenbusch[1]; C Besler[1]; S T Bowen[1]; K Rommel[1]; T Fischer[1]; M Von Roeder[1]; N Rolim[2]; U Wisloff[2]; A Linke[1]; G Schuler[1]; V Volker Adams[1]; P Lurz[1]
[1]University Leipzig, Heart Center, Leipzig, Germany; *[2]Norwegian University of Science and Technology, Trondheim, Norway*

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Aims: Heart failure with preserved ejection fraction (HFpEF) remains a major diagnostic and therapeutic challenge in clinical cardiology. Recent studies suggest that HFpEF is a biventricular disorder with patients also demonstrating impairments of systolic and diastolic function of the right ventricle (RV). However, the underlying mechanisms of impaired RV function in HFpEF are to be characterized. The present study aimed to investigate histological and molecular changes of the RV in a rat model of HFpEF, and to characterize whether exercise training has any impact on these alterations.
Methods: RVs were obtained from obese diabetic Zucker fatty / spontaneously hypertensive heart failure F1 hybrid (ZSF1-obese) rat or ZSF1-lean rats as control group at 20 weeks of age. In a separate group of experiments, ZSF1-obese rats were randomly assigned to either a moderate continuous exercise training or sedentary lifestyle for 8 weeks until the age of 28 weeks. Excised RVs were stained for fibrosis. mRNA expression of TNFα, IL-6 and IL-1β was analyzed by PCR. Quantification of protein carbonylation was used as a measure of reactive oxygen species burden. Expression of pro- and anti-inflammatory enzymes was examined, and TNFα-related profibrotic signaling pathways were characterized.
Results: At the age of 20 weeks, ZSF1-obese rats exhibited signs of HFpEF when compared to the lean counterparts, as evidenced by increased E/e‘ (16.0 ± 2.0 vs. 22.5 ± 1.0), preserved left ventricular ejection fraction (73 ± 2 vs. 71 ± 3%) and reduced exercise capacity, as determined by VO2max (41.4 ± 1.1 vs. 47.8 ± 2.8 ml/kg/min). ZSF1-obese rats displayed a profound increase in RV fibrosis as compared to ZSF-1 lean rats. TNFα levels were higher in RV from ZSF1-obese rats when compared to ZSF-1 lean rats, whereas no change was observed for IL-6 and IL-1 β. Catalase expression was increased in ZSF1-obese rats, suggesting an augmented reactive oxygen species burden in the RVs. Expression of the NADPH oxidase Nox2 homologue did not differ between both groups. At 28 weeks, differences in RV fibrosis between ZSF-1 obese and lean rats persisted. Notably, exercise training led to a decrease in RV fibrosis in ZSF-1 obese rats (11% vs. 8% as compared to sedentary ZSF-1 obese rats, $P < 0.05$), whereas fibrosis in ZSF-1 lean rats was not significantly altered. The favourable effect of exercise training on RV fibrosis in ZSF-1 obese rats was accompanied by decrease in TNFα levels and reactive oxygen species.
Conclusion: The present study is the first to characterize morphological changes of the RV in an in vivo model of HFpEF. The data suggest that inflammation, reactive oxygen species and fibrosis are major characteristics of the RV in HFpEF, and can be reversed by exercise training. The underlying mechanisms are part of ongoing investigations and likely provide important novel insights into the pathophysiology of the disease and potential novel treatment targets for patients with HFpEF.

P627

Protection of cardiomyocytes by E2F6 against drug induced cell death

BS Tuana[1]; JL Major[1]; M Salih[1]
[1]University of Ottawa, Ottawa, Canada

Funding Acknowledgements: Heart and Stroke Foundation of Canada

Background: The E2F pathway impacts the cell cycle to govern growth, differentiation, and death in all cell types but its role in postnatal myocardium in vivo remains elusive. To assess the role of the E2F pathway in postnatal myocardium we expressed a transgene encoding the repressor E2F6 to interfere with endogenous E2F activity. These E2F6 transgenic (tg) mice developed a dilated cardiomyopathy (DCM) in the absence of any apoptosis or growth deficits.
Results: Micro-array analysis and RT-q-PCR revealed a significant increase ($p < 0.05$) in the expression of genes which regulate the DNA damage response including the Chek1 kinase , Rad51 and Blm2 in myocardium from E2F6- (Tg) mice. We examined the sensitivity to apoptotic death of neonatal cardiomyocytes (NCM) isolated from E2F6 tg myocardium to Doxorubicin (Dox) and Colbolt Chloride (CoCl2). Dox treatment of NCMs from Wt and Tg myocytes resulted in caspase 3 activation and p53 induction to a similar level with equivalent effects on cell viability. Surprisingly, Dox (50uM) caused a rapid and dramatic loss of E2F6 protein in cardiomyocytes by 60% at 6hrs ($p < 0.05$) to non detectable levels within 12hrs. On the other hand CoCl2 (at concentrations 0 to 1mM) treatment of neonatal cardiomyocytes isolated from Tg mice demonstrated 6-fold less caspase 3 activation ($p < 0.05$), a 60% lower bax/bcl2 ratio ($p < 0.05$), and higher viability in comparison to their Wt treated counterparts. Although CoCl2 also promoted a dose dependent loss of E2F6 protein in Tg NCMs, it was to a much lesser extent compared with Dox. Unlike CoCl2, Dox activated the p53 death response in cardiomyocytes. In HeLa cells, Dox induced a dose dependent up-regulation of the pro-apoptotic E2F1 protein with a marked reduction in E2F6 levels while CoCl2 caused a reduction in E2F1 without affecting E2F6 levels. In HeLa cells, Dox induced Chek1 and the loss of E2F6 via post-transcriptional mechanisms and this was not observed in NCM.
Conclusion: These data imply that E2F6 may serve to protect cells from apoptosis via distinct mechanisms and strategies to modulate its levels may be a useful therapeutic to mitigate cell death and disease.

P628

Comparison of 12-month kinetics of serum markers of collagen synthesis, transforming growth factor and connective tissue growth factor between patients with recent and chronic dilated cardiomyopathy

P Pawel Rubis[1]; S Wisniowska-Smialek[1]; E Wypasek[1]; E Dziewiecka[1]; P Faltyn[1]; L Khachatryan[1]; A Karabinowska[1]; P Podolec[1]
[1]Department of Cardiac and Vascular Disease, John Paul II Hospital, Institute of Cardiology, Krakow, Poland

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Background: Dynamics of extracellular matrix (ECM) fibrosis process in dilated cardiomyopathy (DCM) may be assessed non-invasively by means of serum markers of fibrosis measurements. Aim: To explore the kinetics of serum markers of fibrosis during 12 month follow-up in DCM.
Methods: We included 70 consecutive DCM patients (pts) (48 ± 12.1 years, EF 24.4 ± 7.4%) with new-onset (n = 35, duration < 6 months) and chronic DCM (n = 35, > 6 months). Markers of collagen type I and III synthesis – procollagens type I and III carboxy- and amino-terminal peptides (PICP, PINP, PIIICP, PIIINP), and ECM metabolism controlling factors – tumor growth factor beta-1 (TGF1-β) and connective tissue growth factor (CTGF) were measured in serum at baseline, 3- and 12-month follow-up. Results: Baseline, 3- and 12-month values of PICP, PINP, PIIICP, PIIINP, TGF-β and CTGF did not differ between pts with new-onset and chronic DCM (Figure 1). Conclusions: Regardless of the disease duration kinetics of serum markers of collagen synthesis, TGF and CTGF were similar in DCM. Better understanding of the kinetics of serum markers of fibrosis in DCM may help to develop tailored therapeutic approach directing ECM fibrosis.

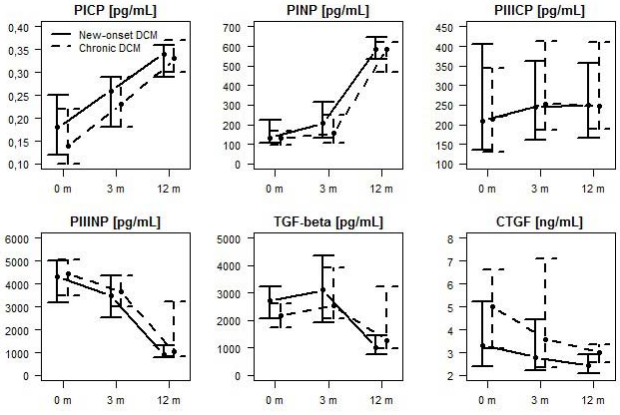


Figure 1

P629

Empagliflozin influence on the course of experimental heart failure in normoglycemic rats

A Aleksandr Kulikov[1]; SV Okovityi[2]; DY Ivkin[2]; AA Karpov[3]; DS Lisitskyi[2]; MM Lubishin[2]; PA Alekseeva[2]; NN Pitukhina[2]; AV Smirnov[1]; IG Kaiukov[1]; EV Parusova[1]

[1]Saint Petersburg Pavlov State Medical University, Saint Petersburg, Russian Federation; *[2]Saint-Petersburg State Chemical Pharmaceutical Academy, Saint Petersburg, Russian Federation*; *[3]Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation*

Purpose: The efficacy of sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin in chronic heart failure in normoglycemic rats was investigated.
Methods: Chronic heart failure (CHF) experimental model in rats was created by permanent ligation of the left coronary artery. Rats were randomly divided into 3 groups: empagliflozin treated CHF group (n = 11), untreated CHF group (n = 11), control group with sham operation (n = 9). Empagliflozin was administered in a dose 1 mg / kg/ per day for 3 months. Echocardiography was performed every month up to the end of the study. Sizes and volumes of the left ventricle (LV), LV ejection fraction, LV stroke volume and minute blood volume were measured. All rats were tested on a treadmill at the end of the experiment to evaluate physical endurance.
Results: CHF model was effective in both study groups, in a month after the surgery rats of the first and the second groups had significantly lower ejection fraction and larger LV sizes than the rats of the control group. At the end of the study animals on empagliflozin treatment had a better exercise tolerance (maximum working time on a treadmill 900 ± 110 s vs. 645 ± 110 s, p = 0.0004), higher minute blood volume at rest (80 ± 30.1 ml / min vs. 57 ± 19,4 ml / min, p < 0,025), bigger LV end-diastolic volume (0,50 ± 0,14 ml vs. 0.39 ± 0,08 ml, p = 0,028) and bigger LV mass (1 09 ± 0.19 g vs 0,69 ± 0,10 g, p = 0,012), than the animals who did not receive treatment. In the course of the empagliflozin treatment an increase of a LV stroke volume, LV end-diastolic volume, LV ejection fraction and minute blood volume were observed. These changes are not documented in CHF rats without treatment.
Conclusion: Antidiabetic drug empagliflozin improves exercise tolerance and the LV functional performance in normoglycemic rats with CHF. Influence of empagliflozin on LV remodeling needs further investigation.

P630

Serum decorin correlates with the heart failure phenotype

P Parminder Chaggar[1]; A Watkins[2]; W Crtichley[3]; A Patel[3]; P Foden[4]; R Venkateswaran[1]; N Yonan[1]; A Trafford[2]; JE Fildes[3]

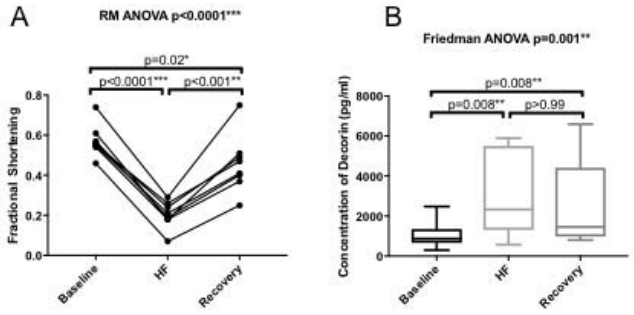
[1]University Hospital of South Manchester NHS Foundation Trust, The Transplant Unit, Manchester, United Kingdom; *[2]University of Manchester, Division of Cardiovascular Sciences, Manchester, United Kingdom*; *[3]University of Manchester, Manchester Collaborative Centre for Inflammation Research, Manchester, United Kingdom*; *[4]University Hospital of South Manchester NHS Foundation Trust, Department of Medical Statistics, Manchester, United Kingdom*

Background: Collagen deposition is the hallmark of cardiac fibrosis which is a feature of adverse remodeling during heart failure. Increased type I and type III collagen deposition impairs ventricular compliance and promotes dilatation. Decorin is a proteoglycan that binds type I and type III collagens, thereby slowing collagen deposition. The temporal dynamics of decorin during myocardial injury and recovery is unknown and warrants further investigation.
Purpose: This study was conducted to define the pattern of serum decorin during myocardial injury and recovery in an ovine model of pacing-induced heart failure.
Methods: 8 healthy Welsh mountain sheep underwent VVI pacemaker implant and paced at 210bpm until they developed overt clinical signs of heart failure. Pacing was then terminated and the animal was allowed to recover. The severity of LV dysfunction was assessed by serial measurements of fractional shortening (FS) on echocardiography at baseline, heart failure and recovery. FS has previously been validated as an accurate measure of LV function in sheep. Serum decorin was quantified via a protein array at baseline, heart failure and recovery. Temporal changes in FS were analysed using repeated measures ANOVA and temporal changes in serum decorin concentration were analysed using a Friedman test.
Results: FS decreased significantly in heart failure compared to baseline and subsequently increased significantly in recovery. The FS in recovery did not reach baseline FS values (Figure 1A). Decorin increased significantly in heart failure compared to baseline and remained elevated during recovery (Table 1 and Figure 1B).
Conclusion: Serum decorin increases significantly with the development of heart failure and this may represent a physiological response to attenuate the effects of adverse remodeling. This is the first study to demonstrate temporal changes in serum decorin during myocardial injury and recovery in a large mammal. Decorin may serve as a biomarker of myocardial injury and could be a target for therapeutic manipulation. These findings require validation in a larger series.

Serum decorin in ovine tachy-paced HF

Decorin (pg/mL)	Baseline	Heart Failure	Recovery
Median	873	2332*	1455*
Interquartile range	665-1348	1310-5501	975-4416
Range	297-2473	572-5887	806-6587

*p = 0.008 compared to baseline



Changes in FS (A) and decorin (B)

P631

Coronary response in the doxorubicin-induced cardiomyopathy

V Cobet[1]; V Lutan[1]; L Tacu[1]; V Rotaru[1]; L Ciobanu[2]; E Cobet[3]; A Rotaru[4]

[1]State University of Medicine and Pharmacy, Chisinau, Moldova Republic of; *[2]Institute of cardiology , Chisinau, Moldova Republic of*; *[3]State University of Moldova , Biopharmaceutical chemistry , Chisinau, Moldova Republic of*; *[4]Harvard Medical School, Cambridge, United States of America*

Background: Coronary reserve and reactivity traits regarding doxorubicin (Dx) cardiotoxicity are less known comparatively to myocardial contraction and inotropic capacities.
Aim: the in vitro evaluation of coronary response to natural vasotropic agent action in Dx-induced cardiomyopathy (Dx-CMP).
Material and methods. Dx-CMP has been reproduced in white rats by Dx administration during 2 weeks (4 i/p Dx injections of 4 mg/kg, cumulative dose 16 mg/kg). The izovolumic isolated heart was perfused by standard Krebs solution according to Langendorff method, and the coronary flow (CF) changes were determined during action of acetylcholine (Ach), adenosine (As), bradykinin (Bk), hydrogen peroxide (H2O2), epoxyeicosatriens 11,12 (EET-11,12) and endothelin 1 (ET-1) in a concentration range of 10-7-10-5 M.
Results: The basal CF in DxCMP did not differ from control index (12,7 ± 0,08 vs 13,4 ± 0,09 ml/min). However, the endothelium dependent coronary functional reserve is impaired, manifested by significant lowered CF value during stimulation by Ach (14,8 ± 0,1 vs 17,3 ± 0,12 ml/min), As (13,9 ± 0,09 vs 15,5 ± 0,11 ml/min) and Bk (13,8 ± 0,08 vs 15,3 ± 0,12 ml/min). Remarkably, the coronarodilation mediated by hyperpolarization was not compromised in Dx-CMP. The coronary reserve inherent to H2O2 action was as 15,7% in Dx-CMP (CF, 14,7 ± 0,12 ml/min) and 14,9% in control series (CF, 15,4 ± 0,13 ml/min). In a similar manner CF increased in response to EET-11,12 action: 14,3% in Dx-CMP (CF, 14,52 ± 0,13 ml/min) and 14,1% in control (CF, 15,29 ± 0,14 ml/min). Thus, the mediated by hyperpolarization coronary artery dilatation could be an alternative tool of coronary functional reserve control in Dx-CMP associated by endothelium dysfunction. Importantly, ET-1 in concentration of 10-7 M determined in Dx-CMP o reduction of CF equal to control pattern (11,3%), but in condition of isolated heart pretreatment by apamin (selective blocker of KCa channels) the coronaroconstriction in Dx-CMP has been more pronounced vs control (-17,1 vs -14,2%). In highest concentration (10-5 M) ET-1 led in Dx-CMP to a bigger decline of coronary flow FC (-16,8 vs -14,5%).
Conclusions: 1. The coronary functional endothelium dependent reserve is significantly reduced in Dx-CMP during Ach, As and Bk action averagely by 39-43,3% comparing to control, but the mediated by hyperpolarization coronarodilation proper to H2O2 and EET-11,12 action is not compromised.
2. In concentration of 10-5 M endoteline-1 induces a bigger fall of CF in Dx-CMP, but in concentration of 10-7 M the decline is similar to control, however CF decreases more if ET-1 action was preceded by KCa channels blocking.

BASIC SCIENCE - THERAPEUTIC APPROACH

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Cardiac gene therapy with phosphodiesterases PDE2A and PDE4B in a mouse model of heart failure

J P Jean Piero Margaria[1]; S Karam[2]; P Mateo[2]; A Varin[2]; J Vinck[2]; C Rubinetto[1]; F Balzac[1]; C Rucker-Martin[3]; A Ghigo[1]; G Vandecasteele[2]; E Turco[1]; E Hirsch[1]; R Fischmeister[2]; J Leroy[2]
[1]University of Turin, Molecular Biotechnology and Health Science, Turin, Italy; *[2]UMR-S 1180, INSERM, Université Paris-Sud, Université Paris-Saclay, Châtenay-Malabry, France*; *[3]Surgical Centre Marie Lannelongue, INSERM UMR-S999, LabEx LERMIT, Le Plessis Robinson, France*

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Purpose: While acute stimulation of β-adrenergic receptors (β-ARs) increases cyclic adenosine monophosphate (cAMP) and improves cardiac function, their chronic activation in heart failure (HF) is detrimental to the heart, by promoting deregulation of intracellular calcium handling and maladaptive remodeling. Multiple phosphodiesterases (PDEs) finely tune β-AR responses by degrading and compartmentalizing cAMP. PDE2A is increased in HF and blunts β-AR responses and the pro-hypertrophic effect of noradrenaline. In contrast, PDE4B is decreased in cardiac hypertrophy and knock-out mice for PDE4B are more susceptible to develop cardiac arrhythmias. Since chronic treatment with PDE inhibitors increases mortality in HF, we hypothesized that decreasing cAMP levels may have therapeutic effects.
Methods: We explored whether serotype 9 adeno-associated viral vectors (AAV9) mediated cardiac overexpression of PDE2A or PDE4B could prevent maladaptive hypertrophy in a mouse model of chronic isoproterenol (Iso) infusion (60 µg/g/day during 2 weeks). Male C57BL/6 mice were injected in the tail vein with AAV9 to increase PDE2A and PDE4B in the heart. Echocardiography allowed cardiac function exploration. PDE4B protein expression in heart extracts was measured by western blot. Heart sections (10 µm thick) were cut from paraffin-embedded specimens and stained with masson's trichrome to quantify fibrosis.
Results: Six weeks after injection, mice showed a five-fold increase in PDE2A and PDE4B protein levels. In control mice injected with a Luciferase-AAV9, chronic Iso treatment induced cardiac hypertrophy (N=10, $p < 0.01$), fibrosis (N=9, $p < 0.01$), and decreased ejection fraction (EF) measured by echocardiography by $31.6 \pm 3{,}5\%$ (N=10, $p < 0.001$). Overexpression of each enzymes did not prevent cardiac hypertrophy (N=10) but abolished the increase in fibrosis (N=9, $p < 0.05$). More importantly, EF was preserved when either PDE2A (N=10, $p < 0.001$) or PDE4B (N=10, $p < 0.001$) were overexpressed in this pathological model.
Conclusions: Altogether, these results suggest that gene therapy with AAV9 encoding PDEs is a potential therapeutic approach for cardiac maladaptive hypertrophy.

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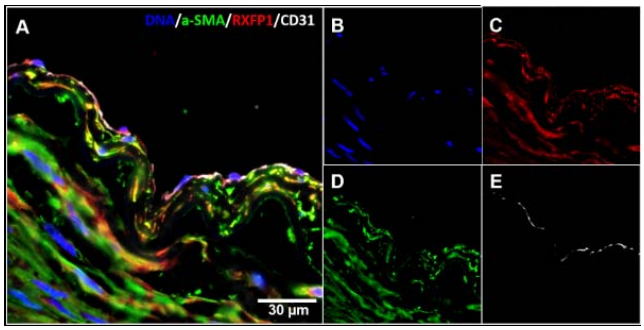
Acute and subacute functional effects of relaxin-2 on human mammary artery

F Francisco Pereira Goncalves[1]; R Martins[1]; L Mendonca[1]; T Laundos Santos[2]; M Pintalhao[1]; F Vasques Novoa[1]; P Pinho[1]; MJ Amorim[1]; DS Nascimento[2]; A Leite Moreira[1]; P Castro Chaves[1]
[1]Faculty of Medicine University of Porto, Departamento de Cirurgia e Fisiologia, Porto, Portugal; *[2]Institute for Research and Innovation in Health, Porto, Portugal*

Introduction: Despite classically associated with pregnancy, relaxin is a hormone with pleiotropic properties and an increasingly unveiled role in the pathophysiology of several cardiovascular diseases. Previous clinical trials have explored its therapeutic role on acute heart failure. However, the exact actions of relaxin on the human vascular territory are scarcely known.
Purposes: To study the acute and subacute functional effects of relaxin-2 on the vasoreactivity of the human mammary artery (HMA). To assess the expression of RXFP1, its main receptor, in this vascular territory.
Methods: HMA from 37 patients subjected to coronary artery bypass graft surgery (median age 69.3 years; 7 female) were sectioned into 2mm rings and mounted on a myograph (DMT myograph system). On one protocol, the vessels were exposed to increasing concentrations of relaxin (10-10-10-7M) or vehicle after pre-contraction with phenylephrine (10-5M), n=5. On a different protocol, the rings were treated for 24h with relaxin (10-7M) or vehicle and afterwards subjected to increasing concentrations of vasoconstrictors (10-9-10-5M) - phenylephrine ($n = 8$), endothelin-1 ($n = 6$) and angiotensin II ($n = 11$) – and of vasodilators (10-10-10-5M) - acetylcholine ($n = 8$) and sodium nitroprusside ($n = 11$). Vessel rings were also incubated for 24h with relaxin or vehicle after endothelium removal, and their response to nitroprusside evaluated (10-10-10-5M; n=7). Immunofluorescence labelling of RXFP1 was performed along with labelling for CD31 (endothelial cells) and α smooth muscle actin (smooth muscle cells). Functional responses are expressed as mean $\pm$ standard error(%).
Results: After acute exposure to relaxin, no differences in the developed active tension were observed between relaxin or vehicle treated groups. Following 24h treatment with relaxin or vehicle, vascular viability and the vasoconstrictor effects of phenylephrine, endothelin-1 and angiotensin II were similar between groups. However, vessel rings treated with relaxin showed higher relaxation when compared to vehicle treated rings, both in response to acetylcholine ($59.1 \pm 6.1\%$ vs $46.2 \pm 6.2\%$; $p < 0.01$) and nitroprusside ($128.9 \pm 4.8\%$ vs $118.7 \pm 5.1\%$ $p < 0.05$). The higher response to nitroprusside was preserved when treatment with relaxin followed endothelium removal ($143.3 \pm 4.1\%$ vs $132.8 \pm 3.3\%$; $p < 0.01$). Immunofluorescence showed labelling for RXFP1 on smooth muscle and endothelial cells (see Figure).
Conclusion: Treatment with relaxin-2 for 24h potentiates HMA vasodilatation without interfering with the effects of several vasoconstrictors, and this effect is at least partially independent of the endothelium. We have also identified for the first time the presence of RXFP1 on the endothelium and smooth muscle cells of HMA. Besides shedding further light on relaxin's role on human vascular physiology, this project may have implications in the understanding of HMA's physiology, an important conduct for coronary revascularization procedures.



Expression of the RXFP1 receptor on HMA

P634

Microencapsulated insulin-like growth factor 1 improves cardiac function after experimental myocardial infarction in comparison to low-dose mesenchymal stem cells

C Baez Diaz[1]; FM Sanchez-Margallo[2]; B Moreno-Naranjo[2]; V Blanco-Blazquez[1]; J Maestre[2]; T Mangas[2]; JG Casado[2]; C Hiemstra[3]; R Steendam[3]; O Franssen[4]; I Diaz-Guemes Martin-Portugues[2]; V Crisostomo[1]
[1]Jesus Uson Minimally Invasive Surgery Centre, Endoluminal Therapy And Diagnosis, Cáceres, Spain; *[2]Jesús Usón Minimally Invasive Surgery Centre, Caceres, Spain*; *[3]Innocore Pharmaceuticals B.V., Groningen, Netherlands*; *[4]Nanomi BV, Oldenzaal, Netherlands*

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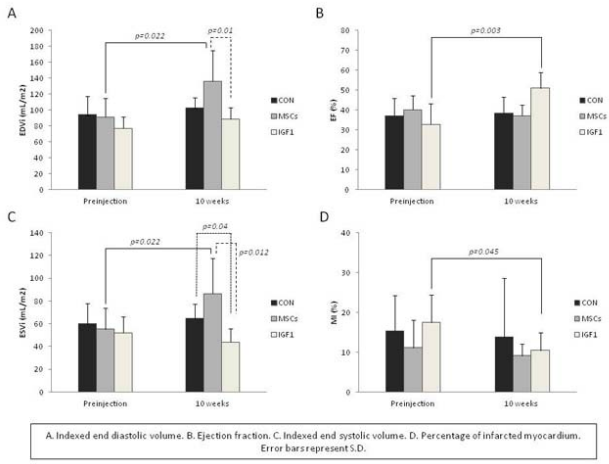
Background: Mesenchymal stem cells (MSCs) have been demonstrated to ameliorate left ventricular remodeling in patients with ischemic cardiomyopathy, with some studies reporting better results after low cell dose administration. Nevertheless, regenerative cardiology is nowadays focusing on cell-less treatment strategies. Insulin-like growth factor-1 (IGF1) has been shown to possess angiogenic effects on endothelial cells. Its microencapsulation allows for sustained release over a specific time.
Purpose: The aim of the study was to evaluate and compare the effect of low-dose allogeneic MSCs and IGF1 loaded microspheres (MSPs) in a porcine myocardial infarction (MI) model.
Methods: Infarcted female pigs (90 minutes mid-LAD occlusion) received an intracoronary (IC) injection of MSCs (30x10^6, n=7), IGF1 loaded MSPs (95µg per MSP, 5x10^6 MSPs, n=8) or saline (CON, n=5) 48 hours after infarction. Safety was evaluated using clinically available tools (ECG and TIMI flow). Cardiac function was studied by magnetic resonance (MR) before injection and at 10 weeks: Indexed end diastolic volume (EDVi), indexed end systolic volume (ESVi), ejection fraction (EF) and percentage of infarcted myocardium (%MI).
Results: Injection was successful in all cases, in absence of major adverse cardiac events. Changes in ECG were seen in one pig belonging to the MSCs group. TIMI flow decreased in 2 animals from the MSCs group (TIMI 2 and TIMI 0), versus 4 swine in the IGF1 group (TIMI 2, n=3 and TIMI 1, n=1), and none in CON. Evolution of cardiac function parameters is shown in the

figure. No differences were seen between groups in any MR-derived parameter before injection. At 10 weeks, however, ESVi was significantly lower in IGF1 (43.82 ± 11.93mL/m2) than in CON (64.60 ± 13.00mL/m2, p = 0.04) and MSCs groups (86.55 ± 31.24mL/m2, p = 0.012). EDVi was significantly different between IGF1 and MSCs groups (88.73 ± 14.23mL/m2 vs. 136.37 ± 38.11mL/m2, p = 0.01). Comparison between pre and 10 weeks post-injection revealed an improvement in EF in IGF1 (32.83 ± 10.41% vs. 50.96 ± 7.89%, p = 0.003), a reduction in %MI (17.50 ± 6.87% vs. 10.50 ± 4.44, p = 0.045) and a limited dilatation with no significant changes to EDVi and ESVi over time, while MSCs animals suffered a significant worsening in EDVi (91.30 ± 23.56mL/m2 vs. 136.37 ± 38.11mL/m2, p = 0,022) and ESVi (55.39 ± 18.44mL/m2 vs. 86.55 ± 31.24mL/m2, p = 0.022). No statistically significant differences were observed in any cardiac function parameter over time in the case of CON group.

Conclusion: Both the IC delivery of MSCs and IGF1 loaded MSPs could impair coronary flow on the short term after experimental MI. Nevertheless, IC administration of 5x10^6 IGF1 loaded MSPs was successful in alleviating myocardial dysfunction over time (limiting ventricular volumes) compared to CON or low-dose MSCs.



Evolution of cardiac function parameters

P635

Pharmacological activation of sphingosine 1-phosphate receptor 1 (S1pr1) enhances arteriole formation and improves cardiac function after myocardial infarction (MI)

L Zhang[1]; LE Bao[1]; XL Li[1]; YZ Zhang[1]; HM Fan[1]
[1]*Tongji University School of Medicine, 1. Research Center for Translational Medicine, Shanghai East Hospital, Shanghai, China People's Republic of*

On behalf of: Research Center for Translational Medicine, Shanghai East Hospital, Shanghai, People's Republic of China
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Background and purpose: Sphingosine 1-phosphate (S1P) is a lipid metabolite and a ligand of five G protein-coupled cell surface receptors S1pr1 to S1pr5. It has been shown that S1P/S1pr1 signaling played an essential role in vascular remodeling during development. However, it is unknown whether S1pr1 regulates vascular remodeling and therefore influences cardiac function after myocardial infarction. We aimed to investigate the effect of pharmacological activation of S1pr1 by SEW2871 in a mouse model of acute myocardial infarction.
Methods: We performed left anterior descending artery (LAD) ligation to induce acute myocardial infarction in mice. We treated operated mice with 5 mg/kg/day S1pr1 agonist, SEW2871, or placebo (DMSO) i.p., respectively, for 4 weeks. We performed echocardiography to investigate cardiac function. We also carried out histological analysis to study vascular remodeling in MI model.
Results: Echocardiography showed that cardiac function was significantly reduced in MI mice (ejection fraction (EF): 76.15 ± 1.65 % Sham group vs. 49.47 ± 2.42 % MI-DMSO group. P < 0.05). S1pr1 agonist, SEW2871, significantly improved cardiac function 4 weeks after myocardial infarction (EF: 49.47 ± 2.42 % MI-DMSO group vs. 60.23 ± 2.38 % MI-SEW2871 group. P < 0.05). Mason's trichrome staining showed that SEW2871 treatment significantly reduced the infarct size: 21.13 ± 1.52 (%) MI-DMSO group vs. 17.01 ± 1.27 (%) MI-SEW2871 group. P < 0.05). Our further isolectin B4 (iB4) antibody staining showed that capillary density in peri-infarct myocardium was similar between MI-DMSO group and MI-SEW2871 group. However, co-staining of iB4 antibody and alpha smooth muscle actin (alpha-SMA) antibody showed that arteriole density in peri-infarct myocardium was significantly increased in MI-SEW2871 group compared to MI-DMSO group.
Conclusions: Our results demonstrate that activation of S1pr1 enhanced arteriole formation and improved vascular remodeling after myocardial infarction, which might contribute to the beneficial effect of S1pr1 agonist on cardiac repair after MI, suggesting that S1pr1 signaling is potential target to therapy post-MI heart failure.

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Raf kinase inhibitor protein regulates fibrosis depending on myocardial oxidative stress

A Andrey Kazakov[1]; A Trouvain[1]; R Hall[2]; S Rodionycheva[3]; F Lammert[2]; H-J Schaefers[3]; C Maack[1]; K Lorenz[4]; M Boehm[1]; U Laufs[1]
[1]*Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany*; [2]*Saarland University Hospital, Department of Internal Medicine II, Gastroenterology, Homburg, Germany*; [3]*Saarland University Hospital, Department of Thoracic and Cardiovascular Surgery , Homburg, Germany*; [4]*University Clinic, Essen, Germany*

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Background: Myocardial fibrosis plays a central role during maladaptive cardiac remodeling. Quantitative Trait Loci (QTL) analyses in BXD recombinant mouse lines identified Raf Kinase Inhibitor Protein (RKIP) as marker of fibrosis.
Methods: To characterize the underlying signaling, 10-week-old C57BL/6 -RKIP-deficient (RKIP-/-) N and RKIP-/- J mice were subjected to transverse aortic constriction (TAC). In the myocardium, reverse-mode nicotinamide nucleotide transhydrogenase (Nnt) is the dominant source for ROS during pressure overload. Due to mutation of the Nnt gene, the C57BL/6J-, but not the N-strain, is protected from oxidative stress.
Results: Myocardial fibrosis, expression of collagen Iα2 mRNA, Ki67 + fibroblasts and markers of oxidative stress such as 8-hydroxyguanosine positive fibroblasts were markedly reduced in RKIP-/- N mice post TAC. The number of fibrocytes in the peripheral blood and bone marrow was also reduced in RKIP-/- N TAC. RKIP-/- N adult cardiac fibroblasts demonstrated decreased migration and fibronectin production. RKIP-/- N TAC showed a two-fold increase of the nuclear expression of nuclear factor erythroid 2-related factor 2 (Nrf2), the main transcriptional activator of antioxidative proteins. In contrast to these findings, the Nnt-deficient RKIP-/- J TAC mice revealed diminished oxidative stress, increased LV fibrosis, collagen Iα2 mRNA and enhanced basal nuclear expression of Nrf2, which was not further increased by TAC. The expression of the gene coding for RKIP, Pebp1, was markedly higher in the N compared to the J mouse strain consistent with increased basal oxidative stress. In human left ventricular myocardium from both non-failing and failing hearts, RKIP-protein correlated negatively with the nuclear expression of Nrf2.
Conclusions: Under conditions of Nnt-dependent enhanced myocardial oxidative stress in response to pressure overload, RKIP plays a maladaptive role for fibrotic myocardial remodeling by suppressing the Nrf2-related beneficial effects.

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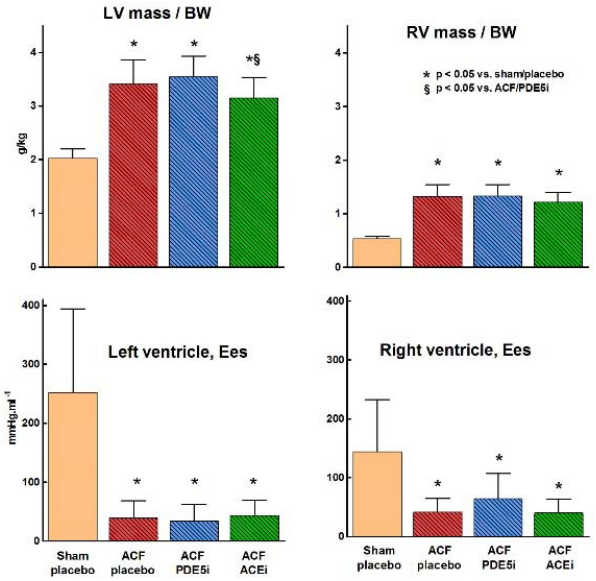
The impact of long-term phosphodiesterase 5 inhibition on right and left ventricular remodelling in chronic heart failure due to volume overload

T Tereza Havlenova[1]; M Kotrc[1]; P Skaroupkova[1]; L Cervenka[1]; V Melenovsky[1]
[1]*Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic*

Background: Chronic inhibition of phosphodiesterase 5 (PED5i) prevents hypertrophy and dysfunction of pressure-overloaded heart, but its impact on volume-overload (VO) induced hypertrophy is unknown. It is also unclear whether right (RV) and left (LV) ventricle differ in their responses to chronic VO or antihypertrophic therapy.
Aim: To elucidate the effect of chronic VO on cardiac structure and function and to address the effect of PED5i and ACEi in VO rat model due to aorto-caval fistula (ACF).
Methods: ACF/sham procedure was performed on 8-week old male HanSD rats. ACF animals were randomized for PDE5i sildenafil (80 mg/kg, n=20), ACEi trandolapril (6 mg/l H2O, n=30) or placebo (n = 30). After 20 weeks, echocardiography and pressure-volume analyses (Millar, AD-Instruments) were performed and animals sacrificed to obtain organ weights and tissue samples for cGMP level measurements. Separate rat cohort (n = 10 - 40/group) served for survival analysis.
Results: ACF led to marked eccentric LV and RV hypertrophy (by 70% and 150%) and reduced load-independent systolic function (end-systolic elastance, Ees, by 85% and 70%, figure). Although RV stroke work increased relatively more than

LV (7x vs. 4x), there was no increase in RV end-diastolic pressure, suggesting better RV adaptation to VO. ACEi, but not PDE5i, attenuated pulmonary congestion, LV dilatation and dysfunction. VO and drug-induced changes in RV and LV mass were proportional, arguing against chamber-specific effects. Median survival in ACF/placebo, ACF/PDE5i and ACF/ACEi was 26, 27 and 37 weeks (p0.05 ACF/ACEi vs. ACF/placebo). ACF/PDE5i rats had increased cGMP levels (by 150%) in the lungs, but not in RV or LV.
Conclusions: Sildenafil had neutral effect on survival, structure and function of the LV and RV and failed to increase myocardial cGMP levels. Cardiac hypertrophy due to volume overload is not cGMP-dependent. Volume overload leads to similar changes in LV and RV mass and contractility.



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BRaf inhibitors, dabrafenib and SB590885, enhance ERK1/2 signalling in cardiomyocytes and increase angiotensin II-induced cardiac hypertrophy.

MA Hardyman[1]; SJ Fuller[1]; SJ Leonard[1]; PH Sugden[1]; A Angela Clerk[1]
[1]*University of Reading, Reading, United Kingdom*

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Purpose: ERK1/2 are phosphorylated and activated by MKK1/2 that are themselves phosphorylated and activated by Raf kinases. The ERK1/2 cascade promotes cardiomyocyte hypertrophy and is protective, but also promotes cancer. V600 mutations in BRaf are commonly found in cancer, and drugs targeting the enzyme are in clinical use (e.g. dabrafenib, SB590885). Some inhibitors have a paradoxical effect and activate ERK1/2 at low concentrations rather than inhibit it. Such activation could be cardioprotective, whilst inhibition is likely to be damaging. Our aim is to determine the effects of BRaf inhibitors on cardiomyocytes and the heart to establish if they may affect cardiac function either alone or in the context of pre-existing hypertension.
Methods: Rat neonatal cardiomyocytes were exposed to dabrafenib or SB590885 and the effects on activation of MKK1/2 or ERK1/2 examined by immunoblotting with antibodies to phosphorylated (i.e. activated) or total kinases. The effects of dabrafenib (3 mg/kg/d) on mouse hearts (male C57Bl6; 12 weeks) in vivo were compared with a MKK1/2 inhibitor, trametinib (1.6 mg/kg/d), alone or in the presence of angiotensin II (AngII, 0.8 mg/kg/d) as a hypertensive model. Echocardiography was performed with a Vevo 2100 system to assess cardiac function. M-mode images of the short axis view were used for analysis of cardiac dimensions. Results. In cardiomyocytes, 10 μM dabrafenib inhibited MKK1/2 and ERK1/2 up to 45 min, but this was followed by a small paradoxical activation. At 0.1 μM, dabrafenib enhanced ERK1/2 signalling to a small degree. SB590885 activated MKK1/2 and ERK1/2 to a greater degree than dabrafenib despite it having a lower IC50 for inhibition of BRaf. SB590885 had a greater effect on cardiomyocyte hypertrophy, increasing myofibrillar organisation and surface area, consistent with increased ERK1/2 signalling. The Raf paradox and potential mechanism will be discussed. In mouse hearts in vivo, dabrafenib enhanced MKK1/2 phosphorylation and increased ANF and BNP mRNA expression, consistent with the in vitro data. Over 10 d, neither dabrafenib nor trametinib alone affected any of the cardiac parameters studied by echocardiography. However, in the presence of AngII, dabrafenib increased ejection fraction and fractional shortening, increased left ventricular (LV) wall thickness in diastole and systole, and this was associated with enhanced reduction in LV volume and internal diameter. This contrasted with the effects of trametinib which reduced the increase in LV thickness induced by AngII and for which there was notable mortality absent from all other groups. Conclusions. Dabrafenib and SB590885 alone do not significantly inhibit ERK1/2 signalling in cardiomyocytes, but enhance the signal and promote hypertrophy. In vivo, the effects are more apparent in the context of hypertension. Thus, cancer patients receiving the BRaf inhibitors alone may experience enhanced cardiac hypertrophy if they are hypertensive.

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Espindolol improved cardiac function and survival in a rat cancer cachexia model

J Ishida[1]; M Saitoh[1]; S Palus[1]; N Ebner[1]; S Von Haehling[1]; S Anker[1]; J Springer[1]
[1]*University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*

Background and aims: Cancer cachexia (CC) is a complex syndrome, characterized by increased proteolysis, lipolysis and anorexia. Moreover, cardiac wasting associated with CC leads to poor prognosis, while both bisoprolol, a beta-1 selective beta blocker, and formoterol, a beta-2 agonist, have recently shown cardioprotective effects in this condition. Purpose: The aim of this study was to investigate the effect of espindolol, a non-selective beta blocker with beta-2 intrinsic sympathetic activity, on cardiac function and survival in a rat model of CC.
Methods: After intraperitoneal injection of 108 Yoshida AH-130 hepatoma tumor cells, Juvenile Wister Han rats were randomized to receive placebo, espindolol 0.3 mg/kg/day (LD) or 3 mg/kg/day (HD). Body weight and body composition were assessed at baseline and day 14, and cardiac function was evaluated by echocardiography on day 11. Results: Espindolol improved survival (hazard ratio [HR] 0.29, 95% confidence interval [CI] 0.16-0.51, $p < 0.001$ for HD; HR 0.51, 95% CI 0.26-1.00, $p = 0.051$ for LD, vs placebo) and preserved lean body mass (170.0 ± 13.5 g, $p < 0.001$ for HD; 145.7 ± 10.4 g, $p = 0.01$ for LD, vs. 118.5 ± 1.6 g for placebo) and fat mass (12.0 ± 2.7 g, $p = 0.02$ for HD; 8.3 ± 1.7 g, $p = 0.57$ for LD, vs. 6.4 ± 0.3 g for placebo). In addition, espindolol increased heart weight (612 ± 40 g, $p = 0.01$ for HD ; 548 ± 27 g, $p = 0.14$ for LD vs. 506 ± 8 g for placebo), improved cardiac systolic function assessed by left ventricular ejection fraction (69 ± 3 %, $p < 0.001$ for HD; 59 ± 4 %, $p = 0.13$ for LD vs. 52 ± 2 % for placebo) and raised cardiac output (71 ± 8 mL/min, $p = 0.001$ for HD; 53 ± 10 mL/min, $p = 0.29$ for LD, vs. 42 ± 3 mL/min for placebo).
Conclusions: Espindolol dose-dependently prevented cardiac wasting as well as loss of skeletal muscle and adipose tissue, and improved survival in a rat model of CC. Espindolol can be a promising treatment option for cardia dysfunction associated with CC.

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Cardioprotective effect of LCZ696 versus valsartan on left ventricular remodeling in experimental model of chronic heart failure

L Lenka Hoskova[1]; V Melenovsky[1]; J Kautzner[1]; I Malek[1]; Z Huskova[2]; L Sedlakova[2]; L Kopkan[2]
[1]*Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic*; [2]*Institute for Clinical and Experimental Medicine (IKEM), Center for Experimental Medicine, Prague, Czech Republic*

Introduction: The renin-angiotensin-aldosterone system (RAAS) plays a key role in the pathogenesis of chronic heart failure (CHF) and its inhibition improves cardiac function and survival. Consequences of RAAS activation are antagonized by endogenous natriuretic peptides. Sacubitril/valsartan (LCZ696) is a new drug that combines angiotensin receptor blocker valsartan (VAL) with sacubitril that inhibits breakdown of natriuretic peptides by neprilysin. The cardiac effects of LCZ696 on volume overload-induced CHF are unknown.
Purpose: To evaluate the effects of LCZ696 or VAL on left ventricular function and geometry in an experimental model of CHF induced by volume overload from aorto-caval fistula (ACF) in rats.
Methods: CHF was induced by ACF in 26 male Sprague-Dawley (SD) rats at 8 weeks of age. Four weeks after ACF, administration of LCZ696 was started in 8 rats (ACF-LCZ group) in a standard dosing at 68 mg/kg/day and valsartan in 8 rats (ACF-VAL, at dose 31 mg/kg/day) for next 16 weeks. Other 10 ACF rats were administered with vehicle. The remaining 8 rats without ACF comprised a control group. At age the end of study protocol (20 weeks), the animals were weighed and anaesthetized, and echocardiography was performed using a 7.5 MHz probe (Vivid

7, GE). Left ventricular (LV) internal dimensions (LVIDd), fractional shortening (FS), stroke volume (SV) and LVmass (LVm) were measured.
Results: In comparison to controls, untreated ACF group displayed marked LV dilatation, (LVIDd 6,2 ± 0,1 vs. 11,9 ± 0,5 mm, p < 0,01). Both SD groups treated with LCZ or VAL exhibited significantly lower LVIDd (9,5 ± 0,5 mm and 10,1 ± 0,3 mm; respectively, p < 0,05). We also observed significantly reduced LV function (FS: 35,2 ± 1,1 vs. 59,9 ± 1,2 %, p < 0,01) and increased SV (1274 ± 164 vs. 225 ± 15 µl/beat, p < 0,01) in untreated ACF group compared to control. In both treated ACF groups, we observed an improvement in LV systolic function, where FS increased in ACF-LCZ (44,3 ± 1,5 %, p < 0,05) or in ACF-VAL (42,5 ± 2,1 %, p < 0,05) and SV significantly decreased in ACF-LCZ (757 ± 122 µl/beat , p < 0,05) and ACF-VAL (835 ± 68 µl/beat, p < 0,05). The LVm was significantly reduced in both ACF-LCZ (1844 ± 129 mg, p < 0,05) and ACF-VAL (1850 ± 58 mg, p < 0,05) compared to untreated ACF (2196 ± 52 mg). We did not observe any adverse effect during the treatments with VAL or LCZ696 confirming the safety of these drugs in this model.
Conclusion: In this animal model of heart failure, both treated normotensive ACF groups (LCZ696 and VAL) showed significant reverse LV remodeling. However, we did not observe any additional effects of treatment on cardiac function with LCZ696 compared to VAL in short term follow-up. Prolonged treatment period is advised to verify cardioprotective benefits of LCZ696 vs.VAL.

P641
Functional recovery in AAV9-shXPO1-treated rats with chronic induced myocardial infarction. A preliminary study

E Esther Rosello-Lleti[1]; E Tarazon[1]; A Ortega[1]; C Gil-Cayuela[1]; F Lago[2]; JR Gonzalez-Juanatey[2]; L Martinez-Dolz[1]; M Portoles[1]; M Rivera[1]
[1]Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain; *[2]Instituto de Investigación Sanitaria de Santiago, Cellular and Molecular Cardiology Research Unit, Santiago de Compostela, Spain*

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Background: In previous studies, we showed that several molecules participating in the nuclear-cytoplasmic transport (EXP-1, IMP-β3, and Nup160) were closely related to ventricular dysfunction in human heart failure. We found the genomic signature of these alterations and the corresponding changes in gene expression, particularly XPO1 (the gene that encodes EXP-1), to be highly related to left ventricular function in patients with heart failure of ischemic etiology.
Purpose: We aim to investigate whether highly significant relationship between XPO1 and ventricular function is a component of causality.
Methods: We induced chronic myocardial infarction (n = 10) by coronary ligation in Sprague-Dawley rats, five of these rats received AAV9-shXPO1 intravenously after four months. Sham rats (n = 5) were healthy non-failing controls and received the placebo AAV9-scramble intravenously. Furthermore, 5 infarcted rats did not receive treatment. Serial echocardiographic assessment was performed before, as well as, two and five months after intravenous injection.
Results: AAV9-shXPO1-treated rats showed improved fractional shortening (16.8 ± 2.8 vs 24.6 ± 4.1%, P < 0.05) and left ventricular systolic (5.10 ± 0.79 vs 3.52 ± 0.88 mm, P < 0.05) and diastolic diameters (6.17 ± 0.95 vs 4.70 ± 0.93 mm, P < 0.05) when comparing measurements obtained before injection and five months after AAV9 injection. We did not observe this improvement in untreated infarcted rats. EXP-1 levels in heart, brain, skeletal muscle, and liver of all rats were determined by western blot. Compared to controls rats, in AAV9-shXPO1-treated rats, EXP-1 levels in cardiac tissue were lower (P < 0.05).
Conclusions: At the five months follow-up, ischemic AAV9-shXPO1-treated rats showed partial recovery of left ventricular myocardial function. No secondary symptoms attributable to AAV9-shXPO1 were observed in the cardiac-related organs. Our findings provide a therapeutic option for patients with ischemic cardiomyopathy.

BASIC SCIENCE - ANIMAL MODELS

P642
Assessment of cardiac dysfunction in diabetes: could speckle-tracking echocardiography become an alternative to invasive hemodynamics?

T Radovits[1]; C Matyas[1]; A Olah[1]; S Braun[1]; M Tokodi[1]; BA Barta[1]; M Ruppert[1]; D Kellermayer[1]; M Torok[1]; BK Lakatos[1]; A Kovacs[1]; B Merkely[1]
[1]Semmelweis University, Heart and Vascular Center, Budapest, Hungary

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Introduction: Diabetic cardiomyopathy is a consequence of diabetes mellitus (DM). Comparison of animal models of T1DM and T2DM may contribute to a deeper pathophysiologic understanding of diabetic cardiomyopathy.
Purpose: We aimed at comparatively investigate diabetic cardiomyopathy by left ventricular (LV) pressure-volume (PV) analysis and by the non-invasive speckle-tracking echocardiography (STE) in rat models of type-1 (T1DM) and type-2 DM (T2DM).
Methods: Rat models of T1DM (induced by 60mg/kg streptozotocin, n=7) and T2DM (32-week-old Zucker Diabetic Fatty rats, n=6) and corresponding control animals (n = 5 and n=8, respectively) were compared. Echocardiography and LV PV analysis were performed. LV short-axis recordings were used for STE analysis. Global circumferential strain (GCS), peak strain rate values in systole (SrS), isovolumic relaxation (SrIVR) and early diastole (SrE) were measured. LV contractility, active relaxation and stiffness were measured by PV analysis.
Results: In T1DM, contractility and active relaxation were deteriorated to a greater extent compared to T2DM. In contrast, diastolic stiffness was impaired in T2DM. Correspondingly, STE described more severe systolic dysfunction in T1DM. Among diastolic STE parameters, SrIVR was more decreased in T1DM, however, SrE referring to diastolic stiffness was more reduced in T2DM. In T1DM, SrS correlated robustly with contractility, SrIVR with active relaxation, while in T2DM SrE was closely related to cardiac stiffness.
Conclusions: Diabetic cardiomyopathy is characterized by overt systolic dysfunction and impaired active relaxation in T1DM, while with increased diastolic stiffness in T2DM. STE corresponds to PV analysis by unveiling key differences between cardiac dysfunction caused by T1DM and T2DM.

P643
A preclinical animal model of heart failure mimics distinct clinical phenotypes of heart failure in humans

X Xiuying Ma[1]; S Tannu[1]; J Allocco[1]; J Pan[1]; M Flaim[1]; E Crain[1]; P Wong[1]
[1]Bristol-Myers Squibb, Cardiovascular Drug Discovery, Pennington, United States of America

Mouse models of chronic heart failure (CHF) post myocardial infarction (MI) have been widely used in HF research. However, current CHF models, most often using the C57Bl/6 mouse strain, do not always resemble the clinical phenotypes observed in patients with HF. Previous findings suggested that BalbC mice may be a preferred mouse strain suitable for HF research, which showed increase in lung weight and the worst cardiac function post-MI among different mouse strains (van den Borne SWM, Cardiovasc Res 2009;84:273-282). The goal of the present study was to fully characterize survival rate, cardiac function, and pulmonary congestion post-MI in BalbC mice with or without enalapril treatment, the current standard of care therapy for patients with HF. After induction of MI by permanent ligation of the left coronary artery, cardiac function was longitudinally assessed by echocardiography: heart weight, lung weight, and pulmonary oedema were all measured at the end of the study. In addition, survival rate was continuously monitored throughout the study. Following MI surgery, the mortality was significantly increased from week 1 to week 7 (4% vs. 30%) compared to sham-operated animals. Cardiac function in the surviving animals started to decline 7 weeks post-MI (stroke volume: 38.2 ± 3.3 vs. 38.3 ± 1.8, 48.2 ± 5.9 vs. 42.2 ± 2.7, and 47.0 ± 4.5 vs. 34.3 ± 3.5 µl at week 1, 4, and 7, sham vs. MI, P < 0.05). Lung weight and water content in the lungs were also significantly increased (152.5 ± 4.5 and 118.9 ± 3.2mg vs. 258.9 ± 22.3 and 204.3 ± 17.8mg, respectively, sham vs. MI, P < 0.05) 7 weeks post-MI indicative of the development of pulmonary congestion. In a subsequent study, survival rate, cardiac function, pulmonary congestion, and plasma BNP concentration were further evaluated in the presence of enalapril (20mg/kg/day, subcutaneous osmotic mini-pump) administered 4 weeks post-MI for 6 weeks. Compared to vehicle, enalapril significantly improved survival (73% to 97%, P=0.009), reduced water content in the lungs (223.9 ± 14.3 vs. 165.7 ± 7.1mg, P < 0.05), plasma BNP concentration (522.9 ± 42.7 vs. 273.8 ± 32.5mg, P < 0.05) and preserved cardiac function. The results presented demonstrate that BalbC mice develop deterioration of cardiac function and pulmonary congestion along with elevated plasma BNP levels post-MI (typical of clinically observed HF in humans) not seen in C57Bl/6 mice and that administration of enalapril effectively improves these parameters. In summary, these data suggest that BalbC mice may provide a better tool to successfully identify novel targets for the treatment of CHF.

P644
Heart failure progression and regression in zebrafish

I Ernens[1]; L Zhang[1]; A Lumley[1]; Y Devaux[1]; DR Wagner[2]
[1]Luxembourg Institute of Health, CVRU, Strassen, Luxembourg; *[2]Hospital Centre, Luxembourg, Luxembourg*

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. New therapeutic strategies are needed to prevent heart failure development or induce heart failure regression. Unlike mammals, zebrafish possess the incredible ability to regenerate cardiac tissue. Thus, this model has been widely used to study cardiac regeneration. Yet, the usefulness of zebrafish to study heart failure progression and regression has not been reported. The aim of this study was to systematically characterize heart failure progression and regression in zebrafish to enable the discovery of new therapeutic targets for patients.
Methods: Eight to ten month-old wild-type AB male zebrafish were treated with phenylhydrazine hydrochloride (PHZ) to induce heart failure development (n = 100-130). Control fish were maintained under normal conditions (n = 20). After 5 weeks of treatment, PHZ was withdrawn and fish were followed for 2 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 either to follow tissue morphology and cellular changes or to generate transcriptomics profiles by microarray analysis.
Results: Five weeks of PHZ-treatment led to a significant increase in ventricle size (+33%) and ventricular wall thickness (+229%), and caused a decrease in heart rate (-11%), fractional shortening (-24%) and swim capacity (-29%) (all $p < 0.05$). Expression of atrial and brain natriuretic peptides was upregulated ($p < 0.05$). Further, greater numbers of apoptotic and proliferative cells were found in the myocardium of PHZ-treated fish. Two weeks following PHZ withdrawal, the ventricle regained its basal size. Cardiac function, tissue morphology and the expression of cardiac stress genes returned to basal levels within 1 week. The figure shows well-defined time-specific transcriptomics clusters in the expected order for the heart failure progression (red arrow) and regression (green arrows) processes.
Conclusion: We showed that the zebrafish constitutes an ideal experimental model to study heart failure progression and regression. This model represents a unique opportunity to study the mechanisms of heart failure and to test novel therapeutic strategies. Through microarray analysis, we identified dozens of new potential therapeutic targets for further analysis.
Figure legend: principal component analysis of microarray data performed at baseline (=normal heart), after 5 weeks of PHZ treatment (=failing heart), and 2, 5 and 9 days post PHZ treatment (=dpt). N=3 per time-point. PC: principal component.

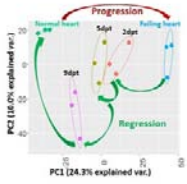

Fig 1

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Head-to-head comparison of two biological acellular scaffolds for myocardial repair: a pre-clinical myocardial infarction swine model

C Carol Galvez-Monton[1]; I Perea-Gil[1]; C Soler-Botija[1]; C Prat-Vidal[1]; I Diaz-Guemes[2]; O Iborra-Egea[1]; V Crisostomo[2]; FM Sanchez-Margallo[2]; S Roura[1]; A Bayes-Genis[3]
[1]*Health Sciences Research Institute Germans Trias i Pujol, Badalona, Spain*; [2]*Minimally Invasive Surgery Centre Jesus Uson, Caceres, Spain*; [3]*Germans Trias i Pujol University Hospital, Badalona, Spain*

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Introduction: Cardiac tissue engineering, which combines cells and biomaterials, is promising for limiting the sequelae of myocardial infarction (MI).1 In this context, decellularized tissues offer a natural microenvironment, driving cellular attachment, survival, migration, proliferation, and differentiation.2,3
Purpose: We assessed myocardial function and histological and immunohistochemical analysis after implanting two different natural decellularized scaffolds in a swine MI model.
Methods: The two tested scaffolds are made of decellularized human pericardium and decellularized porcine myocardium. Forty-eight pigs were distributed into 5 groups as follows: Pericardium + MI (Per-MI) (n = 17), Myocardium + MI (Myo-MI) (n = 8), Pericardium (Per-SHAM) (n = 4), Myocardium (Myo-SHAM) (n = 2), and Control-MI (n = 17). Left ventricular ejection fraction (LVEF), cardiac output (CO), stroke volume (SV), left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) were evaluated non-invasively using magnetic resonance imaging (MRI). Additionally, infarct size, fibrosis, and scaffold vascularization were explored by histopathology.
Results: Upon sacrifice one month after the intervention, MRI detected significant differences between 30 days of follow up and baseline among Per-MI, Myo-MI and Control-MI in LVEF (4.91 ± 1,86% vs. -7.98 ± 4.29% vs. 2.99 ± 3.45%; P=0.015), and ESV (0.56 ± 1.21 mL vs. 8.89 ± 4.95 mL vs. 7.79 ± 2.76 mL; P=0.046). At 30 days, significant differences between groups in LVEF (60.32 ± 1.76% vs. 52.85 ± 2.22% vs. 50.55 ± 2,27%; P=0.005), CO (2.60 ± 0.12 mL vs. 2.88 ± 0.16 mL vs. 3.33 ± 0.21 mL; P=0.010), EDV (54.93 ± 2.84 mL vs. 66.97 ± 5.11 mL vs. 65.59 ± 2 mL; P=0.038), and ESV (21.52 ± 1.28 mL vs. 32.25 ± 3.59 mL vs. 32.26 ± 1.18 mL; P=0.001) were found. Left ventricular infarct size was similar between Per-MI, Myo-MI, and Control-MI animals (P=0.293) (Figure 1). Correct adhesion of the implanted graft with subjacent myocardium after sacrifice was observed in all animals, and, upon sacrifice, scaffolds from Per-MI, Myo-MI, Per-SHAM, and Myo-SHAM animals showed neovessel incorporation. After fibrosis analysis in infarct zone, significant differences between Per-MI, Myo-MI, and Control-MI groups in collagen I (Col I) (P=0.001), collagen III (Col III) (P=0.001), collagen volume fraction (CVF) (P=0.039), collagen I/ collagen III ratio (Col I/Col III) (P=0.050) were detected. Scaffold collagen deposition was also significantly different between Per-MI, Myo-MI, Per-SHAM, and Myo-SHAM in Col I (P=0.019), Col III (P=0.029), CVF ($P < 0.001$), and Col I/Col III (P=0.024).
Conclusions: Human pericardial decellularized scaffold improved cardiac function in a pre-clinical model of MI. These positive results were confirmed by less fibrosis in infarct area, and also in the implanted scaffold. Moreover, the natural decellularized scaffolds, no matter origin, were well-integrated and re-vascularized after 30 days of follow-up.

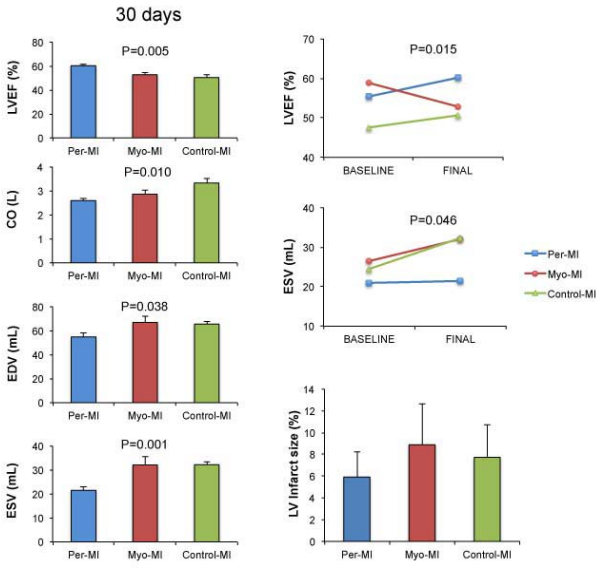

Figure 1

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The characterization of adipose tissue via an obesity-induced cardiomyopathy minipig model

TW Wu[1]; SJ Li[1]; CY Wang[1]; JW Chen[1]; CY Chen[1]
[1]*National Taiwan University, Taipei, Taiwan ROC*

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Background and objective: Distribution of adipose tissue plays an important role in metabolic regulation, however, surplus adipose tissues cause metabolic dysfunction. Excess visceral adipose tissue (VAT) contributes to the pathogenesis of metabolic-related diseases; while epicardial (EAT) and pericardial adipose tissue (PAT) is highly associated with the progression of cardiovascular diseases, thus

attracting more attention recently. We previously established an obesity-induced cardiomyopathy minipig model, and found greater lipid deposited around the heart of obese pigs. To elucidate the link between adipose tissue and cardiac injury induced by obesity, we studied the characteristics of adipose tissues (VAT, EAT and PAT) via our obesity-induced cardiomyopathy minipig model.

Materials and methods: Four-month-old Lee-Sung minipigs were randomly assigned to two groups: control diet (C) and Western diet (W), for a 5-month experimental period. Minipigs were sacrificed and the adipose tissues were isolated for analysis in the end of experiment.

Results: Compared with C group, W pigs exhibited dyslipidemia and cardiac fibrosis. W pigs deposited more VAT and PAT than C group, while C and W pigs deposited similar amount of EAT. The frequency of adipocyte size were equally distributed in PAT and EAT, whereas larger adipocyte size was found in VAT (area >7000 um2). C and W pigs exhibited similar fatty acid composition in EAT and PAT: saturated fatty acids (SFA)> polyunsaturated fatty acids (PUFA) > monounsaturated fatty acids (MUFA). In the VAT of W pigs, higher proportion of MUFA and lower SFA were observed compared with those of the C pigs. Among tissue sites of W pigs, higher PUFA and lower ratio of SFA to PUFA were found in EAT and PAT than those in VAT, suggested that unsaturations in EAT and PAT form the mechanical flexibility to protect the coronary artery against the torsion induced by cardiac contraction. Thiobarbituric acid reactive substances (TBARS) was used as the marker of oxidative stress. Compared with C pigs, W pigs exhibited higher levels of TBARS in the blood and PAT, while no differences were found in the EAT. In the W pigs, the TBARS levels were PAT> VAT > EAT, demonstrating that systemic and local oxidative stress were induced in W pigs, and the local effect from PAT could not be ignored. Interleukin 6 (IL6) was applied as the inflammatory marker. Greater IL6 levels were found in the plasma, PAT and VAT of W pigs than those in C pigs. In the W pigs, PAT secreted more IL6 than VAT did. These results indicated a potential contribution of PAT to the cardiac inflammation.

Conclusion: PAT played a critical role in the obesity-induced cardiomyopathy via the induction of local oxidative stress and inflammation.

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Insulin like growth factor 1-improved cardiac function after experimental infarction in swine is not related to enhanced angiogenesis

C Claudia Baez Diaz[1]; FM Sanchez-Margallo[2]; V Blanco-Blazquez[1]; I Palacios[3]; C Galvez-Monton[4]; J Maestre[2]; T Mangas[2]; R Steendam[5]; C Hiemstra[5]; O Franssen[6]; A Bayes-Genis[4]; V Crisostomo[1]
[1]Jesus Uson Minimally Invasive Surgery Centre, Endoluminal Therapy And Diagnosis, Cáceres, Spain; *[2]Jesús Usón Minimally Invasive Surgery Centre, Caceres, Spain*; *[3]Coretherapix (Tigenix Group), Madrid, Spain*; *[4]ICREC Research Programme, Health Sciences Research Institut Germans Trias i Pujol (IGTP), Badalona (Barcelona), Spain*; *[5]Innocore Pharmaceuticals B.V., Groningen, Netherlands*; *[6]Nanomi BV, Oldenzaal, Netherlands*

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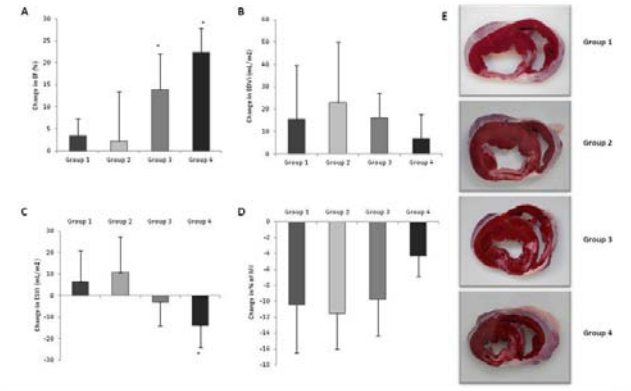
Background: Insulin like growth factor 1 (IGF1) is known as one of the most promising growth factors for promoting cardiorepair, since it decreases ischemia-reperfusion damage and could have angiogenic effects. Intracoronary (IC) infusion of microencapsulated IGF1 allows for site-specific and sustained release of the therapeutic agent over a precise time, which could improve results with a single procedure.

Purpose: We undertook this study to evaluate whether early administration of microencapsulated IGF1 could ameliorate or prevent adverse cardiac remodeling after experimental myocardial infarction (MI).

Methods: Female swine surviving a 90 minutes mid-LAD balloon occlusion received an IC infusion of saline (Group 1; G1, n=7) or IGF1 loaded microspheres (MSPs) (Group2; G2: $3x10^6$, n=4; Group 3; G3: $5x10^6$, n=4; Group 4; G4: $5x10^6$ + nitroglycerin, n=4) two days post-MI. IGF1 dose was 95μg per 10^6 MSPs. Safety was determined by ECG, TIMI flow and troponin I (TnI) values. Cardiac function was evaluated by magnetic resonance (MR) before and 10 weeks post-injection (infarct size (IS), ejection fraction (EF), indexed end diastolic (EDVi) and systolic volumes (ESVi), treatment effect on EF (EF), EDVi (EDVi), ESVi (ESVi), IS (IS). At 10 weeks, TTC staining was performed and tissue samples were obtained from healthy myocardium, border and infarct zones for vascular density analysis with Isolectin B4 immunostaining.

Results: ECG and TnI levels did not reveal significant changes, in any case. While TIMI flow did not alter in G1, it decreased in one pig from G2 (TIMI 2), one animal from G3 and 3 swine belonging to G4 (TIMI 1 or 2). EF improved over time in G3 (40.26 ± 9.12% vs. 54.13 ± 3.81%, p = 0.021) and G4 (25.43 ± 4.86% vs. 47.80 ± 10.20%, p = 0.021). Accordingly, EF was significantly better in G3 (13.90 ± 8.08%) and G4 (22.38 ± 5.48%) compared to G1 (3.48 ± 3.73%) and G2 (2.15 ± 11.24%) (p = 0.018). At 10 weeks the increase in cardiac volumes was limited in G3 and G4, significantly so in the case of EDVi (G1: 121.70 ± 26.09mL/m2; G2: 109.99 ± 14.36 mL/m2; G3: 88.56 ± 14.98 mL/m2; G4: 88.88 ± 15.76mL/m2; p = 0.042). G3 and G4 exhibited an improvement in ESVi (G3: 43.21 ± 9.42mL/m2 vs. 40.26 ± 4.16 mL/m2; G4: 61.16 ± 12.50mL/m2 vs. 47.37 ± 16.77mL/m2) over time, resulting in a trend towards lower systolic volumes compared to G1 (66.09 ± 15.74mL/m2 vs. 72.72 ± 27.18mL/m2) and G2 (54.21 ± 15.99mL/m2 vs. 64.99 ± 5.42mL/m2). TTC staining evidenced that the scar tissue was mixed with viable areas in G3 and G4, but less so in G1 and G2. Quantitative analysis of vascular density revealed no differences between groups.

Conclusion: In this experimental setting, a dose of 5x10^6 IGF1-loaded MSPs was able to improve cardiac function and limit left ventricular remodeling despite an absence of angiogenesis. The IC infusion of IGF1-loaded MSPs may impair coronary flow and caution must be exerted when considering clinical translation.



A. Magnitud of change in EF. Treatment effect was significantly greater in groups 3 and 4 compared to groups 1 and 2; *p<0.05. **B.** Magnitud of change in EDVi. No significant differences were seen. **C.** Magnitud of change in ESVi. Treatment effect was significantly greater in group 4 compared to groups 1 and 2; *p<0.05. **D.** Magnitud of change in percentage of infarcted myocardium. No significant differences were seen. Error bars represent S.D. **E.** Representative TTC-stained heart slice from each group. Mixture of viable and infarcted tissue that is more evident in groups 3 and 4.

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Role of QSOX1 in cardiac adaptation to pressure overload

M Sadoune[1]; P Matteo[2]; C Luc[1]; E Polidano[1]; R Merval[1]; A Mebazaa[1]; J-L Samuel[1]; A Caillard[1]
[1]Hospital Lariboisiere, INSERM UMR-S942, Paris, France; *[2]Université Paris-Sud Orsay, Paris, France*

QSOX1 has been identified as a diagnostic marker of heart failure (ICA), better than BNP in its gray zone in humans. Murine models have shown that the expression of QSOX1 is specifically induced in the heart during the ICA. Moreover, acute cardiac stress by injection of isoproterenol (ISO) combined with a "Knock down" of QSOX1 aggravates the dysfunction of the treated animals. It was possible to demonstrate induction of QSOX1 at 12 days after rat aorta stenosis, correlated with ICA signs. The objective was to study the consequences of an invalidation of this gene in a model of pressure overload induced by aortic stenosis (TAC) in a murine model in order to better define the role of QSOX1 in cardiac function.

The animal model uses 9 week-old male mice (C57BL/6JRj strain) WT and QSOX1 - / - having constricted thoracic aorta (TAC) for 10 days (n = 10 / group) and a control group Sham. A functional and anatomical exploration was performed by transthoracic echocardiography and quantitative phenotypic analysis by RT-qPCR and qualitative by Immunohistology.

In the basal state, QSOX1 - / - mice are viable but in the adult stage they show signs of cardiomyopathy with alteration of the shortening fraction with some signs of endoplasmic reticulum stress and perivascular inflammation. After a TAC, the cardiac phenotype is substantially similar between the WT and QSOX1 - / - mice. On the other hand, the signs of coronary remodeling are more marked in the QSOX1 - / - mice.

These preliminary results show that the expression of QSOX1 is important for a normal function of the heart and moreover it protects the myocardium and more particularly the coronaries against a stress linked to a sudden overload of pressure.

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NLRP3 inflammasome mediated mitochondrial damage in pressure overload-induced heart failure

L Bosch[1]; JJ De Haan[1]; M Brans[1]; SCA De Jager[1]; H El Azouzzi[1]; F Arslan[1]
[1]University Medical Center Utrecht, Experimental Cardiology, Utrecht, Netherlands

Introduction: The NLRP3 inflammasome, responsible for IL-1β and IL-18 maturation, is involved in the pathophysiology of various cardiovascular diseases. However, the role of the inflammasome in pressure overloaded heart failure has never been studied.
Methods: Wild type and NLRP3 deficient C57BL/6J mice underwent transverse aortic constriction (TAC) to induce pressure overload. Cardiac function and geometry was assessed using 3D echocardiography and left ventricular global longitudinal strain (LV GLS) was determined by speckle tracking. Tissue integrity and hypertrophy was determined using immunofluorescence. On left ventricular myocardial tissue, RNA sequencing for whole genome profiling and electron microscopy (EM) for abnormal mitochondrial morphology was performed. Quantification of abnormal mitochondrial morphology was based on the percentage of mitochondria with reduced or abnormal lamellar structure.
Results: NLRP3 deficient mice showed less adverse remodeling after pressure overload: end systolic volume was lower (38.4 ± 11mm3 vs 51.8 ± 12mm3, $p < 0.001$) and ejection fraction higher ($42.1 \pm 11\%$ vs $30.9 \pm 10\%$, $p < 0.001$) compared to wild type mice 6 weeks after TAC. Already 3 weeks after TAC, NLRP3 deficient mice showed improved systolic function by LV GLS compared to wild type ($-15.9 \pm 4\%$ vs $-12.3 \pm 2\%$ respectively, $p = 0.005$). Hypertrophy was less pronounced in the knock-out mice (average cardiomyocyte size: 386 ± 47um2 vs 419 ± 36um2, $p = 0.056$). Furthermore, RNA sequencing revealed increased expression of the mitochondrial respiratory chain in NLRP3 deficient compared to wild type mice 6 weeks after TAC. Preliminary data of mitochondrial numbers assessed by EM 10 weeks after TAC did not show any differences, however mitochondrial morphology did seem to be less affected in the NLRP3 knock-out compared to wild type ($53 \pm 2\%$ vs $32 \pm 19\%$ abnormal mitochondria, n=2, p = NS).
Conclusion: These data indicate a role for the NLRP3 inflammasome in adverse remodelling and the pathophysiology of pressure overload-induced heart failure. A possible mechanism is inflammasome mediated mitochondrial damage. Further studies will have to confirm the influence of inflammasome activation on mitochondrial function in heart failure.

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Exosomes are involved in the transport of miR-21-5p and miR-222-3p in left ventricular remodeling post-myocardial infarction.

H Henri Charrier[1]; E Dubois-Deruy[1]; O Beseme[1]; P Mulder[2]; M Chwastyniak[1]; P Amouyel[1]; V Richard[2]; F Pinet[1]
[1] *Institute Pasteur of Lille, INSERM U1167, Lille, France*; [2] *University of Rouen, INSERM U1096, Rouen, France*

Background: After myocardial infarction (MI), 30% of patients develop left ventricular remodeling (LVR) that is difficult to predict in clinical practice and may lead to heart failure (HF) and death. Previous studies have shown that miR-21-5p and miR-222-3p are up-regulated in plasma (x6.2, $p = 0.003$; x103, $p < 0.0001$ respectively) and LV (x2.3 and x2.1, $p = 0.002$ respectively) of HF rats at 2 months post-MI (induced by left coronary ligation), compared to sham-rats.
Purpose : Our main objectives were i) to identify cardiac cells involved in modulation of miR-21-5p and miR-222-3p and ii) to determine the extracellular transporters (exosomes) of these miRNAs.
Methods: We used an in vitro model of cardiac cells : H9c2 cardiomyoblasts in which hypertrophy was induced by isoproterenol, and neonatal rat fibroblasts. Exosomes from culture medium of both cell types were isolated by filtration-ultracentrifugation.
Results : The levels of miR-21-5p and miR-222-3p were not modulated in hypertrophied H9c2 compared to control H9c2, suggesting that the cardiomyocytes are not the sources of these miRNAs.
Morphological characterization of the isolated vesicles by nanoparticule tracking analysis revealed an exosomal diameter of 115 ± 3.8 nm ($n = 3$), slightly overestimated due to their aggregation observed by electron microscopy. Biochemical characterization of isolated vesicles showed that they express the exosomal biogenesis marker CD63 but not CD9 or TSG101 suggesting a specific exosomal biochemical profile of cardiac cells. The isolated exosomes also express the YB-1 protein known to be a transporter of miRNAs. To validate the potential of cardiac exosomes as extracellular transporters of miRNAs, we quantified the levels of miR-21-5p and miR-222-3p in the exosomes isolated from H9c2 cardiomyoblasts and neonatal rat fibroblasts. The levels of miR-21-5p and miR-222-3p were 25% more expressed in exosomes isolated from fibroblasts compared to H9c2 cells, suggesting that fibroblasts may be the main source of miR-21-5p and miR-222-3p in the circulation. In addition, miR-21-5p appeared to be 100 fold more expressed than miR-222-3p in exosomes derived from fibroblasts. Exosome membranes isolated from fibroblasts were labeled with a fluorescent dye: PKH67, and their integration in H9c2 cells was followed.
Conclusion : These results confirm the role of exosomes in the transport of miR-21-5p and miR-222-3p into the circulation. This preliminary data suggests their role in fibroblast-cardiomyocyte paracrine communication and underlines the potential of cardiac exosomal content as new biomarkers of LVR post-MI.

NURSING INVESTIGATOR AWARD

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Home telemonitoring in patients with heart failure: the experience of a region of northern italy in the EU funded project smartcare

D Radini[1]; GM Apuzzo[1]; K Stellato[1]; G Sola[1]; N Delli Quadri[1]; E Fragiacomo[1]; A Di Lenarda[1]
[1]*Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy*

Background: The care of patients (pts) with chronic non-communicable diseases (CNCD) is one of the main challenges of the future in Europe and in Italy. The EU funded Project SmartCare ("Cohort study on integrated health and social care supported by ICT for European citizens") involved as lead our region with the aim of improving integrated social and health care through the implementation of home telemonitoring (TLM), empowerment, self-care and self-management of heart failure pts.
Methods: The SmartCare project in our region has developed as a cohort study, prospective, randomized, controlled trial that enrolled from 11/2014 to 2/2016 201 pts in home care (>50 years, at least 1 severe CNCD (HF, COPD or diabetes) and ≥1 missing BADL) to intervention arm (INT - automatic BP monitoring, weight, FC, SO2, ECG: n = 100) or usual care (UC; n = 101). The drop-out were 19 (7 UC; 12 INT; p = NS). The patients were followed up by a multiprofessional team (nurses - including a case manager-, GPs, social workers, district doctors and specialists) and stratified for "short term" post-discharge TLM (3-6 months - average 4 ± 1; n = 101) or "long-term" (6-12 months - average 10 ± 3; n = 100) for chronic frail pts already in home health care.
Results: The patients enrolled were elderly (81 years, 54% males), with HF (79%), diabetes (68%) or COPD (38%) and multimorbidity (44% Charlson Index ≥5; 58% ≥7 drugs/day). 58% had a primary level of education, 38% lived alone and 43% were not self-sufficient. In the follow-up of 7 ± 4 months (119 pt-years) were recorded 16 deaths (13.4/100 pt-years) and 126 hospital admissions/access to intermediate care (1758 days of hospitalization). The home care nurses has recorded 3053 contacts (2.14/pt-months; 2417 -79.2% - home accesses of which 160 (6.6%) unplanned; 536 -20.8% - phone calls). In pts enrolled in "long term" INT, TLM has not proven effective. In contrast, in pts enrolled in the "short-term" post-discharge INT was demonstrated a significant reduction in hospital stay (0.9 vs 2.8 pt-months; p = 0.048), due to a reduction of the length of stay (10.2 vs 19.2 days; p = 0.01), associated with a significant increase in unplanned contacts (1.15 vs 0.03/pts; p = 0.04). In particular, each month there was a saving of 1.9 hospital days at the "cost" of 0.7 contacts per patient for control of devices and clinical stability. The same significance was present only in pts with HF.
Conclusion: A postdischarge intensive TLM system supported by ICT of pts with CNCD and in particular with HF, on top of home care, is able to significantly reduce the hospital stay with significant but modest increase use of territorial nursing resources.

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Effects of telemonitoring and disease management on self-care, anxiety and depression: results from the IN TOUCH study

E Edita Lycholip[1]; IT Aamodt[2]; I Lie[2]; H Hillege[3]; I Kraai[3]; A De Vries[3]; J Celutkiene[4]; A Stromberg[5]; T Jaarsma[6]
[1]*Vilnius University, Clinic of Cardiac and Vascular diseases, Vilnius, Lithuania*; [2]*University of Oslo, Oslo University Hospital, Department of Cardiothoracic surgery, Oslo, Norway*; [3]*University Medical Center Groningen, University Hospital Groningen , Groningen, Netherlands*; [4]*Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; [5]*Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*; [6]*Linkoping University, Department of Social- and Welfare studies, Norrkoping, Linkoping, Sweden*

Introduction: Self-care, depression and anxiety are important patient reported outcomes (PRO's) for heart failure (HF) patients and these PRO's might be effected by disease management and/or telemonitoring. Previously no influence of the intervetion on the primary outcomes (mortality, HF-readmission and health-related quality of life) in the IN TOUCH study was reported. However, patient-reported self-care, anxiety and depression were not analysed yet.
Aim: To assess whether telemonitoring (TM) and an Information Communication Technology guided disease management system (ICT-guided-DMS) had effect on self-care behaviour, anxiety and depression and to investigate factors contributing to changes in self-care.
Methods: In the IN TOUCH study 177 patients were randomized to ICT-guided-DMS or to TM + ICT-guided-DMS with a follow-up of nine months. Current analysis included 118 participants who filled the 9-item European Self-care Questionnaire (EHFScBS_9) and Hospital Anxiety and Depression scale (HADs) (mean age 69 ± 11.5 years; 70% male; 81% in NYHA class III–IV; mean left ventricular ejection fraction [LVEF] 27.2 ± 9.9%).
Chi-square, Student's t test, Wilcoxon and Mann–Whitney tests were used. The association of study co-variates including age, quality of life evaluated by Minnesota Living with HF Questionnaire (MLHFQ), NYHA functional class, NT-proBNP level, LVEF, HADs score with the changes in self-care was assessed using multivariable stepwise logistic regression analysis.
Results: The baseline level of self-care was significantly lower in the ICT-guided-DMS group (n = 60) compared to TM + ICT-guided-DMS group (n = 58, p = 0.023) as assessed by the total score of EHFScBS_9. In the course of intervention self-care behaviour significantly improved in the ICT-guided-DMS group (p < 0.01), but not in TM + ICT-guided-DMS group. ICT-guided-DMS significantly improved the consulting behaviour subscore (p < 0.05). During the trial the prevalence of depression and anxiety decreased from 33.8% to 26.3% and from 25.4% to 22.9% respectively. Level of anxiety significantly decreased in the whole study group (p < 0.05), without statistical significance in the separate intervention groups. Self-care behaviour worsened in 46 participants (19 in ICT-guided-DMS and 27 in TM + ICT-guided-DMS group [p = 0.210]). The following baseline factors were significantly associated with decreasing self-care behaviour from baseline to the end of study: physical subscale of MLHFQ (OR 1.76, 95% CI 1.143 – 2.712, per 10 points, p < 0.05), LVEF (OR 0.75, 95% CI 0.587 – 0.959, per 5%, p < 0.05), NYHA class (OR 0.251, 95% CI 0.089 – 0.711, III versus II class, p < 0.05).
Conclusions: ICT guided disease management may improve patients' self-care, specifically in the subscale consulting behaviour, and reduce anxiety, both with and without telemonitoring. Worse physical aspect of quality of life, lower ejection fraction and lower NYHA class were factors associated with poorer self-care.

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Quality of life and fragility in patients with heart failure and mid-range ejection fraction

B Gonzalez[1]; P Gastelurrutia[1]; J Lupon[1]; M Rodriguez[1]; P Moliner[1]; C Rivas[1]; M De Antonio[1]; M Domingo[1]; V Diaz[1]; E Zamora[1]; T Armesto[1]; M Puertas[1]; M Cachero[1]; A Morales[1]; A Bayes-Genis[1]
[1]*Germans Trias i Pujol University Hospital, Badalona, Spain*

Background: Heart failure (HF) is a chronic condition with poor prognosis and is one of the most important chronic diseases that cause quality of life (QOL) impairment. As HF is highly prevalent among older people, fragility is often present among HF patients. Even young HF patients show a high degree of fragility, that also contributes to QoL impairment.
Objective: As the 2016 Heart Failure (HF) ESC Guidelines boost to investigate the "new" subgroup of patients with HF and left ventricular ejection fraction (EF) mildly reduced (HFmrEF) our aim was to assess QoL and the prevalence of fragility in outpatients with HFmrEF, compared with those with HF with reduced EF (HFrEF) and with preserved EF (HFpEF).
Methods: The Minnesota Living with Heart Failure Questionnaire (MLWHFQ) was used for QoL evaluation. Fragility was defined as having at least one abnormal evaluation among four standardized geriatric scales. Predefined criteria for such scales

were: Barthel Index < 90; OARS scale < 10 in women and < 6 in men; Pfeiffer Test >3 (± 1, depending on educational grade); and ≥1 positive response for depression on the abbreviated Geriatric Depression Scale (GDS). The MLWHFQ and the basic geriatric evaluation were performed at the first visit to the Unit.
Results: 185 patients with HFmrEF were evaluated (127 men and 58 women, mean age 67.7 ± 11.7 years, median duration of HF 12 months [Q1-Q3 2–44], ischemic aetiology 58%, 119 (64.3%) and 59 (31.9%) in NYHA class II and III respectively). The mean score in the MLWHFQ was 30.1 ± 18.3. Ninety patients (48.6%) fulfilled fragility criteria. Forty-five patients (24.3%) had a Barthel Index < 90; 25 patients (13.5%) had an anomalous OARS Scale; the score in Pfeiffer Test was abnormal in 10 patients (5.4%); and 60 patients (32.4%) had a positive depression response in abbreviate GDS. Fragility prevalence in HFmrEF patients tended to be higher when compared with 1058 patients with HFrEF (41.9%, p = 0.09) and similar when compared with 162 patients with HFpEF (54.3%, p = 0.29). In contrast QoL was similar when compared with HFrEF patients (MLWHFQ score 30.8 ± 18.5, p = 0.61) and better when compared with HFpEF patients (MLWHFQ score 36.5 ± 20.7, p = 0.003).
Conclusions: HFmrEF patients showed a similar impairment of QoL than HFrEF patients and lower when compared with HFpEF patients. In HFmrEF a high prevalence of fragility (48.6%) was observed, near to that found in HFpEF patients and slightly higher than that observed in HFrEF patients.

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Gender related differences in the prevalence of frailty syndrome among patients with heart failure and cardiac resynchronization

A Mlynarska[1]; R Mlynarski[2]; KS Golba[1]
[1]Medical University of Silesia, Katowice, Poland; *[2]Upper Silesian Cardiology Center, Katowice, Poland*

Frailty is a common geriatric syndrome that embodies an elevated risk of catastrophic declines in health and function among older patients. Frailty's occurrence may vary according to a number of factors and is more often in heart failure population. AIM: to examine gender-related differences in the prevalence of frailty syndrome among patients with advanced heart failure which are treated by cardiac resynchronization (CRT).
Methods: The study included 106 consecutive patients over 60 years (average age 74,9 ± 6,3; 17% women) with implanted cardiac resynchronization therapy devices. All patients had EF < 35%, left bundle branch block and NYHA functional class ≥ 2. In all patients frailty was evaluated by using Tilburg Frailty Indicator. Analysis were performed in three domains: physical domain, psychological domain and social domain. Values ≥ 5 were recognized as frailty syndrome.
RESULTS: In 75% of men and 67% of women frailty syndrome was diagnosed (p = 0,7719). There were no statistically significant differences in the prevalence of frailty syndrome among men and women – exact results are presented below. Analysis of the influence of the ejection fraction of the value of TFI showed significant correlation (the higher value of frailty, the lower ejection fraction) for the entire population r = -0,3083, p = 0,0013 and for the subgroup of men r = -0,2794, p = 0,0084. There was no statistically significant correlation for women (r = -0,4068, p = 0,0939).
Conclusion: Patients with heart failure and implantable cardiac resynchronization are particularly vulnerable to the frailty syndrome presence. There are no gender differences in the prevalence of frailty syndrome. Higher intensification of frailty syndrome is related to reduced ejection fraction.

Tilburg Frailty Indicator results

	Women	Men	p
Global TFI	5,89 ± 2,11	6,19 ± 1,92	0,5476
Physical domain	4,22 ± 1,11	4,46 ± 1,37	0,4816
Psychological domain	1,33 ± 1,19	1,25 ± 1,02	0,7594
Social domain	0,33 ± 0,48	0,47 ± 0,55	0,3022

TFI -Tilburg Frailty Indicator

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Meta-synthesis of the invalidating factors that influence quality of life in patients with an implantable cardioverter defibrillator

M Michela Barisone[1]; AB Bagnasco[1]; G Aleo[1]; G Catania[1]; M Zanini[1]; V Bressan[1]; L Sasso[1]
[1]University of Genoa, Genoa, Italy

Background/Introduction: In 2012, 75% of the health expenditure of the United States was used to cure chronic diseases (CDC, 2013). With regard to heart diseases, the number of patients with Chronic Heart Failure (CHF) is increasing, especially older people with poor health conditions who are often repeatedly readmitted to hospital due to heart failure. The indication to use implantable cardioverter defibrillators (ICDs) to prevent sudden death is now consolidated, although there is no unanimous agreement regarding their impact on quality of life (QoL). Various clinical studies have evaluated the impact of ICDs on patient mortality, survival, and their beneficial effects. Instead, few studies investigate the QoL in patients with ICDs.
Purpose: The purpose of this study is to describe the experiences and perceptions lived by patients with an ICD through a qualitative literature meta-synthesis.
Methods: A qualitative meta-synthesis adopting Confidence in the Evidence from Reviews of Qualitative Research (CERQual) developed by the Grading of Recommendations Assessment Development and Evaluation (GRADE) working group to evaluate the strength of the evidence was conducted. The following database were systematically search: PubMed, CINAHL, and PsycINFO, to identify qualitative studies published between January 2005 and October 2016 that investigate the experience of people living with an ICD. Each selected study was assessed for quality by two reviewers independently using the Critical Appraisal Skills Programme (CASP, 2014)
Results: A total of 17 papers were selected. Five main themes emerged: Sensation of great uncertainty and insecurity, emotional involvement, accepting new life conditions, living with ICD shocks, and need to receive information and advice from physicians.
Conclusion(s): According to the literature, patients' experience with ICDs is very complex and it is often difficult for them to adjust to this new life condition. In fact, the presence of the ICD causes feelings of dependency, psychological discomfort and fear. The patients' most frequent feelings were anxiousness, depression, and self-imposed limitations for some activities of daily living. These results should be used to help clinicians and researchers to develop and explore new research strategies and health policies to improve QoL in these patients.

MODERATED POSTER SESSION 2 – THE GLOBAL PROBLEM OF HEART FAILURE

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Predictors of in-hospital mortality among hospitalized adult heart failure patients in the Philippines

R B Rudy Natividad[1]; BA Tumanan-Mendoza[1]; FER Punzalan[1]; NS Pestano[1]; VL Mendoza[2]; AAA Bermudez-Delos Santos[1]; R Macabeo[1]; LA Shiu[1]
[1]Manila Doctors Hospital, Department of Internal Medicine, Section of Cardiology, Manila, Philippines; *[2]De La Salle Health Sciences Institute, Dasmarinas, Cavite, Philippines*

Background: Majority of the large cohort studies on heart failure involved Western countries and developed nations. The ADHERE International Asia-Pacific study was the only major cohort that included Asian nations, 7.1% of which, (out of a total population of 10,171) were from the Philippines. This research was done in conjunction with a nationwide prevalence study on acute heart failure, which is the first heart failure study to be done encompassing the entire Philippine archipelago.
Purpose: To determine the predictors of mortality among hospitalized adult heart failure patients in the Philippines
Methodology: The study is a nationwide retrospective cohort that involved all adult patients aged 19 years old and above hospitalized for heart failure in 2014. Data was collected from the hospitalization claims database of the Philippine Health Insurance Corporation (PhilHealth), a government corporation that administers the health insurance program for the country. Univariate and multivariate analysis was done in determining predictors of mortality
Results: A total of 44,046 hospitalized heart failure patients were included in the study, with an in-hospital mortality rate of 8.2%. Multivariate analysis was done using logistic regression which showed the following independent factors as predictors of increased in-hospital mortality: government hospital admission (odds ratio (OR) 2.14, 95% confidence interval (CI) 1.89 – 2.42), ward stay (OR 1.24, 95% CI 1.10 – 1.40), and regional classification to regions V (OR 1.42, 95% CI 1.07 – 1.87) and VII (OR 1.31, 95% CI 1.05 – 1.62). Independent variables associated with in-hospital survival are shorter length of hospital stay (OR 0.98, 95% CI 0.97 – 0.99), geographical classification under regions I (OR 0.72, 95% CI 0.58 - 0.89), II (OR 0.31, 95% CI 0.20 - 0.49), IX (OR 0.74, 95% CI 0.58 - 0.96), Cordillera Autonomous Region (CAR) (OR 0.59, 95% CI 0.44 - 0.78) and Autonomous Region of Muslim Mindanao (ARMM) (OR 0.41, 95% CI 0.23 - 0.73) and having hypertension (OR 0.68, 95% CI 0.59 - 0.77) and cardiomyopathy (OR 0.17, 95% CI 0.06 - 0.47) as the etiology of heart failure.
Conclusions: Heart failure patients in the Philippines are relatively younger compared to patients in the Western and developed countries. Government hospital admission, ward admission and residing in regions V and VII are the independent predictors of mortality for hospitalized adult heart failure patients in the country. Living in regions I, II, IX, CAR and ARMM and hypertension as the etiology of heart failure independently predict in-hospital survival. Ward admission and hypertension as the etiology of heart failure, as predictors of in-hospital mortality/survival, should be further validated. Future studies on the outcomes of heart failure should include more variables, clinical or non-clinical, to ascertain the most significant predictors of outcomes

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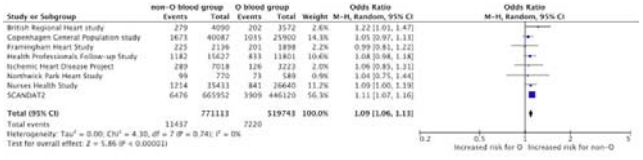
ABO blood group and cardiovascular outcomes in the general population: a meta-analysis

TM Tessa Marthe Kole[1]; N Suthahar[1]; K Damman[1]; RA De Boer[1]
[1]University Medical Center Groningen, Experimental Cardiology, Groningen, Netherlands

Introduction: It has been suggested that carriers of non-O blood groups (ABO groups A, B, and AB) have higher cardiovascular (CV) risk, including risk for myocardial infarction (MI), stroke, heart failure and CV death. However, this assumption is mainly based on case-control studies, which showed a skewed blood group distribution in subjects with CV events, but have a low level of evidence.
Methods: We performed a meta-analysis of prospective studies reporting on blood group and CV events. We searched for terms "ABO blood group" and "myocardial infarction, coronary artery disease, ischemic heart disease, heart failure, stroke, cardiovascular events, cardiovascular mortality and all-cause mortality", and initially retrieved 531 articles. After exclusion of studies with diseased subjects and studies with inappropriate CV endpoints, 9 articles describing 11 prospective cohorts, that reported on CV morbidity and mortality in both O and non-O blood groups, remained.
Results: The total number of subjects included in all studies was 1,362,569, and they experienced 23,154 CV events. The odds ratio's (OR, with 95% Confidence Intervals, CI) for subjects having non-O blood groups compared to O blood group for fatal coronary events, all coronary events and combined CV events were 1.00 (CI 0.85-1.18; p-value: 0.98), 1.09 (CI 1.06-1.13; p-value: <0.00001) and 1.09 (CI 1.06-1.11; p-value: 0.006), respectively. Several sensitivity analyses did not materially change the results.
Conclusion: Our meta-analysis shows that subjects carrying non-O blood group have an increased risk of (nonfatal) CV events, especially myocardial infarction. Underlying mechanisms may vary, although this increased risk has been attributed to a higher concentration of von Willebrand factor and dyslipidemia in subjects with non-O blood group. Further studies should address if the excess CV risk of non O blood group is amenable to treatment.



Coronary events

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Real-world evidence on heart failure: findings from 25 thousand patients in a portuguese primary care database

R Raquel Ascencao[1]; F Fiorentino[1]; M Gouveia[2]; J Costa[3]; P Broeiro[4]; C Fonseca[5]; M Borges[1]
[1]Faculty of Medicine, University of Lisbon, Center for Evidence Based Medicine, Lisbon, Portugal; *[2]Catolica Lisbon School of Business and Economics, Lisbon, Portugal*; *[3]Faculty of Medicine, University of Lisbon, Laboratory of Clinical Pharmacology and Therapeutics, Lisbon, Portugal*; *[4]Agrupamento de Centros de Saúde Lisboa Central, Unidade de Cuidados de Saúde Personalizados dos Olivais, Lisbon, Portugal*; *[5]Centro Hospitalar de Lisboa Ocidental, Heart Failure Unit, Department of Internal Medicine and Day Hospital – Hospital São Francisco Xavier, Lisbon, Portugal*

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Background: Heart failure (HF) is a major health problem in developed countries, accounting for a significant social and economic burden. Published estimates of costs associated with HF patients in the primary care setting are scarce.
Purpose: To determine the clinical and demographic characteristics of adult patients with a HF diagnosis in a Portuguese primary care comprehensive administrative database and to estimate the associated annual costs

per patient.
Methods: Population-based study with real data covering a population of 3.6 million patients attending primary care services in a large health region in Portugal. All adult users coded for HF with at least one visit in 2014 were selected. We analyzed patients' characteristics, comorbidities (anemia, diabetes, hypertension, cerebrovascular disease, atrial fibrillation, ischemic heart disease, cardiomyopathies, valve disease, chronic obstructive pulmonary disease, pulmonary embolism, alcohol abuse), and resource use in 2014 related to medical tests and cardiovascular diagnostic procedures, visits and cardiovascular or anticoagulant medication. Unit costs estimates were based on national sources.
Results: We identified 25,337 patients, with an estimated HF prevalence of 1.4%. This is approximately 30% of number expected according to a previously conducted national community-based epidemiological survey. The difference may be explained by both underdiagnosis and underregistration. Patients with HF are mostly women (58%) and on average 77 ± 11 years old. The large majority of patients (93%) had at least one of the selected comorbidities present, 70% had 2 or more and 38% had 3 or more. About two thirds of patients (65%) had at least one medical test or diagnostic procedure done during 2014. Blood tests, echocardiogram, electrocardiogram and chest x-ray were performed in 61%, 16%, 14% and 11% of patients, respectively. The majority of patients (56%) had at least four office visits during one year. Angiotensin-converting enzyme inhibitor or angiotensin receptor blockers, beta-blockers, and aldosterone blockers were prescribed for 80%, 48% and 20% of patients, respectively. Only 12% of patients were prescribed all three drug classes. The average annual cost per patient was estimated at €552 ± 348, of which 54%, 40% and 6% was associated to medications, medical visits and medical tests or diagnostic procedures, respectively.
Conclusions: This study provides a characterization of patients with HF in a large population in a primary care setting. Surprisingly 70% of the expected number of patients are either not diagnosed or not registered. HF patients are old, mostly women and characterized by multimorbidity. The average annual cost per patient was estimated to be about €550.

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Age- and gender-specific risks of all-cause mortality in patients with newly diagnosed heart failure: a population-based case-cohort study inTaiwan

Y-C Yi-Chih Wang[1]; S-R Chen[2]; C-Y Fann[3]
[1]National Taiwan University Hospital, Internal Medicine, Cardiovascular Division, Taipei, Taiwan ROC; *[2]Novartis (Taiwan) Co., Ltd, Taipei, Taiwan ROC*; *[3]Kainan University, Department of Health Industry Management, School of Healthcare Management, Tao-Yuan, Taiwan ROC*

Funding Acknowledgements: Novartis (Taiwan) Co., Ltd, Taipei, Taiwan

Background: The age- and gender-specific risk of all-cause mortality for newly diagnosed heart failure (HF) patients (pts) comparing with general population is lacking. In Taiwan, the national health insurance (NHI) provides a population-based data with longitudinal follow-up for assessing the issue.
Purpose: We evaluated the relative risk (RR) of all-cause mortality between newly diagnosed HF pts and non-HF subjects.
Methods: The age- and gender-matched case-cohort study estimated the RR of all-cause mortality in HF pts by using all insured data between 2002 and 2013. By excluding prevalent HF pts in 2002, incident and new HF cases should have at least three outpatient visits or one hospital admission with HF (ICD9CM code: 428, 402.01, 402.11, 402.91) between 2003 and 2012. The last insured date was the surrogate endpoint of death. The data in 2013 was to sure those withdrawn before 2012 for at least one year. Each HF pt had a control, randomly sampled from the same age- and gender- subgroup. A total of 1,392,334 subjects including 696,167 HF cases were analyzed. RR was estimated by Poisson and negative-binomial regression models. We further used all-cause mortality from the life table in the whole population to estimate the all-cause mortality of HF.
Results: Two thirds of HF pts were diagnosed at 65 years (yrs) or older. Among HF pts, the RR of all-cause mortality was higher in male (1.33, 95% CI=1.31-1.34), and getting higher with aging (45-64 vs. < 45 yrs: RR=1.4; >=65 vs 45-64 yrs: RR=5.2; both $p < 0.05$). When compared with non-HF subjects, the overall RR of all-cause mortality for HF pts was 2.41 (95% CI:2.40-2.43). In both gender (Figure 1A), the RRs of the younger groups were much higher. Although the age-specific RR for HF pts with either gender were similar, the estimated all-cause mortality in male HF pts was higher due to higher age-specific all-cause mortality in male population (Figure 1B).
Conclusions: When compared with non-HF controls, there remains a more than two-fold risk of all-cause mortality for newly diagnosed HF pts. The mortality burden was much greater on the elderly and male gender. The younger HF pts, however, carry a rather high risk of death, when compared to the non-HF younger population. All suggest the diverse but critical age- and gender-specific burdens of HF among the whole population.

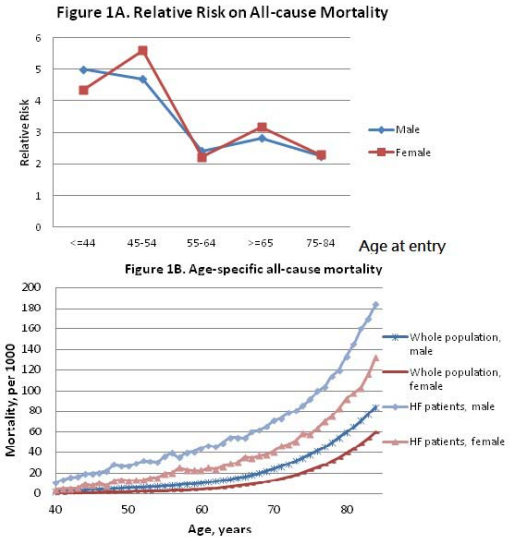

Figure 1A and 1B

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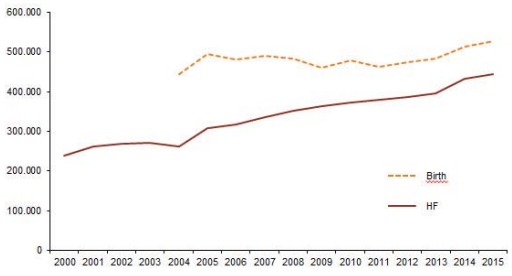
The demographic change in Germany: an analysis by the two leading causes of hospitalisation

S Stoerk[1]; M Doerr[2]; M Christ[3]; HJ Heppner[4]; C Mueller[5]; U Riemer[1]; R Rolf Wachter[1]
[1]University of Göttingen, Göttingen, Germany; *[2]University Medicine of Greifswald, Greifswald, Germany*; *[3]Klinikum Nürnberg-Nord, Notfallmedizin, Nürnberg, Germany*; *[4]Helios Klinikum Schwelm, Schwelm, Germany*; *[5]University Hospital Basel, Basel, Switzerland*

Background: The demographic change, i. e. an increase in elderly people in the general population with an increase in comorbidities, is also reflected within the two leading causes for hospitalization in Germany, which are "Delivery/Birth" (Z38) and "Heart Failure" (I50). We analyzed data available from the German Federal Statistical Office for both diagnoses from 2000 to 2015.
Methods: We used publically available databases for ICD-10-GM diagnoses in Germany and compared the two most common reasons for hospitalization.
Results: Data were available from 2000 to 2015 for heart failure and from 2004 to 2015 for birth. Hospitalization for birth increased by 1.55 %/year from 444,306 (2004) to 526,437 (2015) [+82,131]. Hospitalization for heart failure increased by 4.96 %/year from 260,803 (2004) to 444,632 (2015) [+183,829] effecting heart failure to become the most common cause for disease-related hospitalization in Germany. Should these trends continue, there will be more hospitalizations for heart failure than for birth from 2020 onwards.
Conclusion: The demographic change in Germany will lead to a greater need for comprehensive heart failure care, while the number of hospitalizations for birth only mildly increased at last. Some geographic areas might consider converting labour rooms into comprehensive heart failure clinics.



Trends in Hospitalisation for Birth/HF

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Is public knowledge about heart failure improving over time?

G Burneikaite[1]; E Lycholip[1]; A Grigaliuniene[1]; R Steponeniene[1]; J Celutkiene[1]; A Kavoliuniene[2]; S Stork[3]
[1]*Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; [2]*Lithuanian University of Health Sciences, Department of Cardiology, Medical Academy, Kaunas, Lithuania*; [3]*University of Wuerzburg, Comprehensive Heart Failure Center (CHFC), Wurzburg, Germany*

Background: Heart failure (HF) is an increasing cause of morbidity and mortality. Data of general public views about HF alone and in comparison with other chronic conditions are insufficient. The lack of basic comprehension of HF and self-care was confirmed in the vast majority in HF patients, which manifests itself in suboptimal outcomes in such patients.
Objectives: The aim of this study was to evaluate the changes in knowledge about HF of general population in Lithuania from 2013 to 2015.
Methods: A cross sectional survey study was performed, by using translated questionnaire designed by the German Competence Network Heart Failure. Participants were asked to complete a questionnaire during European Heart Failure Awareness (EHFA) Day activities. Anonymous information was collected and analyzed keeping confidentiality of participant (no personal sensitive data was obtained). Scans of completed questionnaires were made using a dedicated scanning tool and automatically transferred into a database. Data collected during 2013 and 2015 EHFA Day activities in Lithuania were analyzed. The following questions were selected for analysis: participant's gender, age and work experience in the medical area, answers to multiple-choice questions about treatment options, typical complaints and symptoms of HF. A chi-square test was used for comparison between 2013 and 2015 surveys results.
Results: A total of 1025 attendees in 2013 and 459 attendees in 2015 participated in surveys: 39% and 35.6% males, mean age 58.7 ± 6.7 and 55.4 ± 12.5 years, worked in medical area 15% and 21.4%, respectively. In 2013 survey 79% of attendees had heard about HF, meanwhile 65.9% of 2015 survey attendees had known the symptoms of HF. The correct identification of typical complaints and symptoms of HF significantly improved from 2013 to 2015: shortness of breath from 67.4% to 77.3%, tiredness from 55.2% to 66.5%, respectively ($p < 0.001$). The perception of HF as not normal symptom of old age also significantly increased from 31.8% to 37.1% ($p < 0.001$). Major number of 2015 survey participants assumed, that patients with HF should not avoid sport activities, compared to 2013 (41.4% vs 31.8%; $p < 0.001$). Knowledge about available HF treatment options was similar at both time points: respondents marked pharmacotherapy in 76.6% and 70.6%, pacemaker in 49.9% and 50.2%, heart surgery in 47.7% and 47.5%, of cases in 2013 and 2015 surveys, respectively.
Conclusions: The substantial part of participants has reported basic HF knowledge during 2013 and 2015 HFA Day initiatives, but there is still a room for improvement. Knowledge about HF symptoms and nature of the disease seems to be improving over last years. Activities on education and awareness in general population and in HF patients should be continued.

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New predictors of left ventricular hypertrophy in normotensive adults with preserved ejection fraction. Insights from an epidemiologic survey-SEPHAR III

O-F Oana-Florentina Tautu[1]; RO Darabont[2]; A Scafa-Udriste[1]; D Dimulescu[3]; C Sinescu[4]; D Pitic[1]; G Tamasescu[1]; L Radulescu[1]; S Onciul[1]; M Stoian[1]; D Cadil[1]; M Dorobantu[1]
[1]*Emergency Clinical Hospital "Floreasca", University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*; [2]*University Emergency Hospital of Bucharest, Cardiology, Bucharest, Romania*; [3]*Elias Emergency Universitary Hospital, Cardiology, Bucharest, Romania*; [4]*Bagdasar-Arseni Emergency Hospital, Bucharest, Romania*

On behalf of: SEPHAR III TEAM
Funding Acknowledgements: ROMANIAN SOCIETY OF HYPERTENSION

Introduction: Left ventricular hypertrophy (LVH) is an important cause of heart failure with preserved ejection fraction (HFpEF), associated with age, blood pressure values and ponderal status even in normotensive subjects. Up to date, implications of sodium intake throug volume overload, arterial stiffness and BP variability in the development of LVH development have less been adressed in populational studies.
Purpose: We aimed to evaluate the presence and new predictors of left ventricular hypertrophy (LVH) in normotensive adults with preserved ejection fraction enrolled in SEPHAR III survey.
Methods: Adult subjects enrolled in SEPHAR III survey were evaluated throughout two study visits by: anthropometric measurements, 3 sitting BP measurements per visit according to ESC-ESH guidelines, arterial stiffness measurements (with an oscillometric device), volemia measurements by transthoracic bioimpedance, laboratory workup (lipids, fasting plasma glucose, HbA1c, estimation on 24h sodium excretion from morning spot urine sample using Kawasaki formula) and standard echocardiography. Normotensive state was defined as BP below 140/90 mmHg and lack of HT history or treatment. LVH was defined as indexed left ventricular mass (ILVM) > 95g/m2 in females and > 115 g/m2 in males.
Results: From a total of 1970 enrolled subjects we have identified 828 normotensive subjects with preserved EF (mean age 42.66 ± 16.79, 56.9% females). Mean ILVM values was 77.03 ± 27.31 g/m2. LVH was found in 11,4% of the sample (10.4% in males and 12.1% in females). Binary logistic regression adjusted for age and mean arterial pressure validated as independent predictors for LVH in normotensive adult subjects: smoking (OR 1.89; 95% CI for OR: 1.71-2.09), body mass index (OR 1.04; 95% CI for OR: 1.03-1.05), visceral obesity (OR 2.05; 95% CI for OR: 1.83-2.30), hypervolemia (OR 1,23; 95% CI for OR: 1.13-1.33), s.d. SBP (OR 1.02; 95% CI for OR: 1.01-1.03), PWVao (OR 1.14; 95% CI for OR: 1.12-1.15), aortic pulse pressure (OR 1.03; 95% CI for OR: 1.02-1.03). The prediction model has 83.7% accuracy of predicting the presence of LVH in normotensive subjects. Correlation analysis revealed that PWVao, PPao, s.d. SBP and hypervolemia are directly correlated with estimated 24h sodium excretion (mean value: 198.56 ± 62.60mmol/day estimating a mean NaCl dietary intake of 11.62g/day).
Conclusions: Our study reveals that beyond well recognized determinants of LVH (age, BP values, obesity), increased arterial stiffness, central BP parameters, visit-to-visit BP variability and hypervolemia independently contributes to LVH development in normotensive adult subjects, stressing the need of adequate preventing strategies. More, the correlation between these new predictors of LVH with volume overload urge the reduction of dietary sodium intake in preventing new onset on HFpEF.

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Comorbidities in heart failure according to left ventricular ejection fraction: analysis of administrative data of a nationwide population

A Esteban Fernandez[1]; C Fernandez[2]; I Vilacosta[2]; V Bertomeu[3]; J Elola[2]; JL Bernal[4]; JV Segura[5]; C Macaya[2]; R Bover[1]
[1]*Hospital Clinic San Carlos, Heart Failure Unit, Madrid, Spain*; [2]*Hospital Clinic San Carlos, Cardiology Service, Madrid, Spain*; [3]*University Hospital San Juan de Alicante, Cardiology Service, Alicante, Spain*; [4]*University Hospital 12 de Octubre, Madrid, Spain*; [5]*University Miguel Hernandez, Elche, Spain*

Introduction: Comorbidities are an important issue in heart failure (HF) patients. Traditionally, it is thought that they are more relevant in HF with preserved ejection fraction (HF-pef) than in reduced one (HF-ref), but both are present in HF patients. We present the prevalence of comorbidities in HF patients according to the left ventricular ejection fraction 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. The classification includes: systolic, diastolic, systolic and diastolic, hypertensive disease and not specified HF. For this analysis we only consider systolic (HF-ref) and diastolic (HF-pef). Some of the most relevant comorbidities was considered.
Results: 400,861 hospital admissions were recorded, 77,652 with HF as a primary diagnosis (HF-ref 4241 patients and HF-pef 1752 patients). The basal characteristics and main comorbidities of the patients are included in table 1.
Conclusions: According to the results of this Spanish administrative database, both HF-ref and HF-pef have a similar profile with a relevant prevalence of comorbidities, with slight differences in some of them. However, the poor codification of HF at discharge could limit these results.

Parameter	HF-ref	HF-pef
Age	74.1	78.5
Men	65.7	36.7
Ischemic heart disease	36.7	20.5
Arterial Hypertension	59.1	64.6
Diabetes Mellitus	38.5	41.3
Ictus	0.4	0.2
Chronic kidney disease	32.5	30.6
COPD	17.3	15.9
Malnutrition	0.9	1.2
Dementia and senility	14.0	17.4
Functional disability	3.0	2.9
Peripheral arterial disease	66.9	76.3
Advanced cancer	1.2	1.7
Trauma in the last year	2.4	2.7

Table 1. Distribution of comorbidities (%) according to ventricular ejection fraction.

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Prediction of heart failure in asymptomatic type 2 diabetics: an 8 year prospective study following cardiac CT angiography

D A Halon[1]; J Ayman[1]; R Rubinshtein[1]; B Zafrir[1]; M Azencot[1]; BS Lewis[1]
[1]*Lady Davis Carmel Medical Center, Department of Cardiovascular Medicine, Haifa, Israel*

Funding Acknowledgements: European Foundation for the Study of Diabetes

Background and Aims: Heart failure (HF) is a severe complication of diabetes mellitus (DM) but prospective data regarding risk of HF in DM and the role of coronary artery disease (CAD) is limited.
Purpose: In a cohort of asymptomatic type 2 diabetics to identify clinical and cardiac CT angiographic (CTA) findings for prediction of hospitalization for HF or cardiovascular death (HF-CVD).
Methods: Baseline CTA was performed in 735 diabetics aged 55-74 years (51.2% women) with no history of CAD and serum creatinine < 1.4 mg/dl. Chamber volumes, coronary artery calcium (CAC), coronary atherosclerosis and stenosis and clinical data were examined for prediction of HF-CVD events over 7.3-9.3 years based on time to event analysis.
Results: CVD-HF occurred in 41 of 735 subjects (5.6%) (31/600, 5.2% of subjects with full CTA data). HF occurred mostly in subjects without prior myocardial infarction (19/23, 82.6%) and preserved LV contraction. Independent predictors of HF-CVD were left/right atrial volume >1 ($p < .0001$), microvascular disease ($p < .0001$) and systolic blood pressure ($p = .035$)(model C-statistic 0.792 (95%CI. 758-.824).
Conclusions: In asymptomatic diabetics followed for 7-9 years: HF-CVD was independently predicted by hemodynamic (systolic blood pressure), anatomic (LA/RA volume ratio) and microvascular (retinopathy, microalbuminuria) factors but not by CAD.

Baseline Predictors of HF-CVD

Baseline variable	HF-CVD (N=41)	No HF-CVD (N=694)	p-value
Duration of DM (years)	13.5±9.6	9.9±7.4	.004
Systolic BP (mmHg)	148.6±21.1	137.7±19.0	.0004
Albuminuria (>30mcg/mg creatinine)	23 (56.1%)	112 (16.1%)	<.0001
Retinopathy	13 (31.7%)	111 (16.0%)	.011
HbA1c (%)	8.5±2.0	7.4±1.5	<.0001
CAC score (Agatston Units) (median, quartiles)	148 (40, 490)	55 (1, 324)	.004
Left/right atria volume >1	22 (71.0%)	187 (32.9%)	<.0001
Total coronary artery plaque volume (mm^3) (median, quartiles)	241 (80, 648)	139 (22, 411)	.050

CAC=coronary artery calcium

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The interactive smartphone application for the improvement of self-care in patients with heart failure

A Grebennikova[1]; A Stoliarov[2]; T Jaarsma[3]; Y M Yury Lopatin[1]
[1]*Volgograd State Medical University, Volgograd Regional Cardiology Centre, Volgograd, Russian Federation*; [2]*Volgograd State University, Volgograd, Russian Federation*; [3]*Linköping University, Linköping, Sweden*

Background: Patient education and improvement of self-care are considered as key strategies for preventing further deterioration of heart failure (HF). The aim of our study was to evaluate the effectiveness of an interactive smartphone application (app) based on the Russian version of the 9-item European Heart Failure Self-care Behaviour Scale (EHFScBS) for improving self-care management in patients with HF.
Methods: Consecutive 142 patients (mean age 59± 12.2 years, 63% male) with decompensated HF (61% of ischemic etiology), NYHA II-IV (2.8 ± 0.6) and a mean left ventricular ejection fraction of 32 ± 7.0% were included in this study. All patients were provided with general information about HF such as symptoms, principles of self-care, diet, medical therapy and physical activity according to the Russian HF guidelines. Before discharge from the hospital, the original smartphone support app, based on EHFScBS-9, was downloaded on the mobile phones of 47 patients with HF. Other 95 patients with HF who had refused to use the smartphone app became the control group. There were no differences in demographic and clinical characteristics between both groups of patients with HF. The duration of follow-up was 6 months.
Results: On admission, the mean EHFScBS-9 score was similar in the smartphone app group and the control group – 28 ± 6.6 and 27.7 ± 6.3, respectively. However, after 6 months of follow-up, a significant reduction of the mean EHFScBS-9 score was noted in the smartphone app group (/56.4%, $p < 0.05$) but not in the control group (-13.7%, n.s.). The smartphone app group demonstrated the highest adherence to daily weight control, contact with a physician or a nurse in case of increased dyspnea and control of medication intake. Moreover, the rate of repeat hospitalizations in the control group was 21%, whereas among the patients using the interactive smartphone app there were no readmissions. The patients noted that the app was easy to use; and only 10.6% of patients needed the help of relatives.
Conclusion: The interactive smartphone application based on the 9-item European Heart Failure Self-care Behaviour Scale improves self-care behavior in patients with heart failure, provides their continuous and persistent education and may be considered as promising tool in the management of patients with heart failure.

CLINICAL CASE CORNER 2 – THE HORIZON IN PHARMACOLOGICAL THERAPIES, INTERVENTIONS & DEVICE

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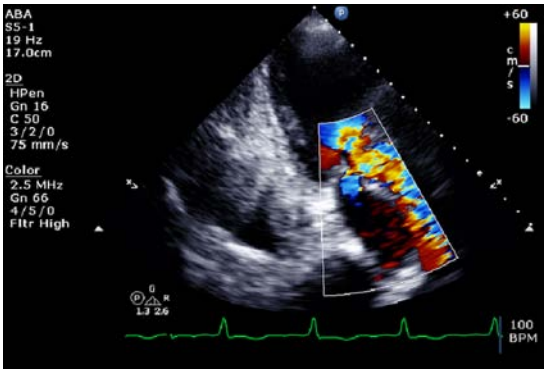
Inotropes and intra-aortic balloon pump counterpulsation in tako tsubo cardiomyopathy: the right treatment when things go wrong?

CD Chue[1]; HS Lim[1]
[1]*Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom*

Case: A 69-year-old female presented with acute chest pain and breathlessness. An electrocardiogram demonstrated anterior ST elevation and lateral T wave changes. Serum troponin levels were elevated at 487ng/l. Coronary angiography showed smooth, unobstructed vessels. Echocardiography demonstrated apical thinning and akinesia with hyperkinesia of the basal segments consistent with tako tsubo cardiomyopathy. Left ventricular ejection fraction was 39% with normal right ventricular function. Within 24 hours of admission the patient developed persistent hypotension with pulmonary oedema on chest radiography. Despite treatment with intravenous diuretics, dobutamine, noradrenaline and intra-aortic balloon pump (IABP) counterpulsation, there was no improvement and advanced mechanical circulatory support was considered. Repeat echocardiography demonstrated persistent left ventricular systolic dysfunction with moderate mitral regurgitation and flow acceleration in the left ventricular outflow tract (LVOT) due to obstruction from systolic anterior motion (SAM) of the mitral valve (Figure). Obstruction of the LVOT was felt to be the principal mechanism of poor cardiac output, exacerbated by inotropes and IABP support. Weaning of these therapies was accompanied by a subsequent reduction in LVOT gradient on repeat echocardiography. The patient improved haemodynamically and biochemically following cessation of all support after 2 days. Problems: 1) Recognition of LVOT obstruction due to SAM in tako tsubo cardiomyopathy as a contributor to low cardiac output and haemodynamic instability. 2) Despite significant impairment of left ventricular systolic function and low cardiac output, inotropes and IABP counterpulsation have deleterious effects on haemodynamic status in this setting. Discussion: LVOT obstruction occurs in approximately 20–30% of tako tsubo cardiomyopathy cases and is associated with reduced cardiac output and cardiogenic shock. Bedside echocardiography is diagnostic. The mechanism is through SAM of the mitral valve apparatus from compensatory hypercontractile function of the left ventricular basal segments. LVOT obstruction should be considered in the setting of cardiogenic shock or persisting haemodynamic instability despite inotrope therapy. Inotropic agents increase sympathetic activation and myocardial contractility, thus exacerbating LVOT obstruction. Greater flow acceleration through the LVOT can worsen SAM, causing further LVOT obstruction. Inotropes and IABP counterpulsation should therefore be avoided in this setting. Conclusion: LVOT obstruction is a cause of reduced cardiac output and cardiogenic shock complicating tako tsubo cardiomyopathy. Inotropes and IABP support can precipitate clinical deterioration and should therefore be avoided.



Transthoracic echocardiogram

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Treatment of patient with acute heart failure due to acute idiopathic giant cell myocarditis using ECMO

NA Beley[1]; OM Druzhyna[1]; OA Loskutov[1]; BM Todurov[2]
[1]*National Medical Academy of Postgraduate Education, Anesthesiology and Intensive Care, Kiev, Ukraine*; [2]*Heart Institute of the Ministry of Healthcare of Ukraine, Kiev, Ukraine*

Introduction and case description: Acute idiopathic myocarditis presents a challenging case for cardiologist often having dramatically fulminant course. Giant cell myocarditis may progress in days to weeks leading to heart failure in 75% of cases. In regard of high rate of refraction to conservative treatment, the use of circulation assisting technologies is highly suggestive. Patient 23 years of age was admitted to our hospital with diagnoses of acute myocarditis and reduced systolic function of left ventricle (EF=18%). On initial examination he presented with dyspnea in rest, lower extremities edema and ascites. No causing factors were found. The disease had acute onset 10 days before. Clinical manifestations were fatigue and drowsiness, dyspnea after walking for 50m. Leg edema and ascites developed by the end of the first week after the symptoms onset. The patient was admitted to the local hospital and on 5th day of treatment he was referred to our Clinic due to worsening of heart failure and lack of response to conservative treatment.
ECG: low voltage, sinus irregular rhythm with HR 100-116 bpm; supraventricular extrasystols; incomplete blockade of right bundle branch.
Echocardiography: end-diastolic volume (EDV) – 100 ml, end-systolic volume (ESV) – 85 ml, stroke volume (SV) – 25 ml, left ventricle ejection fraction (LV EF) – 18%. Polypositional myocardial biopsy shows idiopathic giant cell myocarditis. Brain natriuretic peptide was elevated (1891,6 pg/ml). After two days of conservative treatment with maximum inotropic support, VA ECMO was considered. Beside routine heart failure medications, immunosuppressant therapy was indicated and consisted of cyclosporine 50 mg twice daily and prednisolone with day dosage of 45 mg. ECMO support lasted for 15 days with improving in LV EF from initial 16% to 28% on weaning moment. Patient assessment when discharged shows relative improvement in all investigations. Echocardiography: EDV – 90 ml, ESV – 60%, LV EF – 30%, systolic pressure in right ventricle – 30 mmHg, minimal amount of pleural effusion.
Discussion: Treatment strategy for patients with myocarditis should be guided by etiology, features of clinical course, presence and severity of heart failure. The key point of treatment is hemodynamic correction which is similar to therapeutic approaches for heart failure due to LV dysfunction. Thus, inotropes (dobutamine) is recommended. Failure to support hemodynamics with inotropes suggests consideration of ECMO or mechanical assist devices. These procedures reduce myocardial stress and improve contractile function of myocytes. The main goal of ECMO support is the bridge-to-recovery or the bridge-to-transplant strategy of treatment. Conclusions. ECMO shows effective support in patients with acute idiopathic giant cell myocarditis with fulminant progression in course of heart failure and should be considered as a part of the bridge-to-transplant strategy in such cases.

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Wet, cold and hypertensive: solving the puzzle with levosimendan

A Afonso Felix-Oliveira[1]; MA Goncalves[1]; C Silva[1]; D Matos[1]; M Trabulo[1]; A Tralhao[1]; MJ Andrade[1]; C Aguiar[1]; J Ferreira[1]; M Mendes[1]
[1]*Hospital de Santa Cruz, Cardiology, Lisbon, Portugal*

Acute heart failure is defined as rapid onset or worsening of symptoms and/or signs of HF. The clinical scenario is one of great heterogeneity, either in primary etiology, cause of decompensation or hemodynamic profile presented. Therapeutic options are tailored to each patient and influenced by local expertise, given the absence of a standardized approach. We present the case of a 52 years-old female patient with late-onset anthracycline cardiomyopathy. She was admitted due to worsening fatigue, with symptoms at rest, and increasing weight within the previous week.

Physical examination was characterized by hypertension with 160/90mmHg, sinus tachycardia with 100bpm (QRS <120ms), SaO2 96%, cold extremities with capillary refill time >2s, absence of pulmonary rales and lower leg pitting edema as well as ascites. The patient's condition had been worsening in the last 12 months despite appropriate therapy with Ramipril 10mg/day, Carvedilol 50mg/day and Espironolactone 50mg/day. In spite of being treated with furosemide 180mg/day, congestive features were frequently present. The patient had also a history of severe resistant hypertension, submitted to renal denervation therapy 6 months before current hospitalization. Transthoracic echocardiogram showed a dilated left ventricle, ejection fraction of 26% and global longitudinal strain -5,3%, with estimated cardiac output of 3,3 L/min. E/e′ ratio of 29 and left atrium volume of 58mL/m2 suggesting elevated filling pressures. Right ventricle dysfunction with TAPSE of 13mm, and PSAP of 65mmHg with dilated inferior vena cava. An unusual finding was the presence of elevated arterial pressure, with systolic pressure persistently above 160mmHg, even with additional therapy with Nifedipine ER 30mg/day od and Clonidine 150mg 4id (usual therapy). To define heart transplant eligibility and detail the haemodynamic profile, the patient underwent right heart catheterization with mean PAP of 23mmHg, mean PCWP of 18mmHg, cardiac output of 3.1 L/min (Fick method), PVR of 1,6 Wood and SVR of 3019,4 dynes/sec/cm-5. Being Levosimendan a potent inodilatator, known to decrease systemic and pulmonary resistance and increase cardiac output, a pulse of Levosimendan was successfully administered. In the following week, the patient reported improved fatigue, changing from NYHA IV to NYHA II, and decreased leg swelling and ascites. Arterial hypertension also decreased. Echocardiographic re-assessment showed improved biventricular function as summarized in table 1. This case illustrates an unusual hemodynamic presentation, where "wet/cold" profile occurred together with severe hypertension and very high systemic vascular resistance. Levosimendan obtained a good response, probably due to its arterial and venous vasodilator potency, reinforcing the important role of this drug in the setting of acute heart failure.

Table 1. Echocardiographic Assessment

	Admission	pre-Discharge
Ejection Fraction (%)	26	32
Globo Longitudinal Strain (%)	5,3	7,1
Cardiac Output (L/min)	3,3	3,9
E/A ratio		
E/e' ratio	29	16,5
Left Atrium Volume (mL/m2)	58	
Tricuspid Annular Systolic Excursion (mm)	13	22
PSAP (mmHg)	65	40

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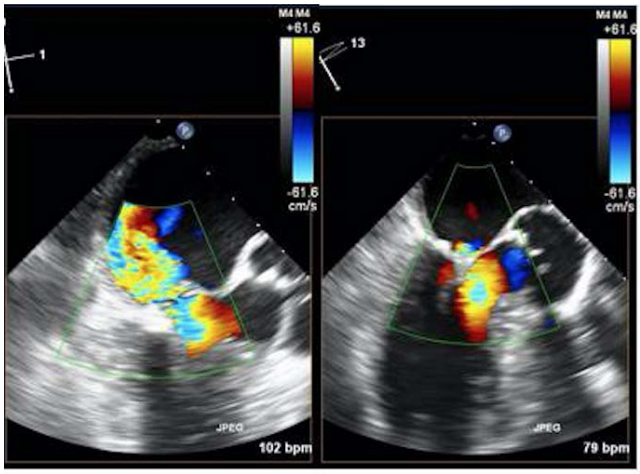
MitraClip for papillary muscle rupture in patient with acute heart failure

K Papadopoulos[1]; M Chrissoheris[1]; P Kourkoveli[1]; K Spargias[1]
[1]*Hygeia Hospital, Transcatheter Heart Valves, Athens, Greece*

Papillary muscle rupture is a devastating and potentially lethal mechanical complication of myocardial infarction that can lead to severe mitral regurgitation (MR) and acute heart failure. An 85 year old woman presented, after several days, to a district hospital with symptoms and signs of myocardial ischemia. The ECG showed a recent anterior STEMI and the patient underwent emergent coronary angiography and revascularization of a totally occluded intermediate (ramus) artery with a drug eluting stent. Echocardiography showed akinetic anterolateral wall with an estimated left ventricular ejection fraction of 40%. On day three post revascularization the patient developed acute pulmonary edema and cardiogenic shock. A transesophageal study revealed partial rupture of the anterolateral papillary muscle with flail anterior leaflet and severe MR. After consideration by the Heart Team, the patient was referred for emergent edge to edge mitral valve repair while being supported with an intra-aortic balloon pump. Two Mitraclips were implanted resulting in marked reduction of MR and dramatic clinical improvement. The patient was discharged home a week later after an uneventful postoperative period. At the 6 month follow up she is clinically well with no re-admissions for heart failure. The case highlights the critical role of edge to edge repair with the MitraClip in patients with acute ischemic mitral regurgitation and refractory heart failure, who are not candidates for surgical repair.



pre and post procedure mitral valve

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LCZ696 as a bridge to candidacy to valve surgery in patients with advanced heart failure with reduced ejection fraction: a case report

D Pellegrini[1]; A Villani[2]; M Oldani[2]; P Gerometta[3]; G Malfatto[2]; G Parati[1]
[1]*University of Milan-Bicocca, Milan, Italy*; [2]*San Luca Hospital of Milan, Milan, Italy*; [3]*Clinical Institute Humanitas Gavazzeni, Bergamo, Italy*

Background: Valvular heart disease (VHD) can impair prognosis significantly in patients affected by heart failure (HF), but these patients are often denied surgery due to excessive operative risk. Even if no data have been published so far on this topic, LCZ696 (sacubitril/valsartan) might improve cardiac function in subjects affected by HF with reduced ejection fraction (HFrEF) and VHD, possibly lowering operative risk and allowing eligibility to valve surgery.
Case report: A 76-year-old man was first diagnosed with HFrEF due to anthracyclines-related cardiotoxicity in 2013. Despite optimal medical treatment for HF and cardiac resynchronization therapy, his clinical conditions slowly worsened (NYHA class III), alongside a gradual worsening of a previously mild aortic and functional mitral regurgitation. In September 2015, an echocardiogram detected a dilated ventricle, a severe reduction of EF, pulmonary hypertension and severe mitro-aortic regurgitation (table, column 1). The patient was then referred for valve surgery, but he was deemed ineligible due to an exceedingly high risk (EuroSCORE II 14.05%). Therefore, palliative infusions of levosimendan and furosemide were started, with mild benefits. In January 2016, we introduced LCZ696, up-titrating the dose to 200 mg b.i.d. over 3 months. In the following months, the patient showed a progressive clinical improvement, reporting resolution of dyspnea (NYHA I) and reduction of diuretic dose. In June 2016 (table, column 2), we observed an overall improvement of cardiac performance and a reduction of mitral regurgitation; aortic regurgitation was unaffected. In October 2016, the hemodynamic burden of valve defects increased again (table, column 3), with a progressive worsening of his clinical conditions; thus, the surgical option was re-evaluated. This time, the pre-operative risk was judged acceptable (EuroSCORE II 5.94%): therefore, the patient underwent aortic valve replacement and mitral valve annuloplasty through a traditional sternotomic approach. No major complications occurred. LCZ696 was restarted a few days later at the lowest dose and up-titrated again. After a hospital-based rehabilitation period, the patient was discharged in NHYA class I-II, with good function of the aortic prosthetic valve, no residual mitral valve regurgitation and stable EF (table, column 4).
Discussion: Beneficial effects of LCZ696 on patients with HFrEF are well known from trials, but experience in clinical practice is still limited. This is the first report on the use of LCZ696 as a "bridge to candidacy", to improve the clinical conditions of a patient, aimed at lowering his predicted operative risk and making him eligible to heart surgery. Thus, LCZ696 administration may pave the way to a new therapeutic approach to patients with advanced HF and VHD, granting larger improvement in prognosis and quality of life than traditional strategies.

Effects of LCZ696 on cardiac function

	Baseline (Sept 2015)	After titration of LCZ696 (June 2016)	Before valve surgery (Oct 2016)	After surgery (Jan 2017)
Ejection Fraction	20%	46%	45%	38%
End-diastolic volume (mL)	348	218	275	230
Pulmonary Artery Systolic Pressure (mm Hg)	60	25	45	30
Mitral regurgitation	+ + +	+/+ +	+ +/+ + +	-
Aortic Regurgitation	+ + +	+ + +	+ + +	-
NT-pro BNP (ng/L)	2007	633	2147	1501

Cardiac ultrasound data and NT-pro BNP values at different times during follow-up

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Effects of LCZ696 on pulmonary arterial pressures in heart failure with reduced ejection fraction, measured with a novel implantable device: a case report

D Dario Pellegrini[1]; A Villani[2]; G Malfatto[2]; M Oldani[2]; F Brasca[2]; GB Perego[2]; G Parati[1]

[1]University of Milan-Bicocca, Milan, Italy; *[2]San Luca Hospital of Milan, Milan, Italy*

Background: LCZ696 (sacubitril/valsartan) can provide a significant improvement in the prognosis of patients affected by heart failure (HF) with reduced ejection fraction (HFrEF). However, trials did not focus on the direct effects of the drug on hemodynamics and on pulmonary arterial pressures (PAP). Novel implantable devices that allow the remote direct monitoring of PAP represent a valuable opportunity to better understand the effects of LCZ696 in these patients.
Case report: A 54-year-old man affected by ischemic HFrEF was followed-up in our center. Despite optimal medical treatment for HF and cardiac resynchronization therapy, no functional nor clinical improvement was observed. He refused both ventricular assist device and heart transplant, so by December 2014 he was dependent on palliative infusions of furosemide and levosimendan, with a NYHA class II-III and a severe reduction of cardiac function (EF 15%), pulmonary hypertension (systolic PAP 50 mmHg), and moderate mitral regurgitation. In January 2015, he received an implantable device for the direct measurement of PAP. The data provided by the device guided therapy optimization in the following months, granting a reduction of 4 mm Hg of mean PAP. No significant clinical improvement was observed, though. In June 2016, we introduced LCZ696, up-titrating it to the target dose of 200 mg b.i.d.: in the following 7 months of follow-up, remote monitoring showed a progressive and significant reduction of PAP (systolic PAP, from 62.6 ± 5.91 to 48.00 ± 3.3 mm Hg; diastolic PAP, from 35.53 ± 4.18 to 27.4 ± 3.01 mm Hg; mean PAP, from 46.07 ± 5.43 to 33.87 ± 3.16 mm Hg; $p < 0.0001$ for all comparisons). Of note, this hemodynamic improvement was paralleled by a progressive down-titration of diuretics and interruption of levosimendan palliative infusions. We also observed a significant increase of thoracic impedance (TI, from 818 ± 16.94 to 876.2 ± 5.61 Ohm, $p < 0.0001$); furthermore, TI values showed an increased stability over time, and the frequency of triggered alarms of fluid overload decreased. No significant changes were observed with cardiac ultrasound and cardiopulmonary exercise test. 6-Minute-Walking Test showed a slight improvement of performance (from 460 to 511 m). Nevertheless, the patient reported a significant subjective improvement of his conditions, reduction of fatigue, resolution of dyspnea and increased low-intensity physical activity at home.
Discussion: In this case LCZ696 produced a significant and progressive reduction of PAP and increase of TI over a relatively short period. The patient experienced a parallel improvement of his clinical conditions and a reduced need for diuretics. This effect appeared to be independent from changes in cardiac function, and may be due to peripheral vasodilation mediated by the drug. Future studies may provide stronger evidence of the effects of LCZ696 on pulmonary pressures and thoracic fluid overload in patients affected by HF.

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Recurrent pump thrombosis: a therapeutic dilemma

M D Avila[1]; JC Leoni[1]; P Patel[1]; DS Yip[1]; J Hosenpud[1]

[1]Mayo Clinic, Transplant, Jacksonville, United States of America

Introduction: Pump thrombosis (PT) remains a devastating complication of left ventricular assist devices (LVAD). To date, there are no guidelines or consensus regarding the management of PT.
Case Report: A 53 y/o male with nonischemic cardiomyopathy underwent HeartWare LVAD placement as a bridge to transplantation. 6 months post implantation, he presented PT which was successfully treated with thrombolytics. He now presents with dark urine, haptoglobin < 14 mg/dl, plasma free hemoglobin 99.1 mg/dl, INR 2.8 and lactase dehydrogenase (LDH) 1,304 u/l. He was hospitalized, started on eptifibatide and unfractionated heparin with improvement of his symptoms and LDH. He remained in the hospital as a status 1A exception on the heart transplant list due to PT. On day 36 of his hospital stay, he presented a third episode of PT which was treated with integrilin. He did not improve and required tissue plasminogen activator (tPA) plus vasopressors. His RAMP study showed inadequate left ventricle unloading in spite of increased speeds. Due to failure to medical therapy, he underwent pump exchange with a HeartWare LVAD via left thoracotomy complicated by cardiogenic shock, respiratory failure and acute kidney injury. He had a chest CT angiography that did not showed thrombus but it did showed that his outflow graft had a 90 degree angle turn posteriorly which may represent a site of obstruction. It was decided that stenting was associated to a moderate risk of stroke which may preclude his heart transplant. He was weaned off vasopressors and had a slow recovery. On day 80, he presented a fourth episode of PT. His prognosis was guarded and at this time he was not a candidate for pump exchange. He was started on tirofiban drip which was unsuccessful. Then, tPA was administered but he continued to deteriorate. He received a second bolus of tPA and became hypotensive followed by pulseless electrical activity refractory to supportive measures. He was declared dead.
Problem and Discussion: This case highlights the difficulty of managing PT in spite of aggressive therapeutic measures. Therapeutic strategies currently available include medical or surgical therapy. Some series have reported success rates of medical therapy of 23-50% with mortality rates of 17-52%. Pump exchange considered a highly morbid procedure has demonstrated low early mortality and low complication rates. There is no head to head trial comparing these strategies. The optimal therapy for patients with PT has not been fully clarified in spite of its increasing incidence in the LVAD population.
Conclusion: The treatment of PT is a complex and challenging medical dilemma. At present, it is unclear what is the appropriate treatment for this morbid condition. The choice of initial therapy depends on patient's characteristics, surgical candidacy and mostly on the center's philosophy based on their experience. Further studies are needed to elucidate which strategy is the most effective and less morbid.

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Role of imaging in patients with a left ventricular assist device implanted

CI Radulescu[1]; L Antohi[1]; A Covaliov[1]; L Chivulescu[1]; R Radu[1]; C Parasca[1]; V Iliescu[1]; O Chioncel[1]

[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania

Introduction: Left ventricular assist devices (LVADs) have revolutionized the treatment of advanced heart failure and LVAD implantation has become a class IIa recommendation therapy in patients with refractory heart failure. A significant number of LVAD recipients have major complications in the first year after the implant, most commonly related to thrombosis/haemorrhage or infections which occur in almost 35% of the patients. Lower rates of infections have been reported for the newer devices, such as HeartWare.
Case Description: This is the case of a 43-years-old man with a history of ischemic cardiomyopathy, severe systolic dysfunction of the left ventricle with an ejection fraction of 20%, implantable cardioverter-defibrillator (ICD) and multiple episodes of decompensated heart failure who became a LVAD recipient (continuous-flow HeartWare device) as a bridge-to-transplantation therapy (9 months prior). The patient presents in the emergency department with signs and symptoms of right ventricular (RV) dysfunction: jugular venous distention (JVD=19 cm), hepatomegaly and peripheral oedema. Systolic blood pressure (SBP) at admission was difficult to assess due to the continuous flow of the device; he also presented with fever, tachycardia and sweating for the last 2 weeks. Chest x-ray showed a large mediastinum, the ICD and the LVAD inflow cannula (Figure 1); initial blood tests asserted leukocytosis with a white blood cell count (WBC) of 16352/µl, a C reactive protein of 80 mg/ml with a high value of the procalcitonin (>10 ng/ml), suggesting an infectious process; we also mention the International Normalized Ratio (INR) of 4,7. The patient was admitted in the Intensive Coronary Care Unit (ICCU) and echocardiography, both transthoracic and transesophageal (Figure 2), revealed a large mass in the anterior mediastinum which compressed the right ventricle with preserved RV systolic function. Computed tomography (CT) scan confirmed the transesophageal echocardiography (TEE) findings and provided more accurate anatomical reports towards the driveline and the inflow cannula (Figure 3,4). Serial blood cultures have been grown and we obtained positive results for Gram-negative pathogens (Pseudomonas aeruginosa). Due to

the urgent situation and the high value of the INR, we decided to perform evacuatory puncture in the fifth right intercostal space with the extraction of a quantity of 600 ml of sero-hemorrhagic fluid. The clinical status of the patient improved significantly immediately after the procedure, ETE showing decompression of the right ventricle (Figure 5). The patient received intravenous antibiotics (ertapenem and moxifloxacin) according to the highest minimum inhibitory concentrations (MIC) for 6 weeks. At the end of the antibiotic treatment the inflamatory blood tests were normalized. The patient remains a candidate for heart transplantation (HTX) without compromising the possibility of performing sternotomy.

Discussions: Right ventricle systolic dysfunction after LVAD implantation has multiple mechanisms, most of them caused by RV contractile dysfunction, but in this case the signs and symptoms of RV dysfunction were produced by extrinsic compression. Mediastinal masses can be the consequences of haemorrhage or systemic infections and distinguishing between them may be clinically challenging. The case is illustrative for managing a difficult complication after LVAD implantation and it attends should be done to conserve the HTX future option.

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Percutaneous paravalvular leak closure for aortic regurgitation after transcatheter aortic valve

M Mariana Castro[1]; JP Abecasis[1]; RC Teles[1]; R Ribeiras[1]; P Freitas[1]; M Neto[1]; M Almeida[1]; MJ Andrade[1]; M Mendes[1]
[1]*Hospital de Santa Cruz, Lisbon, Portugal*

Paravalvular leaks (PVL) are well-recognized sequelae of transcatheter aortic valve implantation (TAVI) with important prognosis impact and difficult management. We present a case of an 87 years patient, underwent transfemoral Corevalve Evolut R 29 complicated with complete atrioventricular block with pacemaker implantation. Immediate pos-TAVI transthoracic echo (TTE) show a mild anterior leak. One year after procedure patient was referred with progressive shortness of breath and recent onset heart failure symptoms, NYHA III. At TTE two PVL were evident one anterior and other posterior globally quantified as moderate, although with severe limitations by this method. Cardiovascular magnetic resonance (CMR) was made to accurately quantify PVL severity, with a regurgitant fraction quantification of 27% (Figure1 A and B). Patient was select to percutaneous treatment with the use of real-time echocardiograpy. Pre-procedure transthoracic echocardiogram (TTE) confirms the severity of the regurgitation and helps to describe leaks: one moderate on a posterior position at 1 o´clock and other smaller anterior at 5 o´clock (Fig 1. C and D), together conditioning severe aortic paravalvular regurgitation. Leak repair was made with TTE guidance (Fig1 E plug at posterior leak (arrow), and anterior leak) using 6-French femoral access and an hydrophilic wire, the defects were successfully crossed with a 5-French Multipurpose catheter and two Amplatzer Vascular Plug IV devices were deployed, resulting in abolition of the posterior aortic leak and minimal residual anterior leak (Fig1. F and G), associated with excellent clinical response. Significant post-procedure aortic regurgitation (AR) is and important predictor of adverse outcome following TAVI. Cardiac imaging, especially two- and three-dimensional transoesophageal echocardiography, plays an essential role in the diagnosis and guidance of intervention but it could fail in the correct quantification. CMR is able to perform accurate flow-imaging and volume-based measurements especially relevant in patients with multiple PVL. Paravalvular leak closure is an established procedure for surgical aortic prostheses; few cases describe percutaneous closure of CoreValve PVL that can be successfully treated with AVP4 device as it can be delivered down standard diagnostic catheters, and easily adapt to leak morphology.

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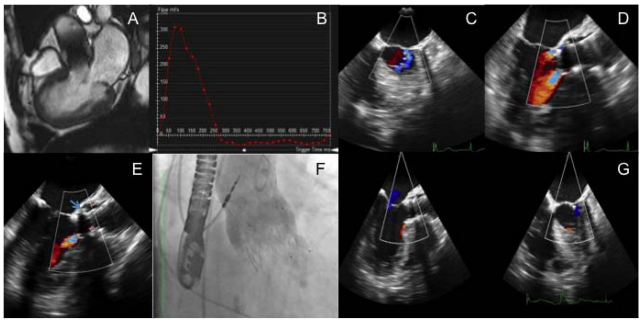
A rare case of heart failure: loculated pericardial effusion after cardiac surgery achieving cardiac compression with focal constrictive pericarditis and mitral stenosis

A Cecchetto[1]; C Ciccio'[2]; A Chiampan[1]; S Bonapace[1]; L Lanzoni[1]; C Dugo[1]; E Barbieri[1]
[1]*Sacred Heart Hospital of Negrar, Cardiology, Negrar-Verona, Italy*; [2]*Sacred Heart Hospital of Negrar, Radiology, Negrar-Verona, Italy*

The interest in this case lies in the difficulty of discerning the main cause of heart failure and the importance of the interpenetration of different imaging techniques to get to the resolution of the case. A 70-years-old male with a medical history of aortic valve substitution with mechanical prosthesis for severe aortic regurgitation, new onset of atrial fibrillation and hepatic cirrhosis, was subjected to our attention for heart failure with bilateral ankle oedema and dyspnoea. Electrocardiogram showed atrial fibrillation and signs of left ventricular hypertrophy. Laboratory tests showed increased natriuretic peptides and chest X ray demonstrated mild pleural effusion. Transthoracic echocardiogram confirmed normal function of aortic prosthesis; hypertrophic left ventricle with thickening of the posterior wall (Fig 1A) and normal systolic function; right ventricle dilatation with mild pulmonary hypertension. We noted an extrinsic mass pressing the infero-lateral wall (Fig. 1A, B, C arrows) with mitral valve prolapse and mitral moderate stenosis (Fig 1 D). The suspect was a cardiac compression for the presence of septal bounce, borderline respiratory variation of the mitral peak E velocity of 20% (Fig. 1E); dilatation of caval and hepatic vein (Fig. 1F); increased left atrium and initial signs of ventricular interdependence on M-mode view of the septum and infero-lateral wall (Fig. 1G). The patient was subjected to thoracic CT that confirmed an inhomogeneous mass with pericardial thickness and calcification (Fig. 1H). To better define the characteristics of the mass, CMR was executed. It showed a loculated chronic pericardial effusion (Fig. 1 I, L, M, arrows) compressing the lateral wall of the left ventricle with an asymmetric hypertrophy (Fig. 1 I, L, M, stars) and causing anterior mitral leaflet prolapse. Then we saw a thickening of the pericardium (3-4 mm) with calcification in particular in the basal inferior and lateral segments. Finally, on real time cine sequences we noted a flattening of the interventricular septum, with signs of ventricular interdependence (Fig. 1N). The patient was treated with diuretics with a period of benefit. During the follow up, he died for a severe sepsis due to mitral valve endocarditis. Analyzing the case, the possible causes of heart failure in this patient could be a dysfunction of the bioprosthesis, the onset of atrial fibrillation, liver cirrhosis, diastolic dysfunction secondary to ventricular hypertrophy, mitral stenosis, constrictive pericarditis. Probably in this case more elements have contributed to the development of heart failure. However it seemed predominant, also in relation to a predominant right heart failure, focal constrictive pericarditis. Constrictive pericarditis is a condition in which a thickened, scarred, inelastic, and often calcified noncompliant pericardium limits diastolic filling of the ventricles. The etiologies are diverse, including cardiac surgery. In patients with suspected constriction, imaging tests can focus on diagnostic information, including pericardial thickness, interventricular dependence, other associated abnormalities (valvular, myocardial, or coronary artery disease). On the basis of its ability for comprehensive morphologic assessment of the heart as well as the pericardium and hemodynamic characteristics, echocardiography remains the initial imaging test, and can provide a definite diagnosis of constrictive pericarditis for most patients. In those situations in which echocardiographic findings are equivocal, additional imaging testing (CT or CMR) is needed to make the diagnosis with more confidence. In some patients, hemodynamic cardiac catheterization may be necessary to establish the diagnosis.



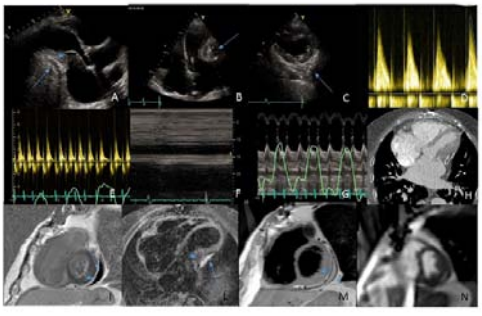


Figura 1

YOUNG INVESTIGATOR AWARD: CLINICAL

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Plasma based cBIN1 correlates with myocardial health in HFpEF patients

A Andriana Nikolova[1]; TC Hitzeman[1]; R Baum[1]; D Geft[1]; D Chang[1]; J Moriguchi[1]; A Hage[1]; B Azarbal[1]; L Czer[1]; M Kittleson[1]; J Patel[1]; J Kobashigawa[1]; M Hamilton[1]; TT Hong[1]; R Shaw[1]

[1]*Cedars-Sinai Medical Center, Los Angeles, United States of America*

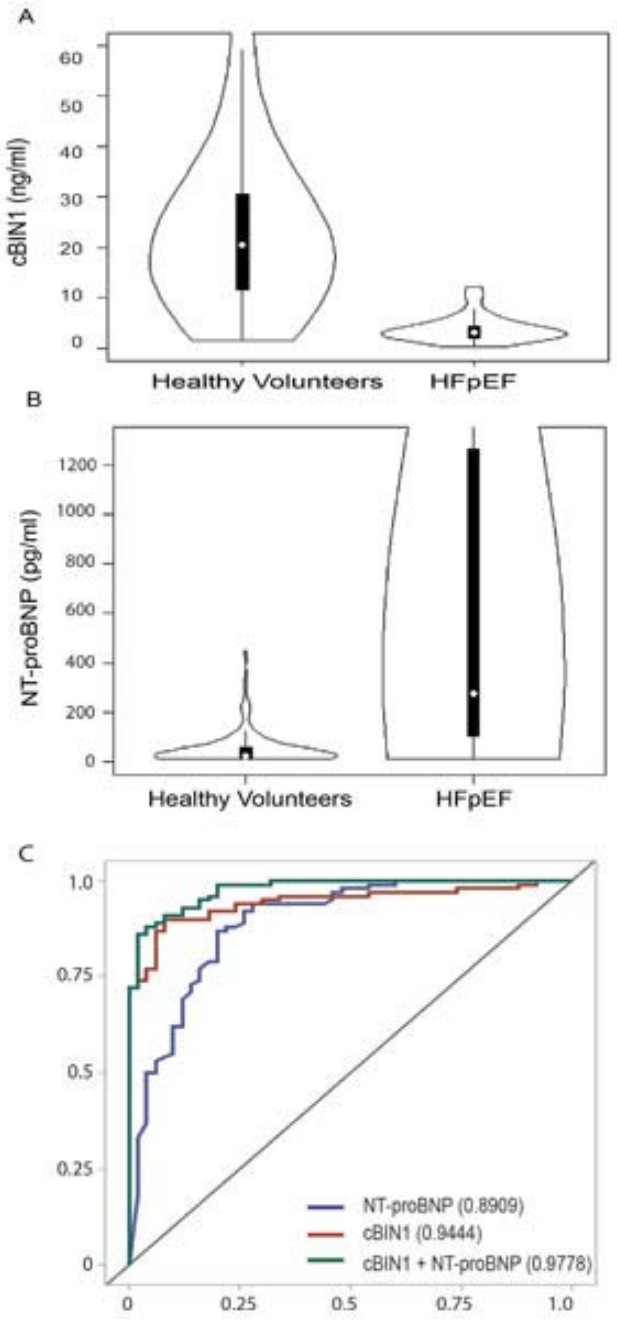
Funding Acknowledgements: American Heart Association, Department of Defense, National Institute of Health, National Heart, Lung, and Blood Institute

Introduction: Heart failure with preserved ejection (HFpEF) is an elusive pathological entity due to lack of diagnostic tools or evidence-based therapies. It accounts for half of the heart failure burden worldwide. Key underlying pathophysiological mechanism in heart failure has been shown to be abnormal calcium regulation. We postulated that a newly found molecular player, Bridging Integrator 1 and particularly its cardiac isoform cBIN1, could be the long-sought marker of myocardial health. cBIN1 is a membrane scaffolding protein which organizes the T-tubule dyads - essential players in calcium cycling.

Methods: The studied cohort (referred to as HFpEF) consisted of 52 patients with various forms of cardiomyopathy with preserved left ventricular (LV) ejection fraction (EF) and stable chronic heart failure symptoms. The comparator cohort included 104 age and sex matched healthy volunteers. IRB approval and full informed consent was obtained from all participants. cBIN1 concentration was determined with a cBIN1 specific ELISA which involved mouse monoclonal anti-cBIN1 exon 17 as capture antibody and a HRP-conjugated exon 13-specific detection antibody. The assay above has been previously validated in our lab. Detailed patient characteristics were obtained per chart review. The HFpEF patients were followed retrospectively for a minimum of 1 year post cBIN1 lab draw or until their most recent clinic visit, whichever is longer.

Results: Plasma cBIN1 levels are substantially reduced in the HFpEF population with a median of 1.62 ng/mL as compared to 10.24 ng/mL in the healthy cohort. Unlike pro-BNP which shows a wider variation in the sick patient cohort, cBIN1 appears to be a better diagnostic test as demonstrated by higher positive and negative predictor value per receiver operator curve. Half of the HFpEF patients had an echocardiogram (TTE) performed within 3 months of cBIN1draw. LV mass as estimated by standard TTE parameters showed an inverse correlation with cBIN1 and no correlation with pro-BNP. cBIN1 correlated well with NYHA class of symptoms and severity of diastolic dysfunction. In addition, cBIN1 level of less than 1.6 was found to be good prognosticator of worse outcomes as shown by the Kaplan Meyer curves of cardiovascular hospitalizations.

Conclusion: cBIN1 is a crucial player in myocardial calcium signaling and it also appears to be a promising new marker for myocardial health. In the current cohort of 52 patients with preserved ejection fraction it performed as well as pro-BNP and showed a better inverse correlation with LV hypertrophy. Additionally cBIN1 < 1.6 appears to be a good prognostic indicator of worse clinical outcomes.



cBIN1 marker in HFpEF patients

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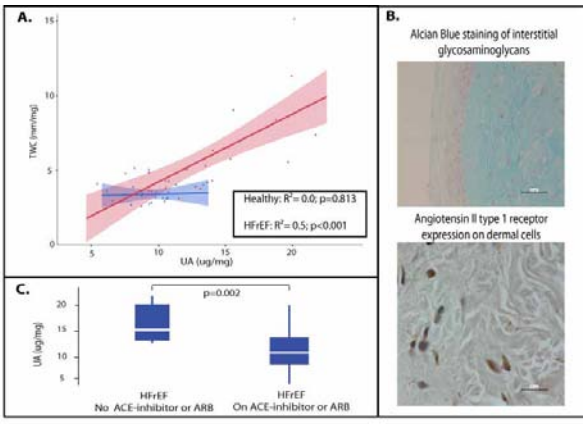
Dermal interstitial alterations in patients with heart failure and reduced ejection fraction are associated with volume status

P Petra Nijst[1]; P Martens[1]; P Hilkens[2]; M Olinevic[2]; M Dupont[1]; W Tang[3]; I Lambrichts[2]; JP Noben[2]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*; [2]*Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt (3500), Belgium*; [3]*Cleveland Clinic Foundation, Cleveland, United States of America*

Background: The occurrence of edema is poorly correlated with cardiac filling pressure in heart failure patients with reduced ejection fraction (HFrEF). Other factors than increased capillary hydrostatic pressure might also determine the occurence of extracellular edema. Large networks of glycosaminoglycans (GAGs) in the interstitium help to regulate water homeostasis. Factors present in HFrEF might increase GAG density and sulphation, leading to interstitial GAG-network dysfunction and fluid accumulation.
Objectives: The aims of this study are to demonstrate in HFrEF patients 1) that interstitial GAG density is increased, 2) that GAG-networks can become dysfunctional contributing to interstitial fluid accumulation and the clinical presentation of edema, and 3) that there is a link between GAG dysfunction and the renin-angiotensin-aldosterone system (RAAS).
Methods: Two punch biopsies of the skin of the lower leg were obtained in healthy subjects (n = 18) and HFrEF patients (n = 29, Left ventricular ejection fraction 32 ± 10%). Alcian blue staining and immunostaining for the angiotensin II type 1 receptor was performed. After obtaining tissue water content (TWC), total interstitial GAG (Uronic Acid (UA)) and sulphated GAG (sGAG) density were quantified with ELISA techniques. A venous blood sample, clinical investigation and echocardiography were simultaneously obtained.
Results: Significant higher interstitial GAG density and sulphation was observed in HFrEF patients compared to healthy controls (UA: 13.1 ± 4.2 vs 9.6 ± 1.6 mg/mg ; $p < 0.0001$; sGAG 15.9 ± 5.9 vs 10.1 ± 1.2 mg/mg; $p = 0.0021$) and in HFrEF patients with versus without presence of lower extremity edema (Table 1). In healthy subjects TWC was stable over a range of interstitial GAG density. In contrast, there was a strong correlation between TWC and UA in HFrEF patients (Figure 1A.). Expression of the angiotensin II type 1 receptor is found on dermal cells responsible for GAG synthesis. Moreover, use of ACE-inhbitors/ARB is associated with significantly lower levels of interstitial GAGs in HFrEF patients (Figure 1B and C).
Conclusion: Interstitial GAG concentration is increased in HFrEF patients compared to healthy control subjects, and correlated with tissue water content and clinical signs of volume overload. Expression of the angiotensin II type 1 receptor was demonstrated on dermal cells. ACE-inhibitors/ARB use is associated with lower levels of interstitial GAGs. A better appreciation of the interstitial compartment might improve current management of volume overload in HF.

	HFrEF without edema (n = 13)	HFrEF with edema (n = 16)	p-value
Skin biopsy- TWC	4.0±0.9	6.5±3.0	0.001
(ml/mg)- sGAG (ug/mg)-	13.3±3.1	17.9±6.8	0.057
UA (ug/mg)	10.9±2.5	14.8±4.5	0.010

sGAG: sulphated GAG, TWC: Tissue water content; UA: uronic acid



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Employment status at time of first hospitalization for heart failure independently predicts mortality and rehospitalization for heart failure

RASMUS Roerth[1]; EL Fosbol[1]; UM Mogensen[1]; K Kragholm[2]; GH Gislason[3]; C Torp-Pedersen[2]; L Kober[1]; SL Kristensen[1]
[1]*Rigshospitalet - Copenhagen University Hospital, Heart Center, Department of Cardiology, Copenhagen, Denmark*; [2]*Aalborg University, Department of Health, Science and Technology, Aalborg, Denmark*; [3]*Gentofte University Hospital, Department of cardiology, Gentofte, Denmark*

Background: Employment status at time of first heart failure (HF) hospitalization may be an indicator of both self-perceived and objective health status as well as it may potentially impact subsequent disease trajectory in terms of adherence to evidence based therapy and cardiac rehabilitation. In this study we set out to examine the association between employment status and the risk of all-cause mortality and recurrent HF hospitalization in a nationwide cohort of HF patients.
Methods: We identified all patients of working age (18-60) with a first HF hospitalization between 1997-2012 in Denmark and stratified them according to whether they were part of the workforce or not. The primary outcome was death and secondary outcome was recurrent HF hospitalization. Cumulative incidence curves and cox regression models were used to assess outcomes. All analyses were adjusted for age, sex, educational level and comorbidity.
Results: Of 21455 patients with a first hospitalization for HF, 11880 (55%) were part of the workforce at baseline. Patients in the workforce were younger (median age 53 vs 55), more were men (76% vs 65%) and fewer had ischemic heart disease (21% vs 28%) and diabetes (12% vs 23%). During a mean follow-up of 1005 days (SD 742), 1883 (16%) died in the workforce group and 2930 (31%) in the non-workforce group, unadjusted Hazard ratio(HR) 2.09 (95% CI 1.97-2.21). Rehospitalization for HF occurred in 4705 (40%) in the workforce group and 3998 (42%) in the non-workforce group, unadjusted HR 1.10 (95% CI 1.05-1.14). In adjusted analyses, HF patients not part of the workforce at baseline had a 1.5 times increased risk of death (Hazard ratio: 1.49 [1.40–1.59]; $P < 0.0001$; figure 1) whereas the risk of rehospitalization for HF was less markedly increased (Hazard ratio: 1.12 [1.07–1.17]; $P < 0.0001$). Not being part of the workforce was associated with a higher likelihood of death than history of diabetes and stroke; figure 1.
Conclusion: Employment status at time of first HF hospitalization is associated with subsequent mortality and to a lesser degree recurrent HF hospitalization, even after multivariable adjustment including comorbidity and socioeconomic factors.

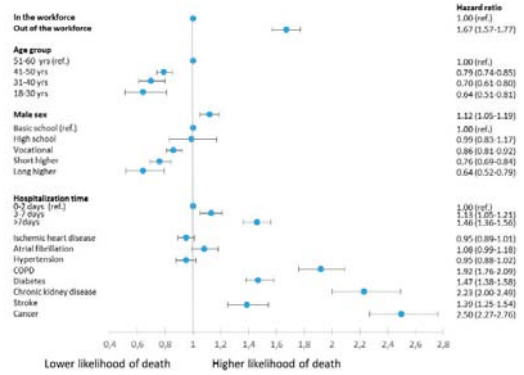

Figure1: Forest Plot

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Extracellular volume expansion in cardiac amyloidosis: validation of cardiac magnetic resonance T1 mapping against endomyocardial biopsy

F Franz Duca[1]; C Zotter-Tufaro[1]; AA Kammerlander[1]; A Panzenboeck[1]; S Aschauer[1]; B Boerries[1]; H Agis[2]; R Kain[3]; D Bonderman[1]; J Mascherbauer[1]
[1]*Medical University of Vienna, Cardiology, Vienna, Austria*; [2]*Medical University of Vienna, Oncology, Vienna, Austria*; [3]*Medical University of Vienna, Pathology, Vienna, Austria*

Background: Cardiac amyloidosis (CA) is caused by extracellular deposition of amyloid fibrils within the myocardium, thus expanding the extracellular volume (ECV). The gold standard for ECV quantification is the histological assessment of

endomyocardial biopsies (EMB). However, this method is limited by procedural risk and therefore not ideal for the monitoring of response to treatment. Cardiac magnetic resonance (CMR) T1 mapping has recently been shown to allow accurate ECV measurement in various cardiac diseases. Thus far it has not been investigated weather CMR-ECV accurately measures ECV in CA.

Methods: Between July 2011 and December 2016, 21 CA patients were enrolled in our study. All patients underwent EMB and CMR for invasive and non-invasive ECV quantification. EMBs were stained with modified Trichrome (n = 21). Additionally, immunohistochemical staining (n = 15) with specific amyloid antibodies was performed. ECV in EMBs was quantified using TissueFAXS software in Trichrome stained (Histo-ECV) as well as in immunohistochemically stained samples (Immunohisto-ECV). ECV by CMR was quantified with T1 mapping using the Modified Look-Locker Inversion recovery (MOLLI) sequence (MOLLI-ECV). Spearman's correlation and Bland-Altman plots were used for correlation analysis and assessment of agreement.

Results: The study population consisted of 7 (33.3%) wild-type transthyretin and 14 (66.6%) light chain CA patients. Median Histo-ECV was 50.2% (IQR: 39.7 – 59.8), median Immunohisto-ECV was 37.4% (IQR: 23.8 – 55.2) and median MOLLI-ECV was of 48.4% (IQR: 41.7 - 59.2). MOLLI-ECV was strongly correlated with Histo-ECV (r=0.774, p < 0.001, Fig.1A) and Immunohisto-ECV (r=0.814, p < 0.001, Fig. 1C). Additionally, MOLLI-ECV showed good agreement with Histo-ECV (Fig. 1B) as well as Immunohisto-ECV (Fig. 1D).

Conclusion: MOLLI-ECV accurately reflects the amount of amyloid deposited within the myocardium. In CA patients, ECV by CMR has the potential of becoming a monitoring tool for new therapeutic agents.

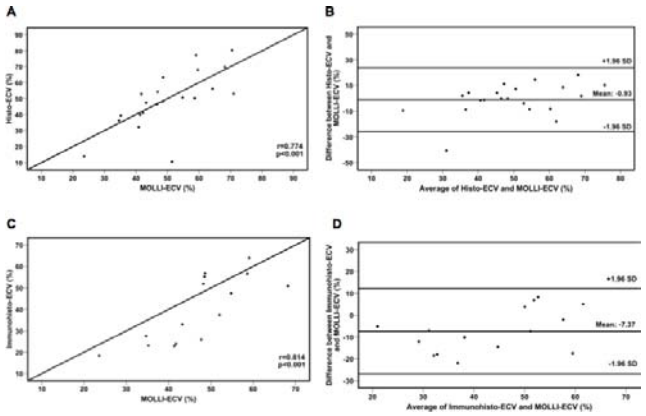
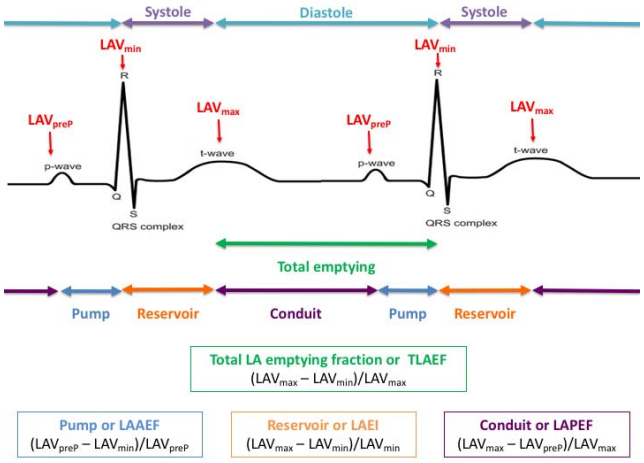


Figure 1

Table 1

Variable	All patients (n = 117)	No SFMR (n = 46)	SFMR (n = 71)	P
Age (y)	63,4±11,2	63,0±11,8	63,6±10,9	ns
NYHA class	2,58±0,81	2,26±0,79	2,79±0,75	0,001
LAVI (ml/m^2)	54,1±20,2	44,6±18,0	59,6±19,4	0,0001
LVEDVi (ml/m^2)	113,1±38,4	100,0±34,1	120,6±39,0	0,009
LVEF (%)	30,1±8,8	31,8±9,2	29,0±8,5	ns
E/E′ ratio	17,8±7,5	14,0±5,9	20,5±7,3	0,0001
sPAP (mmHg)	42,9±14,2	35,8±9,6	47,6±14,8	0,0001
TAPSE (mm)	17,,4±3,6	18,6±3,9	16,7±3,2	0,009
Reservoir LAEI (%)	78,5±52,1	95,1±63,4	64,7±35,8	0,019
Pump LAAEF (%)	24,5±11,7	28,2±12,1	21,5±10,5	0,022
TLAEF (%)	40,4±13,3	44,9±13,0	36,7±12,6	0,013
Reservoir strain	11,8±5,8	13,8±6,2	10,2±4,9	0,019
Pump strain	6,2±4,4	7,9±5,2	4,8±3,2	0,008



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Significant functional mitral regurgitation affects left atrial function and determines clinical status and pulmonary hypertension in HFrEF patients

G Palmiero[1]; L Ascione[1]; G Carlomagno[1]; R Ascione[1]; A Ferro[1]; P Caso[1]
[1] *AO dei Colli-Monaldi Hospital, Department of Cardiology, Naples, Italy*

Functional mitral regurgitation (FMR) is a well-known prognostic factor in patients with HFrEF. Similarly, the left atrial function and the pulmonary hypertension are determinants of outcomes and clinical status in this setting. Aim of this study is to explore the possible interplay between those factors.

Methods: 117 patients with HFrEF, sinus rhythm and FMR were studied with echocardiography. Patients dichotomized based on the presence of SFMR (3-4+). LA volumes were measured at three time-points and the different components of LA function were thus calculated (See Figure 1). The deformation indices were calculated using 2D speckle-tracking.

Results: Patients with SFMR displayed: worse clinical status, larger LV and LA volumes and more impaired LA reservoir and contractile function. LAF was inversely correlated with NYHA class and sPAP. Univariate and multivariate linear regression analysis showed severe FMR, TLAEF and LV filling pressures as predictors of PH, while LA contractile function and the presence of PH were independent predictors of NYHA class.

Conclusions: Our data suggest that the presence of SFMR seems to affect LA reservoir and contractile function HFrEF patients, independently of LVEF. SFMR and the LA dysfunction may play a complimentary role in determining PH and functional impairment in this population.

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Refractory electrical storm rescued by venoarterial extracorporeal membrane oxygenation

G Baudry[1]; G Lebreton[1]; G Hekimian[1]; N Brechot[1]; A Nieszkowska[1]; CE Luyt[1]; JL Trouillet[1]; P Leprince[1]; A Combes[1]; M Schmidt[1]
[1] *Hospital Pitie-Salpetriere, Paris, France*

Introduction: Electrical storm refers to a state of cardiac electrical instability characterized by multiple episodes of ventricular tachycardia or ventricular fibrillation within 24 hours despite antiarrhythmic drugs or device-related therapies (defibrillation or anti-tachycardia pacing) and for which overall mortality was 22-82% in previous series. Triggering factors for this condition include worsening heart failure, early postoperative period, electrolyte abnormalities, and myocardial ischemia. Since Venoarterial extracorporeal membrane oxygenation (VA-ECMO) can be used as a rescue therapy in this setting, we reviewed our experience and assessed the outcomes of patients who received VA-ECMO for refractory electrical storm in our center.

Method: We retrospectively collected demographic, pre ECMO, post ECMO data and in-ICU mortality of patients who received VA-ECMO for refractory electrical storm in our 26-bed intensive care unit from March 2007 to March 2015.

Results: Of the 1286 VA-ECMO patients treated in our ICU during the study period, 38 had ECMO for refractory electrical storm after a median time of 24 (8-168) hours. Median age, SAPS II and SOFA scores at admission were 58 (49-62) years, 80 (55-87) and 13 (11-15), respectively. Electrical storm was secondary to myocardial infarction in 26 (68%) patients. Cannulation was performed during and after cardiac arrest in 5 (13%) and 17 (45%) patients, respectively. Overall ICU survival was 47%

(one patient got a heart transplant and one a left ventricular assist device). Survivors spent 5 (4-10) days on ECMO, 14 (9-25) days in ICU and 52 (34-59) days in hospital. Patients discharged alive from the ICU had lower body mass index, lower SOFA score before ECMO and at day 1 and received less inotropes in the 24h following cannulation ($p = 0.02$). No difference was identified between alive and deceased patients regarding pre-ECMO anti-arrhythmic treatments and number of electrical shocks.

Conclusion: Refractory electrical storm is a very severe condition that might be rescued by VA-ECMO support. The 47% ICU survival rate we observed in this series parallels that of other cardiogenic shock populations rescued by VA-ECMO. Earlier ECMO support in the course of the disease might allow a rapid decrease in inotrope doses and less organ failures, which were both associated with more favorable outcomes.

YOUNG INVESTIGATOR AWARD: BASIC SCIENCE AND TRANSLATIONAL SCIENCE

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The dimer interface of ERK1/2 provides a potential strategy for selective inhibition of pathological cardiac hypertrophy

A Tomasovic[1]; S Kramer[1]; M Huemmert[1]; HA Katus[2]; O Mueller[2]; K Lorenz[3]
[1]*University of Wuerzburg, Institute of Pharmacology and Toxicology, Wuerzburg, Germany*; [2]*University Hospital of Heidelberg, Internal Medicine III, Heidelberg, Germany*; [3]*Leibniz-Institute for Analytical Sciences - ISAS, Dortmund, Germany*

Background and purpose: The extracellular signal-regulated kinases 1 and 2 (ERK1/2) have a central role in cardiac hypertrophy. This involves ERK1/2 dimerization, a trigger for an autophosphorylation of ERK1/2 at threonine 188 (pERKT188), which was shown to induce pathological hypertrophy. However, it is well known that ERK1/2 are essential for cardiomyocyte protection from cell death. Therefore, it is needed to selectively interfere with the hypertrophic ERK1/2 function. Here, we investigated, the ERK dimer interface as potential strategy for selective pERKT188 inhibition.
Methods: To evaluate the impact of monomeric ERK on cardiac integrity, we used the dimerization-deficient ERK2Δ174/177 mutant and a peptide that interferes with ERK dimerization. Cardiomyocyte size, ERK1/2 activity and target activation by Western blot, TUNEL positive cells and ERK localization using confocal microscopy were analyzed. Mice with cardiac overexpression of ERK2Δ174−177 (ERK2Δ174−177-tg) were generated and characterized in response to transverse aortic constriction (TAC) or running wheel exercise. An adeno-associated virus serotype 9 (AAV9) vector construct was used to evaluate the peptide.
Results: Monomeric ERK2Δ174−177 significantly reduced hypertrophic response to phenylephrine (PE) stimulation in neonatal rat cardiomyocytes (NRCM) but, interestingly, did not exacerbate cardiomyocyte death in contrast to ERK1/2 inhibition by PD98059. Similarly in vivo, ERK2Δ174−177 overexpression attenuated the hypertrophic response to TAC and did not increase apoptosis compared to controls. Moreover, cardiac function of ERK2Δ174−177-tg was well preserved; and even after dobutamine infusion, speed of contraction and relaxation were indistinguishable to control mice. In addition, mRNA levels of collagen and brain natriuretic peptide (BNP) were significantly reduced in ERK2Δ174−177-tg after TAC. In contrast to TAC, a physiological stimulus, i.e. running exercise, did not impair cardiac growth in ERK2Δ174−177-tg.
As monomeric ERK2 seems "save" for the heart, we generated a peptide that interferes with ERK dimerization to test the impact of ERK dimers. In line with our hypothesis, the peptide prevented pERKT188 and nuclear translocation of ERK2. In NRCM, the peptide also reduced pERKT188 and led to an attenuated hypertrophic response to PE compared to control cells. Of note, the peptide neither impaired ERK1/2 activation nor cardiomyocyte survival, but efficiently inhibited nuclear ERK target phosphorylation. The potency of the peptide in vivo was investigated in TAC-induced heart failure: AAV9-mediated gene transfer protected from pathological cardiac hypertrophy, an increase of heart failure markers and impaired cardiac function and even decreased cardiomyocyte apoptosis compared to control mice.
Conclusion: These data indicate that the ERK interface is a promising target for the prevention of ERK1/2-mediated pathological cardiac growth without cardiac adverse effects.

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Hypercontractile heart and delayed cardiomyopathy in mice with cardiac-specific ablation of the RIalpha subunit of cAMP-dependent protein kinase

I Bedioune[1]; S Karam[1]; A Varin[1]; M Gandon-Renard[1]; P Lechene[1]; D Mika[1]; P Mateo[1]; G Pidoux[1]; J Leroy[1]; C Stratakis[2]; JJ Mercadier[1]; JP Benitah[1]; AM Gomez[1]; R Fischmeister[1]; G Vandecasteele[1]
[1]*Université Paris-Sud, Université Paris-Saclay, Signaling and Cardiovascular Pathophysiology, INSERM UMR-S1180, Châtenay-Malabry, France*; [2]*National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health & Human Development, Bethesda, United States of America*

Heart failure (HF) is a major health problem in which excessive activation of β-adrenergic receptors (β-AR) and the cAMP-dependent protein kinase (PKA) are critically involved. PKA is a heterotetramer of two regulatory (R) and two catalytic (C) subunits and comprises two subtypes, PKAI and PKAII, defined by the nature of their regulatory subunits, RI and RII respectively. Whereas PKAII is thought to play a key role in β-AR regulation of cardiac contractility, the function of PKAI remains unclear. To address this question, we generated mice with cardiomyocyte-specific and conditional invalidation of the Prkar1α gene, encoding for the RIα subunit of PKA, the predominant constituent of PKAI in the heart. Tamoxifen injection (40 mg/kg/day during 2 days) in 8 weeks old mice resulted in a >70% decrease in RIα protein without modification of other PKA subunits. In Langendorff-perfused heart preparations, spontaneous heart rate was similar whereas basal LV pressure and maximal rate of contraction, as well as maximal rate of relaxation were increased >2-fold in mutant (RIα KO) versus wild type (WT) mice (N=9 in each group, $p < 0.05$). In paced hearts (650 bpm), β-AR stimulation with isoprenaline (Iso) increased cardiac contraction >3-fold in WT versus 1.5-fold in RIα KO. Basal L-type Ca2+ current density was increased in ventricular myocytes from RIα KO and β-AR stimulation (Iso, 30 nM, 15s) was decreased by ~50% ($p < 0.05$, n=38 cells for WT and 40 for RIα KO). The relaxation phase of Ca2+ transients was accelerated, along with a 3-fold increase in PLB phosphorylation at Ser16 (PKA site) in RIα KO myocytes. With age, RIα KO mice develop a dilated cardiomyopathy with depressed ejection fraction, massive interstitial fibrosis, cardiac dilation, and pulmonary congestion which eventually led to death in 50% of RIα KO mice at 50 weeks (versus 0% in WT, $p < 0.01$). These results indicate that PKAI plays a previously unsuspected role in cardiac excitation-contraction coupling and identify RIα as a critical buffer of C subunits in the heart.

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Rac1 regulates mineralocorticoid receptor mediated pro-fibrotic remodeling through 11beta hydroxysteroid dehydrogenase type 2

D Daniel Lavall[1]; N Jacobs[1]; A Kazakov[1]; U Laufs[1]; M Boehm[1]
[1]*Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany*

Purpose: The aim of the study was to characterize the role of Rac1 GTPase for the mineralocorticoid receptor (MR) mediated pro-fibrotic remodeling in atrial fibrillation.
Methods and Results: Transgenic mice with cardiac overexpression of constitutively active Rac1 (RacET) develop an age-dependent phenotype with atrial dilatation, fibrosis and atrial fibrillation. Expression of MR was similar in RacET and wild-type (WT) mice. The expression of 11β-HSD2 was up-regulated in the atria ($665 \pm 378\%$ compared to WT, $p < 0.05$) and the left ventricles ($452 \pm 415\%$, $p < 0.05$) of RacET mice. Statin treatment inhibiting Rac1 geranylgeranylation decreased 11β-HSD2 expression ($185 \pm 25\%$ in statin vs. $324 \pm 94\%$ in vehicle-treated RacET, $p < 0.05$). Rac1-bound 11β-HSD2 was enhanced in RacET compared to WT mice ($167 \pm 20\%$, $p < 0.01$). Samples of human left atrial myocardium showed a positive correlation between Rac1 activity and 11β-HSD2 expression (r=0.7169, $p < 0.05$). In cultured H9c2 cardiomyocytes, Rac1 activation with L−buthionine sulfoximine increased ($174 \pm 47\%$, $p < 0.05$), Rac1 inhibition with NSC23766 decreased 11β-HSD2 expression ($21 \pm 7\%$, $p < 0.05$). Connective tissue growth factor (CTGF) up-regulation induced by aldosterone was prevented with NSC23766 ($312 \pm 88\%$ vs. $77 \pm 6\%$, $p < 0.01$). Cardiomyocyte transfection with 11β-HSD2 siRNA abolished the aldosterone-induced CTGF up-regulation ($181 \pm 35\%$ vs. $123 \pm 9\%$, $p < 0.05$). Aldosterone-stimulated MR nuclear translocation was blocked by the 11β-HSD2 inhibitor carbenoxolone ($213 \pm 70\%$ vs. $46 \pm 45\%$, $p < 0.01$). In cardiac fibroblasts, nuclear MR translocation was inhibited by NSC23766 (Aldosterone, 0.84 ± 0.69, vs. Aldosterone + NSC23766, 0.21 ± 0.17, $p < 0.001$) and spironolactone (0.25 ± 0.3, $p < 0.001$). NSC23766 prevented the aldosterone-induced up-regulation of CTGF ($182 \pm 55\%$ vs. $39 \pm 5\%$, $p < 0.01$) and fibronectin ($181 \pm 43\%$ vs. $94 \pm 27\%$, $p < 0.05$).
Conclusion: Rac1 GTPase regulates 11β-HSD2 expression, MR activation and MR-mediated pro-fibrotic signaling.

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Supercomplex-dependent improvements in mitochondrial function with the mitochondria-targeting peptide elamipretide

JB Perry[1]; EM Sullivan[2]; ME Allen[1]; AB Bandara[1]; F Moukdar[3]; BL Stauffer[4]; SR Shaikh[2]; DA Brown[1]
[1]*Virginia Tech, HNFE, Blacksburg, VA, United States of America*; [2]*East Carolina University, Biochemistry and Molecular Biology, Greenville, United States of America*; [3]*East Carolina Heart Institute, Physiology, Greenville, United States of America*; [4]*University of Colorado, Denver, CO, United States of America*

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Background: Elamipretide is a novel mitochondria-targeting peptide currently being investigated in several heart failure clinical trials. This peptide has shown efficacy in improving bioenergetics in explanted failing human heart and across pre-clinical heart failure models. In spite of these promising findings, the mechanism of action is not fully understood. Electron transport chain proteins typically aggregate into functional 'supercomplexes'. Supercomplex formation is postulated to directly influence mitochondrial ROS production, and decreased supercomplex formation has been observed in several cardiac pathologies.
Purpose: Determine whether elamipretide preserved supercomplex-dependent bioenergetics and lowered ROS emission in cardiac mitochondria.
Methods: Mitochondrial supercomplexes were isolated from post-ischemic rat left ventricle, extracted from the blue-native PAGE gel, and placed in a high-resolution respirometer to determine electron transport chain complex-dependent mitochondrial respiration. In separate studies, measurement of mitochondrial ROS production was comprehensively determined using elamipretide concentrations ranging from 1uM to 1pM.
Results: Mitochondrial supercomplex density was significantly lower in post-ischemic hearts compared to control (2321 ± 374 v. 3300 ± 153 AU, respectively; $P < 0.05$), and preserved with elamipretide (3238 ± 173 AU). Complex-I dependent respiration was significantly reduced in supercomplexes isolated from post-ischemic mitochondria (complex I-dependent respiration decreased to $48 \pm 8\%$ of control, $P < 0.05$). Elamipretide treatment significantly improved complex I-dependent respiration to $85 \pm 24\%$ of normoxic control. Complex IV-dependent supercomplex respiration was not impaired in post-ischemic mitochondria, and there was no discernible effect of elamipretide on complex IV-dependent respiration. In separate studies elamipretide significantly reduced mitochondrial production of ROS from complex I. Complex I-mediated ROS production was 5.10 ± 0.13 nmol/mg in untreated mitochondria, and reduced with 1nM (4.16 ± 0.05nmol/mg), 100pM (3.65 ± 0.05nmol/mg), and 10pM (3.53 ± 0.04nmol/mg) elamipretide ($P < 0.05$ for 1nM-10pM). No effect was observed on complex I-dependent ROS production with 1pM elamipretide.
Conclusions: Elamipretide preserved supercomplex integrity, resulting in improved electron transport chain function and reduced emission of ROS. These data highlight the therapeutic potential of this peptide to lower mitochondrial ROS production and improve bioenergetics in cardiac pathology.

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Accumulation of 5-oxoproline in myocardial dysfunction and the protective effects of OPLAH

A Van Der Pol[1]; A Gil[2]; H H Sillje[1]; J Tromp[1]; E Ovchinnikova[3]; I J Domian[4]; B Van De Sluis[5]; J M Van Deursen[6]; A A Voors[1]; D J Van Veldhuisen[1]; E Berezikov[3]; P Van Der Harst[1]; R A De Boer[1]; R Bischoff[2]; P Van Der Meer[1]
[1]*University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; [2]*University of Groningen, Deparment of Pharmacy and Analytical Biochemistry, Groningen, Netherlands*; [3]*University of Groningen, Laboratory of Stem Cell Regulation and Mechanisms of Regeneration, Groningen, Netherlands*; [4]*Massachusetts General Hospital, Cardiovascular Research Center, Department of Medicine, Boston, United States of America*; [5]*University Medical Center Groningen, Department of Pediatrics, Molecular Genetics Section, Groningen, Netherlands*; [6]*Mayo Clinic, Department of Pediatrics, Rochester, United States of America*

Introduction: In response to heart failure (HF), the heart reacts by returning to a more fetal-like gene profile, which is thought to take place by repressing adult and re-expression of fetal genes.
Purpose: In this study we set out to further characterize the fetal-like gene program in HF, and investigate whether identified genes can serve as a therapeutic targets.
Methods: and Results: Genes associated with the fetal-like gene program were identified by means of next-generation RNA-sequencing on RNA from murine cardiac tissue during development and ischemia/reperfusion (IR) induced HF. Our screen identified 5-oxoprolinase (OPLAH), a member of the γ-Glutamyl cycle, that functions by scavenging 5-oxoproline and converting it to glutamate. OPLAH was shown to be expressed during cardiac development, while repressed in cardiac disease. OPLAH was regulated by the nuclear receptor, Estrogen related receptor alpha (ERRα). Administration of the ERRα antagonist, XCT-790, to human ESC-derived cardiomyoctes resulted in a $\pm 60\%$ reduction in OPLAH expression and thereby increasing oxidative stress. OPLAH levels in cultured cardiomyocytes were manipulated by adenoviral transduction of short-hairpin RNA directed at OPLAH or human OPLAH over-expression (hOPLAH) constructs. A depletion in OPLAH lead to a 2-fold increase in oxidative stress, while over-expression displayed a cardio-protective effect. To test the in vivo physiological effects of OPLAH over-expression, αMHC-hOPLAH (TG) mice were developed and exposed to IR injury. The TG mice had less oxidative stress upon myocardial infarction and smaller infarct sizes, ultimately resulting in an improved cardiac function, assessed by cardiac MRI and invasive hemodynamic measurements (Fig 1). Furthermore, the increase in oxidative stress observed in the wild-type (WT) littermates upon cardiac injury was linked to elevated levels of tissue and plasma 5-oxoproline, measured by LC-MS. Interestingly, when measured in a large cohort of HF patients, elevated plasma levels of 5-oxoproline were associated with an impaired outcome (Fig 2).
Conclusions: Collectively these data describe the identification of OPLAH, a novel cardiac gene involved in oxidative stress, possessing a cardio-protective effect post myocardial infarction, and its substrate 5-oxoproline as a putative novel circulating biomarker for HF.

Fig 1. MRI of Sham and IR hearts of WT and TG mice

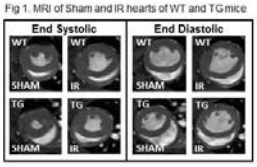
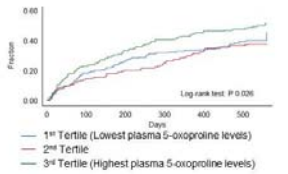


Fig 2. All-cause mortality and HF hospitalization at 18 months



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Investigation of myocardial sarcomerdynamics and myocardial sarcomeric protein alterations in a rodent model of physiological hypertrophy

A Olah[1]; B Bodi[2]; J Tamas[2]; M Torok[1]; C Matyas[1]; A Lux[1]; D Kellermayer[1]; M Ruppert[1]; AA Sayour[1]; B Barta[1]; E Urban[1]; K Stark[1]; B Merkely[1]; Z Papp[2]; T Radovits[1]
[1]*Semmelweis University, Heart and Vascular Center, Budapest, Hungary*; [2]*University of Debrecen, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary*

Funding Acknowledgements: National Research, Development and Innovation Office (NKFIH) of Hungary (K 120277)

Background: In contrast with pathological myocardial hypertrophy, long term exercise-induced cardiac enlargement is associated with functional amelioration. Thus understanding the cellular and molecular processes leading to physiological hypertrophy induced by exercise training might provide a novel therapeutic approach to prevent or treat heart failure.
Purpose: We aimed at determining left and right ventricular (LV and RV) cardiac sarcomeric modifications at cellular and molecular levels in a rat model of athlete's heart and additionally, examining the reversibility of the observed alterations.
Methods: Young rats were divided into control (Co) and exercised (Ex) groups. Trained rats swam 200 min/day for 12 weeks. To investigate reversibility, detrained rats remained sedentary for 8 weeks after completion of the training protocol. LV morphology was examined by echocardiography, while in vivo hemodynamic porperties were provided by LV pressure-volume analysis. Force assessments on isolated permeabilized cardiomyocytes and molecular biological measurements (qRT-PCR, Western blot) were applied to reveal underlying mechanisms.
Results: Echocardiographic and post mortem measured organ weight data confirmed training-induced cardiac hypertrophy, while pressure-volume analysis revealed increased LV contractility in exercised hearts. The $Ca2+$-activated force production of isolated cardiomyocytes was improved (Factive: LV 28.0 ± 1.4 kN/m^2 Ex vs. 15.8 ± 0.8 kN/m^2 Co, $P < 0.05$; RV 16.8 ± 1.1 kN/m^2 Ex vs. 12.1 ± 1.0 kN/m^2 Co, $P < 0.05$) along with increased $Ca2+$ sensitivity and rate constant of force redevelopment in trained rats. $Ca2+$-independent passive tension did not differ between the groups. Exercise training did not affect myocardial gene expression of α- and β-myosin heavy chain (MHC). Cardiac troponin I phosphorylation was decreased (cTnI relative phosphorylation level: LV 0.66 ± 0.06 Ex vs. 1.00 ± 0.02 Co, $P < 0.05$; RV 0.65 ± 0.05 Ex vs. 1.00 ± 0.03 Co, $P < 0.05$), whereas the phosphorylation of titin and cardiac myosin binding protein-C was not altered in physiological hypertrophy. Complete reversibility of the observed alterations was detected in detrained rats.
Conclusions: Exercise-induced hypertrophy is associated with increased $Ca2+$-activated force and $Ca2+$ sensitivity of force production of LV and RV cardiomyocytes, which might be associated with hypophosphorilation of cardiac troponin I. Cellular and molecular alterations regressed completely after 8 weeks of detraining.

MODERATED POSTER SESSION 3 – DIAGNOSIS

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Biomarker profiling in heart failure with mid-range ejection fraction

P Moliner[1]; J Lupon[1]; J Barallat[1]; M De Antonio[1]; J Nunez-Villota[2]; M Domingo[1]; E Zamora[1]; S Altimir[1]; C Pastor[1]; M Rodriguez[1]; M Boldo[1]; M Puertas[1]; MI Troya[1]; V Diaz[1]; A Bayes-Genis[1]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; *[2]University Hospital Clinic of Valencia, Valencia, Spain*

Background: Recently the ESC created a new classification of heart failure (HF) according to left ventricular ejection fraction (LVEF): reduced (HFrEF) when LVEF is <40%, mid-range (HFmrEF) when LVEF is between 40% and 49%, and preserved (HFpEF) when LVEF is >50%. The intermediate group of HFmrEF has been less studied in the past.
Purpose: We sought to explore a panel of biomarkers in patients with HF based on 2016 ESC HF classification and assess whether they have different prognostic value in HFmrEF.
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 diabetes mellitus). Serum concentrations of NTproBNP (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), Cystatin-C (N=804), Neprilysin (N=1069), and soluble transferrin receptor (sTfR) (N=794) 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 death and the composite all-cause death or HF-related hospitalization and CV death or HF-related hospitalization were assessed.
Results: Biomarkers levels according to ESC HF classification are shown in the table. NTproBNP in HFmrEF patients was significantly lower than in HFrEF patients and was similar than in HFpEF patients. In contrast, and remarkably, all the other biomarkers were similar between HFrEF and HFmrEFpatients. On the other hand, ST2 and Cystatin-C were significantly lower in HFmrEF patients than in HFpEF patients and Galectin-3 and STfR also tended to be lower, without achieving statistical significance.
Conclusions: Although HFmrEF patients are acknowledged frequently as intermediate between HFrEF and HFpEFclinically, from a multi biomarker point of view HFmrEF seems quite similar to HFrEF except for NTproBNP, that was lower.

Blood concentration of biomarkers

	HFrEF (1) (N=800)	HFmrEF (2) (N=134)	HFpEF (3) (N=135)	P (1-2)	P (2-3)
NTproBNP, ng/L	1389 (586-3176)	1008 (316-2497)	956 (417-2241)	0.02	0.88
hs-TnT, ng/L	22.5 (10-8-38.6)	21.2 (9.4-41.2)	23.8 (11.5-41.6)	0.64	0.55
ST2, ng/ml	37.5 (30.4-49.4)	37.1 (29.1-48.8)	44.4 (32.3-57.3)	0.62	0.02
Galectin-3 ng/mL	16.1 (12.4-21.5)	16.1 (12.1-23.9)	19.2 (13.6-25.9)	0.75	0.07
hs-CRP, mg/L	3.53 (1.25-7.99)	3.02 (1.21-9.59)	4.77 (1.69-9.27)	0.99	0.34
Cystatin-C, mg/L	1.30 (1.07-1.73)	1.32 1.02-1.89)	1.55 (1.20-2.08)	0.82	0.01
Neprilysin, ng/mL	0.63 (0.38-1.10)	0.68 (0.38-1.32)	0.74 (0.44-1.62)	0.44	0.39
STfR, mg/L	3.60 (2.80-4.60)	3.55 (2.9-4.68)	4.00 (3.20-5.28)	0.80	0.08

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Cardiac123I-mIBG scintigraphy as a gatekeper for ICD implantation?

DO Derk Verschure[1]; JR De Groot[2]; S Mirzaei[3]; O Gheysens[4]; K Nakajima[1]; BLF Van Eck - Smit[1]; GA Somsen[5]; HJ Verberne[1]
[1]Academic Medical Center of Amsterdam, Nuclear Medicine, Amsterdam, Netherlands; *[2]Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands*; *[3]Wilhelminen Hospital, Nuclear Medicine, Vienna, Austria*; *[4]University Hospitals (UZ) Leuven, Nuclear Medicine, Leuven, Belgium*; *[5]Cardiology Centers of the Netherlands, Amsterdam, Netherlands*

Aim: Chronic heart failure (CHF) is a life-threatening disease, partly due to sudden cardiac death (SCD). Implantable cardioverter defibrillators (ICD) for primary prevention of SCD have improved overall survival of CHF patients. However, a high percentage of patients never receives appropriate ICD therapy. This prospective multicentre study evaluated whether cardiac sympathetic activity assessed by planar 123I-mIBG scintigraphy could optimize selection for ICD implantation.
Materials and Methods: 135 stable CHF subjects (age 64.5 ± 9.3 years, 79% male, LVEF 25 ± 6%) referred for ICD implantation for primary prevention in 13 European institutions were enrolled. All subjects underwent planar and SPECT 123I-mIBG scintigraphy. Planar images were acquired at 15 minutes (early) and 4 hours (late) after administration of 123I-mIBG. Early and late heart-to-mediastinum (H/M) ratio, 123I-mIBG washout (WO) and late summed scores were calculated. Cross-calibrated phantom study-data were used to correct for different gamma camera-collimator use. The primary endpoint was appropriate ICD therapy. The secondary endpoint was the combined endpoint of all first cardiac events: appropriate ICD therapy, progression of heart failure (HF) and cardiac death
Results: During a median follow-up of 30 months (6-68 months), 24 subjects (17.8%) experienced a first cardiac event (appropriate ICD therapy [12], HF progression [6], cardiac death [6]). The combination of late H/M ratio (HR 0.461 [0.281-0.757]) and LVEF (HR 1.052 [1.021-1.084]) was significantly associated with freedom of appropriate ICD therapy ($p < 0.001$). Late H/M ratio was independently associated with the combined endpoint (HR 0.135 [0.035-0.517], $p = 0.001$).
Conclusion: Planar myocardial 123I-mIBG-derived late H/M ratio and LVEF were associated with freedom of appropriate ICD therapy. In addition there was a significant association between late H/M ratio and the combined endpoint. Therefore, 123I-mIBG scintigraphy seems to be able to optimize the selection of CHF subjects who might benefit from ICD implantation.

Table 1

	Variable	HR (95% CI)	X2	p-value
Freedomofappropriate ICDtherapy	LVEFLate H/M ratio	1.052 (1.021-1.084) 0.461 (0.281-0.757)	17.542	<0.001
Combinedendpoint	Late H/M ratio	0.135 (0.035-0.517)	10.136	0.001

Multivariate Cox regression analysis for freedom of appropriate ICD therapy and combined endpoint of first cardiac events

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Enhanced insulin clearance in advanced non-diabetic heart failure

V Vojtech Melenovsky[1]; J Benes[1]; A Tura[2]; B Borlaug[3]; K Kovar[1]; T Pelikanova[1]
[1]Institute for clinical and experimental medicine, Prague, Czech Republic; *[2]CNR, Institute for Neuroscience, Padua, Italy*; *[3]Mayo Clinic, Dept of Cardiovascular Disease, Rochester, United States of America*

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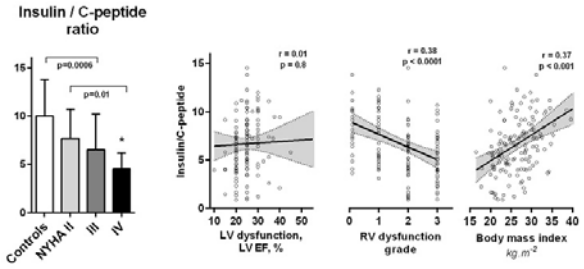
Background: The relevance of impaired glucose homeostasis intrinsically caused by heart failure (HF) are poorly understood. The goal of the study were to examine glucose regulation in non-diabetic (DM) patients with advanced HF and to analyze pancreatic β-cell secretory function.
Methods: 140 advanced HF patients without known DM and 21 sex-, age- and BMI-matched controls underwent body composition (DEXA) and oral glucose tolerance (OGT) assessment with measurements of insulin, glucagon, glucagon-like peptide (GLP-1) and pro-insulin split product C-peptide in 0, 60, 90 and 120 min.

Pancreatic insulin secretion was estimated using C-peptide level deconvolution model.
Results: Compared to controls, HF patients were more insulin resistant. Insulin secretion was not impaired (by modeling of β-cell secretory response) and positively correlated with insulin resistance (HOMA-IR), GLP-1 and glucagon. Despite elevated insulin secretion, fasting insulin decreased with increasing HF severity. The ratio of fasting insulin to C-peptide (IRI/CP ratio), that reflect the balance between insulin production and clearance (in liver and systemic circulation), was decreasing with NYHA class (Figure left) or terticles of natriuretic peptides. IRI/CP ratio correlated with low cardiac output, liver impairment, right ventricular dysfunction, BMI (Figure right) and preceeding change of body weight.
Conclusions: Patients with advanced non-diabetic HF may have enhanced insulin clearance, linked to right heart failure. Because insulin is an important anabolic hormone, enhanced insulin degradation in congested liver may be one of the mechanisms promoting cardiac cachexia in advanced HF.



819

Lifelong arrhythmic risk stratification in arrhythmogenic right ventricular cardiomyopathy: distribution of events and impact of periodical reassessment

C Cappelletto[1]; D Stolfo[1]; A De Luca[1]; B Pinamonti[1]; G Barbati[1]; A Pivetta[1]; M Gobbo[1]; F Brun[1]; M Merlo[1]; G Sinagra[1]
[1]University Hospital Riuniti, Cardiovascular department, Trieste, Italy

Funding Acknowledgements: We deny any relation with the industry and any source of financial support

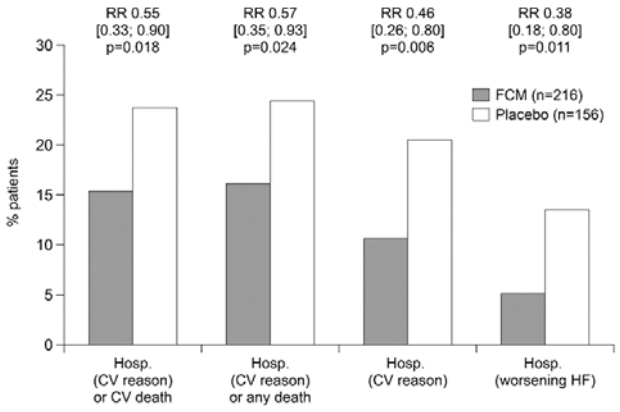
Aims: The arrhythmic risk stratification of Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) remains controversial. We evaluated the long-term distribution of life-threatening arrhythmic events assessing the impact of periodical risk reassessment.
Methods: Ninety-eight ARVC patients with no previous major ventricular arrhythmias were retrospectively analyzed. Patients were assessed at baseline, at 22 (interquartile range [IQR] 16-26), 49 (IQR 41-55) and 97 months (IQR 90-108).
Results: The primary endpoint was a composite of sudden cardiac death, ventricular fibrillation, sustained ventricular tachycardia or appropriate implanted cardioverter-defibrillator intervention. During a median follow-up of 91 months (IQR 34-222) 28 patients (29%) experienced the composite endpoint. The median time for the primary event was 35 months (IQR 18-86 months), and 39% of events occurred beyond 49 months of follow-up. History of syncope (HR 4.034; 95%CI, 1.488 to 10.932; p value=0.006), non-sustained ventricular tachycardia (NSVT; HR 3.534; 95%CI 1.265-9.877; p value=0.016), premature ventricular contractions (PVC) >1000/24h (HR 2.761; 95%CI 1.120-6.807; p value=0.027) and right ventricular fractional area change (RVFAC; HR 0.945; 95% CI 0.906-0.985; p value=0.008) were found as independent predictors at baseline multivariate analysis. Nevertheless, when the prognostic impact of each variable was reassessed overtime only NSVT (HR 3.282; 95%CI, 1.122 to 9.598, p value=0.023) and RVFAC (HR 0.351, 95%CI, 0.157 to 0.780; p value=0.010) remained independent predictors throughout the whole follow-up.
Conclusions: In our cohort of ARVC patients only NSVT and RVFAC maintained their independent prognostic impact in predicting arrhythmic events during the long-term follow-up. Periodical re-assessment of risk in these patients is strongly recommended.

820

An individual patient data meta-analysis of outcomes in 4 randomized double-blind trials of iron-deficient patients with HFrEF and renal dysfunction treated with IV ferric carboxymaltose

P Ponikowski[1]; IC Macdougall[2]; M Bohm[3]; J Comin Colet[4]; G Filippatos[5]; B Roubert[6]; DJ Van Veldhuisen[7]; SD Anker[8]
[1]Medical University, Military Hospital, Department of Heart Disease, Wroclaw, Poland; *[2]King's College Hospital, Department of Renal Medicine, London, United Kingdom*; *[3]University of the Saarland, Department of Internal Medicine and Cardiology, Homburg/Saar, Germany*; *[4]University Hospital of Bellvitge, Cardiology Department, Barcelona, Spain*; *[5]Attikon University Hospital, Heart Failure Unit, Athens, Greece*; *[6]Vifor Pharma, Department of Biometry, Glattbrugg, Switzerland*; *[7]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; *[8]University Medical Center Gottingen (UMG), Department of Cardiology & Pneumology, Gottingen, Germany*

Background. Renal dysfunction is common in patients with heart failure (HF) and linked with poor outcomes. Iron repletion with IV FCM (ferric carboxymaltose) improves symptoms and functional capacity in iron-deficient patients with HF and reduced ejection fraction (HFrEF), but data on outcomes for those with renal dysfunction are lacking.
Purpose: To assess the effect of IV iron therapy with FCM on hospitalization and mortality in iron-deficient patients with heart failure with HFrEF and renal dysfunction.
Methods: Data from four randomized, double-blind, placebo-controlled trials (FER-CARS-01, FAIR-HF, EFFICACY-HF and CONFIRM-HF) were included in an individual patient data meta-analysis. Each study enrolled ambulatory HFrEF patients (NYHA class II/III) with iron deficiency, randomized to IV FCM or placebo, followed for 12–52 weeks. Event rates in the subpopulation with chronic kidney disease stage ≥3 (estimated GFR [eGFR, CKD-EPI] <60mL/min/1.73m^2) were analyzed using a log-link negative binomial regression model.
Results: In total, 372 patients were included in the analysis (FCM 216, placebo 156): males 52%, mean age 72 years, mean LVEF 33%, mean eGFR 43mL/min/1.73m^2, mean ferritin 62ng/mL, mean TSAT 17.7%, mean Hb 12.0g/dL (median Hb 11.9g/dL). A composite of hospitalization for cardiovascular (CV) reasons and CV death was significantly less frequent with FCM vs placebo (rate ratio 0.55, 95% CI [0.33; 0.90], p = 0.018). FCM was also associated with a lower risk for hospitalization for any CV reason or any death, hospitalization for CV reasons, or hospitalization for worsening HF (Figure). The median length of stay in hospital due to worsening HF was 8.5 vs 13 days in the FCM and placebo groups, respectively. The effect on all-cause mortality was neutral. The safety profile of FCM was similar to placebo based on the incidences of adverse events per 100 patient years (FCM 44.6, placebo 45.9) and study drug-related adverse events leading to study drug withdrawal (FCM 0.7, placebo 0.4).
Conclusions: Correction of iron deficiency with IV FCM in patients with ambulatory HFrEF and renal dysfunction is associated with a reduced risk for CV-related or HF-related hospitalization and mortality, a significantly reduced need for hospitalization, and fewer days in hospital for worsening HF.
Figure: Observed incidence, and rate ratios (RR) [95% CI] based on number of events, for outcomes with FCM vs placebo



821

Baseline characteristic and prognosis of patients with cardiac amyloidosis referred in the French Amyloidosis Expert Center.

T Thibaud Damy[1]; A Galat[2]; S Rouffiac[2]; J Badie[2]; S Guendouz[2]; M Kharoubi[2]; K Ayad[2]; N De Nadai[2]; V Plante-Bordeneuve[2]; F Lebras[2]; F Amiot[2]; C Radu[2]; L Hittinger[2]; D Bodez[2]
[1]AP-HP - University Hospital Henri Mondor, Creteil, France; *[2]GRC-Amyloid Research Institute - APHP - INSERM, Creteil, France*

On behalf of: GRC Amyloid Research Insitute
Funding Acknowledgements: PFIZER, Alnylam, GSK.

Introduction: Amyloidosis is a disease caused by infiltration of tissues by an amyloid protein. The most frequent cardiac amyloidosis are light chain (AL) amyloidosis, hereditary transthyretin (TTR-h) and wild transthyretin (w-TTR).
Objective: Describe baseline clinical, biological, echocardiographic characteristics and prognostic of patients referred for cardiac amyloidosis in the Amyloidosis expert cente.
Methods: From 2010 to July 2016, all patients referred to the expert center of our Hospital for suspected cardiac amyloidosis were included. Baseline demographic, clinical, laboratory and ultrasound characteristics were recorded and patients were followed-up for major events including death, cardiac transplantation and left ventricular assistance implant. Results: Of the 942 patients referred for suspicion of CA, 502 had confirmed CA of whom162 had AL amyloidosis, 203 h-TTR and 141 w-TTR. CA were men in 60%, the median age was 69 years w-TTR amyloidosis were older (83 [79; 87], $p < 0.001$) and more men (86%, $p < 0.001$) than the two other types of CA. NYHA III-IV dyspnea was more frequent in AL amyloidosis (60%) and w-TTR (54%, $p < 0.001$)compared to h-TTR, while neurological symptoms were more predominant in h-TTR (62% $p < 0.001$). Creatinine, NT-proBNP and troponin were higher in AL amyloidosis and w-TTR ($p < 0.001$) than in h-TTR. w-TTR amyloidosis had thicker Interventricular septum thicker, lower LVEF, higher global strain E/A and E/Ea ratios than the two other types of CA ($p < 0.001$). During follow-up 137 major events occured. Median follow-up was 22(8-36) months. The survival without major event was 59% for AL amyloidosis, 79% for w-TTR, 81% for h-TTR versus 88% for patients without amyloidosis ($p < 0.001$). In multivariate analysis, only NYHA class III-IV, hyponatremia, elevation of creatinine, troponin and NTproBNP were independent prognostic factors ($p < 0.001$).Conclusion: Cardiac amyloidosis is more frequent than initially thought, with very different layouts depending on the type of amyloid protein involved. Its prognosis is poor at short term. The challenge is to achieve earlier diagnosis to improve prognosis

822

Cardiac biomarkers dynamics in amateur marathon runners

E Roca[1]; J Lupon[2]; L Nescolarde[1]; J Lupon[2]; J Barallat[2]; C Pastor[2]; A Bayes-Genis[2]
[1]Polytechnic University of Catalonia, Barcelona, Spain; *[2]Germans Trias i Pujol University Hospital, Badalona, Spain*

Background: Strenuous exercise such a marathon race might induce an increase of the blood concentrations of some cardiac biomarkers usually measured for diagnosis and prognosis prediction of heart diseases. However the behavior of different cardiac biomarkers around a marathon race in people of both genders has not been well elucidated.
Objective: 1) To assess baseline, just after the marathon race and 2 days after the race blood concentrations of NTproBNP, hs-TnT and ST2; 2) Try to find some relationship between the observed changes and demographic and performance characteristics.
Subjects and methods: 79 subjects (72.2% men), with a mean age of 39 ± 6.2 years (70.9% $\geq$ 35 years) were studied. Three blood samples were obtained: 24-48 h before the race, in the immediate hours after the race and 48h hours after the race.
Results: Baseline data: hs-TnT blood levels tended to be higher in women ($p = 0.07$). Only NTproBNP correlated with age ($p = 0.007$). hs-TnT ($p = 0.01$) correlated with weekly training hours and inversely correlated with the real time for completing the race ($p = 0.009$). No biomarker correlated with the years of training. Biomarkers' dynamics: Blood levels of the three cardiac biomarkers significantly increased during the race (Table, $p < 0.001$ for all). NTproBNP and ST2 decreased to similar pre-race values 48h hours after the race, while hs-TnT blood levels decreased but their remained higher than those pre-race (Table, $p < 0.001$). Relationship with biomarker dynamics: We found higher increase of hs-TnT in women ($p = 0.03$). We did not found any significant relationship between increase in the studied biomarkers and age or years of training. We found inverse relationship between weekly training hours and ST2 increase ($p = 0.007$), and direct relationship between race time and hs-TnT ($p < 0.001$) and ST2 ($p = 0.052$) increase. In multivariable lineal regression analyses including age, sex and those variables with a p-value ≤ 0.10 in the correlation analyses, race time remained independently associated with ST2 ($p = 0.031$) and hs-TnT ($p < 0.001$) increase. Conclusions: cardiac biomarkers significantly increased during a marathon race in amateur runners. Such increase reached abnormal values for hs-TnT and ST2, and was significantly associated with worse athlete performance.

	Baseline	Immediately post-race	48 h after race
NTproBNP, ng/L	70 (70-70)	92 (70-147)	70 (70-70)
ST2, ng/mL	34.2 (24.7-40.9)	54.2 (38.2-72.4)	33.7 (28.9-42.3)
hs-TnT, ng/L	2.85 (1.7-7)	46.9 (24.1-91.1)	4.65 (2.4-8.85)

823

Brain natriuretic peptide improves risk stratification of EuroSCORE II in cardiac surgery: beyond statistical significance, clinical relevance

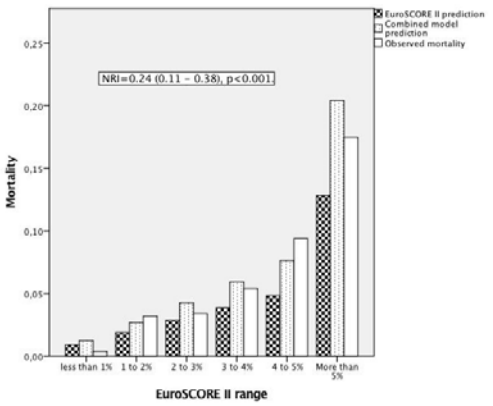
L S Nguyen[1]
[1]Clinique Medico-Chirurgicale Ambroise Pare, Critical Care Department, Neuilly sur Seine, France

Purpose: Our goal was to evaluate the additional prognosis value provided by pre-operative BNP combined to EuroSCORE II regarding intrahospital mortality after cardiac surgery.
Methods: In a prospective cohort of 2209 patients, we validated the performance of EuroSCORE II and a combined model (EuroSCORE II with preoperative BNP). Multivariable logistic regression analysis was used to assess adjusted odd-ratios (OR). Discrimination performance was evaluated using receiver-operator-characteristics analysis area under curve (ROC AUC). Inter-model comparison was performed using the net reclassification index (NRI).
Results: Intrahospital mortality rate was 4.8%. EuroSCORE II had a ROC AUC of 0.81; 95%CI 0.77-0.85, $p < 0.0001$; however there were significant differences between predicted and observed mortality ($p < 0.0001$). Elevated BNP (above 100 ng/l) was an independent risk factor of intrahospital mortality (2.9% vs. 6.5%; adjusted OR 1.83; 95%CI 1.17-2.87, $p = 0.008$). The combined model had a ROC AUC of 0.81; 95%CI 0.78-0.85, $p < 0.0001$. BNP reclassified 1180 (53.4%) patients. Moreover, BNP significantly improved risk stratification of EuroSCORE II with an NRI of 0.24; 95%CI 0.11-0.38, $p < 0.001$.
Conclusion: Preoperative BNP improved the predictive capabilities of EuroSCORE II. Half the patients were reclassified; those with elevated BNP had a theoretical risk multiplied by 1.8 regarding intrahospital mortality after cardiac surgery.

Multivariable logistic regression

	Adjusted OR	95%CI	p-value
Regression with continuous BNP			
EuroSCORE II	1.10	1.07-1.13	< 0.0001
BNP (per 1 log-BNP)	1.45	1.01-2.07	0.04
Regression with categorical BNP			
EuroSCORE II	1.10	1.08-1.13	< 0.0001
Elevated BNP (>100 ng/l)	1.83	1.17-2.88	0.008

BNP as a continuous variable was log-transformed to account for its skewed distribution. Elevated BNP cut-off value was based on the Youden index computed from ROC analysis. OR: odd-ratio; 95%CI: 95% confidence interval.



Observed and predicted mortality

CLINICAL CASE CORNER 3 – METABOLIC ISSUES IN HEART FAILURE: DON'T FORGET PERIPHERY!

824

Acute right heart failure in thyroid storm: warranting early thyroidectomy

O Ossama Abou Hassan[1]; S Mansour[1]; A Zakharia[1]; H Skouri[1]
[1]*American University of Beirut Medical Center, Internal Medicine, Beirut, Lebanon*

Introduction: Thyroid storm may manifest in acute right ventricular failure due to elevated pulmonary vascular resistance. A heightened catecholaminergic state is central to the disease and its cardiac manifestations. We discuss the presentation and management of a patient with idiopathic dilated cardiomyopathy and acute decompensated right heart failure due to thyroid storm.
Description: A 44-year-old man known to have idiopathic dilated cardiomyopathy presents with heart failure exacerbation requiring LVAD procedure. His peri-operative stay is complicated with atrial fibrillation and hyperthyroidism. This is followed by thyroid storm intra-operatively. He developed acute RV failure with intractable ventricular arrhythmias during surgery requiring a temporary RV assist device insertion with emergent thyroidectomy. Questions and Problems: 1. The treatment of atrial fibrillation in bi-ventricular failure sets a challenge due to the pathophysiology of hyperthyroidism in the setting of cardiogenic shock. 2. Should RV afterload reduction be considered in those patients? 3. Inotropic support of bi-ventricular failure in light of a heightened catecholamine state (hyperthyroidism) sets another challenge and requires aggressive measures earlier. 4. The optimal time of LVAD surgery is not studied in patients with hyperthyroidism. Is thyroidectomy warranted before the LVAD in high risk patients?
Discussion: The initial management of hyperthyroidism and thyroid storm is central to all the cardiac manifestation and should be dealt with promptly. The quantitative evidence of thyroid hormone suppression may not help prevent a thyroid storm, and so, the time of surgery should not be linked to the levels of thyroid hormones. Digoxin and beta blocker requirements for treatment of atrial fibrillation may be higher due to increased drug metabolism. In cardiogenic shock, the use of beta-blockers in those patients should be used cautiously. In hyperthyroidism, pulmonary hypertension occurs due to elevated pulmonary vasculature resistance. The role of pulmonary vascular vasodilators should be contemplated in acute event of RV failure. Inotropic support of bi-ventricular failure in the setting of a catecholaminergic state (hyperthyroidism) may be counterproductive and increases the risk of arrhythmias. An earlier bridge through ECMO may stabilize the patient prior to LVAD surgery and thyroidectomy.
Conclusion and Implications: Thyroid storm must always be suspected in refractory cases of cardiac arrhythmia, new onset right sided heart failure or worsening left heart failure. The RV is expected to fail in hyperthyroid states due to the pulmonary vasculature physiology. An ECMO bridge to LVAD is warranted due to the complicated state of heightened catecholaminergic release. We suggest early ECMO followed by combined surgery of LVAD and thyroidectomy with or without a temporary right sided mechanical assist device.

825

It is possible to avoid an ICD implantation with empagliflozine?

J Jose Morgado[1]; JRG Roa[1]; PRO Rodriguez[1]; MTRM Moraleda[1]; JFDF Diaz Fernandez[1]
[1]*Hospital Juan Ramon Jimenez, Cardiology, Huelva, Spain*

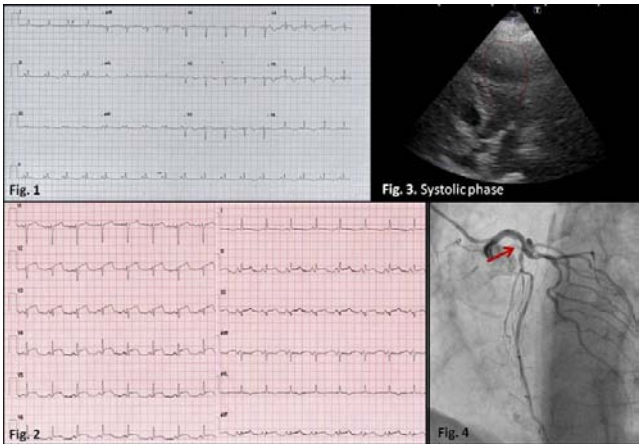
Introduction: We report a case of a 67-year-old female with diabetes mellitus and nonischemic dilated cardiomyopathy. She was being treated with ramipril 10 mg once daily, bisoprolol 10 mg once daily, eplerenone 25 mg once daily, furosemide 40 mg daily and metformine 850 mg three times daily. Her functional class was II of classification of New York Heart Association (NYHA), and had suboptimal metabolic control, with 7.5% of Hemoglobin A1c (HbA1c), her Body mass index (BMI) was 33.5. We decided introduce another oral antidiabetic to improve HbA1c, we choosed empagliflozine due to possible benefits in heart failure (HF) situation, as we learned with is´s clinical trial. She received 10 mg once daily, and one month later 25 mg of empagliflozine once daily. 4 weeks later, she improved her funciontal class, with no symptoms of heart failure, and lower level of natriuteric peptides. We reevaluated the decision of implantable cardioverter-defibrillator (ICD) need, but she had no symptoms of HF, so we refused the implant of ICD. 3 months later, she has no admissions due to heart failure and better metabolic control, with 6.7% of HbA1c. Conclusions and implications for clinical practice Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a new class of diabetic medications indicated for the treatment of type 2 diabetes which had shown benefits in heart failure situation and development of this same. We present a case with improvement in HF situation and metabolic control, being possible the change of indication for ICD therapy.

826

Simultaneous anterior and inferior ST segment elevation during hypoglycemia: myocardial infarction or Tako-tsubo cardiomyopathy?

S Sonia Ferretto[1]; R Turri[2]; C Penzo[2]; L Leoni[1]; S Iliceto[1]; R Bellu[3]
[1]*University Hospital of Padova, Cardiac, Vascular and Thoracic Science, Padua, Italy*; [2]*Mirano Hospital, Mirano, Italy*; [3]*Multi-specialty and Thermal Clinic of Abano Terme, Cardiology, Abano Terme, Italy*

Introduction: Simultaneous ST-segment elevation in the precordial and inferior leads is a rare ECG finding. In literature this aspect is associated to the presence of an occlusion of a "wrapped" left anterior descending artery (LAD) below the first diagonal branch, so to a LAD that perfuses at least one-quarter of the inferior wall. Tako-tsubo cardiomyopathy (TTC) manifests with a clinical scenario mimicking acute myocardial infarction (AMI) and several cases of TTC associated with obstructive coronary artery disease have been reported. We present a case of ST segment elevation occurred during hypoglycemia in which the differential diagnosis between of AMI and TTC results particularly challenging. Case report. An 85-year-old female patient presented to the Emergency Department for pulmonary edema associated with high arterial blood pressure. A routine ECG performed one year ago was completely normal. She had a history of diabetes and hypertension and experienced a severe hypoglycemic episode (glucose 20 mg/dl) two days before. She did not report chest pain episodes. The ECG at the admission showed negative T waves in the precordial leads and slightly negative T waves in the peripheral leads (fig. 1). The echocardiogram demonstrated moderate reduction of the left ventricular ejection fraction due to akynesia of the apical segments and moderate mitral regurgitation. The pulmonary edema resolved with non invasive ventilation, nitrates and diuretics. The Troponin T (TnT) arose until 267 ng/l (normal value < 14 ng/L) in six hours and then decreased. Two days later, during the night, the patient presented a new hypoglycemic episode (glucose 40 mg/dl) severely symptomatic for dyspnea and profuse sweating. She did not report chest pain. The ECG during hypoglycemia showed ST-segment elevation from V2 to V6, in DII, DIII and aVF (fig. 2) that only partially resolved after normalization of glucose level and resolution of symptoms. The echocardiogram showed severe reduction of the left ventricular ejection fraction (25%) due to akynesia of the apical segments (fig. 3). The TnT following this episode continued its descending trend (from 119 ng/l before the episode, to 98 and 94 ng/l three and six hours respectively after the episode). The patient underwent coronary angiography which showed an ulcerated lesion of the left main branch and a subocclusion of the proximal "un-wrapped" LAD (fig. 4), treated with two drug eluted stents. After two days the echocardiographic left ventricular function markedly improved. The ECG at discharge presented negative T waves in the precordial leads. Conclusion. Our case report shows that AMI and TTC are often difficult to distinguish and that the presence of CAD should not be considered an exclusion criteria at all for the diagnosis of TTC, but symptoms, instrumental and biochemical data should be carefully evaluated to formulate the correct diagnosis.



827

Metabolic cardiomyopathy with heart failure: a late, reversible complication of bariatric surgery.

G Pela*[1]; M Li Calzi[1]; P Demola[1]; L Ceriello[1]; MI Gioia[1]; M Gianfreda[1]; F De Rosa[1]; A Crocamo[1]

[1]*University Hospital of Parma, Medicine, Parma, Italy*

Introduction: Dilated cardiomyopathy (DCM) is characterized by cardiac enlargement and impaired left ventricular systolic function, mostly caused by coronary artery disease, which may be effectively treated with myocardial revascularization techniques. However, besides other generally progressive aetiologies of DCM, such as the idiopathic form, there are also reversible causes of DCM, including those secondary to arterial hypertension and alcoholism or to metabolic-nutritional imbalances, such those operating in the present case. Case presentation: We report the case of a 74 years old woman, referred to the University Hospital of Parma because of progressive dyspnoea and peripheral oedema lasting from three months. In her clinical history, almost 30 years before the onset of the symptoms, she underwent a jejuno-ileal bypass surgery for severe obesity, with consequent 40 Kg weight loss. First clinical examination showed an undernourished (body mass index 16 Kg/m2), symptomatic subject with marked peripheral oedema and resting dyspnoea. Blood pressure levels were low (82/59 mmHg). ECG showed a sinus tachycardia with non-specific intraventricular conduction delay and flattened T-waves in the left precordial leads. An early echocardiogram demonstrated a left ventricular dilation with severe systolic dysfunction (end-diastolic diameter 60 mm, ejection fraction 22 %) and severe functional mitral regurgitation (MR) (Fig. 1). Coronary angiogram excluded significant coronary artery disease. Laboratory blood tests showed: normal renal function, markedly reduced values of the main serum electrolytes (2.1 mEq/L potassium; 0.76 mEq/L ionized calcium; 0.6 mg/dL magnesium; 1.4 mg/dL inorganic phosphorus) and of the albumin (1.9 g/dL); significant anaemia (8.7 g/dL haemoglobin) and depletion of iron, folate and Vitamin D; a 346 pg/mL serum concentration of PTH indicated secondary hyperparathyroidism; BNP was elevated (1647 pg/mL), while enzymes of myocardial injury were negative. On the assumption of a malabsorption syndrome as the cause of dilated cardiomyopathy resulting in congestive heart failure, the patient received transfusion of 3 red blood cell units and a three-weeks' lasting intravenous supplementation of potassium, magnesium, calcium, phosphorus, iron and vitamins, with early clinical and laboratory improvement. Then a sustained oral supplementation was initiated and continued after discharge from the Hospital. She also received pharmacological therapy with beta-blocker and angiotensin-receptor blocker (ARB), while loop diuretic treatment, initially needed to control oedema and dyspnoea, was permanently discontinued. At the follow-up the patient felt progressively better with significant improvement of the functional class (NYHA – from IV to I). Serial echocardiographic exams showed a left ventricular ejection fraction rising to 35% within one month, with downgrading of MR to a moderate degree, and to 65% after eight months, with complete regression of left ventricular dilation (51 mm end-diastolic diameter) and a further recovery of MR to a mild degree. Conclusions: This observation reports a rare case of bariatric surgery induced metabolic cardiomyopathy, which completely regressed after correction of nutritional abnormalities.

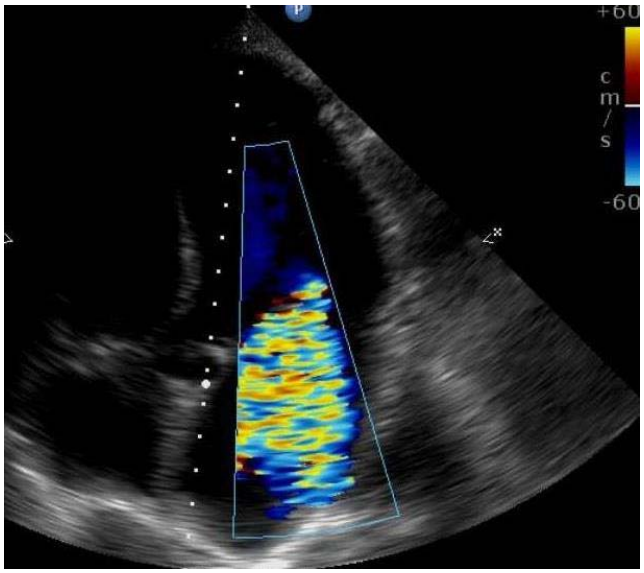


Figure 1

828

An unusual cause of dilated cardiomyopathy

AB Mendez[1]; M Panelo[1]; G Caldentey[1]

[1]*Capio Hospital General de Catalunya, Department of Cardiology, Sant Cugat del Vallès, Spain*

Introduction: A 36-year-old female with no significant previous medical history presented to the outpatient clinic complaining of progressive shortness of breath (NYHA III-IV) and weakness for 4 months. No recent history of cold, diarrhea or any other symptom. Blood pressure was 149/94 mmHg and she was not tachycardic. Signs of congestion were noted (mild bilateral lung rales and peripheral oedema). She also presented exophthalmos and reported weight gain in the last months of trunk predominance. No alcohol or other toxics consumption.

Description of the problem, procedures: Electrocardiography showed sinus rhythm with no ischemic signs. Chest radiography revealed cardiomegaly and increased pulmonary vascularity. Blood test evidenced a normal hemogram, kidney and liver function. NT-ProBNP was raised at 2770 ng/L and troponin was negative. Echocardiogram evidenced a dilated left ventricle with severe systolic dysfunction (EF 19%), no segmental abnormalities or valvulophaties. were noted. Cardiac magnetic resonance confirmed the diagnosis and showed no fibrosis areas. Optimal medical treatment for dilated cardiomyopathy was initiated.

Questions, problems or possible differential diagnosis: Facing the diagnosis of dilated cardiomyopathy potential causes of systolic dysfunction such as ischemic heart disease, myocarditis or infiltrative myocardiopathy were rule out. With the initial suspicion of possible thyroid alteration, the patient was referred to Endocrinology. Thyroid function was normal, but plasma and urinary cortisol levels were high, the dexamethasone suppression test showed an abnormal response suggesting an adrenal alteration. Abdominal CT scan confirmed the presence of an adrenal adenoma. Laparoscopic surgical intervention was initially performed, which was complicated by haemorrhagic shock after 48 hours due to a splenic laceration requiring laparotomy and splenectomy. The patient was discharged 8 days after surgery. Over the following months, left ventricular dilation and ejection fraction progressively improved till almost normal values (Figure 1 A and B: chest X ray before-after surgery; C and D: cardiac-MRI before-after surgery).

Answers and discussion: Cushing's syndrome is an uncommon but potentially reversible cause of dilated cardiomyopathy, most often reported in patients with hypercortisolism arising from an adrenal adenoma. After adenoma excision, our patient presented a significant clinical improvement. Left ventricular diameters reduced till normal values, although mild left ventricle sphericity and borderline EF (50%) is still present 24 months after surgery. She is currently in NYHA I.

Conclusions and implications for clinical practice: Dilated cardiomyopathy and left ventricular failure are rare presentations of Cushing's syndrome. It is important to consider this diagnosis because cardiomyopathy can be reversed following successful treatment of Cushing's syndrome, as shown in our patient.

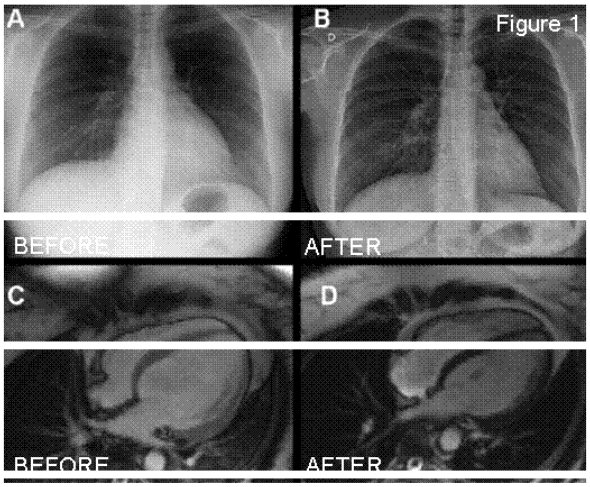


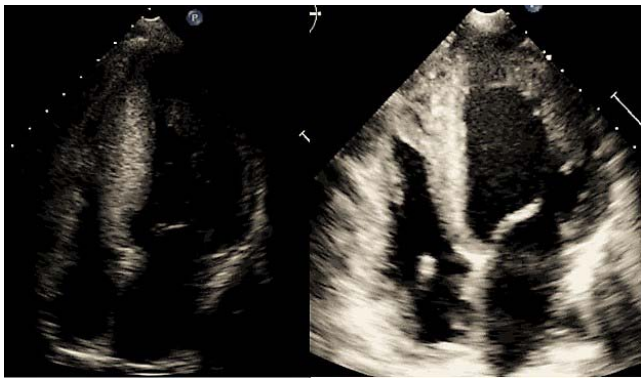
Figure 1

829

Diabetes, deafness and hypertrophic cardiomyopathy: is it just a coincidence?

V Veronica Angela Rial Baston[1]; AM Iniesta Manjavacas[1]; P Meras Colunga[1]; FJ Irazusta Cordoba[1]; SO Rosillo Rodriguez[1]; L Pena Conde[1]; O Gonzalez Fernandez[1]; JL Lopez-Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain

A 45 year-old white female with past history of diabetes mellitus (diagnosed at a very early age) and sensorineural deafness that required cochlear implant, was first diagnosed in 2007 of a non-obstructive hypertrophic cardiomyopathy. The same year, an ablation of three accessory pathways due to Wolff-Parkinson-White syndrome was performed. During follow-up she progressively developed asymptomatic left ventricular systolic dysfunction and in 2012 during an in-hospital admission secondary to a third-degree atrio-ventricular block that required implantation of a definite pacemaker, an echocardiogram was performed revealing severely depressed left ventricular systolic function. In 2015 she was admitted at our center because of acute heart failure. On physical examination, blood pressure was 80/50 mmHg and heart rate was 77 bpm. Heart sounds were rhythmic with no murmurs and pulmonary auscultation revealed bilateral rales at lung bases. NT-proBNP levels rose up to 6903 ng/ml. An electrocardiogram showed ventricular paced rhythm and an echocardiogram revealed severe left ventricular systolic dysfunction and moderate right ventricular systolic dysfunction. Intravenous diuretics were initiated but ACE inhibitors had to be interrupted due to hypotension. She also required conventional analgesics to treat frequent headaches. During hospital admission inquiry of family history was especially striking, as three out of her seven sisters were also diabetic and wore a cochlear implant, therefore suggesting a hereditary disorder. Considering her cardiovascular history (non-obstructive hypertrophic cardiomyopathy and cardiac conduction abnormalities), symptoms such as headaches, hearing impairment and early type 2 diabetes, a mitochondrial disease was suspected. A genetic study was requested revealing mitochondrial mutation in the MT-TL1 gene encoding tRNA, changing adenine to guanine at position 3243 of the mtDNA (m.3243A>G). The diagnosis of MELAS syndrome was then established and the patient was discharged after seven days with low-dose of bisoprolol, eplerenone, oral furosemide and nutritional supplements. During follow-up, an up-grade to TRC-D was scheduled and completion of a cardiac rehabilitation program achieved. Nevertheless, she continued to be on NYHA class III, being then referred to a cardiac transplantation center. Conclusion: Mitochondrial diseases are inherited disorders caused by mutations in mitochondrial DNA which result in an incapacity to generate enough ATP to meet energy needs. They include a wide range of clinical entities which have multi-organ involvement. Despite the importance of an early diagnosis (which would allow genetic counseling), they are often under diagnosed. These disorders must be suspected by cardiologists when they assess patients with cardiomyopathies, cardiac conduction abnormalities and multi-organ manifestations such as: strokes, lactic acidemia, myopathy, deafness or epilepsy.



Echo in 2007 (left) and 2015 (right)

830

Case of acute decompensation in patient with diastolic left ventricul dysfunction and extraordinary obesity

O Olha Vasylenko[1]; I Prudkyi[1]; I Katsytadze[1]; YU Sychenko[1]; I Gorda[1]
[1]National O.O. Bohomolets Medical University, Kiev, Ukraine

Case report description: A female patient of 72 years and BMI 68,6 (height 162cm, weight 180kg) was hospitalized in cardiac ICU with acute onset dyspnea, arterial BP 105/60mmHg (office BP 150/95 mmHg), SpO2 - 82-84%. Anamnesis: permanent AFib, diabetus melitus type 2. On ECG: AFib, QIIISI, HR64. D-dimer - 3097 (N≤500), NTproBNP -1843 (N≤125). Echo: MV- mid reg, TV - severe reg, LA - 58×45mm, RA - 54×40mm, RV - 43mm, PAH - 75 mmHg, ESV - 44 ml, EDV - 92ml, EF - 50%, IVS - 12,5mm, PW - 12mm. Diastolic dysfunction, type 1.
Contrast CT of the chest: no data for pulmonary embolism (PE). Excess fatty tissue, compressive atelectasis of posterior segments.
Ultrasound of lower limbs: lymphedema, no data for thrombosis. Central venous pressure: 280mmH2O. In 3 days after hospitalization, respiratory acidosis increased, we found increasing of potassum, creatinine, breath disorders appeared. CPAP-BIPAP ventilation has been started. We marked elevation of plasma renin and low level of aldosterone/renin relation. Description of the problem. The main problem of this case was a 3rd degree obesity and non-specific symptoms of acute decompensated heart failure, in a combination with adrenal insufficiency, diabetus melitus, chronic anemia and severe respiratory acidosis, as well as PE symptoms and also difficulties to correct the main cause of disease. Answers and discussion. First of all, our main goal of the treatment was weight correction and correction of respiratory acidosis with support of effective breathing. In cooperation with dietologists we prescribed optimal diet and in 3 weeks, she lost 22 kg. We started CIPAP-BIPAP lung ventilation, and the problem of acidosis and hypercapnia was solved. Renal function in this case improved in 48-72hours after correction of acidosis, and potassum level decreased to normal ranges accordingly. In a month after admission to hospital, our patient was discharched in well condition with slight symptoms of dyspnoe and normal ranges of SpO2, BP, HR, pH, creatinine and renin levels. NTproBNP dicreased significantly, but still was elevated. In 4 month of follow up, the patient adheres to a diet and has 148kg.
Conclusion: Importance of comorbities in heart failure prognosis is well known, but sometimes the value of their impact is crusial and the only way to imrove cardiac function and regress HF symtoms is a succesful treatment of main causes.

Main hemodinamic and lab parametres

	BP, mmHg	HR, bpm	CVP, mmH2O	RBC	Hb, g/l	Potassium	Plasma renin, ng/l	ARR	pH	pCO2	pO2
D1	100/60	64	280	2,9	77	7,68	61	0,47	7,22	76	36
D7	95/50	127	240	2,7	71	5,83	-	-	7,29	46	46
D29	120/65	80	140	4,3	116	5,3	38	2,5	7,34	34	65

D1 - admission date, D29 - discharge date, ARR - aldosterone-renin relation

831

Over-correction of symptomatic hyponatremia in chronic HF that required specific therapeutic adjustments against possible osmotic demyelination syndrome. An apparently counterintuitive approach.

R De Vecchis[1]; C Ariano[2]

[1]*Cardiology Unit, Presidio Sanitario Intermedio "Elena d'Aosta", Naples, Italy*;
[2]*Neurorehabilitation Unit, Clinica' S.Maria del Pozzo', Somma Vesuviana, Italy*

Introduction: Hyponatremia (serum Na + <135 mEq /L) in chronic heart failure (CHF) is associated with reduced survival and can be accompanied by various neurological symptoms, including postural instability, gait disorders, attention deficit and increased risk of falls, especially if values of ≤116 mEq/L are attained. Moreover, patients with CHF and chronic hyponatremia are more likely to develop complications from rapid sodium repletion, such as osmotic demyelination syndrome(ODS). Case description A female 74 year old patient presented to the emergency department with a CHF clinical picture, coupled with new onset neurological symptoms. In particular, the patient had problems of her motor function ,i.e., inability to walk with staggering posture, and her speech was difficult to understand. Clinical history and diagnosis. The patient was smoker and slightly obese. She suffered from chronic alcoholism and chronic atrial fibrillation. She had been treated with biological prosthetic valve five years earlier for mitral steno-insufficiency. Moreover, along with usual therapy for CHF(digoxin, enalapril , carvedilol, warfarin), she was taking some drugs known to stimulate the arginine vasopressin secretion, such as a thiazide(one tablet/day of hydroclorothiazide 50 mg plus amiloride 5 mg), and an antidepressant drug belonging to the class of SSRIs (fluoxetine, 10 mg/day). The serum Na +, measured on admission, was 98 mEq / L. Based on this laboratory finding and neurological picture as well as the negative results of CT scan of the brain and electromyography, the diagnosis of symptomatic hyponatremia in CHF patient was made. Therapy and clinical outcome A correction of the low serum Na + was programmed. It was planned that the upper limit for the speed of correction should not have exceeded 6 mEq / L per day (NaCl 2M, i.e., 11.6% NaCl; 10 ml vials; 5 vials in electric syringe, 7.5 ml/h, plus furosemide 20 mg as a slow IV bolus twice daily). However, after 72 h, serum Na+ rose to 126 mEq / L, i.e., a value much higher than the expected target. Subsequently the patient developed marked dysarthria, with slowed slurred speech, which was regarded compatible with the initial stage of the osmotic demyelination syndrome (ODS). Thus, the administration of furosemide and hypertonic saline(HSS) was discontinued and the patient was treated with hypotonic solutions (NaCl 0.45%) and subcutaneous desmopressin (a synthetic analog of arginine-vasopressin), at doses of 2 micrograms more times a day for some days. After ten days in hospital, the patient was discharged in NYHA class II, after retrieval of her normal serum sodium levels together with complete regression of the neurologic disorders. Discussion The unexpected very quick correction of hyponatremia was attributed to the combination of the infusion of HSS and the rapid restoration of capacity of producing an adequately diluted urine output. This was presumably caused by the loss of the stimulating effect on arginine-vasopressin secretion by the fluoxetine, that had been stopped, along with the discontinuation of the thiazide diuretic. In this case, chronic hyponatremia required a well-tailored correction because a high speed of Na+ correction could instead be burdened by the risk of ODS.

Conclusions: Considering that even moderate grades of hyponatremia can cause symptoms (dullness, reduced level of attention, postural instability, etc.), hyponatremia occurring during CHF should be systematically treated with appropriate pharmacologic approach while paying attention not to elicit ODS.

RAPID FIRE 3 – ACUTE HEART FAILURE – FROM DIAGNOSIS TO PROGNOSIS

876

The changing non-cardiovascular comorbidity profile of patients hospitalized with heart failure: Insights from the Get With The Guidelines-Heart Failure registry

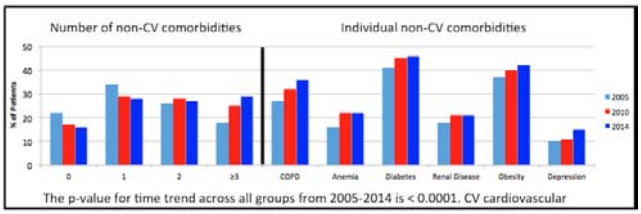
A Sharma[1]; X Zhao[1]; BG Hammill[1]; AF Hernandez[1]; GC Fonarow[2]; GM Felker[1]; C Yancy[3]; PA Heidenreich[4]; JA Ezekowitz[5]; AD Devore[1]
[1]Duke Clinical Research Institute, Durham, United States of America; *[2]University of California Los Angeles, The Ahmanson– UCLA (University of California, Los Angeles) Cardiomyopathy Center, Los Angeles, United States of America*; *[3]Northwestern University, Feinberg School of Medicine, Chicago, United States of America*; *[4]VA Medical Center, Palo Alto, United States of America*; *[5]Mazankowski Alberta Heart Institute, Edmonton, Canada*

Funding Acknowledgements: Get With The Guidelines American Heart Association (AHA) research grant and a AHA Strategically Focused Research Network grant

Introduction: Co-morbid conditions are frequent among patients hospitalized for acute heart failure (HF). There is increasing recognition that non-cardiovascular (CV) comorbidities impact the outcomes of patients with HF. We assessed trends in non-CV comorbidities over time regarding the (1) the prevalence; (2) the total burden; and (3) the association with in-hospital outcomes among patients admitted with HF.
Methods: Using data from the GWTG-HF registry from 2005 to 2014, we assessed 6 key non-CV comorbidities (chronic obstructive pulmonary disease [COPD], anemia, diabetes, renal disease, obesity [BMI ≥ 30 kg/m2], and depression). We evaluated the association between the number of non-CV comorbidities (0,1, 2, and ≥3) with in-hospital mortality and length of stay (LOS).
Results: We analyzed 207,984 HF patients with hospitalizations. 18% of patients had 0 non-CV comorbidities, 30% had 1, 27% had 2, and 25% of patients had ≥3. Patients with increasing numbers of non-CV comorbidities were younger and more likely to have HF with preserved ejection fraction. Over 9 years, there was an increase in the prevalence of all non-CV comorbidities over time (figure). There was an increase in the proportion of patients with ≥3 non-CV comorbidities over time (figure). Patients with an increasing number of non-CV comorbidities were at an increased risk of in-hospital mortality and length of stay > 4 days (table).
Conclusion: The increasing burden of non-CV comorbidities among patients hospitalized with HF over time reflects a shift in the profile of patients with HF. Strategies to manage and treat the growing burden of non-CV comorbidities will be required and should be included in the delivery of in-hospital HF care pathway.

Number of non-CV comorbidities	MortalityAdjusted odds ratio (95% CI); p-value	Length of stay > 4 daysAdjusted odds ratio (95% CI)
0	Reference	Reference
1	1.09 (1.00-1.12); p = 0.04	1.16 (1.12-1.19); p < 0.0001
2	1.32 (1.21-1.43); p < 0.0001	1.32 (1.27-1.36); p < 0.0001
≥3	1.54 (1.39-1.72); p < 0.0001	1.67 (1.60-1.75); p < 0.0001

Figure: Time trends of non-cardiovascular comorbidities among patients admitted with heart failure



877

In hospital changes in natriuretic peptide levels and prediction of outcomes in patients with preserved versus reduced ejection fraction hospitalized for acute decompensated heart failure

K Salah[1]; YM Pinto[1]; LW Eurlings[2]; P Bettencourt[3]; M Metra[4]; JM Pimenta[3]; A Bayes-Genis[5]; V Verdiani[6]; S Stienen[1]; JG Tijssen[1]; WE Kok[1]
[1]Academic Medical Center, Heart failure Research Center, Department of Cadiology, Amsterdam, Netherlands; *[2]VieCuri Medical Center, Department of Cadiology, Venlo, Netherlands*; *[3]Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal*; *[4]University of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Brescia, Italy*; *[5]Germans Trias i Pujol Hospital, Department of Cadiology, Badalona (Barcelona), Spain*; *[6]Careggi University Hospital (AOUC), Department of Internal Medicine and Emergency, Florence, Italy*

Background: A single measurement of NT-proBNP, either at admission or discharge of a hospitalization for acute decompensated HF (ADHF), has been reported to provide equal prognostic information for patients with either reduced (HFREF) or preserved (HFPEF) ejection fraction. However, HFPEF patients have lower absolute NTproBNP levels and less evidence for prognostically relevant medication. Therefore, the change in NT-proBNP levels is expected to be of lesser magnitude in HFPEF.
Purpose: We assessed the change in NT-proBNP levels in HFPEF versus HFREF, stratified for baseline levels. We readdressed the prognostic significance of NT-proBNP changes compared to levels at admission and discharge, in both groups.
Methods: This study is a pooled individual patient data-analysis assembled from 7 prospective cohorts comprising 1131 patients. The endpoint was all-cause mortality within 180 days after discharge. NT-proBNP levels were measured at admission and at discharge. Patients with LVEF ≥45% were categorized as HFPEF (n = 319) , and those with < 45% as HFREF (n = 812). Percent NT-proBNP reduction from baseline levels was calculated for HFPEF versus HFREF, each stratified for admission NT-proBNP categories. Contributions to prognosis of admission and discharge NT-proBNP levels (in four categories) and of relative NT-proBNP reductions (in three categories) were assessed in both groups by Cox regression analysis.
Results: Patients with HFPEF had significantly lower median NT-proBNP levels than those with HFREF both at admission (4432, vs. 7074 pg/ml, p < .001) and at discharge (2148, vs. 3851 pg/ml, p < .001). All-cause 180-day mortality was non-significantly lower in patients with HFPEF compared to patients with HFREF (12% versus 16%, p = 0.13). Within each NT-proBNP quartile at admission, HFPEF responded with a similar percent reduction in NT-proBNP as HFREF. A ≤30% percentage reduction in NT-proBNP carried similar 180 day mortality risks for HFPEF and HFREF (HR 3.72, 95% CI 1.39-9.97; HR 4.62, 95% CI 2.64-8.08, respectively), adjusted for admission NT-proBNP levels and other known predictors. Similar pattern was found, with somewhat lower HR's, for a ≤30% percentage reduction adjusted for NT-proBNP values at discharge (HR 2.94, 95% CI 0.89-7.27; HR 2.19, 95% CI 1.21-3.95, respectively). Finally, we showed that particularly for HFPEF patients the value of the risk estimates increased after adding the reduction

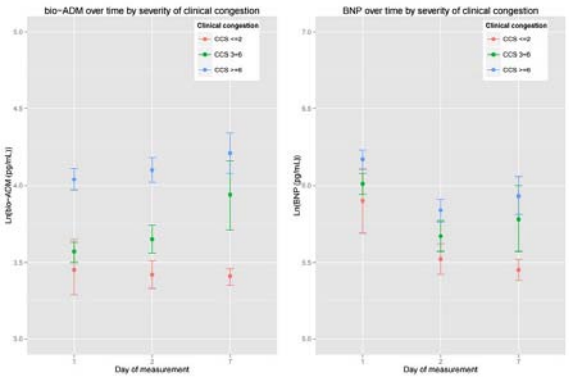
percentage to increasing absolute NT-proBNP levels, while for HFREF patients this effect remained modest.
Conclusions: For patients hospitalized for ADHF, a change in NT-proBNP during hospitalization determines prognosis in HFPEF and HFPEF alike, and these changes in NTproBNP are also equally possible. For absolute NT-proBNP levels HR's apply for both HFPEF and HFREF patients following the concept of the lower the better; adding information of change in NTproBNP is particularly of influence on the prognostic information of absolute levels in HFPEF patients.

878

Bio-ADM: a novel marker of congestion in patients with acute heart failure

D Kremer[1]; BG Demissei[1]; J Rubio-Gracia[2]; J Struck[3]; A Bergmann[3]; JM Ter Maaten[1]; JG Cleland[4]; M Metra[5]; G Cotter[6]; BA Davison[6]; MM Givertz[7]; K Damman[1]; DJ Van Veldhuisen[1]; AA Voors[1]
[1]University of Groningen, University Medical Center Groningen, Groningen, Netherlands; *[2]Clinical University Hospital Lozano Blesa, Servicio de Medicina Interna, Zaragoza, Spain*; *[3]Sphingotec, GmbH, Hennigsdorf, Germany*; *[4]National Heart and Lung Institute, Royal Brompton and Harefield Hospitals, Imperial College, London, United Kingdom*; *[5]University of Brescia, Brescia, Italy*; *[6]Momentum Research Inc., Durham, United States of America*; *[7]Brigham and Women's Hospital, Boston, United States of America*

Background: Congestion is the main reason for hospitalization and the main target of therapy in patients with acute heart failure (AHF). There is an unmet need for a reliable measure of sub-clinical congestion, that can help in clinical decision-making. Adrenomedullin, a vasoactive hormone, is stimulated by volume overload, prevents vascular leakage and oedema and is thus tightly related to congestion.
Objectives: We studied the potential role of plasma biologically active adrenomedullin (bio-ADM), as a marker of congestion in AHF. In addition, we evaluated bio-ADM's added prognostic value on top of predefined models and clinically assessed congestion.
Methods: Plasma bio-ADM was evaluated at baseline, days 2 and 7 in 1562 patients admitted for AHF (enrolled in the PROTECT cohort). Clinical congestion was assessed using a composite score (ranging from 0 to 9) encompassing peripheral oedema, orthopnoea and jugular venous pressure.
Results: Median [IQR] baseline bio-ADM level was 44.1 pg/mL [25.9-82.7] (compared to healthy subjects, median: 20.7 pg/mL, 99th percentile: 43 pg/mL). Amongst a large number of clinical and biochemical variables, bio-ADM had the strongest association with clinically assessed congestion (OR=1.76, 95%CI: 1.56-1.99; $p < 0.001$) and bio-ADM was the strongest predictor of the presence of significant residual congestion by day 7 (OR=1.87, 95%CI: 1.62-2.17; $p < 0.001$). In patients with residual congestion at day 7, bio-ADM levels remained high while BNP levels decreased. At day 7, bio-ADM was an independent predictor of 60-day heart failure rehospitalization on top of predefined predictors and clinically assessed congestion at day 7 (HR=1.30, 95%CI: 1.04-1.63; $p = 0.019$), while BNP was not.
Conclusions: In patients hospitalized for AHF, plasma bio-ADM is strongly associated with clinically assessed congestion and an independent predictor of early rehospitalization.



Bio-ADM and BNP by congestion status

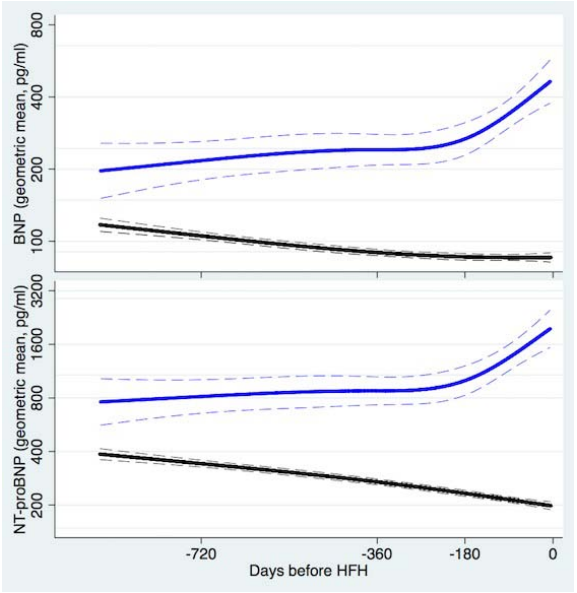
879

Increases in natriuretic peptides precede heart failure hospitalization in patients with a recent coronary event and type 2 diabetes

B Claggett[1]; E Wolsk[2]; MA Pfeffer[1]; R Diaz[3]; K Dickstein[4]; HC Gerstein[5]; LV Kober[2]; FC Lawson[6]; EF Lewis[1]; AP Maggioni[7]; JJV Mcmurray[8]; JL Probstfield[9]; MC Riddle[10]; SD Solomon[1]; J-C Tardif[11]
[1]Brigham and Women's Hospital, Cardiology, Boston, United States of America; *[2]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*; *[3]Estudios Cardiologicos Latinoamerica (ECLA), Rosario, Argentina*; *[4]Stavanger University Hospital, Stavanger, Norway*; *[5]McMaster University, Hamilton, Canada*; *[6]Sanofi US, Bridgewater, NJ, United States of America*; *[7]Research Center of the Italian Association of Hospital Cardiologists, Florence, Italy*; *[8]University of Glasgow, Glasgow, United Kingdom*; *[9]University of Washington, Seattle, United States of America*; *[10]Oregon Health & Science University, Portland, United States of America*; *[11]Montreal Heart Institute, Montreal, Canada*

Funding Acknowledgements: Sanofi

Background: Natriuretic peptides (NP) are used clinically to aid in the diagnosis of heart failure (HF) and considered for monitoring clinical status in patients with this syndrome. The timing of any such changes prior to a HF hospitalization (HFH) remains less well explored. We implemented a novel statistical approach to better characterize temporal changes of NP prior to HFH.
Methods: B-type natriuretic peptide (BNP) and N-terminal prohormone B-type natriuretic peptide (NT-proBNP) were measured in 5450 patients with type 2 diabetes and a recent coronary event in the ELIXA trial (NCT01147250). Measurements were done at baseline and at weeks 24, 76, and 108; patients were included in the present analysis if they had measurements at both baseline and 24 weeks with no intervening HFH. To characterize potentially non-linear temporal changes in NP levels preceding adjudicated HFH, we utilized all measurements available prior to HFH in a post-hoc, retrospective repeated-measures analysis using restricted cubic splines, with non-HFH patients as a control group. NP values are summarized using geometric means at various time points prior to HFH.
Results: During a median follow-up of 26 months, 151 patients (3%) experienced HFH. Patients who experienced HFH had higher baseline NP levels compared to patients without HFH (BNP [234 pg/ml vs. 101 pg/ml, $p < 0.001$]; NT-proBNP [862 pg/ml vs 304 pg/ml; $p < 0.001$]). Geometric mean levels of patients who did not experience HFH declined slowly with time (Figure). In those who experienced a HFH, NP levels remained relatively constant until about 6 months prior to HFH, and subsequently increased approximately two-fold by the time of HFH (BNP: 478 pg/ml, NT-proBNP: 2059 pg/ml) [Figure].
Conclusion: In patients with type 2 diabetes and a recent coronary event, a novel analysis revealed that, while elevated NP levels are associated with future HFH in general, more dramatic increases in NP levels typically precede HFH by about 6 months, suggesting that detectable cardiac deterioration accelerates prior to HFH.
Figure: Geometric mean concentrations (±95% CI) of BNP (panel A) and NT-proBNP (panel B) before HFH – blue line, compared with patients with no HFH – black line (no HFH: n=5299, HFH: n=151).



NP Concentrations prior to HFH

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The continuous conundrum of hyponatremia in acute heart failure: from depletion to dilution, different phases for different outcomes

G Ruocco[1]; FH Verbrugge[2]; R Nuti[1]; A Palazzuoli[1]
[1]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy; *[2]Hospital Oost-Limburg (ZOL), Department of Cardiology, Genk, Belgium*

Background: Hyponatremia is the most common electrolyte abnormality found in hospitalized patients with acute heart failure (AHF) and is related to poor prognosis.
Purpose: In this study we compared dilutional versus depletional hyponatremia (defined on the basis of hematocrit values) in terms of congestion and renal dysfunction; we also investigated the two pattern respect to short/long term outcome.
Methods: This was a retrospective single center study including subjects, with a primary diagnosis of AHF screened from Diur-HF trial. Serum creatinine, blood urea nitrogen (BUN), serum electrolytes and B-type Natriuretc Peptide (BNP) were assessed with 24 hours from admission and at discharge at a central laboratory. We categorized hyponatremia in dilutional (serum sodium $<$ 135mEq/L with hematocrit values $<$35%) and depletional (serum sodium $<$ 135mEq/L with hematocrit values $\geq$35%). Congestion score was evaluated considering five principal signs and giving for each sign 1 point (third heart sound, pulmonary rales, jugular venous stasis, hepatomegaly, and peripheral edema). Patients were followed for six months and composite outcomes were considered the sum of death or rehospitalization for AHF.
Results: Our definitive sample consisted of 233 AHF patients, and hyponatremic patients were 68. 27 patients had dilutional hyponatremia and 41 patients had depletional hyponatremia. Patients with dilutional hyponatremia showed lower serum levels of admission hematocrit (30 ± 3 vs 40 ± 4 vs 38 ± 6 %; $p < 0.001$), admission hemoglobin (10.0 ± 1.1 vs 13.0 ± 1.4 vs 12.2 ± 2.0 g/dL; $p < 0.001$), admission potassium (3.8 ± 0.5 vs 4.0 ± 0.5 vs 4.1 ± 0.5 mEq/L; $p = 0.04$) and EF (33 ± 8 vs 35 ± 13 vs 38 ± 12 %; $p = 0.04$). Mean furosemide home daily dosage was higher in patients with dilutional hyponatremia respect to patients with dilutional hyponatremia and patients with normal serum sodium levels (181 ± 36 vs 176 ± 21 vs 150 ± 46 mg/die; $p < 0.001$). Univariate and multivariable Cox regression model evaluating 60 days death or rehospitalization showed that dilutional hyponatremia was related to poor outcome (U-HR 2.64 [1.40-4.99]; $p = 0.003$. M-HR 2.17 [1.08-4.37]; $p = 0.03$). Univariate analysis for 180 days death or rehospitalization, univariate analysis demonstrated that both dilutional hyponatremia (HR 2.17 [1.32-3.55]; $p = 0.002$) and depletional hyponatremia (HR 1.71 [1.11-2.62]; $p = 0.01$) were related to poor prognosis; multivariable analysis confirmed the same trend.
Conclusions: Our findings showed that dilutional hyponatremia was related to lower EF, higher congestion degree, higher rate of CKD, higher mean of home furosemide dosage and to poor outcome both 2 and 6 months of follow up. Therefore, dilutional hyponatremia could be defined as the last phase of AHF with severe clinical congestion and diuretic resistance. Depletional hyponatremia represented the previous phase respect to dilitional hyponatremia reflecting better outcome and clinical status.

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Clinical characteristics and predictors of one-year outcome in patients hospitalized for heart failure: results from the Polish part of the ESC-HF-Pilot and ESC-HF-LT Registries

S Borodzicz[1]; P Balsam[1]; K Ozieranski[1]; M Peller[1]; A Tyminska[1]; A Kaplon-Cieslicka[1]; M Marchel[1]; J Drozdz[2]; G Opolski[1]; M Grabowski[1]
[1]Medical University of Warsaw, 1st Chair and Department of Cardiology, Warsaw, Poland; *[2]Medical University of Lodz, Department of Cardiology, Lodz, Poland*

Introduction: The Heart Failure (HF) Association of the European Society of Cardiology (ESC) created the Heart Failure Pilot Survey (ESC-HF Pilot) and Heart Failure Long-Term Registry (ESC-HF-LT) which are prospective, multicentre, observational registries aimed to evaluate the clinical profile, pharmacotherapy and one-year outcomes of HF patients in the European countries.
Purpose: The aim of the study was to compare the clinical characteristics and one-year outcome, as well as predictors of mortality and hospital readmissions in patients hospitalized for HF enrolled in the ESC-HF-Pilot or ESC-HF-LT Registry.
Methods: The analysis included hospitalized Polish patients enrolled in the ESC-HF-Pilot Registry and in the phase I of the ESC-HF-LT Registry. The primary endpoint (PE) was all-cause death at one year, while the secondary endpoint (SE) was composed of all-cause death or rehospitalization for worsening HF at one year.
Results: The total Polish cohort of both Registries included 2 019 patients. The final analysis consisted of 1 415 inpatients, 650 from the ESC-HF-Pilot and 765 from the ESC-HF-LT Registries. The PE was reached by 209 of the 1361 patients (15.4%); in the ESC-HF-Pilot Registry the PE occurred in 89 of the 650 patients (13.7%), whereas in the ESC-HF-LT Registry the PE was observed in 120 of the analyzed 711 patients (16.9%; $p = 0.11$). The SE occurred in 423 of the 1172 patients (36.1%), including 201 of the 509 patients from the ESC-HF-Pilot Registry (39.5%) and 222 of the 663 patients from the ESC-HF-LT Registry (33.5%; $p = 0.04$). The independent predictors of PE in the total population from both registries were older age, chronic obstructive pulmonary disease (COPD), higher New York Hear Association (NYHA) class at admission, lower serum sodium at admission, support of inotropics during index hospitalization, lower systolic blood pressure (SBP) at discharge, higher heart rate at discharge, and amiodarone at discharge. The prescription of beta-blockers at discharge was associated with significantly decreased mortality. The independent predictors of SE were diabetes, myocardial infarction, NYHA class at admission, lower serum sodium at admission, lower serum potassium at admission, support of inotropics during index hospitalization, use of diuretics intravenously during index hospitalization and lower SBP at discharge.
Conclusions: The results of the present study reveal, that patients hospitalized for HF remain at high risk for adverse outcomes, including death and HF rehospitalization. The recent progress in diagnosis and treatment of HF changes the patients' clinical profile and frequency of HF readmission.

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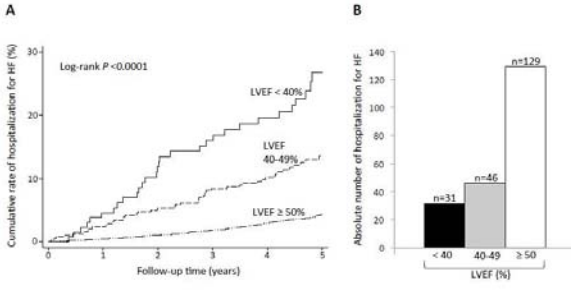
Hospitalization for heart failure in stable coronary artery disease outpatients: determinants, role of interim myocardial infarction, and prognosis

N Nicolas Lamblin[1]; T Meurice[2]; O Tricot[3]; P De Groote[1]; G Lemesle[1]; C Bauters[1]
[1]Lille University Hospital, Institut Coeur Poumon, Lille, France; *[2]Clinique du Bois, Lille, France*; *[3]Centre Hospitalier de Dunkerque, Dunkerque, France*

On behalf of: CORONOR registry group
Funding Acknowledgements: Fédération Française de Cardiologie, Paris, France

Background. There is a lack of recent data on incidence, correlates, and prognosis associated with the development of heart failure (HF) in patients with stable coronary artery disease (CAD).
Objectives: To analyze the risk of hospitalization for HF, together with relevant associated factors, and related mortality, in stable CAD outpatients.
Methods: The multicenter CORONOR registry enrolled 4184 unselected outpatients with stable CAD (ie myocardial infarction (MI) and/or coronary revascularization >1 year previously). Five-year clinical follow-up was achieved for 3785 (98%) of the 3781 patients who had no history of hospitalization for HF at inclusion.
Results: Hospitalization for HF occurred in 6.1% of the patients at 5-year and was a powerful predictor of mortality in a time-dependent analysis (age and sex adjusted HR = 7.62 [6.0-9.68]; $P < 0.0001$). Six variables were independently associated with hospitalization for HF: left ventricular ejection fraction (LVEF), age, diabetes mellitus, atrial fibrillation, history of hypertension, and low estimated glomerular filtration rate. As most patients had a normal LVEF at inclusion (mean=59 ± 10%; 86% with LVEF $\geq$ 50%), although low LVEF was a strong predictor of hospitalization for HF, a majority of them (62%) occurred in patients with preserved LVEF. Interim MI was strongly associated with hospitalization for HF (HR=3.63 [2.17-6.08]; $P < 0.0001$) but was a relatively rare circumstance (7.6% of the patients hospitalized for HF).
Conclusions: HF development remained relatively frequent in patients with stable CAD and was associated with a high risk of mortality. Although the LVEF at inclusion was a strong predictor of HF, we emphasized that the majority of cases of HF occurred in patients with preserved LVEF at inclusion and without an interim MI.



Hospitalization for heart failure

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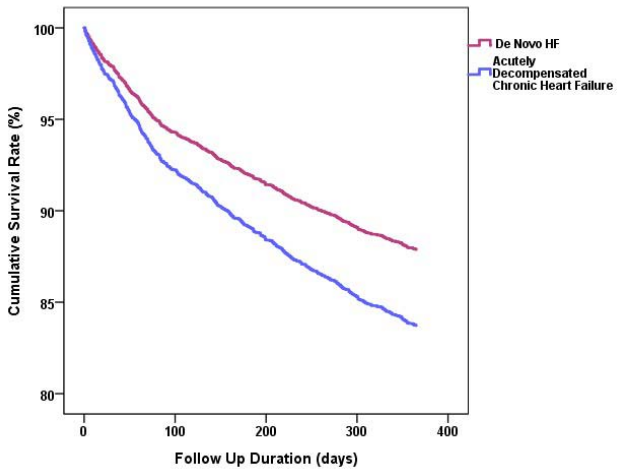
Not all acute heart failure syndromes are the same: de novo acute heart failure vs. acutely decompensated chronic heart failure.

J-H Ju-Hee Lee[1]; DH Bae[1]; KK Hwang[1]; MC Cho[1]
[1]Chungbuk National University Hospital, Cardiology, Cheongju, Korea Republic of

On behalf of: KorAHF Registry Investigators

Background: Acute heart failure syndromes (AHFS) can be classified into heart failure (HF) which presenting for the first time (de novo) or acutely decompensated chronic HF (AD-CHF). We compared the differences between de novo HF and AD-CHF regarding their clinical features and prognosis.
Method: We evaluated the AHFS patients hospitalized in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to February 2014.
Results: Among the 5,625 patients who were registered at KorAHF Registry, 2,944 patients (52.3%) were classified as de novo HF and 2,681 patients (47.7%) were classified as AD-CHF. AD-CHF patients were older, more often women, and more likely to have hypertension, diabetes, ischemic heart disease, chronic kidney disease and atrial fibrillation. Regarding precipitating factors, infection, renal failure, anemia or bleeding, noncompliance and recent addition of negative inotropic drugs were predominant in AD-CHF, whereas ischemic event, severe hypertension, excessive alcohol or illicit drug use and endocrine abnormalities were predominant in de novo HF. AD-CHF patients showed lower serum sodium and hemoglobin, higher blood urea nitrogen and serum creatinine, and higher B-type natriuretic peptide level. De novo HF patients showed higher LV EF, smaller LV end-diastolic dimension and LA size, and lower RV systolic pressure. Although the use of renal replacement therapy was comparable, de novo HF patients were more frequently supported by mechanical ventilator and mechanical assisting device including IABP, PCPS and AD-CHF patients used inotropes more frequently. While in-hospital mortality was comparable between two groups (5.0% in AD-CHF vs 4.6% in de novo HF, P=0.396), 1-year mortality was significantly higher in AD-CHF patients (22.9% vs 13.9%, P < 0.001). In multivariate analysis adjustment for 13 risk variables including age, sex, and brain natriuretic peptide, the hazard ratio for the mortality was increased in patients with AD-CHF. (Figure)
Conclusion: Independent of other key prognostic variables, AD-CHF had significantly worse prognosis than de novo HF. They also showed many differences in clinical presentation, risk factors and laboratory values. Better understanding on these differences between de novo HF and AD-CHF is needed to improve outcomes for AHFS.



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Acutely decompensated heart failure with preserved and reduced ejection fraction present with comparable hemodynamic congestion

LNLC Van Aelst[1]; M Arrigo[2]; R Placido[3]; E Akiyama[4]; N Girerd[5]; F Zannad[5]; P Manivet[6]; P Rossignol[5]; M Badoz[7]; M Sadoune[6]; JM Launay[6]; E Gayat[8]; A Cohen-Solal[9]; A Mebazaa[8]; MF Seronde[7]
[1]Catholic University of Leuven, Department of Cardiovascular Diseases, Leuven, Belgium; *[2]University Heart Center, Division of Cardiology, Zurich, Switzerland*; *[3]University Hospital De Santa Maria, Serv Cardiologia I, Lisbon, Portugal*; *[4]Yokohama City University Medical Center, Division of Cardiology, Yokohama, Japan*; *[5]Clinical Investigation Centre Pierre Drouin (CIC-P), Nancy, France*; *[6]Inserm UMR-S 942, Paris, France*; *[7]Regional University Hospital Jean Minjoz, Department of Cardiology, Besancon, France*; *[8]Hospital Lariboisiere, Department of Anesthesia and Critical Care, Paris, France*; *[9]Hospital Lariboisiere, Department of Cardiology, Paris, France*

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Introduction: Distinctive clinical, echocardiographic and biochemical features of chronic heart failure with preserved and reduced ejection fraction (HFPEF and HFREF) are well known, yet insights into the presentation of acute HFPEF and HFREF are scarce.
Objectives: This study aimed at characterizing acute HFPEF (defined as left ventricular (LV) EF ≥ 40%), HFREF (LVEF < 40%) and acute dyspnea of non-cardiac origin, with special emphasis on congestion, right ventricular (RV) and kidney dysfunction at admission.
Methods: Included patients derived from MEDIA-DHF (NCT02446327), investigating diagnostic and prognostic potential of echocardiographic measurements and biomarkers of congestion (MR-proANP and sCD146) in the initial, early presentation (< 4 hours of admission) of acutely decompensated heart failure (ADHF) and acute non-cardiac dyspnea.
Results: One hundred and forty-six patients with acute dyspnea were included in the study: 101 ADHF patients (60 classified as HFPEF, 41 as HFREF, with LVEF 50% [40-60] and 29% [20-33] respectively) and 45 with dyspnea of non-cardiac origin (LVEF 60% [54–65]). At admission, clinical characteristics were similar in ADHF and non-cardiac dyspnea patients, yet echocardiographic analysis of congestion, RV and LV systolic and diastolic function as well as biochemical analysis of kidney function, inflammation, fibrosis, cardiovascular stress and congestion differentiated between ADHF and non-cardiac dyspnea. Apart from indices of LV systolic function, HFPEF and HFREF patients presented similar echocardiographic alterations at admission, including comparable RV dysfunction (TAPSE 17 mm [14-20] and 17 mm [15-21] respectively, p > 0.05) and comparable signs of hemodynamic congestion (enlarged inferior vena cava and right atrium), except for a larger left atrium in HFREF (29 ± 8 cm2) compared to HFPEF (25 ± 7 cm2; p = 0.015). HFPEF and HFREF had similarly elevated plasma levels of MR-proANP and sCD146 that were both associated with poor outcome. Furthermore, HFPEF and HFREF had similar impairment of eGFR though parameters of congestion associated with kidney dysfunction in HFREF (eGFR and surface right atrium: r = -0.5474; p = 0.0428 ; eGFR and IVC diameter: r = -0.559 ; p = 0.0016), yet not in HFPEF (eGFR and surface right atrium: r = -0.132 ; p = 0.6274 ; eGFR and IVC diameter: r= 0.034 ; p = 0.8557).
Conclusion: In acute conditions, HFPEF and HFREF presented in a comparable state of hemodynamic congestion, with similarly altered RV and kidney function. The circulating biomarkers MR-proANP and sCD146 were reliable markers of global congestion as well as one-year prognosis in ADHF.

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True worsening renal function identifies patients with acute heart failure with an ominous outcome

M Sokolski[1]; R Zymlinski[2]; J Biegus[1]; P Siwolowski[2]; S Nawrocka-Millward[2]; JM Krzysztofik[1]; EA Jankowka[3]; W Banasiak[2]; P Ponikowski[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland; *[2]Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland*; *[3]Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland*

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Background: Recent studies in acute heart failure (AHF) challenge a traditional approach connecting every rise in creatinine level with kidney injury/dysfunction and further unfavorable consequences. We apply the new definition of worsening renal function (WRF) linking the changes in serum creatinine with clinical status of the patients.
Purpose: The aim of the study was to characterize prevalence, determinants and prognostic significance of true WRF in AHF.
Methods: In 266 patients (mean age: 67 ± 12 years, 71% men), admitted with AHF, serum levels of creatinine were measured at baseline, day 2, and day 3. Patients who developed WRF (an increase of ≥0.3 mg/dL in serum creatinine or a >25% decrease in the estimated glomerular filtration rate from the baseline value during the first 3 days of hospitalization) were differentiated into those with true WRF (presence of deterioration or no improvement in clinical status during first 3 days) vs. pseudo-WRF (improvement in clinical status).
Results: True WRF and pseudo-WRF occurred in 11 (4%) and in 27 (10%) patients, respectively whereas remaining 228 (86%) patients did not develop WRF. At admission, those with true WRF had more often peripheral oedema (91 vs. 44 vs. 62 %), ascites (36 vs. 4 vs. 18 %), lower ejection fraction (36 ± 16 vs. 43 ± 11 vs. 34 ± 14 %), lower haemoglobin (11.6 ± 1.4 vs. 13.5 ± 2.2 vs. 13.1 ± 1.9 g/dL),lower albumins (3.6 ± 0.4 vs. 4.0 ± 0.4 vs. 3.8 ± 0.7 mg/dL), higher bilirubin (1.6 [0.7-2.3] vs. 0.9 [0.7-1.4] vs. 1.4 [0.8-2.4] mg/dL) and higher concentration of C-reactive protein (29 [19-42] vs. 5 [3-26] vs. 13 [6-33] mg/L) (true WRF vs. pseudo-WRF vs. without WRF, all P<0.05). Regarding treatment before hospitalization and at admission there were no significant differences between groups. During 1-year follow-up all-cause mortality was significantly higher in patients with true WRF (82%) compared to patients

with pseudo-WRF (11%) and those without WRF (27%), P=.00005. The occurrence of true WRF was an independent predictor of all-cause mortality (hazard ratio [95% confidence interval]: 4.43 [2.09-9.42], P=0.00012).
Conclusions: In patients with AHF, only true WRF identifies those with extremely high risk of death whereas development pseudo-WRF does not affect long-term outcome.

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Functional mitral regurgitation predicts short-term adverse events in acute heart failure patients with reduced left ventricular ejection fraction

R De La Espriella Juan[1]; ES Enrique Santas[2]; GM Gema Minana[2]; AM Anna Mollar[2]; EV Ernesto Valero[2]; SGB Sergio Garcia-Blas[2]; JS Juan Sanchis[2]; SM Salvador Morell[1]; JN Julio Nunez[2]
[1]University General Hospital of Valencia, Department of Cardiology, Valencia, Spain; *[2]University Hospital Clinic of Valencia, Cardiology, Valencia, Spain*

Background: Functional mitral regurgitation (FMR) is a common finding among patients with acute heart failure (AHF) and reduced left ventricle systolic function (rLVSF). However, the short-term prognostic impact of FMR at discharge in AHF remains unclear. We aimed to evaluate the association between the severity of FMR and short-term adverse outcomes following a hospitalization for AHF.
Methods: We prospectively included 1180 consecutive patients with rLVSF discharged with a diagnosis of AHF. Of these, 242 patients (20.4%) with organic mitral valve disease, congenital heart disease or aortic valve disease were excluded, leaving the study sample in 938 patients. FMR was assessed semi-quantitatively by colour Doppler analysis of the regurgitant jet area and its severity categorized as: a) none or mild (grade 0-I), b) moderate (grade II) or severe (grade III or IV). The primary end-point was the composite of all-cause mortality and rehospitalization at 90 days. Multivariate analyses were performed using Cox proportional hazards models.
Results: At discharge, 533 (56.8%), 253 (26.9%) and 152 (16.2%) patients showed none-mild, moderate and severe FMR. At 90-day follow-up, 161 patients (17.2%) either died (49 patients) or were readmitted (112 patients). Rates of the composite endpoint were higher for patients with moderate and severe FMR as is shown in figure below. After multivariable adjustment, compared to patients with none or mild FMR, those with moderate and severe FMR had a significantly higher risk of reaching the endpoint [(HR=1.50; 95% CI: 1.04 – 2.17; p = 0.027 and HR=1.63; 95% CI: 1.07 – 2.48; p = 0.023, respectively].
Conclusion: FMR is a dynamic condition among patients with AHF and rLVSF. According to our results, more than mild FMR present at discharge identify a subgroup of higher risk of adverse clinical outcomes at short-term.

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High serum bilirubin is associated with short-term mortality following a myocardial infarction complicated by heart failure and/or left ventricular systolic dysfunction

Z Frikha[1]; JP Ferreira[1]; E Bozec[1]; JJ Mcmurray[2]; B Pitt[3]; K Dickstein[4]; P Rossignol[1]; F Zannad[1]; N Girerd[1]
[1]INSERM, Centre d'Investigations Cliniques 9501, Université de Lorraine, CHU de Nancy, Institut Lorrain du cœur et des vaisseaux, Nancy, France and INI-CRCT F-CRIN Network, Vandoeuvre-les-Nancy, France; *[2]University of Glasgow, BHF Cardiovascular Research Centre, Glasgow, United Kingdom*; *[3]University of Michigan, School of Medicine, Ann Arbor, United States of America*; *[4]Stavanger University Hospital, Department of Cardiology, Stavanger, Norway*

Objectives: Higher serum bilirubin has been associated with poorer prognosis in patients with heart failure (HF). We examined the association between serum bilirubin and clinical outcomes in patients with clinical signs of HF and/or left ventricular systolic dysfunction following acute myocardial infarction (MI).
Methods: 7467 patients from the High-Risk MI Database Initiative (which merged the datasets of the CAPRICORN, EPHESUS, OPTIMAAL and VALIANT trials) with an available baseline total bilirubin concentration were studied. The association between baseline bilirubin concentration and cardiovascular mortality, hospitalization for HF and all-cause mortality was assessed using Cox proportional hazards models.
Results: The mean baseline total bilirubin concentration was 12 ± 7 μmol/l and was above the normal range (>17.1 μmol/l) 1053 (14.1%) patients. In multivariable analysis, with adjustment for baseline characteristics (demographic, co-morbidity, Killip score, left ventricular ejection fraction and laboratory variables), patients with bilirubin >17.1 μmol/l were at significantly higher risk for 90-day cardiovascular mortality (HR=1.45, CI=1.14–1.86, p = 0.003), cardiovascular mortality or hospitalization for HF (HR=1.26, CI=1.05–1.51, p = 0.02) and all-cause mortality (HR=1.51, CI=1.20-1.91, p < 0.001). The addition of bilirubin in the survival model was associated with a significant improvement in reclassification to predict cardiovascular mortality (continuous net reclassification improvement=6.4%, CI=0.7%-9.6%, p = 0.04).
Conclusions: In MI patients complicated with HF and/or systolic dysfunction, bilirubin concentration is an independent predictor of mortality and improves risk stratification. This low-cost routinely available biomarker may improve risk assessment in this population.

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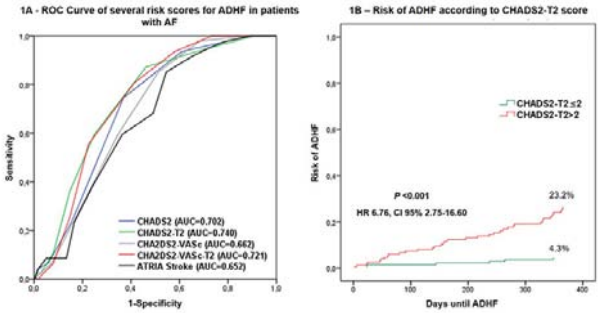
CHADS2-T2 - a new risk score to predict acute decompensated heart failure in patients with atrial fibrillation

J B Augusto[1]; M Borges Dos Santos[1]; D Roque[1]; D Faria[1]; H Ferreira[1]; J Urzal[1]; C Santos[2]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal; *[2]Hospital Santo Andre, Leiria, Portugal*

Background: Atrial fibrillation (AF) is a frequent comorbidity in patients with heart failure (HF). Currently, there are several tools for prediction of acute decompensated heart failure (ADHF).
Purpose: We aimed to evaluate the prognostic value of two new scores (CHADS2-T2 and CHA2DS2-VASc-T2) based on well-known AF stroke risk scores, in the prediction of ADHF in patients with AF at 12-month follow-up.
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. We evaluated medical charts in order to calculate AF stroke scores at discharge: CHADS2, CHA2DS2-VASc and ATRIA Stroke. We added 2 points if there was a documented troponin I exceeding the 99th percentile of the reference population: CHADS2-T2 and CHA2DS2-VASc-T2. Primary outcome was the incidence of ADHF 12 months after discharge.
Results: We included 348 patients who were successfully discharged and who had at least one troponin I measurement during hospital admission (mean age of 71.8 ± 0.7 years, 39.4% males). In receiver-operating characteristic (ROC) analysis (Figure 1A), CHADS2-T2 score performed better than other scores in predicting ADHF (CHADS2 – c-index 0.702, p < 0.001; CHADS2-T2 – c-index 0.740, p < 0.001; CHA2DS2-VASc – c-index 0.662, p = 0.001; CHA2DS2-VASc-T2 – c-index 0.721, p < 0.001; ATRIA Stroke – c-index 0.652, p = 0.002). A CHADS2-T2>2 (Figure 1B) had a sensitivity of 85.7% (CI 95%: 71.5-94.6%) and a specificity of 53.0% (CI 95% 46.6-59.3%) for prediction of ADHF at 12-month follow-up.
Conclusions: The new CHADS2-T2 score is an easy and simple tool with high sensitivity, which can predict the risk of ADHF in patients with AF.



Scores and Risk of ADHF

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Prognostic impact of right ventricular function in acute heart failure

C Daneluzzi[1]; D Stolfo[1]; M Merlo[1]; C Faggioli[1]; G Barbati[1]; A Scagnetto[1]; V De Paris[1]; P Lesizza[1]; S Albani[1]; P Gentile[1]; J Cristallini[1]; B Ortis[1]; S Franco[1]; A Di Lenarda[1]; G Sinagra[1]
[1]University Hospital Riuniti, Cardiovascular department, Trieste, Italy

Background: Acute decompensated heart failure (ADHF) is a major health problem worldwide. Prognostic stratification in the acute phase remains challenging despite several scores combining demographic, clinical and laboratory parameters have been proposed. Left ventricular (LV) systolic function is not generally a major determinant of outcome and in large registries the prognosis did not clearly diverged among patients with reduced or preserved ejection fraction (EF). On the other hand, right ventricular (RV) function is emerging as a strong outcome predictor in chronic HF but was not previously evaluated in ADHF setting.

Purpose: In the present study we sought to evaluate the impact of RV dysfunction on 2-years survival in a large cohort of patients admitted for ADHF and to assess the short-term in-hospital evolution of RV function after appropriate treatment.
Methods: We retrospectively screened all consecutive patients admitted for ADHF in our Department from January 2009 to December 2014. RV systolic function was assessed on echocardiography <24 h from admission and at discharge (median time 8 days). RV dysfunction was defined by a TAPSE $<$ 16 mm and/or a RV fractional area change $<35\%$. The primary endpoint was 2-years all-cause mortality.
Results: Globally, 560 patients with available RV function assessment were included. Mean age was 69 ± 12 years, 70% were males and 49% were ischaemic. Mean systolic blood pressure (SBP) at admission was 128 ± 26 mmHg, mean creatinine and median BNP values were respectively 1.36 ± 0.64 mg/dl and 776 (95% CI 707-845) pg/ml. RV function was impaired in 241 patients (43% of the overall cohort). In these patients non-ischaemic etiology of HF was more frequent (54% vs 41% of ischaemic, $p < 0.002$). They were younger (age 66 ± 14 years vs 72 ± 10, $p < 0{,}001$) with a lower rate of comorbidities. SBP at presentation was lower (120 ± 23 vs 133 ± 27 mmHg, $p < 0.001$). RV dysfunction was more frequent among patients with reduced LVEF (56%) compared to patients with mid-range EF (20%) and preserved EF (31%). 2-years survival was similar among ranges of LVEF (EF $<40\%$ vs EF 40-49% vs EF>50%, p>0.05), instead patients with RV dysfunction exhibited a worst outcome (2-years mortality 52% vs 40% in patients with preserved RV function, $p < 0.01$). Finally, at a median time of 8 days, RV function was reassessed in 479 patients showing a normalization after therapy in 46 % of patients.
Conclusions: In ADHF right ventricular function rather than LV ejection fraction showed an impact on prognosis. Larger prospective studies are needed to confirm our preliminary data and to assess the effect of targeted supportive therapy for RV function in this specific setting.

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Early post-discharge ST2 and NTproBNP for predicting 30-day heart failure readmission in a very old and co-morbid population with predominantly HFpEF

C Pacho[1]; M Domingo[1]; R Nunez[1]; J Lupon[1]; E Revuelta[2]; J Barallat[1]; P Moliner[1]; B Gonzalez[1]; M Rodriguez[1]; C Rivas[1]; V Diaz[1]; J Santesmases[1]; M De Antonio[1]; J Tor[1]; A Bayes-Genis[1]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; *[2]Health Research Institute Germans Trias, Badalona, Spain*

Background: Heart failure (HF) is associated with a high rate of readmissions within 30 days post-discharge. This figure is even higher in the old and co-morbid patients, mainly affected from HFpEF. Attempts to predict short-term outcome in such population have not been particularly successful. Data on biomarkers in such especial population are scarce.

Purpose: To assess the usefulness for predicting 30-day outcome of early post-discharge blood levels of ST2 and NTproBNP in a very old and co-morbid HF population.
Methods: Blood sample were obtained at first visit in the specific HF-Clinic shortly after discharge from a HF-related hospitalization (mean 4.9 ± 2 days). HF-related rehospitalization and the composite end-point all-cause mortality or HF-related rehospitalization were the primary end-points.
Results: 522 patients (57.1% women, mean age 82 ± 8.7 years, 25% older than 88 years) were included. Mean LVEF (available in 390 patients) was $58.8\% \pm 14$. Main aetiologies were: hypertensive (40%), ischemic (29%) and valvular (13%). Diabetes, anaemia and renal failure were present in 53%, 65% and 79% respectively. Mean Barthel index was 70 ± 25 and mean Charlson index was 5.6 ± 2.2. 30-days HF-related re-hospitalization occurred in 36 patients (6.9%), death in 13 (2.5%) and the composite end-point in 45 (8.6%). In the univariate analyses urea ($p < 0.05$), diabetes ($p = 0.006$), Charlson index ($p = 0.001$) and ST2 ($p = 0.002$) were associated with 30-days HF-related rehospitalization, and NTproBNP showed borderline results ($p = 0.07$); whereas diabetes ($p = 0.01$), urea ($p = 0.04$), Barthel index ($p = 0.01$), Charlson index ($p < 0.001$), NTproBNP ($p = 0.001$), and ST2 ($p < 0.001$) were associated with the composite end-point. In the multivariable analyses female sex (OR 2.24 [1.03-4.82], $p = 0.04$), Charlson index (OR 1.27 [1.08-1.48], $p = 0.004$), and ST2 (OR 1.41 [1.03-1.93], $p = 0.03$) were the only independent variables associated with 30-days HF-retated rehospitalization and also with the composite end-point (female sex OR 2.22 [1.11-4.43], $p = 0.02$, Charlson index OR 1.30 [1.12-1.50], $p < 0.001$, and ST2 OR 1.60 [1.20-2.13], $p = 0.001$). The clinical model including age, sex, diabetis, urea, and Charlson index obtained an AUC of 0.67 [95%CI 0.58-0.76] for the risk prediction of HF-related rehospitalization. Adding NTproBNP, ST2 or both biomarkers, the results were 0.71, 0.72 and 0.73 respectively. For the risk prediction of the composite end-point the clinical model including the same variables plus Barthel index obtained an AUC of 0.69. Adding NTproBNP, ST2 or both biomarkers, the results were 0.73, 0.73 and 0.75 respectively.
Conclusions: In a very old and co-morbid population with mainly HFpEF,early post-discharge ST2 performed better than NTproBNP for the risk prediction of 30-days HF-related rehospitalization and for the composite end-point including all-cause mortality. The inclusion of both biomarker in a predictive model improve C-statistics for both end-points.

POSTER SESSION 2

ACUTE HEART FAILURE

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Immune-mediated inflammation and acute left ventricular failure in myocardial infarction

AR Aida Babaeva[1]; AA Tarasov[1]; SI Davydov[1]; MA Gordeeva[1]; AL Emelyanova[1]
[1]*Volgograd State Medical University, Volgograd, Russian Federation*;

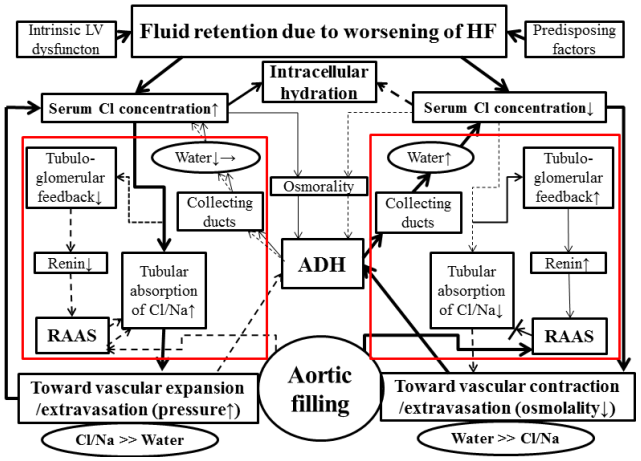
Background: Myocardial infarction (MI) is the commonest cause of acute left ventricular failure (ALVF) and cardiogenic shock. Our previous studies have revealed dramatically elevated levels of circulating pro-inflammatory cytokines and anti-connective tissue antibodies in MI patients.
Purpose: of this investigation was to assess the relationship between circulating markers of immune-mediated inflammation and ALVF in the setting of MI.
Methods: 215 pts with determined MI were included in the investigation. ALVF was diagnosed in 32 (14.88%) pts on the basis of the clinical and echocardiography data. The levels of pro-inflammatory cytokines (TNFα, IL1β, IL6) and anti-connective tissue antibodies (ACTA): antibodies against collagen (ACA), hyaluronic acid (AHA) and chondroitin sulfate (ACSA) were measured by ELISA in sera samples from MI pts and 50 controls.
Results: The serum levels of TNFα, IL1β, IL6, ACA, AHA and ACSA were significantly higher in MI pts than in controls. The most prominent abnormalities were revealed in STEMI complicated by ALVF, especially in cardiogenic shock and in pulmonary edema. There were significant differences between mean levels of key pro-inflammatory cytokines and ACTA in MI groups with ALVF and without one. Moreover the strong correlation was determined between hemodynamic abnormalities according to Killip's classes and levels of IL6 and AHA (r=0.78, 0.72 respectively). Moderate correlation was found between Killip's classes on the one hand and TNFα, IL1β, ACA on the other hand (r=0.56, 0.59, 0.62 respectively).
Conclusion: Obtained data show that ALVF in MI is associated with dramatically increased levels of key pro-inflammatory cytokines and ACTA. This phenomenon can be concerned as reflection of the severity of myocardial damage in MI. Assessment of the serum pro-inflammatory cytokines and anti-connective tissue antibodies can be used for diagnostic and prognostic purposes.

P897

The chloride theory, a unifying hypothesis for renal handling and body fluid distribution in heart failure pathophysiology

H Hajime Kataoka[1]
[1]*Nishida Hospital, Oita, Japan*

Background– A unifying hypothesis for heart failure (HF) pathophysiology based on serum biochemical solute(s) has yet not been developed.
Purpose: Chloride is an established key electrolyte for tubuloglomerular feedback and subsequent body fluid reabsorption in the kidney. Elucidation of the involvement of chloride in body fluid distribution under transition of HF status will contribute to the development of a unifying hypothesis of HF pathophysiology.
Methods: Data from 47 HF patients that experienced worsening and subsequent recovery of HF were analyzed. Blood tests included peripheral blood and serum albumin/solutes (sodium/potassium/chloride/urea nitrogen/creatinine). Relative change in the plasma volume (%PV) was determined by the Strauss method based on changes in the hemoglobin and hematocrit.
Results: (1) Worsening HF–When divided into two groups based on the median %PV, the clinical features of the expansion group (%PV [range 11%-36%]; n=24) included a lower incidence of crackles (13 vs 52%,p = 0.005) and a tendency toward preserved renal function defined by a decrease in serum creatinine (83% vs 57%,p = 0.06) in comparison with the non-expansion group (%PV [range -19% to 10.8%]; n=23). Multivariate logistic regression analysis revealed an independent association between the increase in %PV and the increase in the serum chloride concentration from stability to worsening HF (OR:12.5, 95%CI:1.89-82, p = 0.009). (2) Recovery after HF therapy–Multivariate regression analysis demonstrated an independent association between preserved %PV and an increased or preserved serum chloride concentration after conventional diuretic therapy (OR:8.71, 95%CI:1.20-63.0, p = 0.032).
Conclusions: The present study propose a unifying hypothesis of HF pathophysiology based on the "chloride theory" (Figure). This hypothesis is the first to unify the two main platforms of the body fluid-processing organs through one key electrolyte, chloride, in both 1) the kidney, which reabsorbs body fluid via main control by the renin-angiotensin-aldosterone system, and 2) the body, an organ with dynamic body fluid storage in the intracellular, intravascular, and interstitial compartments.



Chloride theory for worsening HF

P898

Risk factors and outcomes of hospital-acquired heart failure in medical patients with no pre-existing cardiac dysfunction

V Kittipibul[1]; P Torvorapanit[1]; S Gonlachanvit[1]; A Ariyachaipanich[1]
[1]*Chulalongkorn University, Department of Medicine, Faculty of Medicine, Bangkok, Thailand*

Background: Heart failure (HF) is a common complication in hospitalized patients with known cardiac dysfunction and associated with higher mortality and longer hospital stay. Little is known about new-onset, hospital-acquired or iatrogenic HF in patients with no pre-existing cardiac dysfunction. This study aims to study risk factors, impacts of fluid balance, and outcomes of hospital-acquired HF in patients with no pre-existing cardiac dysfunction.
Methods: We conducted a case-control study by prospectively reviewing consecutive medical patients with no pre-existing cardiac dysfunction who developed new-onset HF during hospitalization for non-cardiac diagnoses from January 2015 to December 2015. Two control patients who have no pre-existing cardiac dysfunction were chosen per case with matched age, gender, and date of admission. When this was not possible, at least 1 control patient was selected. Patient characteristics, treatments, and outcomes were gathered. Chi-square test, T-test, and binary logistic regression were used for analysis.
Results: We identified 27 cases of hospital-acquired HF (mean age 64 ± 20 years and 67% female) with various primary diagnoses (52% infection, 28% cancer, 11%

gastrointestinal bleeding, and 11% pancreatitis) and 45 control patients (mean age 65 ± 17 years and 64% female). There was no significant difference in demographics, primary diagnoses, medications and laboratory values between 2 groups. Median time from admission to the onset of hospital-acquired HF was 3 (range 1 to 19) days. There were no differences in total fluid intake over 1, 3 and 7 days prior to onset of hospital-acquired HF between cases and controls (1,108 ± 226 ml vs 1,341 ± 202 ml; p = 0.229, 7,287 ± 2414 ml vs 7051 ± 3139 ml; p = 0.807 and 8261 ± 4282 ml vs 7,906 ± 6239 ml; p = 0.805, respectively). Positive fluid balance over 1, 3 and 7 days prior to onset of hospital-acquired HF were higher in a case cohort (1,755 ± 1260 ml vs 952 ± 1084 ml; p = 0.008, 4,294 ± 2535 ml vs 1635 ± 2402 ml; p = 0.003 and 4829 ± 2871 ml vs 943 ± 3358 ml; p < 0.001, respectively). Hospital-acquired HF was associated with increased use of urinary catheterization (30% vs 9%, p = 0.024), mechanical ventilation (22% vs 2%, p = 0.005) and prolong hospital stay (27 ± 22 days vs 20 ± 19 days, p = 0.013). There were 2 HF-related mortalities among case cohort.
Conclusion: Positive fluid balance, but not total fluid intake, is associated with developing of hospital-acquired HF in medical patients with no pre-existing cardiac dysfunction. Hospital- acquired HF can lead to morbidities such as the increased rate of urinary catheterization, mechanical ventilation, and prolonged hospitalization.

P899

Biological variation of extracellular matrix biomarkers in patients with stable chronic heart failure

T Tobias Taeger[1]; H Froehlich[1]; A Corletto[1]; HA Katus[1]; L Frankenstein[1]
[1]*University Hospital of Heidelberg, Department of Cardiology, Heidelberg, Germany*

Funding Acknowledgements: Thiw work was supported by a grant by novartis

Background: Extracellular matrix (ECM) biomarkers such as matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) are up-regulated in chronic heart failure (HF). Serial measurements of MMPs and TIMPs may be useful for therapy guidance and risk stratification of patients with CHF. However, interpretation of time-dependent changes requires knowledge about the biological variation of ECM biomarkers.
Methods: We performed measurements of MMP-2, MMP-9, TIMP-1, and TIMP-4 in 50 patients with chronic HF who met rigid criteria for clinical stability at 3-hour, 6-hour, 1-week and 2-week time intervals. In addition, clinical and haemodynamic assessment was performed at baseline, at 1-week and 2-week intervals. Haemodynamic variables were measured using inert gas rebreathing and impedance cardiography. Heart rhythm was monitored with external ECG event recorders throughout the complete study. Reference change values (RCVs) and minimal important differences (MIDs) were determined for MMP-2, MMP-9, TIMP-1, and TIMP-4.
Results: Clinical and haemodynamic variables were stable over time. Depending on the time-interval, RCVs ranged between 4.9% and 11.7% for MMP-2, 26.4% and 56.7% for MMP-9, 10.8% and 30.7% for TIMP-1, and 16.0% and 47.4% for TIMP-4, respectively. The MIDs varied between 43.38 and 65.22 ng/ml for MMP-2, 28.71 and 40.96 ng/ml for MMP-9, 52.32 and 156.07 ng/ml for TIMP-1, and 293.92 and 798.04 pg/ml for TIMP-4, respectively.
Conclusion: The biological variation of ECM biomarkers differs with respect to individual biomarkers and time intervals. MMP-2 may be most suitable for serial biomarker measurements, as the biological variation is low irrespective of the time interval between measurements.

P900

Clinical and analytical patterns and the different mechanisms of cardiorenal syndrome.

H De Barros Viegas[1]; P Freitas[1]; G Amaral Mendes[1]; B Lobao[1]; S Marques[1]
[1]*Hospital Center of Setúbal, Internal Medicine, Setúbal, Portugal*

Background/Introduction: In recent years new data on physiopathology of cardiorenal syndromes has been collected but the impact in acute management is still to be found.
Purpose: We tried to find different patterns using simple clinical and analytical data that could point to the main decompensated mechanism using a retrospective cohort sample of patients from a level 2 intermediate care unit. We also accessed the impact of Non-invasive ventilation (NIV), the need for ultrafiltration and a strategy of diuretic plus slight hydration on these different patterns.
Methods: We selected 110 patients with decompensation of heart or renal function but excluded 53 for not having cardiorenal syndrome or with acute type 5 (sepsis).
Results: We had 56,34% males with a mean age of 76,3 years, mostly type 1 76,74%, fewer type 3 20,93% and 1 case of type 2. 44,19% presented worst renal function at admission (less than 24 hours) and 37,21% after 3 to 5 days, this groups were statistically different. Mortality rate was 27,27%.
Conclusions: More data is being processed and validated but we have found a statistical difference at the time of worst renal function and this was not associated with the degree of basal chronic renal disease or the type of cardiorenal syndrome. It appears to be related with the degree of congestion and with the use of pulsed diuretic. The ones with worst renal function at admission appear to have a better diuresis in response to diuretic therapy. This finds suggest that the different mechanism of cardiorenal syndrome type 1 or 3 can make a difference in the initial approach in an acute setting and this data gives the basis for a much needed prospective study.

P901

Demographics, prognostic variables and clinical outcomes in patients with heart failure with mid range ejection fraction (HFmrEF)

J Jessica Webb[1]; J Draper[1]; T Teall[1]; E Bolca[1]; L Fovargue[2]; S Rivolo[2]; R Rajani[1]; S Piper[3]; A Mcdiarmid[1]; S Kapetanakis[1]; T Mcdonagh[3]; R Razavi[1]; G Carr-White[1]
[1]*St Thomas' Hospital, Cardiology Department, London, United Kingdom*; [2]*King's College London, Division of Imaging Sciences and Biomedical Engineering, London, United Kingdom*; [3]*King's College Hospital, Cardiology Department, London, United Kingdom*

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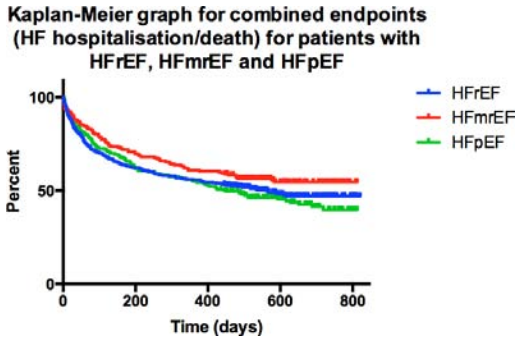
Background: In 2016 the ESC published updated guidelines for the diagnosis of patients with heart failure, introducing the category Heart Failure with mid-range Ejection Fraction (HFmrEF).
Aims: This study sought to define the demographics, prognostic variables and clinical outcomes in patients with HFmrEF from a large unselected population of heart failure patients admitted to a Tertiary Hospital in the United Kingdom.
Methods: 2077 consecutive patients over a 12 month period were screened for heart failure through our heart failure (HF) service and were followed up for a mean of 15.8 ± 8.7 months from September 2014 to September 2015. Patients were categorised as heart failure with preserved ejection fraction (HFpEF), HFmrEF and heart failure with reduced ejection fraction (HFrEF) according to the 2016 ESC guidelines. Echocardiography was used to determine LVEF and NTproBNP was measured at presentation. Patient demographics (age, gender, ethnicity), risk factors and outcome (time to HF hospitalisation or all cause death) were recorded.
Results: 632 patients with HF were identified (mean age 72.6 ± 15.4 years, 60% male). 136 patients were identified with LVEF 40-49%; with 87.1% satisfying ESC criteria for diagnosis of HFmrEF with evidence of diastolic dysfunction and/or structural heart disease. These patients with 'true' HFmrEF patients had lower plasma sodium levels (137.6 ± 3.5 v 142 ± 0.1, p < 0.05), higher MCV (91.9 ± 9.4 v 84.5 ± 9.2, p < 0.05) and were less likely to have coronary artery disease (40.8% v 68.8%, p < 0.05) than the 16 patients with HF, raised NTproBNP and LVEF 40-49% but no evidence of diastolic dysfunction and/or structural heart disease.
Demographics and prognostic markers differed by heart failure diagnosis. Compared to patients with HFrEF, patients with HFmrEF were older (70 ± 15.1 v 74.5 ± 13.3, p < 0.05) had lower NTproBNP (12,130.6 ± 16001.8 v 8796.7 ± 12,054.4, p < 0.05) and were more likely to be hypertensive (54.6% v 67.6%, p < 0.05) and/or have obstructive sleep apnoea (2.8% v 8.8%, p < 0.05). Whereas compared to HFpEF, HFmrEF patients were more likely male (42.3% v 52.2%, p < 0.05), less likely to be afrocaribbean (25.3% v 16.9%, p < 0.05), with higher NTproBNP (4670.7 ± 6960.9 v 8796.7 ± 12,054.4, p < 0.05) and fewer risk factors (3.7 ± 1.6 v 3 ± 1.6, p < 0.05).
Patients with HFmrEF had better clinical outcomes than both the HFpEF and HFrEF groups, with higher mortality in the HFrEF population and higher HF rehospitalisation rates in the HFpEF population.
Conclusions: HFmrEF accounted for 16.9% of all the symptomatic heart failure patients admitted from a large unselected population of heart failure patients. When defining patients' demographics, blood tests, risk factors, the HFmrEF population were statistically distinct from the HFrEF and HFpEF population. Patients with HFmrEF had better outcomes, compared to high rates of mortality seen in patients with HFrEF and high rates of HF hospitalisations seen in patients with HFpEF.



Kaplan-Meier graph

P902

Relationship between high admission glucose and in-hospital heart failure in patients with AMI

S Chimed[1]; B Khuyag[2]
[1]*Institute of Medical Sciences, Department of Cardiology, Ulaanbaatar, Mongolia*;
[2]*The State Third Central Hospital, Coronary Care Unit, Ulaanbaatar, Mongolia*

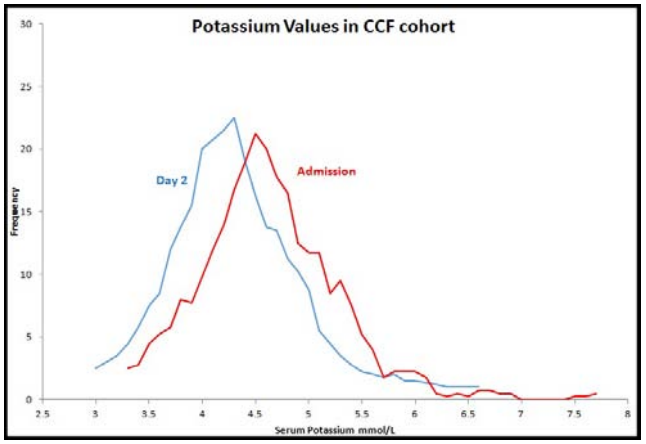
Background: Patients with acute myocardial infarction (AMI) often had high admission glucose, regardless previous history of diabetes mellitus (DM). Previous studies demonstrated that hyperglycemia in patients AMI is associated with adverse outcomes.
Aims: In this study, we aimed to reveal relationship between high admission gluocse and in-hospital heart failure (HF) in patients with AMI.
Material and methods: Patients with AMI who treated by primary PCI were prospectively selected. Plasma glucose level is measured on admission in all patients. Hyperglycemia was defined as admission plasma glucose ≥11.1 mmol/l. In-hospital HF was defined according to the Killip classification. Multiple logistic regression analysis was used to assess relationship between admission glucose level and in-hospital HF.
Results: A total of 428 patients (59 ± 13, 84% male) were included in this study. 122 patients had high plasma glucose (≥11.1 mmol/l) on admission and classified as a hyperglycemia. 306 patients had normal plasma glucose (< 11.1mmol/l) on admission and classified as a normoglycemia. Occurrence of in-hospital HF was significantly higher in patients with hyperglycemia compared with normoglycemia (30% vs. 21%, $p < 0.05$). In multivariable logistic regression analysis was showed that admission glucose level is independently associated with in-hospital HF after adjustment of age, gender, hypertension, previous myocardial infarction, previous heart failure, previous coronary artery disease, chronic kidney disease, heart rate, multivessel disease, LAD culprit vessel and final TIMI flow grade in non-diabetic patients (OR 1.10, 95% CI 1.02-1.18, $p < 0.01$). Furthermore, univariable logistic regression analysis revealed that every 1 unit increase of admission glucose level is associated with 1.07 fold increased probability of in-hospital HF (OR 1.07, 95% CI 1.01-1.15, $p < 0.05$) in non-diabetic patients.
Conclusion: Our results suggest that admission glucose level was independent predictor of in-hospital HF in patients with AMI. However, this relationship is only evident for non-diabetic patients.

P903

Is hypokalaemia during acute exacerbations of heart failure preventable or predictable?

D Daniel O'hare[1]; C O'connor[1]; Z Coyne[1]; G Balan[1]; C Macsweeney[1]; K Tuite[1]; J Fay[1]; R Murphy[1]; C Daly[1]
[1]*St James Hospital, Dublin, Ireland*

Background: Heart failure activates the renin-angiotensin aldosterone system, which leads to hypokalaemia. This is aggravated by upregulated sympathetic drive and the use of increased amounts non-potassium sparing diuretics during acute exacerbations. Mild hypokalaemia has been shown to increase cardiovascular events in a treated heart failure population. In patients with NYHA class I to III patients, elevations of serum potassium have been shown to reduce the incidence of fatal arrhythmias and sudden cardiac death. There is growing evidence that serum potassium levels should be maintained above 4 mmol/l in heart failure patients.
Methods: We performed a retrospective review of all patients admitted to a tertiary refferal centre during a one year period from 1st January 2015 to 31st December 2015, with a principal diagnosis of congestive cardiac failure. A total of 330 patients were included. Blood results on admission, 24 hours and the final result prior to discharge were included for analysis.
Results: On admission, 67 (22%) of the 309 patients with admission bloods had a serum potassium value of less than 4.0 mmol/l. Of the sub-group of patients that had bloods taken at both admission and 24 hours, ($n = 287$) the percentage of patients with a serum potassium less than 4.0 mmol/l at 24 hours significantly increased from 21% to 36% ($p < 0.001$).
The average serum potassium of all patients fell significantly during the first 24 hours from 4.44 mmol/L to 4.17 mmol/l ($p < 0.0001$). This resulted in significantly more patients (11% vs 5%) with a potassium value of less than 3.5mmol/l after 24 hours. ($p < 0.001$)
Patients who had a serum potassium of less 3.5mmol/l after 24 hours had a significantly lower serum magnesium on admission than the patients whose 24 hour potassium result was within the normal range. (0.71 mmol/L vs 0.81 mmol/L, $p < 0.001$)
Of the patients surviving to discharge, over 33% were discharged with serum potassium values less than 4.0mmol/l.
Conclusion: Our results demonstrate that a significant number of patients with heart failure have lower than desirable serum potassium levels on admission, through their inpatient stay and on discharge. Within a cohort of patients hospitalised for exacerbations of heart failure, serum potassium levels fall during the first 24 hours. There is a significant correlation between hypomagnesaemia on admission and the prediction of hypokalaemia 24 hours later. Hypokalaemia has been shown to be an independent predictor of mortality in heart failure. This study highlights the importance of close monitoring of serum potassium levels early in the admission, and suggests that identification of hypomagnesaemia can predict hypokalaemia at 24 hours. The authors advise early consideration of aldosterone antagonists or potassium replacement in these patients.



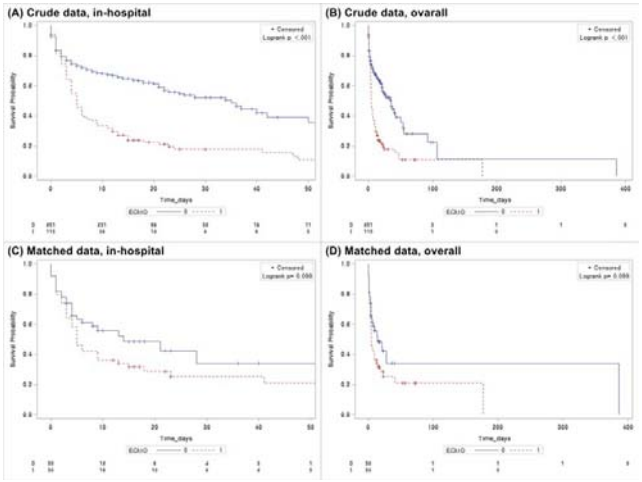
Visual representation of potassium trend

P904

Role of extracorporeal membrane oxygenation in acute myocardial infarction complicated by cardiogenic shock

H W Lee[1]; JW Park[1]; JH Ahn[1]; JS Park[1]; JH Oh[1]; JH Choi[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]; JC Choi[1]; SH Lee[1]; DY Kim[1]; JY Shin[1]
[1]*Pusan National University Hospital, Department of Cardiology, Busan, Korea Republic of*

Purpose: The role of extracorporeal membrane oxygenation (ECMO) in refractory cardiogenic shock is increasing. Among the various roles, temporary support for myocardial stunning during the peri-myocardial infarction (MI) period is of utmost importance. We evaluated the role of ECMO in such patients.
Methods: Of 11,974 acute MI cases between March 2006 and December 2014 from the Korea Acute Myocardial Infarction Registry, 1,022 patients (8.5%) were complicated with cardiogenic shock (CS) during index hospitalization. Of 766 CS patients with available data, 115 (15%) were in the ECMO group and 651 (85%) were in the NO-ECMO group. Clinical outcomes were survival analysis, and complications during hospitalization. We evaluated both crude- and propensity-matched cohorts. Cox regression analysis evaluated the factors associated with long-term mortality. Results: Patients in the ECMO group were younger, had lower initial mean BP, larger infarct size, and more left-sided coronary artery disease as the target vessel. Crude- and propensity-matched data showed significantly higher major and minor bleeding complications. However, there were no statistical differences in in-hospital and long-term survival between the ECMO and NO-ECMO groups in propensity-matched data. Cox regression analysis revealed that ECMO application was not a significant predictor for mortality (hazard ratio 1.505; 95% confidence interval 0.907-2.498; $p = 0.11$). Conclusions: ECMO application did not affect survival in this study population in spite of increased bleeding risk. Early ECMO application was associated with increased survival.



Clinical outcomes

P905

Outcomes of VA ECMO in cardiogenic shock - Bridging to recovery, ventricular assist device and transplantation

S Jaamaa-Holmberg[1]; B Salmela[1]; R Suojaranta-Ylinen[2]; K Lemstrom[1]; J Lommi[1]
[1]Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland; *[2]Helsinki University Central Hospital, Anesthesiology and Intensive Care, Helsinki, Finland*

Funding Acknowledgements: The Finnish Medical Foundation, Governmental grant for research in health/ Helsinki University Hospital, Heart and Lung Center

Background: The use of venoarterial extracorporeal membrane oxygenation (VA ECMO) in refractory cardiogenic shock have expanded rapidly during the last years. Data on its´ benefit in patient subgroups is though still limited.
Purpose: To evaluate the outcome and prognostic factors for ECMO in cardiogenic shock.
Methods: Retrospective analysis of 142 consecutive VA ECMOs in a transplant center in 2007-2016.
Results: Mean age was 51.4 years (SD 12.2), 70% were men, and 92% Intermacs profile 1. Mean duration of ECMO was 7.5 days (SD 6.8) and of ICU stay 21.1 days (SD 22.2). The most frequent indications for ECMO were postcardiotomy shock (26%), acute coronary syndrome (ACS) (23%), cardiomyopathy (18%), primary graft failure (17%), and fulminant myocarditis (11%). In total, 30-day survival was 72%, hospital discharge rate 63% and one year survival 61%. Hospital discharge rates according to indication of ECMO were: myocarditis 81%, cardiomyopathy 75%, postcardiotomy shock 65%, primary graft failure 58% and ACS 50%. 75 (53%) patients were weaned from ECMO with no need to further procedures, 13 (9%) received ventricular assist device (VAD) from ECMO, and 15 (11%) underwent emergency heart transplantation (HTx). Survival rates to hospital discharge for these groups were 87%, 77% and 93%, respectively. For patients bridged with ECMO to VAD, the most frequent diagnosis was cardiomyopathy (54%) while for patients bridged to HTx, cardiomyopathy and myocarditis were equally common, both 27%. 39 (27%) patients died during ECMO, of which 23 (62%) had been resuscitated prior to ECMO.
There was no significant difference in age (50.0 vs 53.1 years, $p = 0.12$), body mass index (27.8 vs 28.1, $p = 0.86$), gender ($p = 0.79$), or duration of ECMO (7.3 vs 7.8 days, $p = 0.71$) between hospital survivors and non-survivors. The amount of red blood cells (RBC) transfused during the ICU stay was significantly higher for non-survivors (mean 6.2 units/day vs 1.4 units/day, $p < 0.001$) than for hospital survivors. Cardiac arrest prior to ECMO implantation ($n = 49$; OR 3.2, $p < 0.01$), initiation of ECMO or emergency perfusion followed by ECMO during resuscitation ($n = 29$; OR 3.7, $p < 0.01$), lower blood HCO3 prior to ECMO (15.0 vs 18.2 mmol/liter, $p < 0.001$) and higher blood lactate (9.8 vs 6.1 mmol/liter, $p < 0.001$) associated with increased hospital mortality. Most frequent complications were stroke (16%), limb ischemia (13%) and need of fasciotomy (8%). Simultaneous use of intra-aortic balloon pump associated with increased risk of lower limb ischemia (OR 3.2, $p < 0.05$).
Conclusions: ECMO can enable recovery to hospital discharge for over 60% of selected patients with severe cardiogenic shock. In our cohort, ECMO benefitted most the patients with myocarditis or cardiomyopathy, both as a bridge to recovery of heart and as a bridge to VAD or HTx. Cardiac arrest, ECMO implantation during resuscitation and need of high amounts of RBCs transfused associated with increased risk of hospital death.

P906

Acute heart failure in the real world: are elderly patients managed in accordance to current guidelines? Data from the ATHENA registry

A Pratesi[1]; S Baldasseroni[1]; S Parlapiano[1]; A Herbst[1]; A Berni[2]; G Ciuti[2]; AC Baroncini[1]; C Ghiara[1]; G Baglioni[1]; L Poggesi[2]; A Moggi Pignone[2]; L Gabbani[1]; C Nozzoli[2]; N Marchionni[3]; F Orso[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

Background: Heart failure (HF) has a high prevalence in the elderly. Adherence to HF guidelines improves prognosis and is very high in randomised clinical trials (RCTs), it also seems to be quite high in clinical registries which represent the so-called "real world". However, HF registries may maintain a certain level of selection bias by including only patients hospitalised in cardiology wards while administrative data show that the majority of HF patients are admitted to internal medicine and geriatrics wards where adherence to guidelines could be less optimal.
Purpose: to compare adherence to current clinical guidelines in the management of elderly patients hospitalised for acute HF in differnt settings of care: cardiology, internal medicine and geriatrics.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of acute HF to the emergency department (ED) of a tertiary University teaching-hospital and transferred to the above described settings of care. We evaluated adherence to current European Society of Cardiology (ESC) guidelines regarding echocardiogram performance during hospitalisation, body weight measurement on admission and at discharge, follow-up (FU) schedule and evidence based prescriptions at discharge.
Results: 342 patients composed the study population; 17.8% were hospitalised in cardiology, 17.3% in geriatrics and 64.9% in internal medicine. Mean age was 83.7 years, females were 54.1%. 28.1% of the patients had not performed any echocardiographic evaluation during hospitalization: 3.3% in cardiology, 17% in geriatrics and 37.8% in internal medicine ($P < 0.001$). Body weight measurement on admission and at discharge was collected only in 24% of patients and in 44% of patients no information regarding body weight measurement was collected during hospitalisation (1.6% in cardiology, 41.4% in internal medicine and 54.2% in geriatrics; $p < 0.001$). We analysed evidence based prescription rates at discharge in the subgroup of patients with HF with reduced ejection fraction (HFrEF, 49% the total population) for beta-blockers, ACE-inhibitors, angiotensin receptor blockers and mineralocorticoid receptor antagonists that were 81,3% 39,6%, 23,1% and 48,4%, respectively, without significant differences across the considered settings of care. A clinical FU at the discharge was scheduled only in 16.0% of the total study population, 70.0% in cardiology, 7.0% in geriatrics and in 5.0% of those discharged from internal medicine (P=0.001).
Conclusions: in elderly patients hospitalised for acute HF a low adherence to current international guidelines recommendations regarding HF management could be observed particularly in patients hospitalised in non-cardiological settings. This was particularly evident for non-pharmacological strategies that are known to reduce the risk of rehospitalisation.

P907

Protocol of the IMPACT-study: Improve Management of Heart Failure with Procalcitonin

M Mockel[1]; A Anna Slagman[1]; J Searle[1]; S Ebmeyer[2]; J C Wiemer[2]; J O Vollert[2]; A Maisel[3]
[1]Charite - Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany; *[2]Thermo Fisher Scientific, Global Medical Affairs, Hennigsdorf, Germany*; *[3]University of California San Diego, Division of Cardiovascular Medicine, San Diego, United States of America*

Background: Patients with acute HF and pulmonary infections are not uncommon in the acute health care setting and often present with overlapping signs and symptoms. Procalcitonin (PCT), is a precursor protein of the hormone calcitonin, consisting of 116 amino acids. Procalcitonin blood levels reflect the presence and severity of bacterial infection.
Purpose: To evaluate an advantage of PCT guided antibiotic treatment over established treatment practice with respect to 90-day all-cause mortality.
Methods: The IMPACT study is a prospective, multicentre, randomized-controlled, interventional biomarker study. In patients randomized to the intervention group, antibiotic therapy is guided by PCT-measurements on day 0 and day 1 (figure 1).
Expected study results: 792 patients (396 per group) are planned. The study employs an adaptive design. An interim analysis is conducted to allow for sample size adaptation. At this point in time, the sample size for this study is estimated based on a difference in 90 day mortality between the groups of 7% (11% PCT guided vs. 18% standard care). This effect size was estimated by applying stratified

Cox models to BACH study data. Based on a two-sided chi-square test for two independent proportions 396 subjects per study arm would be sufficient to detect this difference with a power of 80% at an alpha level of 5% in a study design with fixed sample size. The study however employs an adaptive design including an interim analysis after 198 patients per study arm completed their 90 days follow-up to allow for sample size adjustment as required.
Conclusions: The IMPACT study is the first study to evaluate the concept of PCT-guided antibiotic treatment applying a randomized design in this specific setting. Provided that the study result is positive, the IMPACT study will prove the beneficial effect of a PCT-guided antibiotic therapy on top of standard diagnostic and therapeutic procedures in patients with acute decompensated heart failure.

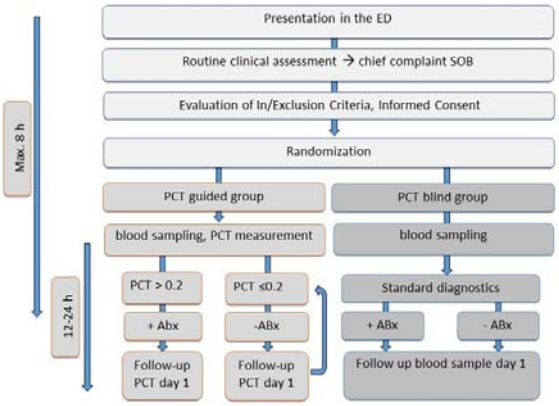


Figure 1: Design of the IMPACT-study

P908
Noninvasive ventilation in acute cardiogenic pulmonary edema

MJ Vieira[1]; L Reis[1]; P Dinis[1]; M Madeira[1]; J Ribeiro[1]; A Fernandes[1]; F Caetano[1]; M Alves[1]; R Teixeira[1]; C Lourenco[1]; L Goncalves[1]
[1]Hospital Santarém, Cardiology, Santarém, Portugal

Introduction: Noninvasive ventilation (NIV) is commonly used to treat patients (Pts) with acute cardiogenic pulmonary edema (ACPE) with some immediate beneficial effects. However, there is some conflicting evidence about the role of NIV in the prognosis of these Pts.
Aim: Determine whether NIV improves in-hospital survival in Pts with ACPE.
Methods: A retrospective analysis was performed, including 81 consecutive Pts hospitalized in a Cardiac Intensive Care Unit with a clinical diagnosis of ACPE as initial presentation. For this study, Pts were divided in two groups according to the use of NIV. Demographic, clinical, laboratory and echocardiographic parameters were evaluated. The primary endpoint was in-hospital mortality (IHM).
Results: In this population, 44 Pts (54%) were treated with NIV (NIV group) and 37 Pts (46%) were treated without NIV (WVNI group). There were no differences between the two groups regarding demographics, cardiovascular risk factors, vital parameters at admission, except for the presence of previous history of coronary disease, which was higher on the WVNI group (35 vs 59%, P = 0.032). Regarding laboratory values at admission, there were no significant differences between both groups, namely in relation to biomarkers such as troponin and NTproBNP, as well as in relation to the left ventricular ejection fraction. Patients in the NIV group had a higher incidence of cardiorenal syndrome (65 vs 39%, P = 0.02), higher maximum daily dose of furosemide (225 vs 120mg, P < 0.001), and increased use of noradrenaline (16 vs 2%, P = 0.026).
Regarding IHM, there were no significant differences between the two groups. Moreover, NIV didn't influenced length of stay. With a multivariate logistic regressions analysis, the development of cardiorenal syndrome was the only independent variable associated with the use of NIV (OR: 2.75; 95% CI: 0.88-7.6; P = 0.049), in a model adjusted for sex, age, previous history of coronary disease and use of noradrenaline.
Conclusion: According to our data, in ACPE patients, the use of NIV was not associated with better in-hospital survival or a shortened length of hospital stay. Some authors have suggested that in patients with high filling pressures, positive pressure ventilation may compromise venous return (a known risk factor for the development of cardiorenal syndrome). In this study, we were able to confirm a higher incidence of cardiorenal syndrome, but the exact mechanism behind this association remains to be clarified.

P909
Acute heart failure in the elderly: real world evidence from the ATHENA registry.

A Herbst[1]; F Orso[1]; S Parlapiano[1]; A Pratesi[1]; F Bacci[2]; G Ciuti[2]; A Berni[2]; A Crociani[2]; AC Baroncini[1]; C Nozzoli[2]; L Poggesi[2]; A Moggi Pignone[2]; L Gabbani[1]; N Marchionni[3]; S Baldasseroni[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA study group

Background: Acute heart failure (AHF) is a common disease that typically affects the elderly. Clinical registries represent the so-called "real world" in contrast to clinical trials that are known to have a selection bias. However, HF registries may maintain a certain level of selection by including only patients hospitalised in cardiology wards. Administrative data show that only a minority of these patients (about a quarter) is hospitalised in cardiology units, with the majority being admitted to internal medicine and geriatrics wards.
Purpose: to compare clinical characteristics and prognosis of elderly patients hospitalised for AHF in the settings of care of usual management: cardiology, internal medicine and geriatrics.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of AHF to the Emergency department (ED) of a tertiary University teaching-hospital and transferred to the above described settings of care in the period 01.12.2014-01.12.2015.
Results: 342 patients composed the study population; 17.8% were hospitalised in cardiology, 17.3% in geriatrics and 64.9% in internal medicine. Mean age was 83.7 years, resulting higher in geriatrics (86.9 years) versus internal medicine (83.6 years) and cardiology (81.0 years), P=0.001. Females were 54.1%: 55.7% in cardiology, 55.0% in internal medicine and 49.2% in geriatrics (P=0.700). Patients with HFpEF were 61.0% and were hospitalised less frequently in cardiology (49.1%) compared to geriatrics (62.5%) and internal medicine (65.0), P=0.116. Total in-hospital length of stay (including subsequent transferral to other wards before discharge) was 9.5 days and was higher for patients initially admitted to cardiology (15.0 days) compared to geriatrics (13.3 days) and internal medicine (7.8 days), p = 0.001. In-hospital mortality was 7.3% and it was higher in cardiology and geriatrics (11.0%) compared to internal medicine (5.0%), (P=0.075). Independent predictors of in-hospital mortality were evaluated using two different models: the ADHERE-like model which showed a significant correlation with age (OR=1.20, CI=1.07-1.34, P=0.002), systolic blood pressure (OR=0.96, CI=0.94-0.98, P=0.005) and Blood Nitrogen Urea (OR=1.01, CI=1.01-1.02, P=0.020) measured at the ED entry; the ATHENA model, which tested these variables with others more typical of geriatric patients (comorbidity and disability scores) and with the setting of care: a significant correlation was confirmed for age (OR=1.18 CI=1.05-1.32, P=0.002), systolic blood pressure measured at the ED entry (OR=0.96, CI=0.94-0.99, P=0.011) and for the setting of care (OR=0.32, CI=0.12-0.87, P=0.025) with a protective effect of cardiology ward assignment.
Conclusions: elderly patients with AHF are significantly different in terms of clinical characteristics and prognosis according to the different settings of care. Multidisciplinar research is needed in this field.

P910
Safety and effectiveness of oral rivaroxaban versus standard anticoagulation for the treatment of acute pulmonary embolism: a propensity-matched analysis of 478 patients

P Pedro Freitas[1]; AR Santos[2]; A Oliveira[1]; M Goncalves[1]; A Santos[2]; J Oliveira[2]; M Gago[2]; R Mamede[2]; D Correia[2]; N Vale[1]; J Mesquita[1]; M Castro[1]; J Brito[1]; J Ferreira[1]; M Mendes[1]
[1]Hospital de Santa Cruz, Cardiology, Lisbon, Portugal; *[2]Hospital de Sao Francisco Xavier, Lisbon, Portugal*

Background: Real-world data about the safety and effectiveness of oral rivaroxaban for the treatment and secondary prevention of acute pulmonary embolism (APE) is scarce.
Purpose: The objective of this study was to compare the safety and effectiveness of oral rivaroxaban against standard anticoagulation in an unselected real-world population hospitalized with APE.
Methods: We identified 534 patients diagnosed with APE by computed tomographic angiography in a single centre, between 2009 and 2015. A total of 56 patients were excluded because thrombolysis was performed or follow-up was incomplete. All

patients were discharged with oral rivaroxaban or low molecular weight heparin (LMWH)/warfarin for a minimum period of 6 months. A propensity-matched analysis based on 20 covariates was applied (absolute standardized mean difference < 20% for all variables in the paired population). Safety endpoints – total, fatal, major (ISTH criteria) and minor bleeding – and efficacy endpoints – all-cause death or venous thromboembolism (VTE) – at 6 months were analysed according to Cox regression.

Results: A total of 478 patients were included for analysis. Median age was 76 years (IQR 65 – 83), 39% males. Patients treated with LMWH/warfarin had higher prevalence of active cancer. In the propensity-matched population, rivaroxaban was associated with a lower risk of major bleeding (HR = 0.32; 95% CI: 0.087 – 1.182) and all-cause death or VTE at 6 months (HR = 0.24; 95% CI: 0.051 – 1.131) even though statistical significance was not reached. Figure attached summarizes the study findings.

Conclusions: In this retrospective study with a real-world unselected population, rivaroxaban showed to be at least as safe and effective in the treatment of APE as conventional anticoagulation with warfarin/LMWH at 6 months of treatment.

	Overall			Propensity-matched population		
	Warfarin/LMWH (n= 383)	Rivaroxaban (n=95)	P value	Warfarin/LMWH (n=95)	Rivaroxaban (n=95)	P value
Safety Endpoints % (at 6 months)						
Total bleeding	12	7.4	0.188	12.6	7.4	0.208
Fatal bleeding	0.5	0	0.661	0	0	NA
Major bleeding	8.6	3.2	0.086	9.5	3.2	0.087
Minor bleeding	3.1	4.2	0.620	3.2	4.2	0.720
Efficacy Endpoints % (at 6 months)						
All cause death + VTE	8.4	2.1	0.052	8.4	2.1	0.071
All cause death	7.1	1.1	0.057	5.3	1.1	0.135
VTE	2.1	1.1	0.514	3.2	1.1	0.337

Figure - Overall and propensity matched

P911

The patient view of hospitalisation with acute heart failure. Results from a qualitative study of the acute heart failure pathway.

J Riley[1]; C Keane[2]; M Walshe[2]; J Gallagher[2]; P Kalra[3]; M Cowie[1]; M Ledwidge[2]; K Mcdonald[2]

[1]Royal Brompton Hospital, London, United Kingdom; *[2]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*; *[3]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*

Unplanned hospital admissions are expensive for healthcare systems and stressful for the patient and family. To improve the use of healthcare resources and patient experience of care increasing public awareness of the common symptoms of heart failure (HF) and empowering and supporting those with HF to actively engage in their care is encouraged. This study explored the views of patients and GPs to identify issues that could be improved in the acute heart failure (AHF) pathway

Patients where recruited from a large Irish hospital following an unplanned HF admission. An established HF Unit provides monitoring, optimises therapies and provides patient education for 3 months post-discharge. We also interviewed GPs. Data were collected by semi-structured interview and analysed using an inductive, thematic process involving constant comparison.

Twenty-four patients were recruited: Mean age of 81 yr: 12 (50%) > 80 yr: 10 (41%) > 85 yr: Male 15 (63%), 9 (37%) de-novo HF, 17 (71%) had > 3 comorbidities and 8 (33%) > 3 non-cardiovascular comorbidities. 11 (46%) lived alone. 6/15 patients with an existing diagnosis of HF had > 3 admissions in previous 12 months. Seven GPs took part in the study.

Key themes: Understanding of HF. Patients had a poor understanding of HF. They interpreted their symptoms as related to comorbid conditions or age: breathlessness due to lung disease: fatigue due to old age. These symptoms did not fit with patient's views of HF (palpitations or chest pain) or their view of the type of person who developed HF (sedentary lifestyle). This understanding appeared derived from a general knowledge of heart disease.

Continuity of care: Patients described a close relationship with their GP that developed from monitoring related to comorbidities, on-going medication review and ease of access. They viewed the GP as a 'trusted' source of knowledge. The majority turned to the GP when they sought resolution for symptoms. Following hospital discharge the HFU scheduled face-to-face and telephone follow-up. Patients appreciated the regular contact and were reassured by monitoring.

Fragmentation of care: GPs described barriers to obtaining diagnostic tests in primary care. This left them unable to give patients a formal diagnosis or start conversations about HF.

Patients described limited access to the HFU for support or information. Some experienced frustration as they navigated between systems: HFU, GP and ED.

Patients in this study were elderly. They had multiple comorbidities that led to a reliance on the GP. Limited knowledge of HF resulted in them identifying HF symptoms as related to a comorbidity. Fragmentation of care between primary and secondary care were barriers to prompt treatment and to timely provision of information and support. These factors contributed to unplanned hospital admission and provided a negative experience of care. These results are now being validated in a larger population and different healthcare organisation.

P912

Worsening renal function during hospital stay following acute heart failure is associated with decreased venous congestion

E Akiyama[1]; LNL Van Aelst[2]; M Arrigo[3]; J Motiejunaite[1]; E Gayat[4]; MF Seronde[5]; A Mebazaa[4]

[1]Inserm UMR-S 942, Paris, France; *[2]KU Leuven, Leuven, Belgium*; *[3]University Hospital Zurich, Zurich, Switzerland*; *[4]Hospital Lariboisiere, Paris, France*; *[5]University Hospital Jean Minjoz, Besançon, France*

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Background: Impaired renal function is an important prognostic factor in patients with heart failure (HF) and increased central venous pressure which means venous congestion is associated with worsening renal function in patients with advanced decompensated HF with reduced left ventricular (LV) ejection fraction (EF) (HFREF) who underwent right heart catheterization.

Purpose: The purpose of this study was to investigate correlation between changes in renal function during hospitalization and severity of venous congestion in patients with acute HF (AHF).

Methods and Results: Of 101 hospitalized patients with AHF derived from MEDIA-DHF cohort, 60 had preserved LVEF (HFPEF) and 41 had HFREF. In patients with AHF, renal function worsened during hospital stay (median: estimated glomerular filtration rate (eGFR) 59 [40-75] at admission, 48 [31-67] ml/min/1.73m2 at discharge, $p < 0.001$, Cystatin C 1.50 [1.20-2.27] at admission, 1.78 [1.33-2.59] mg/L at discharge, $p < 0.001$, neutrophil gelatinase associated lipocalin (NGAL) 127 [95-260] at admission, 167 [104-263] ng/mL at discharge, $p = 0.004$, urea nitrogen 8.9 [6.9-13.2] at admission, 10.2 [7.6-16.0] mmol/L at discharge, $p = 0.006$) with few differences between HFPEF and HFREF: Estimated GFR decreased more in HFREF than in HFPEF (HFPEF 59 [40-74] at admission, 53 [28-73] ml/min/1.73m^2; at discharge, $p = 0.02$, HFREF 59 [45-76] at admission, 42 [34-56] ml/min/1.73m^2 at discharge, $p < 0.001$). At the same time, echocardiographic examinations showed signs of venous "decongestion" with decreased inferior vena cava (IVC) diameter at rest and increased respiratory variability of IVC diameter during hospitalization (median: IVC diameter 22 [16-24] at admission, 13 [11-18] mm at discharge, $p = 0.009$, variability 32 [8-44] at admission, 43 [29-70] % at discharge, $p = 0.04$) and no changes in left atrial and right atrial areas (median: left atrial area 25 [21-28] at admission, 25 [20-32] cm^2 at discharge, $p = 0.77$, right atrial area 18 [16-22] at admission, 17 [16-23] cm^2 at discharge, $p = 0.36$). Although eGFR negatively correlated with IVC diameter at admission, eGFR positively correlated with IVC diameter at discharge ($n = 93$, $r = -0.33$, $p = 0.001$ at admission, $n = 20$, $r = 0.47$, $p = 0.04$ at discharge).

Conclusions: Renal function worsened despite echocardiographic signs of venous "decongestion" during hospitalization in patients with AHF.

P913

Dopamine is associated with the worst outcome among inotropes used in acute heart failure: observations from the ESC-HF-LT registry

A Mebazaa[1]; J Motiejunaite[2]; E Gayat[1]; E Akiyama[2]; MG Crespo-Leiro[3]; LH Lund[4]; AP Maggioni[5]; O Chioncel[6]; F Ruschitzka[7]; G Filippatos[8]

[1]Hospital Lariboisiere, Department of Anesthesiology and Critical Care, Paris, France; *[2]Inserm UMR-S 942, Paris, France*; *[3]Complexo Hospitalario Universitario A Coruna, CHUAC, Unidad de Insuficiencia Cardiaca Avanzada y Trasplante Cardiaco, La Coruna, Spain*; *[4]Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden*; *[5]ANMCO Foundation For Your Heart, Florence, Italy*; *[6]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; *[7]University Heart Center, Department of Cardiology, Heart Failure Clinic and Transplantation, Zurich, Switzerland*; *[8]Attikon University Hospital, Athens, Greece*

On behalf of: on behalf of ESC-HF-LT registry investigators

Introduction: Intravenous (IV) inotropes and vasopressors are widely used in the initial treatment of acute heart failure (AHF). There is a continuing controversy about whether one agent is superior to the other. Our aim was to analyze current real-life use of inotropes and/or vasopressors, and their association with all-cause long-term mortalityin a large AHF cohort.

Methods: The European Society of Cardiology Heart Failure Long – Term Registry (ESC-HF-LT) was conducted between 2011 and 2013 and included 12785 patients (pts) in 21 countries in Europe, Northern Africa and the Middle East. Median duration of follow-up was 381 [363; 457] days. 833 (6.5%) AHF pts who received IV inotropes and/or vasopressors were identified for the post-hoc analysis. Propensity score for inotrope and/or vasopressor treatment was estimated using 35 clinically relevant baseline variables. Matching was made 1:1 on inotropic medication versus no inotropic medication and derived 606 pts in each treatment group. Hazard ratio (HR) for all-cause long-term mortality was estimated.
Results: Mean age of pts was 67(±13) years and 33.4% were women. Mean systolic blood pressure at presentation was 112(±27) mmHg. 45.7% of pts treated with inotropes had signs of hypoperfusion and 19.0% presented with cardiogenic shock. The 3 most widely used inotropes were dobutamine (42.5%), dopamine (24.7%) and levosimendan (13.1%), although their use varied among different regions (table 1). Median duration of treatment was 36.0 hours (h) [23.0; 72.0] for dobutamine, 36.0h [20.0; 72.0] for dopamine and 24.0h [24.0; 24.0] for levosimendan. Adjusted HR confirmed a significant association between the use of dopamine and all-cause long-term mortality (1.628 [1.031-2.572]) in the matched cohort. By contrast, no such association was seen with patients receiving dobutamine or levosimendan (HR 1.055 [0.727-1.531] and 1.229 [0.618-2.445] respectively).
Conclusions: Most commonly used inotropes in AHF patient population were dobutamine, dopamine and levosimendan. Compared to other inotropes, the use of dopamine was associated with markedly higher all-cause long-term mortality.

Inotropes in different regions

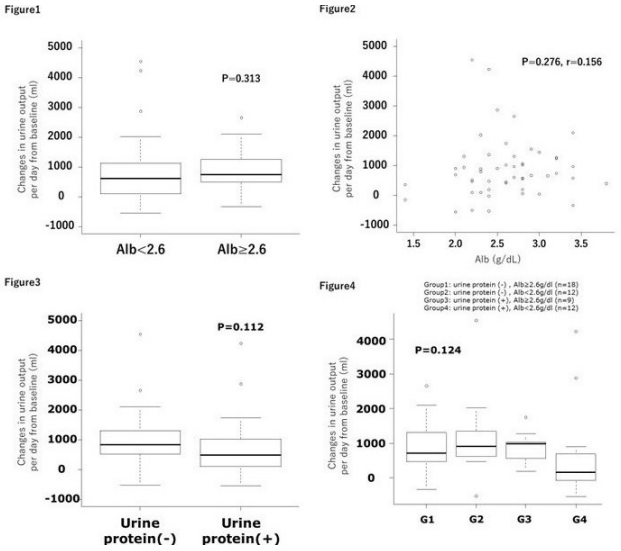
IV inotrope	Eastern Europe (n = 303)	North Africa and Middle East (n = 148)	Northern and Western Europe (n = 90)	Southern Europe (n = 292)	All (n = 833)
Dobutamine	40.6%	61.5%	53.3%	31.5%	42.5%
Dopamine	30.4%	23.6%	10.0%	24.0%	24.7%
Levosimendan	6.6%	0.0%	22.2%	23.6%	13.1%
Other	22.4%	14.9%	14.4%	20.9%	19.7%

P914

A novel therapeutic approach with additional tolvaptan for the patients with hypoalbuminemia or proteinuria.

K Takagi[1]; N Sato[1]; N Sato[1]; S Shigihara[1]; S Shigihara[1]; S Ishihara[1]; S Ishihara[1]; W Shimizu[2]; W Shimizu[2]
[1]Nippon Medical School Musashi-Kosugi Hospital, Department of Cardiology and Intensive Care Unit, Kanagawa, Japan; *[2]Nippon Medical School, Department of Internal Medicine and Cardiology, Tokyo, Japan*

Backgrounds: Hypoalbuminemia and proteinuria are independent prognostic factors in hospitalization for heart failure (HHF) and they are related to resistance to loop diuretics. Tolvaptan is an oral non-peptide, competitive antagonist of vasopressin receptor-2. It has been used for the treatment of volume overload in HHF patients in several Asian countries. Several studies have demonstrated marked improvement in congestion in HHF patients. However, it has not been clarified whether or not tolvaptan is useful for HHF patients with hypoalbuminemia and/or proteinuria.
Methods: We examined the diuretic response to tolvaptan in HHF patients with hypoalbuminemia and/or proteinuria. We defined hypoalbuminemia as a serum level of albumin < 2.6 g/dl and proteinuria as positivity by a point-of-care test tape. Fifty-one HHF patients were received additional tolvaptan upon therapies with loop diuretics. The subjects were divided into 4 groups with or without hypoalbuminemia and proteinuria.
Results: The changes in urine output per day were not different between with and without hypoalbuminemia (+610 (range, 100–1032); +742 (505–1247) ml, respectively, P=0.313, Figure1). The serum level of albumin did not correlate with changes in urine output per day after tolvaptan treatment (P=0.276, r=0.156, Figure2). The changes in the urine output per day were not different between with and without proteinuria (476 (range, 100–1020) vs. 834 (534–1309), respectively, P=0.112, Figure3). Fifty one patients were divided into 4 groups: group1, urine protein (-), Alb≥2.6g/dl (n = 18); group2, urine protein (-), Alb<2.6g/dl (n = 12): group3, urine protein (+), Alb≥2.6g/dl (n = 9); group4, urine protein (+), Alb<2.6g/dl (n = 12). The changes in urine output per day were significantly increased in the group 1, 2, and 3 after tolvaptan administration, but not in the group 4. Kruskal-Wallis tests indicated that changes in urine output per day did not differ among those 4 groups (P=0.124, Figure4),
Conclusion: Thus, additional administration of tolvaptan elicited a good diuretic response in HHF patients with hypoalbuminemia and/or proteinuria, although less response in the patients with both hypoalbuminemia and proteinuria. The present study suggested a novel therapeutic approach with additional tolvaptan for the patients with hypoalbuminemia or proteinuria.



Figure

P915

Long-term sacubitril/valsartan therapy improved central pulse wave parameters in patients with stable heart failure with reduced ejection fraction

Z Kobalava[1]; S Villevalde[1]; O Lukina[1]; L Babaeva[1]; I Meray[1]
[1]RUDN University, Moscow, Russian Federation

Objective: Angiotensin receptor-neprilysin inhibitor (ARNI) is recommended to further reduce the morbidity and mortality for patients with chronic symptomatic heart failure with reduced ejection fraction (HFrEF) according to the new ESC guidelines. Increased arterial stiffness has been shown to correlate with adverse cardiovascular events. The aim of the study was to assess long-term sacubitril/valsartan effects on parameters of arterial stiffness in patients with stable HFrEF.
Methods: In the open-label follow-up to PARADIGM HF study 16 patients with stable HFrEF (14 male, 69 ± 9 years (M ± SD), arterial hypertension 88%, previous myocardial infarction 88%, diabetes mellitus 43%, dyslipidemia 63%, LVEF 32 ± 6%, serum creatinine 122 ± 23 μmol/l, eGFR 55 ± 13 ml/min/1.73m2, potassium 4.43 ± 0.38 mmol/l) were enrolled. Patients received a stable background treatment for at least a month (ACEI 94%, beta-blockers 100%, aldosterone receptor antagonists 81%, loop diuretics 75%). ACEI treatment was interrupted for 36 h and replaced with sacubitril/valsartan 50, 100 or 200 mg BID according to baseline brachial BP (mean dose 185.7 ± 36.3 mg BID). Arterial stiffness was assessed by applanation tonometry baseline and after 6 and 12 months sacubitril/valsartan therapy. Parameters of LV efficacy were calculated. Wilcoxon and Spearman test was considered significant if $p < 0.05$.
Results: After 6 months of sacubitril/valsartan therapy carotid-femoral pulse wave velocity (PWV) significantly decreased (11.5 ± 2.9 vs 10.2 ± 2.9 m/s, $p < 0.05$) while other parameters of arterial stiffness did not change (p>0.05). After 12 months sacubitril/valsartan therapy was associated with significant decrease of aortic augmentation pressure (AP) (15.3 ± 8.9 vs 10.5 ± 5.0 mmHg, p = 0.002), increase of reflected wave transit time (RWTT) (132 ± 9 vs 143 ± 29 ms, p = 0.02), subendocardial viability ratio (SEVR) (164 ± 25 vs 177 ± 37 % p = 0.009). Changes of PWV between 6 and 12 months were nonsignificant (10.2 ± 2.9 vs 10.8 ± 2.0 m/s; p>.05). There was significant correlation between changes of augmentation pressure and changes of SEVR (R=-0.56), augmentation index (AIx) (R=0.52), stroke volume (R=0.52), potential energy (R=0.71), $p < 0.05$ for all. There was significant correlation between changes of SEVR and stroke volume (R=-0.85), stroke work (R=-0.81), potential energy (R=-0.95), $p < 0.05$ for all. There was statistically significant correlation between changes of RWTT and AIx (R=-0.68).
Conclusion: In stable symptomatic patients with HFrEF long-term sacubitril/valsartan therapy is associated with significant improvement of central pulse wave parameters: decrease of aortic AP, increase of RWTT. Sacubitril/valsartan therapy was associated with beneficial increase of SEVR, index that reflects the subendocardial oxygen supply-demand ratio.

Table 1. P915

	Improved (n = 2530)			Unchanged(n = 173)			Worsened(n = 229)		
	admission	discharge	p	admission	discharge	p	admission	discharge	p
Body Weight (kg)	79±14.6	77±23.1	0.032	78.9±19.0	77.4±16.5	0.0039	78.5±26.1	77.9±16	0.095
SBP (mmHg)	143.1±23.2	129.6±16.5	< 0.0001	138±25	127.1±19	< 0.0001	128.4±29	119±16	< 0.001
HR (heats/min)	96.5±23	80.04±21	< 0.001	99.5±26	90.2±18	< 0.0001	98.3±16	97.9±25	0.069
RR (breaths/min)	22.8±4	20.9±6	0.0057	24.3±6	22.9±8	0.053	26.1±9	24.9±11	0.0487
Na (mmol/L)	134.9±3.2	134.7±2.1	0.193	133.9±4	134.1±2.8	0.092	131.4±4.1	131.0±3.8	0.175
K (mmol/L)	4.6±0.9	4.5±0.7	0.437	4.3±0.6	4.1±0.8	0.049	4.2±1.1	4.1±1.3	0.263
BUN (mg/dl)	59±42	55±53	0.069	68±49	61±39	0.027	86±65	84±4.8	0.058
Creatinine (mg/dl)	1.3±0.4	1.3±0.5	0.2571	1.4±0.6	1.3±0.7	0.092	1.7±1.2	1.9±1.2	0.026

SBP systolic blood pressure. HR heart rate. RR respiratory rate. BUN blood urea nitrogen

P916

Clinical profile and symptom status at discharge among patients hospitalized for heart failure; an analysis of the RO-AHFS registry

E-L Elena-Laura Antohi[1];
M Chivulescu[1]; C Radulescu[1]; RI Radu[1]; C Macarie[1]; A Ambrosy[2]; S Collins[3]; M Gheorghiade[4]
[1]*Institute of Emergency for Cardiovascular Diseases "Prof. Dr. C.C.Iliescu", Bucharest, Romania*; [2]*Stanford University Medical Center, Stanford, United States of America*; [3]*Vanderbilt University Medical Center, Department of Emergency Medicine, Nashville, TN, United States of America*; [4]*Center for Cardiovascular Innovation, Northwestern University Feinberg School of Medicine, Chicago, United States of America*

On behalf of: The Romanian Acute Heart Failure Syndromes Registry
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Background: There are few heart failure (HF) registries accurately describing in hospital patient clinical journey. Also, lack of improvement in patient self-assessed symptoms at discharge may also represent a neglected end-point which may relate to hard outcomes.
Aim: To evaluate the value of clinical and biological variables in predicting self assessed symptom improvement during HF-hospitalization.
Methods: The RO-AHFS registry prospectively enrolled 3224 consecutive patients admitted for acute HF over a 12-month period. The clinical course of patients surviving to discharge has been evaluated as: improved, unchanged, worsened. In parallel with patient's self assessment clinical status, body weight, SBP, HR, RR, serum Na, K, BUN and creatinine have been evaluated at admission and discharge.
Results: At discharge 86.3% of patients reported their status to be improved, 5.9% unchanged, 7.8% worsened. When patient self-assessed clinical status was analyzed by clinical profile, substantial variation emerged; patients classified as cardiogenic shock and right HF were less likely to report improvement (55% and 80%, respectively), compared to chronic hospitalized HF (97%). There was minimal variation when patients were stratified by age and ejection fraction. Clinical and biological data collected at admission and discharge, are presented in Table 1. A trend for lower betablocker use was noted in patients that reported their status worsened.
Conclusion: Of the surviving patients, a proportion of 13% do not experience symptom improvement. The variation of known biological prognostic markers does not appear to predict the incidence of this outcome, while the patients clinical course may be more relevant.

P917

Prognostic value of mid-range ejection fraction in patients with acute coronary syndrome and heart failure

RM Rosa Maria Agra Bermejo[1]; A Cordero[2]; JM Garcia Acuna[1]; I Gomez Otero[1]; A Varela Roman[1]; I Gomez Otero[1]; M Rodriguez Manero[1]; JR Gonzalez Juanatey[1]
[1]*UNIVERSITY CLINICAL HOSPITAL OF SANTIAGO DE COMPOSTELA, DEPARTMENT OF CARDIOLOGY, SANTIAGO DE COMPOSTELA, Spain*; [2]*University Hospital San Juan de Alicante, Cardiology, Alicante, Spain*

Background: The new 2016 European Society of Cardiology Heart Failure (HF) Guidelines propose a new HF classification according to the level of LVEF, as follows: HFrEF is < 40%, mid-range HF is an LVEF range from 40–49%, and HFpEF is ≥ 50%. HFmrEF characteristics and prognosis in acute coronary syndrome complicated with HF are unkown.
Purpose: The aim of our study was to analyse the HFmEF in patients with acute coronary syndrome and Killip [3]2.
Material and methods: This is a retrospective observational study of 1444 consecutively patients admitted in for acute coronary syndrome (ACS) and Killip[3]2 in two different hospitals. Baseline patient characteristics were examined for each patient and a follow-up period was stablished for registry of death and re-hospitalization by HF as the primary endpoint. The observed event risk was calculated as a Kaplan–Meier estimate.
Cox regression models performed survival analyses once proportional risk test were verified. Multivariate analysis were performed using all variables that obtained p values < 0.1 in the univariate analysis. The incidence of HF could be affected by patients' death and, therefore, the usual techniques for time-to-event analysis would provide biased or un-interpretable results due to the presence of competing risks. With the aim of avoiding such effects we applied the model introduced by Fine and Gray to test the competing events.
Results: Among the study participants 523 (45,7%) had HFrEF, 123 (10, 7%) HFmrEF and 498 (43,5%) HFpEF. Patients with HFmrEF had a demographic and clinical profile with many intermediate features between HFrEF and HFpEF. They were similar to HFrEF in terms of age, sex, hypertension, hemoglobine, heart rate, STEMI and use of ACEIS, MRAS and diuretics. They were similar to HFpEF in terms of previous HF, Killip II, systolic blood pressure and GRACE score. All other characteristics were similar between groups.
There were no significant differences in terms of mortality or readmission to HF between the three groups.
When we performed the multivariate analyses only the HFpEF was associated with less HF readmission (HR 0,49, CI 95% 0,395-0,624, p < 0,01)
Conclusions: HFmrEF patients represent a small group in acute coronary syndrome complicated with HF. They have intermediate characteristics between HFpEF and HFrEF but not differences between the three groups in terms of mortality or heart failure readmission were observed.

P918

The POP-HF score to predict heart failure expression in patients after coronary artery bypass grafting: A substudy of the POP study

P Predrag Mitrovic[1]; B Stefanovic[1]; M Radovanovic[1]; N Radovanovic[1]; D Rajic[2]; G Matic[2]; I Subotic[2]; N Mitrovic[2]; N Mijic[2]
[1]*University Institute for Cardiovasculari Diseases, CCS, School of Medicine, University of Belgrade, Belgrade, Serbia*; [2]*Clinical Center of Serbia, Institute for Cardiovascular Diseases, Belgrade, Serbia*

On behalf of: The POP Study Group
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Presentation of heart failure (HF) has different influence on new coronary events expression in patients with previous coronary artery bypass grafting (CABG), than in patients without CABG. Heart failure is one of the most important major adverse cardiovascular events (MACE) in patients after previous CABG. This substudy aimed at evaluating the usefulness of the POP-HF score (PostOperative Prognosis-HeartFailure score), originally developed for the prediction of 60-day, 1-year, 5-year, 10-year, 15-year and 20-year MACE, after CABG.
From April 1988, we analyzed 2028 consecutive patients who underwent CABG. Expression of HF was the predefined end point. Models discrimination and calibration to predict HF was tested using receiver-operating characteristics curves and the goodness-of-fit (GoF) test. Sensitivity analyses and 1000-resample bootstrapping were used to evaluate the model's performance. The rate of HF was 44.6 %, respectively. Compared with controls, the cumulative HF group was associated with much higher rates of adverse clinical outcomes at 60-day follow-up (adjusted odds ratio (OR) for death 6.96), at 1-year follow-up (adjusted OR for death 7.18), at 5-year follow-up (adjusted OR for death 7.64), at 10-year follow-up (adjusted OR for death

7.88), at 15-year follow-up (adjusted OR for death 8.26) and at 20-year follow-up (adjusted OR for death 8.32). Internal validation confirmed a reasonably good discrimination and calibration of thePOP-HFscorefor the prediction of HF (area under the curve (AUC) 0.72, GoF 0.34), after CABG.
Conclusion: The risk of HF in patients after previous CABG, could be accurately assessed using the POP-HF score, which might help in deciding upon measures aimed at preventing adverse prognosis.

P919

Fate of acute heart failure patients with mid-range ejection fraction

H B Hye Bin Gwag[1]; GY Lee[1]; JO Choi[1]; ES Jeon[1]; JY Lee[1]; ES Ju[1]
[1]Samsung Medical Center, Cardiology, Seoul, Korea Republic of

On behalf of: KorAHF
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Background: Outcomes of acute heart failure (HF) with mid-range ejection fraction (EF) are limited, and optimal medical treatment for these patients are not well-established. Especially, there are few data on follow-up left ventricular EF (LVEF) in these patients. Therefore, we investigated mortality and improvement of LVEF in acute HF patients with mid-range EF.
Methods: The study population was selected from the multicenter prospective cohort registry. Patients were categorized into three groups according to baseline LVEF: HF with reduced EF (HFrEF) group (LVEF < 40%), HF with mid-range EF (HFmrEF) group (40% ≤ LVEF < 50%), and HF with preserved EF (HFpEF) group (LVEF ≥ 50%). Follow-up LVEF reported at least 90 days after discharge was used to assess the improvement of LV systolic function in HFmrEF group. 'Improved LVEF' was defined as %LVEF change ≥ 5% with follow-up LVEF ≥ 50%, and 'worsened LVEF' was defined as %LVEF change ≥ 5% with follow-up LVEF < 40%.
Results: Of the 3085 patients included in the present study, 2123 (68.8 %) had HFrEF, 454 (14.7%) had HFmrEF, and 508 (16.5%) had HFpEF. Among 276 patients in HFmrEF group who underwent follow-up echocardiography, 94 (34.1%) showed improved LVEF. Survival rate was significantly higher in HFmrEF patients with improved LVEF than those with no change of LVEF or worsened LVEF. Multivariate analysis showed that improvement of follow-up LVEF, lower blood urea nitrogen level, and maintenance of renin-angiotensin blocker or aldosterone antagonist were significantly associated with better survival.
Conclusion: HFmrEF patients with improved LVEF had better survival rate than those with no change of LVEF or worsened LVEF. Improved LVEF, and maintenance of renin-angiotensin blocker or aldosterone antagonist were independent prognostic factors for mortality in acute heart failure patients with mid-range EF.

P920

Mean platelet volume / platelet count ratio at discharge: a new tool to predict hospitalization for de novo acute heart failure

D Candeias Faria[1]; J B Augusto[1]; M Borgues Dos Santos[1]; D Roque[1]; H Ferreira[1]; J Urzal[1]; C Santos[2]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal; *[2]Hospital Santo Andre, Leiria, Portugal*

Background: Acute heart failure (AHF) is a powerful predictor of future readmissions and mortality in patients with atrial fibrillation (AF). Mean platelet volume (MVP) / platelet count ratio is associated with coronary occlusion and cardiovascular events in ischemic heart disease. However, there is limited knowledge about its effects in patients with AF.
Purpose: We aimed to evaluate the impact of MVP/platelet count ratio at discharge as a noninvasive predictor of de novo AHF in patients with AF.
Methods: We included retrospectively 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period. Among them, 423 patients were admitted for in-hospital management. Patients who had previous known heart failure (n = 101) were excluded. We recorded MPV (fL) and platelet count (normal range 150.000-400.000 platelets/μL) at discharge and calculated MPV/platelet count ratio. Primary outcome was the incidence of hospitalization for de novo AHF 12 months after discharge.
Results: We included 253 AF patients who were successfully discharged and followed for 12 months (mean age of 70.7 ± 12.6 years, 37.5% males). Median MPV/platelet count ratio was 4.63x10^3fL/platelets/μL, interquartile range 2.85 – 3.27x10^3fL/platelets/μL. MPV/platelet count at discharge was significantly higher in patients who were admitted for de novo AHF (mean 1.59x10^3fL/platelets/μL vs 0.74x10^3fL/platelets/μL; p = 0.019). Kaplan-Meier analysis (Figure) revealed that patients who had a MPV/platelet count at discharge >4.0x10^3fL/platelets/μL had significantly more hospitalizations for de novo AHF 12 months after discharge (26.1 vs. 9.6%; log-rank p = 0.011). Cox regression analysis controlled for age and chronic kidney disease revealed that MPV/platelet count was an independent predictor of de novo AHF (HR 2.59; CI 95% 1.03 – 6.490; p = 0.042). There was a significant trend towards a higher mortality rate after discharge in AF patients with >4.0x10^3fL/platelets/μL (26.1 vs. 10.0%; p = 0.034).
Conclusions: MPV/platelet count ratio at discharge is associated with future hospitalizations by de novo AHF in patients with AF

P921

Elevated heart rate at discharge is associated with worse long-term cardiovascular outcomes among patients hospitalized for acute heart failure

A Ravera[1]; C Giacopini[1]; V Carubelli[1]; E Sciatti[1]; CM Lombardi[1]; M Metra[1]
[1]University of Brescia, Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, Brescia, Italy

Background: Drugs acting on heart rate (HR), namely beta-blockers (BB), are among the pillars of chronic heart failure (HF) therapy. However, the effects of HR in acute HF (AHF) have been analysed only in a few studies.
Purpose: This study assessed the relationship between HR measured at discharge and long term outcomes after a hospitalization for AHF.
Methods: We enrolled 938 patients admitted in our hospital for AHF. We evaluated HR at discharge (HRds), and we divided the patients in 2 groups: those with HRds < 70 beats per minute (bpm), and those with HRds≥70bpm. We followed-up the enrolled patients to assess outcomes up to 180 days after discharge. We performed statistical analysis with Cox regression for survival analysis and we used the Kaplan-Meier method to obtain time-to-event curves.
Results: At discharge, 525 subjects (56%) had HRds < 70bpm and 413 subjects (44%) had HRds≥70bpm. Higher HRds was associated with male gender (p < 0.001) and arterial hypertension (p = 0.018). Patients with lower HRds were more likely to have ischemic heart disease and less likely to have valvular heart disease (p = 0.008). No difference was found in age or other important comorbidities between the 2 groups. Patients with higher HRds had higher NYHA class at baseline (p = 0,014) and discharge (p < 0.001). N-terminal pro b-type natriuretic peptide (NT-proBNP) at baseline was similar in the 2 groups, whereas NT-proBNP at discharge was higher in patients with higher HRds (p < 0,001). At discharge 80 subjects with HRds < 70bpm (15.2%) and 129 subjects with HRds≥70bpm (31.2%) were not on BB. Among patients on BB, we found no difference in percent target dose prescribed at discharge (p = 0.776). After adjustment for covariates, we found that HRds ≥70bpm was associated with a significant higher risk of day-180 all-cause (AC) death (adjusted hazard ratio, HR 1.86, 95% confidence interval, CI, 1.10-3.16, p = 0.021) and cardiovascular (CV) death (adjusted HR 2.40, 95% CI 1.34-4.28, p = 0.003). No impact of HRds on day-180 HF hospitalization (HFH) was found. The composite endpoint of CV death and HFH did not demonstrate statistical significance, due to lack of observed effect of HRds on HFH. Among patients with atrial fibrillation (AF), HRds was not significantly associated with any of the evaluated outcomes, after adjustment. In the subset of patients in sinus rhythm (SR), HRds ≥70bpm was significantly associated with day-180 AC death (adjusted HR 2.76, 95% CI 1.31-5.81, p = 0.008) and CV death (adjusted HR 3.57, 95% CI 1.55-8.23, p = 0.003).
Conclusions: Patients hospitalized for AHF with elevated HR at discharge have an increased risk of death. This finding was confirmed in the subset of patients in SR at discharge, whereas among patients with AF, a higher HR at discharge was not significantly associated with higher CV and AC mortality at day 180.

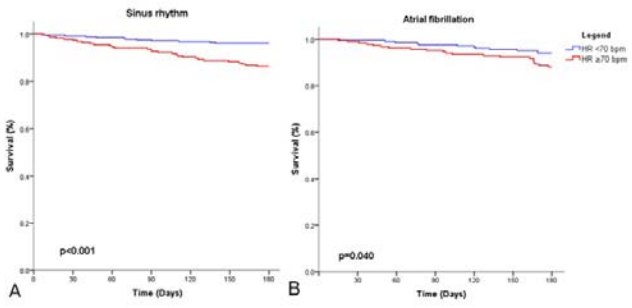

Figure. Kaplan-Meier survival curves for cardiovascular mortality among patients in sinus rhythm (A) and atrial fibrillation (B).

P922

Hemoconcentration during hospitalization is associated with better outcomes in patients with decompensated heart failure

A Klimenko[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: Patients with decompensated heart failure (DHF) are usually admitted with severe systemic congestion. Volume overload is the known main driver for morbidity, mortality and readmission to the hospital. Hemoconcentration (HC) has been proposed as a surrogate marker of decongestion during hospitalization.
Purpose: The aim of the study was to determine the prevalence of HC in DHF patients and to evaluate the impact of HC on short-term (30-days mortality) and long-term (6 months rate of HF rehospitalizations) outcomes.
Methods: In 183 patients admitted with ADHF (125 male, 69 ± 9 years (M ± SD), arterial hypertension (AH) 87%, ischemic heart disease (IHD) 56%, myocardial infarction (MI) 53%, atrial fibrillation 51%, diabetes mellitus (DM) 36%, known chronic kidney disease (CKD) 40%, ejection fraction 44 ± 15%) the prevalence of HC was assessed. HC was defined as increase in both hemoglobin and hematocrit levels between baseline and discharge. Mann-Whitney and multiple logistic regression analysis were performed. $P < 0.05$ was considered statistically significant.
Results: 33% of patients developed HC during hospitalization. There were no differences between groups in clinical presentation of systemic congestion (comparable rates of oedema, orthopnea, S3, pulmonary rales, Rg-hydrothorax), level of EF (47 ± 14 vs 43 ± 15%, p>0.05), level of NT-proBNP (11151 ± 1633 vs 13414 ± 4093 fmol/ml, p>0.05) and frequency of prior HF hospitalizations (70 vs 81%, p >0.05). Patients without HC were older (70 ± 8 vs 67 ± 12 years, $p < 0.05$), had lower resistance R/h (238 ± 61 vs 266 ± 43 Ohm/m, $p < 0.05$) and reactance Xc/h (19 ± 6 vs 25 ± 6 Ohm/m, $p < 0.05$), which were assessed by bioimpedance vector analysis (BIVA). Patients with HC had higher levels of R/h (290 ± 35 vs 261 ± 64 Ohm/m, $p < 0.05$) and reactance Xc/h (27 ± 5 vs 21 ± 6 Ohm/m, $p < 0.05$) at discharge, which correspond to less evident congestion assessed by BIVA. Patients without HC compared to patients with HC had higher rate of acute kidney injury (AKI) during hospitalization (57 vs 20%, ×2= 15, $p < 0.001$), higher rate of 30-days mortality (11 vs 0%, ×2=5, $p < 0.05$) and there was tendency to higher 6 months rate of HF rehospitalizations (39 vs 30%, p>0.05).
Conclusions: 33% of patients admitted with DHF developed HC. Development of HC during hospitalization was not associated with higher level of AKI. HC was associated with better short-term and long-term outcomes and less evident hyperhydration by BIVA at discharge. Evaluation of HC during hospitalization added useful information to standard clinical parameters and could be used as a marker of prognosis in patients with DHF.

P923

Nutritional risk index predicts 1 year mortality in patients with acute decompensated heart failure

J Y Jae Yeong Cho[1]; KH Kim[1]; HY Lee[2]; ES Jeon[3]; MS Kim[4]; JJ Kim[4]; KK Hwang[5]; SC Chae[6]; SH Baek[7]; SM Kang[8]; DJ Choi[9]; BS Yoo[10]; HY Park[11]; MC Cho[5]; BH Oh[2]
[1]*Chonnam National University Hospital, Cardiology, Gwangju, Korea Republic of*; [2]*Seoul National University Hospital, Seoul, Korea Republic of*; [3]*Samsung Medical Center, Seoul, Korea Republic of*; [4]*Asan Medical Center, Seoul, Korea Republic of*; [5]*Chungbuk National University Hospital, Cheongju, Korea Republic of*; [6]*Kyungpook National University Hospital, Daegu, Korea Republic of*; [7]*Seoul St. Mary's Hospital, Seoul, Korea Republic of*; [8]*Severance Hospital, Seoul, Korea Republic of*; [9]*Seoul National University Bundang Hospital, Seongnam, Korea Republic of*; [10]*Wonju Christian Hospital, Wonju, Korea Republic of*; [11]*National Institute of Health, Osong, Korea Republic of*

On behalf of: KorAHF registry
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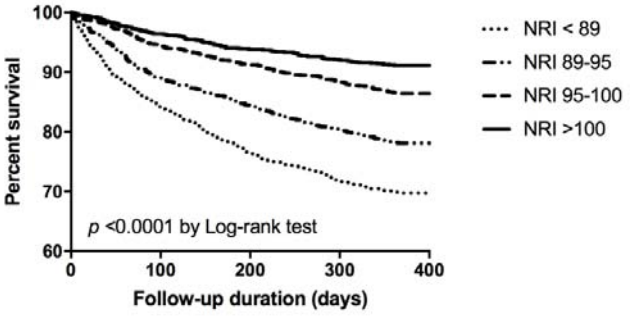
Background: Nutritional status is associated with adverse clinical outcomes in various cardiovascular diseases. Nutritional Risk Index (NRI) is a useful tool in identifying the patients at risk of malnutrition, but the role of NRI in patients with acute decompensated heart failure (ADHF) has been poorly studied. Therefore, the aim of this study was to investigate the impacts of NRI on long-term mortality in patients with ADHF.
Methods: Among 5,625 cohort patients enrolled in Korean Acute Heart Failure Registry (KorAHF), a total of 5,531 patients who were possible to calculate NRI were enrolled. NRI was calculated by the following formula; NRI = (1.519 x serum albumin[g/dl]) + (41.7 x weight [kg]/ideal body weight [kg]). The patients were divided into 4 groups according to the NRI quartile; Q1 < 89 (n = 1268, 69.9 ± 14.5 years, 632 males), Q2 89-95 (n = 1295, 69.7 ± 14.4 years, 677 males), Q3 95-100 (n = 1570, 68.8 ± 14.0 years, 849 males), Q4 >100 (n = 1398, 65.6 ± 14.5 years, 779 males). Primary end point was all-cause mortality at 1-year clinical follow-up. Results: Proportion of male sex increases with increasing NRI quartile (49.8% vs. 52.3% vs. 54.1% vs. 55.7%, linear p = 0.001). History of ischemic heart disease was more prevalent in lower NRI (29.3% vs. 28.6% vs. 30.1% vs. 24.8%, linear P=0.030). Atrial fibrillation (22.9% vs. 28.6% vs. 28.9 vs. 29.0%, linear p = 0.001), history of smoking (36.3% vs. 37.7% vs. 39.7% vs. 40.5%, linear p = 0.014), and history of alcohol intake (34.2% vs. 34.7% vs. 38.7% vs. 45.1%, linear $p < 0.0001$) were more prevalent in higher NRI quartile. One year mortality was 17.2% in Korean patients with ADHF. The 1-year mortality was significantly increased as the NRI quartile increased, and the highest NRI quartile was associated with the highest 1-year mortality (Q4: 27.5% vs. Q3: 20.9% vs. Q2: 12.9% vs. Q1: 8.7%, linear $p < 0.0001$). On Kaplan-Meier survival analysis, the significant inter-quartile difference was observed ($p < 0.0001$ for all). Conclusion: Poor nutritional status as assessed by NRI and quartile grading of NRI was associated with 1-year mortality in Korean patients with ADHF. The assessment of nutritional status by NRI may provide additional prognostic information and thus would be useful in the risk stratification of the patients with ADHF.

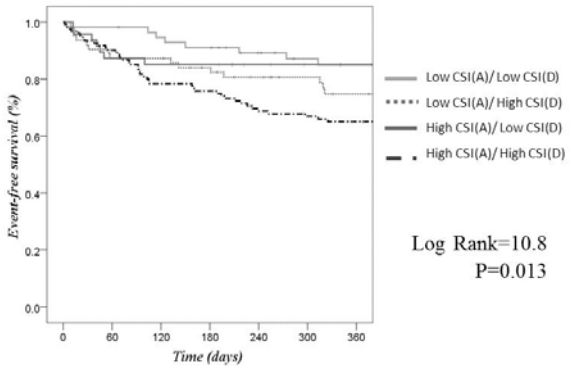


P924

Congestion trajectories and long-term outcomes in acute heart failure evaluated by chest radiographic congestion score

MK Kobayashi[1]; MW Watanabe[1]; YI Ito[1]; YI Iwasaki[1]; AY Yamashina[1]
[1]*Tokyo Medical University Hospital, Tokyo, Japan*

Aims: Residual pulmonary congestion has association with poor prognostic value in heart failure (HF), but there is challenging to evaluate the quantification of congestion by a simple and accurate measure. The aim of this study was to assess the prognostic value of chest radiographic congestion and to investigate the relationship between congestion trajectories and outcomes.
Methods and Results: 292 ADHF patients retrospectively enrolled with clinical examination, echocardiography, laboratory findings and chest roentgenogram that was blindly scored for the presence and severity of lung edema at both admission and discharge. Patients were stratified by radiographic congestion score index (CSI) of both admission (median=1.33) and discharge (median=0.33). The study group were CSI(A) < 1.33/ CSI(D) < 0.33 (n = 57), CSI(A) < 1.33/ CSI(D)≧0.33 (n = 63), CSI(A)≧1.33/ CSI(D) < 0.33 (n = 48), and CSI(A)≧1.33/ CSI(D) ≧0.33 (n = 124). Hb, eGFR, BNP, EF and PASP were not significant differences both these groups. Concerning about one-year event-free survival for the primary endpoint (all-cause death and HF hospitalization), high CSI(A)/high CSI(D) group had a highest risk of developing the events (log rank=10.8, P=0.013). In multivariable Cox regression analysis, CSI(D) was associated with the combined endpoint (HR [95% CI], 1.91 [1.07 to 3.4]; P=0.029).
Conclusion: Residual pulmonary congestion assessed by chest radiographic scoring may predict poor prognostic value beyond BNP and physical assessment. Discharge congestion identifies cardiac prognosis for 1-year cardiovascular outcome compared with admission congestion.



survival curve for the combined outcome

P925

Peak exercise oxygen uptake predicts recurrent admissions in heart failure with preserved ejection fraction

P Palau Sampio[1]; E Dominguez Mafe[1]; JM Ramon Ferrandis[2]; L Lopez[3]; J Melero Lloret[1]; J Gonzalez[2]; R Heredia[2]; A Bellver[1]; E Santas Olmeda[2]; E Valero Picher[2]; E Nunez Botero[2]; FJ Chorro[2]; J Nunez Villota[2]

[1]Hospital General de Castellón. Universitat Jaume I, Cardiology Department, Castellón, Spain; *[2]Hospital Clínico Universitario, INCLIVA. Universitat de València, Cardiology Department, Valencia, Spain*; *[3]Universitat de València, Facultat de fisioteràpia, Valencia, Spain*

Background: Heart failure (HF) with preserved ejection fraction (HFpEF) is a highly prevalent syndrome with elevated morbimortality risk. To date, there is scarce evidence about the role of peak exercise oxygen uptake (peak VO2) for predicting the morbidity burden in HFpEF. We sought to evaluate the association between peak VO2 and risk of recurrent hospitalizations in patients with HFpEF.
Methods: A total of 74 stable symptomatic patients with HFpEF underwent a cardiopulmonary exercise test between June 2012 and May 2016. Negative binomial regression method was used to determine the association between percent of predicted peak VO2 (pp-peak VO2) and recurrent hospitalizations. Estimates of risk were reported as incidence rate ratios (IRR).
Results: Mean age was 72.5 ± 9.1 years, 53% were women and all patients displayed NYHA II-III. Mean peak VO2 and median pp-peak VO2 were 10 ± 2.8 ml/min/kg and 60% (47-67), respectively. During a median follow-up of 276 days (IQR: 153-1231), 84 all-cause hospitalizations in 31 patients (41.9%) were registered. A total of 15 (20.3%) deaths were also ascertained. In a multivariate analysis, accounting for mortality as a terminal event, pp-peak VO2 was independent and linearly associated with the risk of recurrent admissions (figure 1). Thus, and modeled as continuous, a 10% decrease of pp-peak VO2 increased by 32% the risk of recurrent hospitalizations [IRR: 1.32 (1.03-1.68), p = 0.028]
Conclusions: In symptomatic elderly patients with HFpEF, pp-peakVO2 predicts all-cause recurrent admissions.

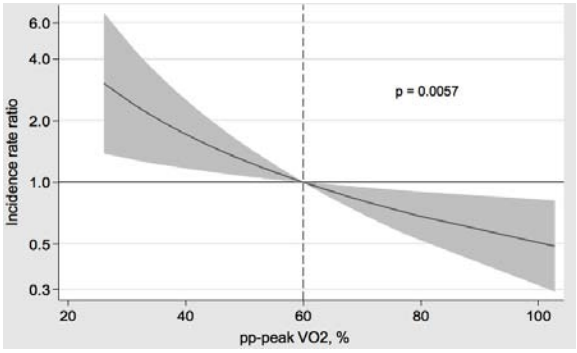


Figure 1

P926

Mortality risk of patients with heart failure with mid-range ejection fraction following a hospitalization with acute heart failure

I Ingrid Cardells Beltran[1]; E Santas Olmeda[1]; A Paya Chaume[1]; R Heredia Cambra[1]; D Escribano Alarcon[1]; G Minana Escriva[1]; A Bayes Genis[2]; J Lupon Roses[2]; J Sanchis Fores[1]; FJ Chorro Gasco[1]; J Nunez Villota[1]

[1]University Hospital Clinic of Valencia, Valencia, Spain; *[2]University Hospital Trias i Pujol, Barcelona, Spain*

Introduction. According European Society of Cardiology guidelines, patients with left ventricular ejection fraction in the range of 40-49% are now defined as heart failure with mid-range ejection fraction (HFmEF). There is scarce information about the long-term prognostic course of these subset of patients, especially after an episode of acute heart failure (AHF).
Purpose: In this work, we aimed to compare the risk of long term all-cause and cardiovascular (CV) mortality among patients with acute heart failure and reduced (HFrEF), mid-range and preserved ejection fraction (HFpEF).
Methods: We prospectively included 2642 consecutive patients with AHF in a single teaching center. Left ventricular ejection fraction (LVEF) was assessed by two-dimensional echocardiography during index hospitalization. Patients were grouped according LVEF status: < 40% (HFrEF), 40-49% (HFmEF) and ≥50% (HFpEF). Traditional Cox and Cox adapted for competing events were used to evaluate the risk of total and CV-death, respectively.
Results: Patients with HFrEF, HFmEF and HFpEF represented the 31.3%, 15.3% and 53.4% of the sample, respectively. During a median follow-up of 2.3 years (0.8-4.2), 1322 (50%) deaths were registered (73.7% of them were of CV etiology). Similar rates (per 100 person-years) across the 3 categories were found for all-cause [16.4, 18.8 and 17.1 for HFrEF, HFmEF and HFpEF, respectively (log-rank p = 0.591) and CV-mortality [12.8, 14 and 12.1, respectively (log-rank p = 0.486)]. After a multivariate adjustment, compared to patients with HFrEF, patients with HFmEF showed a similar risk of total (HR:1.07, CI 95%: 0.78-1.24, p = 0.446) and CV-death (HR:0.98, CI 95%: 0.90-1.27, p = 0.882).
Conclusion: Patients with AHF and HFmEF show a similar mortality burden than patients with HFrEF and HFpEF.

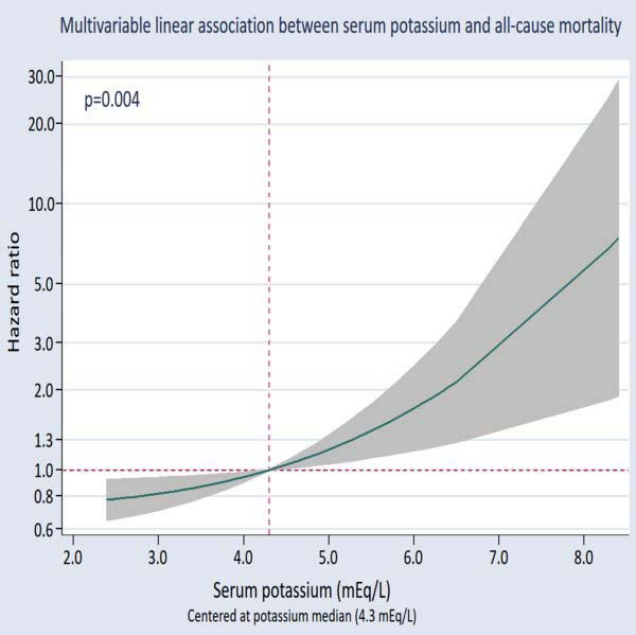
P927

Serum potassium levels and 6-month mortality in acute heart failure

J Jana Gummel[1]; R Farcasan[1]; J Parra[1]; A Paya[1]; R Heredia[1]; G Minana[1]; I Cardells[1]; A Mollar[1]; E Santas[1]; S Garcia-Blas[1]; E Valero[1]; FJ Chorro[1]; J Sanchis[1]; J Nunez[1]

[1]University Hospital Clinic of Valencia, Valencia, Spain

Background: Serum potassium abnormalities are frequent in patients with acute heart failure (AHF); however, information about its prognostic meaning is limited. In this work, we sought to evaluate the independent association between serum potassium on admission and the risk of 6-month all-cause mortality.
Methods: Potassium at admission was prospectively measured in 1090 patients with AHF. Patients were grouped according to low potassium (<3.5 mEq/L), normal potassium (3.5 to 5.0 mEq/L), and high potassium (>5.0 mEq/L) levels. The independent association between serum potassium and 6-month mortality was assessed through Cox regression analysis. The gradient of risk along the continuum of serum potassium was evaluated by fractional polynomials.
Results: The mean age of patients was 73.6 years, 53.5% were men and 50.8% showed left ventricular ejection fraction (LVEF) ≥50%. Median (IQR) N-terminal pro brain natriuretic peptide (NT-proBNP) was 3631 pg/ml (1694-8292). Low potassium was present in 84 patients (7.7%), normal potassium in 871 (79.8%), and high potassium in 136 (12.5%). At 6-month follow-up, a total of 126 patients (11.6%) died. Compared to patients with normal and low potassium, those with potassium >5.0 mEq/L almost doubled the rates of death [10.5%, 11.9% and 19.8% for normal, low and high potassium, respectively (p = 0.014)]. After a multivariate adjustment that included established prognosticators and important potential confounders (final model included the following covariates: age, prior admission for AHF, systolic blood pressure, LVEF, hemoglobin, NTproBNP, and treatment with antialdosteronics and angiotensin converting enzyme inhibitors or angiotensin receptor blockers), the association lost strength, but patients with potassium >5.0 mEq/L remained showing a statistical trend to higher risk of 6-month mortality compared to patients with normal potassium (HR=1.49; CI 95%: 0.94-2.38, p = 0.088). When evaluated as continuous, serum potassium was significantly associated with the endpoint; this association is best described as monotonically positive (Figure 1) with exponential increments from 6 to 6.5 mEq/L and up.
Conclusion: In patients with AHF, high serum potassium at admission is associated with higher risk of 6-month death. This association is especially attributable to very high potassium levels.



P928

N-terminal pro-B-type natriuretic peptide is no related with prognosis in patients hospitalized for heart failure with mid-range ejection fraction. The REDINSCOR II Registry.

I Gomez Otero[1]; A Varela-Roman[1]; R Agra Bermejo[1]; A Ferrero-Gregori[2]; D Pascual-Figal[3]; J Delgado Jimenez[4]; J Alvarez Garcia[2]; F Worner Diz[5]; F Fernandez Aviles[6]; R Vazquez Garcia[7]; M Rivera[8]; J Cinca[2]; JR Gonzalez-Juanatey[1]

[1]University Hospital of Santiago de Compostela, Cardiology Department, Santiago de Compostela, Spain; *[2]Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain*; *[3]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology Department, Murcia, Spain*; *[4]University Hospital 12 de Octubre, Cardiology Department, Madrid, Spain*; *[5]Hospital Arnau de Vilanova, Cardiology Department, Lleida, Spain*; *[6]University Hospital Gregorio Maranon, Cardiology Department, Madrid, Spain*; *[7]University Hospital Puerta del Mar, Cardiology Department, Cadiz, Spain*; *[8]Hospital Universitario y Politécnico La Fe, Cardiology Department, Valencia, Spain*

On behalf of: REDINSCOR II
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Background/Introduction: The prognosis impact of the N-terminal pro-B-type natriuretic peptide (NT-proBNP) during hospitalization for acute heart failure (HF) is controversial. The new ESC HF guidelines include a new HF category with mid-range EF (HFmrEF) (LVEF 40-49%). To date has not been described the NT-proBNP levels and the prognosis in this group.
Purpose: We describe the NT-proBNP levels and the prognosis of HFmrEF hospitalized for acute HF in the REDINSCOR II Registry.
Methods: A prospective observational study was conducted with 1420 patients classified according to ejection fraction as follows: HFrEF <40%; HFmrEF, 40%-49%; and HFpEF, ≥50%. Baseline patient characteristics and outcomes at 1-, 6-, and 12-month follow-up were examined.
Results: Among the study participants, 583 (41%) had HFrEF, 227 (16%) HFmrEF, and 610 (43%) HFpEF. The mean value of NT-proBNP during hospitalization was 6242.4 pg/ml in HFrEF, 4349.3 pg/ml in HFmrEF and 2845.9 pg/ml in HFpEF, p < 0.001. Despite these differences there were no significant differences in all-cause mortality, or heart failure readmissions (table 1).
Conclusions: Despite marked differences in NT-proBNP levels between three categories during hospitalization for acute HF, no significant differences in the prognosis were observed during 1-year follow up. Our findings suggest a limited value of NT-proBNP levels in HFmrEF patients in these setting.

	HFrEF < 40% n=583 (41,1%)	HFmrEF 40 to 49% n=227 (16,0%)	HFpEF >=50% n=610 (43,0%)	P
Age, y	68,2 (12,8)	72,5 (11,1)	75,0 (10,7)	< 0,001
Isquemic HF etiology	266 (50,5%)	83 (43,5%)	142 (26,4%)	< 0,001
Hypertension	415 (71,7%)	179 (79,2%)	489 (80,3%)	0,001
Diabetes mellitus	276 (47,7%)	109 (48,2%)	279 (45,8%)	0,746
Atrial fibrillation on admission	195 (34,5%)	92 (42,2%)	253 (43,0%)	0,009
Estimated GFR (CKD-EPI, mL/min/1,73m^2)	61,6 (26,3)	58,5 (24,6)	60,1 (24,0)	0,266
NT-proBNP pg/ml,	6.242,4 (3.299,1-10.960,2)	4.395,9 (2.308,1-8.262,5)	2.845,9 (1.287,4-5.903,6)	< 0,001
In-hospital deaths	21 (3,8%)	9 (4,1%)	23 (3,9%)	0,972
1-month mortality	31 (5,3%)	19 (8,4%)	37 (6,1%)	0,265
6-month mortality	84 (14,4%)	41 (18,1%)	88 (14,4%)	0,370
12-month mortality	116 (19,9%)	55 (24,2%)	118 (19,3%)	0,278
HF readmision at 1 month	58 (9,9%)	21 (9,3%)	57 (9,3%)	0,924
HF readmision at 6 months	147 (25,2%)	55 (24,2%)	142 (23,3%)	0,738
HF readmision at 12 months	178 (30,5%)	67 (29,5%)	182 (29,8%)	0,947

P929

The association of baseline hyponatremia with ethnicity and gender in acute heart failure admissions

V Vikas Sunder[1]; R Alvarez[1]; E Carabelli[1]; M Weiner[1]; E Hamad[1]

[1]Temple University School of Medicine, Cardiology, Philadelphia, United States of America

Background: Hyponatremia, defined by a serum sodium concentration less than 135 mEq/L, is an electrolyte abnormality seen in approximately 25% of patients admitted with congestive heart failure (CHF). Baseline hyponatremia on admission has been shown to increase in-hospital mortality and to be an independent predictor of 6-month mortality in CHF patients. Prior work has shown that CHF patients with baseline hyponatremia are more likely to be Caucasian, but without further investigation. Heart failure does not impact patients of different ethnic backgrounds in the same manner. African-Americans have more than twice hospitalization rate of Caucasians. Given its prognostic significance and pathophysiologic role in the heart failure syndrome, hyponatremia and its association with patient characteristics warrants further study
Purpose: To examine the association between baseline hyponatremia and the patient characteristics ethnicity and gender in a sample of heart failure admissions
Methods: Administrative data from admissions to Temple University Hospital between August 2011 and July 2015 was extracted and merged with inpatient laboratory data. We queried for unique admissions with a DRG code of "291-293" to represent a heart failure admission. We identified unique heart failure admissions that had a first sodium lab value after admission available. We used the identifiers "Ethnicity" and "Gender" to categorize the data. Chi-square tests were performed to examine association between first Na < 135 mEq/L and ethnicity, gender, or ethnic/gender sub-group. All statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, NC). Statistical significance was defined as $p < 0.05$.
Results: 976 CHF admissions with a first Na lab value were identified. 884 admissions were identified by ethnicity as either "African-American", "Caucasian (Non-Hispanic)" or "Hispanic". There was no association between first Na < 135 and ethnicity (Chi-squared=2.31; p = 0.31). 976 admissions were identified as either "male" or "female". There was no association between baseline hyponatremia and gender (Chi-squared=1.17; p = 0.27). 768 patient admissions could be classified by both ethnicity and gender. The "African-American/ Female" sub-group had the lowest proportion of admissions with first Na < 135 at 10.4%.The association between baseline hyponatremia and ethnic/gender sub-group did not achieve statistical significance (Chi-squared=9.49; p = 0.09)

Conclusion(s): Our study demonstrates no statistically significant association between baseline hyponatremia and the patient characteristics ethnicity and gender in a small sample of heart failure admissions. There was a trend toward a lower proportion of "African-American/Female" admissions having baseline hyponatremia as compared to other ethnic/gender sub-groups. Further examination of the association between hyponatremia and patient characteristics is needed using a larger sample

P930

Heart failure and preserved ejection fraction: clinical and prognostic observation after long follow-up. (from the ABC-3 study on acute coronary syndrome)

G Giuseppe Berton[1]; R Cordiano[2]; R Palmieri[2];
F Cavuto[3]; B Segafredo[3]; A Cati[1]; M Centa[1]; S Cuckon[1]; M Pasquinucci[1]
[1]Conegliano General Hospital, Conegliano, Italy; *[2]Adria General Hospital, Adria, Italy*; *[3]Bassano General Hospital, Bassano, Italy*

On behalf of: ABC Study on Heart Disease
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Objective: to examine clinical characteristics and long term prognosis of patients with heart failure (HF) and preserved left ventricular ejection fraction (HFpEF), and compare them to patients with HF and reduced LVEF (HFrEF).
Methods: The ABC 3-Study on Acute Coronary Syndrome is an ongoing, prospective investigation designed to reflect, as closely as possible, an unbiased population of patients with acute coronary syndrome (ACS). The present study includes 529 patients with ACS, enrolled in three intensive coronary care units, followed up for 17 years. HF was evaluated according to Killip classification: class 1: no HF, class 2: pulmonary rales, class 3: pulmonary oedema, class 4: cardiogenic shock. We considered left ventricular ejection fraction (LVEF)=45% as a cut-off, higher values were considered as preserved systolic function. Baseline, clinical and laboratory data were all obtained within the first 7 days of hospitalization. All patients were followed up to 17 years of observation or time to death. Only 3 patients did not complete the follow-up and their time was censored before 17 years. Survival analysis was realized using Cox regression models. All analyses were made with STATA 14.
Results: Among the 529 ACS-patients, 87 (48%) had HFpEF, and 95 (52%) had HFrEF. All the other patients had Killip class=1. We did not observe differences between the two groups regarding age (mean ± SD: 69.7 ± 10.1 years; 71.8 ± 10.7 years respectively, $p = 0.16$); gender, $p = 0.27$; BMI, $p = 0.46$; presence of hypertension, $p = 0.49$; diabetes mellitus $p = 0.70$; total plasma cholesterol, $p = 0.65$. Remarkably, the CK-MB peak (log-transformed), an indicator of necrosis extension, did not differ between the two groups ($p = 0.78$), while indicators of renal function (estimated glomerular filtration rate (eGFR)=77.7 ± 31.6 and 64.8 ± 28.3 respectively, $p = 0.002$) and endothelium dysfunction ,evaluated by means of 24-hours urinary albumin to creatine ration (ACR)=39.8 ± 74.1 mg/g and 71.6 ± 116.1 mg/g respectively, $p = 0.009$ in log-transformed data) showed relevant divergence. Among HFpEF patients, 62 (71.3%) died during the follow-up, while 89 (93.7%) died among those with HFrEF, chi2=16.1, $p = < 0.0001$.
At Cox surviving analysis, we observed lower mortality risk among HFpEF patients (HR=2.3; 95%CI=1.7-3.3; $p < 0.0001$). In the adjusted model (age, gender, ACR, GFR) still the risk difference remained consistent (HR=1.8; 95%CI=1.2-2.5; $p = 0.001$).
Conclusion: We observed that HFrEF patients had worse renal function and endothelium dysfunction in comparison with HFpEF patients. Besides, patients with HFrEF showed higher long-term mortality risk as compared to those with HFpEF.

P931

In ADHF patients, difference between serum BNP on admission and the one that is detected at discharge predicts six- month mortality more reliably compared to BNP on admission

R De Vecchis[1]; C Ariano[1]; G Di Biase[2]
[1]Cardiology Unit, Presidio Sanitario Intermedio "Elena d'Aosta", Naples, Italy; *[2]Neurorehabilitation Unit, Clinica" S.Maria del Pozzo", Somma Vesuviana, Italy*

Background According to some authors, a single isolated measurement of serum B-type natriuretic peptide (BNP) executed on hospital admission would not be a sufficiently accurate method to predict the outcome of patients with acute decompensated heart failure (ADHF).
Aims: For verifying this assumption, a retrospective study was conducted on patients hospitalized for ADHF. Our main objective was to ascertain whether there was any difference in midterm mortality among patients with rising BNP at discharge as compared to those with decreasing BNP at discharge.
Methods: Medical records were examined so as to make a partition of the ADHF patient population into two groups, the former characterized by a rise in BNP during hospitalization, and the latter exhibiting a decrease in BNP in the measurement taken at hospital discharge.
Results: 177 patients were enrolled in a retrospective study. Among them, 53 patients(30%) had increased BNPs at the time of discharge, whereas 124 (70%) showed decreases in serum BNP during their hospital stay. The group with patients who exhibited BNP increases at the time of discharge had higher degree of congestion evident in the higher frequency of persistent jugular venous distention and persistent orthopnea at discharge. Moreover, patients with increased BNP at the time of discharge had a lower reduction in inferior vena cava maximum diameter [1.58 ± 2.2 mm vs. 6.32 ± 1.82 mm; p (one-way ANOVA)=0.001]. In contrast, there was no significant difference in weight loss when patients with increased BNP at discharge were compared to those with no such increase. A total of 14 patients (7.9%) died during the six-month follow-up period. Multivariable Cox proportional-hazards regression analysis revealed that BNP increase at the time of discharge was an independent predictor of six-month all-cause mortality after adjustment for persistent jugular venous distention, persistent orthopnea, reduction in inferior vena cava maximum diameter at discharge, weight loss, serum urea, systolic blood pressure at admission and BNP at admission (hazard ratio= 30.5424; 95% CI: 1.7409 – 535.8294, $p = 0.0199$).
Conclusions: Among patients with history of ADHF, more elevated BNP levels at the time of discharge from the hospital compared to those detected at admission identify a patient subset with higher grade of congestion and higher six-month mortality.

P932

Transient versus persistent worsening renal function during hospitalization in acute heart failure: different phenotypes for different outcome

G Ruocco[1]; R Nuti[1]; M Beltrami[1]; A Giambelluca[1]; C Daniello[1]; B Franci[1]; A Palazzuoli[1]
[1]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy

Background: Role of Worsening renal function (WRF) in acute Heart Failure (HF) is still debated: it could be an index of over-diuresis but also a poor prognostic index. Our hypothesis is that the timing of WRF development could differently influence clinical decongestion and outcome.
Purpose: The aims of this study were: 1- to evaluate transient WRF versus persistent WRF in terms of clinical decongestion efficacy in acute HF patients; 2- to compare transient WRF and persistent WRF in relation to rate of adverse events at six months.
Methods: We enrolled 161 patients admitted to our department with diagnosis of acute HF screened from DiurHF Trial. All patients underwent systematic clinical congestion scoring and laboratory assessment (BNP, creatinine, BUN) at admission and at discharge. WRF was defined as creatinine increase ≥ 0.3 mg/dL at any time during hospitalization. Persistent WRF was defined as a sustained rise above this level throughout the hospitalization whilst transient WRF was defined as creatinine increase ≥ 0.3 mg/dL within 72 hours from the initiation of loop diuretics with return to creatinine levels below this threshold. Congestion score was evaluated using 5 signs (peripheral edema, pulmonary rales, jugular venous distention, third heart sound, hepatomegaly). Efficacy decongestion was considered when at least 3 signs resolving by the time of discharge. All patients were followed for six months for death or re-hospitalization due to cardiovascular causes.
Results: Of 161 patients, 12 patients were excluded for lacking laboratory or follow-up data. 93 patients (62%) experienced adverse events during 180 -days follow-up period. Among all patients developing WRF (n = 71) 48 had persistent and 23 had transient WRF. Patients who developed persistent WRF demonstrated similar rate of decongestion compared to those with transient or no WRF (72% vs 73% vs 74% respectively $p = 0.984$). Conversely transient WRF patients had lower adverse events rate respect to patients with persistent WRF and stable creatinine (30 % vs 81% vs 60%; $p < 0.001$). Stratification of the groups by previous Chronic Kidney Disease (CKD) revealed a significant lower rate of basal renal dysfunction in transient WRF group respect to persistent WRF and stable creatinine groups (21% vs 45% vs 50%; $p = 0.05$). Cox regression analysis showed that persistent WRF was related to poor outcome (U-HR 1,70 [1,11-2,61]; $p = 0.01$. M-HR 1,75 [1,12-2,74]; $p = 0.01$) oppositely transient WRF was related to improved prognosis (U-HR 0,42 [0,19-0,93]; $p = 0.03$. M-HR 0,42 [0,18-0,98]; $p = 0.04$). Kaplan-Meier survival curves confirmed the same trend.
Conclusions: Our data suggest that the timing of WRF has different prognostic significance: Transient WRF is associated with lower adverse events rate. Conversely persistent WRF is related to poor prognosis. These findings suggest the prognostic relevance of WRF is related to timing evaluation and it could reflect true and false renal dysfunction.

P933

Mean systolic blood pressure after admission for myocardial infarction is associated with one year mortality among elderly patients.

B Basile Mouhat[1]; C Guenancia[1]; M Zeller[1]; G Cartigny[1]; G Porot[1]; L Lorgis[1]; C Toucas[1]; M Benalia[1]; L Rosier[1]; C Khalil[1]; T Pommier[1]; Y Cottin[1]
[1]*University Hospital of Dijon, Department of cardiology, Dijon, France*

OBJECTIVE: Optimal blood pressure after acute myocardial infarction (AMI) is still debated. After admission for AMI, the target mean systolic blood pressure (mSBP) is unknown, especially in the elderly patients.
Methods: All patients older than 75 years admitted for AMI in our university hospital from 01/02/2012 to 31/01/2015 were screened to participate at this prospective observational study. Exclusion criteria were cardiogenic shock, end-stage renal disease, less than 3 collected blood pressure values. We completed a one-year follow-up. The primary endpoint was all-cause mortality at one year while additional criteria were major adverse cardiac and cerebrovascular events at one year. The mSBP was defined by the mean of at least 3 measurements over the first 48 hours following admission for AMI.
RESULTS: In our population, a ROC curve study on the relationship between mSBP and one-year mortality suggested a cut-off value of mSBP of 125 mmHg. 517 patients (mean age 82 years) were divided into 2 groups according to mSBP (<125mmHg vs ≥125mmHg). There was a higher rate of one year all-cause mortality in the mSBP<125mmHg group with 58 deaths (22.3%) versus 31 (12.1%)(p = 0,002) in the mSBP≥125mmHg group, and also an increased cardiovascular mortality in the mSBP<125mmHg group with 43 deaths (16.5%) versus 22 (8.6%) (p = 0,006). A multivariate analysis identified 4 independents factors of all-cause mortality at 1 year after AMI: initial GRACE score > 140, LVEF < 40%, history of stroke and mSBP<125mmHg.
Conclusions: In our elderly AMI population, low mSBP within 48 hours after admission was an independent and powerfull predictor of one-year mortality. Our results raise the question of the timing implying the introduction of usual pharmacological therapies in this high-risk population. Our cut-off of mSBP remains to be validated in further studies.

P934

Trends in gender differences in cardiac care and outcome after acute myocardial infarction in western Sweden

E Elmir Omerovic[1]; O Angeras[1]; P Petursson[1]; I Haraldsson[1]; C Dworeck[1]; J Odenstedt[1]; D Ioaness[1]; P Albertsson[1]; B Redfors[1]
[1]*Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: Cardiovascular disease is the most common cause of death for both genders. Debates are ongoing as to whether there exists sex-specific differences in clinical course, diagnosis and management of acute myocardial infarction (AMI) and to what extent these differences can be alleviated by changes in clinical praxis.
Methods: We compared all men and women who were treated for AMI at a cardiac care unit in Västra Götaland County between January 1995 and October 2014 by obtaining data from the prospective SWEDEHEART registry (Swedish Websystem for Enhancement of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies). We performed unadjusted and adjusted Cox proportional hazard and logistic regression analyses on complete case data as well as on imputed datasets.
Results: 48.118 patients (35.4% women) were diagnosed with acute myocardial infarction and were included in the analysis. Women as a group had better age-adjusted prognosis than men but this survival benefit was absent for younger women (<60 years) and for women with ST-elevation myocardial infarction (STEMI). Compared to men, younger women and women with STEMI were more likely to develop pre-hospital cardiogenic shock (adjusted OR 1.67, 95%CI 1.30 – 2.16, p < 0.001 and adjusted OR 1.31, 95%CI 1.16 – 1.48, p < 0.001) and were less likely to be prescribed evidence based treatment at discharge (p < 0.001 for beta blockers, angiotensin converting enzyme inhibitor/angiotensin receptor antagonist, statins and P2Y12 antagonists). Differences in treatment between the genders did not decrease over the course of the study period (p>0.1 for all treatments).
Conclusions: Younger women and women with STEMI have higher risk to develop cardiogenic shock and have worse short- and long-term prognosis after acute myocardial infarction. Women are less likely than men to be prescribed evidence based treatment after acute myocardial infarction.

P935

Dynamics of epidemiological characteristics of the prevalence of cardiovascular and some noninfectious diseases among the women of fertile age in Fergana Valley

S Saidrakhim Lukmonov[1]; O Usmonov[1]; I Xaydarov[1]; M Usmonova[1]; M Rozikova[1]; D Mamedov[1]; SH Shamsiyev[1]; M Turdikulova[1]; M Ismailov[1]; A Ismatov[1]; E Mirzakarimov[1]; D Toirova[1]; G Suyunova[1]; N Melikova[1]; S Mingbayeva[1]
[1]*Tashkent Medical Academy, Department of faculty and hospital treatment, medical and pedagogical faculty, Tashkent, Uzbekistan*

Purpose: To study 9-year dynamics of prevalence of main cardiovascular and non-infectious diseases (MCNID) among the population of women of fertile age (FAW) in Fergana Valley.
Material and methods: During epidemiological study with use method of monitoring there was evaluated 9-year dynamics of MCNID prevalence among FAW (912 women in Andijan-city and 2360 women in Namangan). In two researches with interval 9 years the lists of election campany before onset of investigations were the resources for formation of the selection. There were used epidemiological criteria for diagnosis of MCNID (Oganov R.G. et al, 2003).
Results: During the period from 1996 to 2004 in FAW the statistic significant increase in prevalence of MCNID by 5,4% was found (from 26,1% to 31,5% respectively from 1 to 2 investigation, P < 0,05). This grow of MCNID formed due to their increase in various patterns in the following age groups: from 10,1 - 19,2% or by +9,1% at 15 years-19 years (P < 0,05); from 17,2 -29,4%, or by +12,2% - at 20-29 years (P < 0,05); from 24,0 to 37,8% or by 13,8% - at 30-39 years (P < 0,05) and from 16,6% to 28,8% or by 12,2% at 40-49 years (P < 0,05).The marked growth of MCHID was noted in age group of 30-39 years, comparatively less this grow was observed in groups of women of 15-19 years, 20-29 and 40-49 years.
Conclusion: During the 9-year follow-up of FAW in comparison with initial data the growth of cases of MCNID was significantly accelerated – from 9,1% (15-19 years) to 13,3% (30-39 years) in dependence on age. These results may be recommended for optimization of the strategy of preventing programs or for determination of the groups of high risk for development of chronic multiple diseases in women of the age 15-49 years.

P936

Prognostic role of cystatin C and other biomarkers in heart failure

A Adriana Tamburello[1]; G Carollo[1]; G Novo[1]; F Ricupati[1]; S Novo[1]
[1]*University Hospital Paolo Giaccone, Cardiology, Palermo, Italy*

Background: Cystatin C is a valid alternative to test renal function and it recently showed some features, in terms of long-term predictive value of mortality and re-hospitalization for acute heart failure, compared to measurement of serum creatinine and/or levels of NT-proBNP.
Materials and methods: We studied 79 patients (Men= 38, Women= 41; average age 74.10 ± 8.45 years) consecutively admitted at the Cardiology Unit for heart failure. The final diagnosis of heart failure was made in accordance with the recent ESC Guidelines 2016, based on clinical history, signs, symptoms experienced, and echocardiographic alterations (Abnormalities in E/e′ ratio and/or increased left atrial volume were also considered)
We evaluated serum concentrations of cystatin C and NTproBNP within 24 hours of hospitalization and at discharge, the classification of the New York Heart Association (NYHA), the speed ratio of the transmitral flow (ratio E/A) to assess diastolic function.
It was conducted a one year follow-up with telephone interview, regarding any re-hospitalizations or mortality for all-causes or cardiac causes.
Results: The levels of Cystatin C, NT-proBNP were significantly related to NYHA class and lower ejection fraction (r = 0.603 P < 0.001, r = 0.331 P < 0.001 and r = 0.321 P < 0.001, respectively).
Patients with Cystatin C levels less than 1.5 mg/l had a higher E/A ratio than those with cystatin C levels greater than 1.5 mg/l. Cystatin C was significantly associated with both NYHA classification and E/A ratio even after adjusting for creatinine clearance.
We found an area under the ROC curve of 0.741 (SE 0.0969, 95% CI 0.610 to 0.846) for NTproBNP and 0.824 (SE 0.0596, 95% CI 0726-0897) for Cystatin C. In these conditions, the values with the high prognostic accuracy appear to be> 590 pg/ml for NTPRO-BNP (95.9% sensitivity, 87.0% specificity) and cystatin C> 2.16 mg/L (sensitivity 89.1%; specificity 88.2%).
Conclusions: Both Cystatin C and NT-proBNP are related to worse NYHA classification, ejection fraction and increased rate of MACEs and mortality. Independent of renal function, higher serum concentrations of cystatin C correlates with days of hospitalization (P = 0,0002) and abnormal cardiac diastolic properties in patients with heart failure.

P937

Association between iron deficiency and post-discharge outcomes in patients hospitalized for heart failure

M Monica Chivulescu[1]; L Antohi[1]; I Cosei[1]; C Radulescu[1]; J Butler[2]; G Tatu-Chitoiu[3]; IM Coman[1]; SP Collins[4]; M Gheorghiade[5]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; [2]*Stony Brook University Medical Center, Stony Brook, United States of America*; [3]*Emergency Clinical Hospital Floreasca, Bucharest, Romania*; [4]*Vanderbilt University, Nashville, United States of America*; [5]*Northwestern University, Chicago, United States of America*

Background: Iron deficiency (ID) is common in chronic heart failure (HF) patients and is associated with a negative prognosis, but its prevalence and clinical relevance remain unknown in hospitalized patients with worsening chronic heart failure (WCHF).
Aims: To determine the prevalence of ID in a cohort of patients hospitalized for WCHF and to describe the epidemiological characteristics of this sub-population. The relationship between ID and post-discharge outcomes was prospectively evaluated.
Methods: FERIC-RO study was designed as a prospective national observational study which enrolled 138 consecutive patients hospitalized for WCHF. Iron status was assesed at discharge in all patients and ID was defined as ferritin < 100 mcg/L or 100-299 mcg/L and TSAT < 20%. Patients were divided in two groups according to the presence or absence of ID.
Results: A proportion of 54% of the patients had ID, and of these 19% had ID without anemia, while 35% had ID and anemia. Differences in baseline characteristics between ID+ and ID- are shown in Table 1. Patients with ID had higher 3-month mortality compared to those without ID (9.9% vs 7.9% P=0.002). In univariate analysis, ID was predictive for 3-month mortality (HR=1.21; 95% CI 1.04-1.32). When adjusted for 9 clinical variables including demographic, baseline treatments, history and left ventricular ejection fraction, ID wasn´t found as a predictor of 3-month all cause mortality (HR=1.12; CI 95% 0.98-1.19)
Three month-HF rehospitalizations were higher in patients with ID as compared with patients without ID (12.0% vs 9.1% P=0.002). ID was independently predictive for 3-month HF rehospitalizations even after adjusting for the same clinical variables (HR=1.38; CI 95% 1.11-1.46).
Conclusion: ID is a common comorbidity in patients hospitalized for WCHF and it is associated to higher risk for post-discharge adverse events. ID should be regularly checked at discharge and may be a therapeutical target in WCHF.

	ID + n=75	ID-n=63	P
Age (years)	71.4±11	70.3±9	0.04
Male gender (%)	61	63	0.08
LVEF (%)	31.4±10	33.5±9	0.005
Ischemic etiology (%)	60.4	61	0.1
NT-proBNP (pg/ml)	3875±1950	2510±1730	<0.001
CKD (eGFR 60ml/min)	48	41	0.002

LVEF left ventricular ejection fraction. CKD chronic kidney disease. eGFR estimated glomerular filtration rate disease.

P938

Adherence to treatment guidelines and its association with length of hospital stay for patients with decompensated heart failure and reduced ejection fraction

G Gediminas Aucina[1]; J Motiejunaite[2]; V Juknevicius[3]; D Kablucko[3]; E Paleviciute[3]; A Montvilaite[4]; E Kavaliunaite[4]; A Mebazaa[5]; A Kavoliuniene[2]; J Celutkiene[3]
[1]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [2]*Lithuanian University of Health Sciences, Kaunas Clinics, Department of Cardiology , Kaunas, Lithuania*; [3]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; [4]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [5]*University Paris Diderot , U942 Inserm, Hospital Lariboisière, Paris, France*

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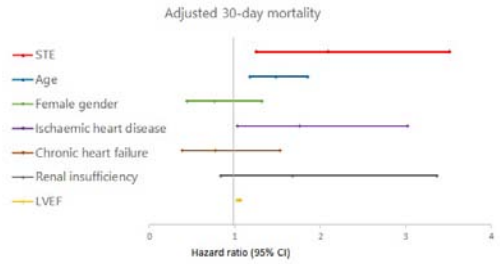
Introduction: Heart failure (HF) is a major and growing public health problem. Currently, HF is the main reason of hospitalisation for patients aged over 65 and it imposes a significant economic burden on health care systems. Medication nonadherence is associated with an increased risk of all-cause mortality and cardiovascular hospitalisations in patients with HF.
Purpose: We aimed to investigate adherence to HF guidelines for drug therapy and the association between adherence and length of hospital stay for HF patients hospitalised due to acute dyspnea.
Methods: Prospective observational cohort study enrolled 837 consecutive patients admitted to the emergency department with acute dyspnea between March 2015 and December 2016. Out of 837 examined patients, 187 patients (22.3%) were included in the analysis after being hospitalised and discharged with final diagnosis of acute HF with reduced left ventricular ejection fraction (LVEF <40%). Patients presenting dyspnea related to HF with LVEF >40% (9.2%), cardiac arrhythmia (8.8%), pulmonary embolism (6.9%), pulmonary infection (6.8%), acute coronary syndrome (4.5%), chronic obstructive pulmonary disease (4.3%), cancer (3.0%), hypertension (1.8%), anxiety (1.6%) were excluded. Adherence was evaluated using guideline adherence indicator (GAI3), which is defined as the proportion of care across main three therapeutic classes (angiotensin-converting-enzyme inhibitors (ACEIs), beta-blockers (BBs) and mineralocorticoid receptor antagonists (MRAs)) according to current European Society of Cardiology (ESC) HF treatment guidelines. Patients were categorised into 3 groups based on the GAI3 values (good, 100% intermediate, 50–67% poor, 0-33%). A general linear model was used to assess the effect of pre-hospital GAI3 on the length of hospital stay.
Results: We evaluated 187 patients (mean age, 69.1 years, 66% men) with the mean GAI3: pre-hospital – 56.7% (23%, 40% and 37% showed good, intermediate, and poor adherence, respectively), at discharge – 68.4% (34%, 43% and 23% showed good, intermediate, and poor adherence, respectively). BBs (68%) were used more frequently in pre-hospital HF treatment than ACEIs (60%) and MRAs (42%). This trend was also observed in medication prescribed at discharge (BBs 81%, ACEs 66%, MRA 58%). The length of hospital stay was significantly longer in poor adherence patients group (11.7 ± 0.98 days) in comparison with intermediate (8.1 ± 0.84 days) and good (10.8 ± 1.59 days) adherence groups ($p < 0.05$).
Conclusions: Pre-hospital and discharge treatment showed intermediate adherence to HF treatment guidelines. Poor adherence to ESC HF guidelines could be associated with increased length of hospital stay.

P939

ST-segment elevation in baseline electrocardiogram predicts mortality in cardiogenic shock

T Javanainen[1]; HEV Tolppanen[1]; VP Harjola[2]; J Lassus[3]; T Tarvasmaki[1]; MS Nieminen[1]; J Spinar[4]; A Sionis[5]; M Banaszewski[6]; R Jurkko[1]
[1]*Helsinki University Central Hospital, Helsinki, Finland*; [2]*Helsinki University Central Hospital, Emergency medicine, Helsinki, Finland*; [3]*Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland*; [4]*University Hospital Brno, Department of Internal Medicine and Cardiology, Brno, Czech Republic*; [5]*Hospital de la Santa Creu i Sant Pau, Intensive Cardiac Care Unit, Cardiology Department, Barcelona, Spain*; [6]*Institute of Cardiology, Warsaw, Poland*

Background: The most common aetiology of cardiogenic shock (CS) is acute coronary syndrome (ACS), but 20 % of CS is caused by other disorders. ST-segment deviations in electrocardiogram (ECG) have previously been investigated in patients with CS caused by ACS but not in those with other CS aetiologies.
Purpose: The aim was to explore the prevalence of different ST-segment patterns and their association with the aetiology and 30-day mortality in CS.
Methods: We analysed the baseline ECG of 196 patients who were included in a multinational prospective cohort study of CS. The patients were divided into three groups according to their ECG: 1) ST-segment elevation (STE): ST-segment elevation at the J point in two contiguous leads with following cut-points: ≥ 0.1 mV in all leads other than leads V2 – V3 where the following cut points apply: ≥ 0.2 mV in men ≥ 40 years; ≥ 0,25mV in men < 40 years, or ≥ 0.15 mV in women. 2) ST-segment depression (STDEP): horizontal or down-sloping ST-depression ≥ 0.05 mV in two contiguous leads. 3) No ST-segment deviation or ST-segment impossible to analyse (NSTED). The multivariable model was adjusted for age, gender, left ventricular ejection fraction and comorbidities.
Results: Mean age was 66 years, 74 % were men, and 81 % had ACS as CS aetiology. The prevalence of any ST-segment deviation was 80 % (n = 157). Half of the patients had STE (n = 105, 54 %) and one fourth had STDEP (n = 52, 27 %). Remaining 20 % (n = 39) comprised NSTED group. The prevalence of ACS aetiology was higher in patients with STE (93 %) in comparison with STDEP (71 %, p < 0.01) and NSTED (59 %, p < 0.01). Overall, 30-day mortality was 36%; in STE group 42 %, STDEP 31 % and NSTED 28 % (p = 0.18). In multivariable analysis, STE was an independent predictor of mortality (HR 2.09, 95 % CI 1.25 - 3.51) along with increasing age, previous ischaemic heart disease and left ventricular ejection fraction (Figure).
Conclusions: Most CS patients have ST-segment deviations in baseline ECG. STE is strongly associated with ACS aetiology. Interestingly, CS aetiology was other than ACS in one third of patients with STDEP. Furthermore, CS was caused by ACS in over half of the NSTED patients. Importantly, STE is an independent predictor of 30-day mortality.



Figure

P940

Characteristics of patients with acute heart failure according to new ESC guidelines derived-LVEF classification

D Damien Logeart[1]; T Damy[2]; R Isnard[3]; M Saval[4]; P Degroote[5]; F Roubille[6]; C Tribouilloy[7]; R Trochu[8]; F Piccard[9]; G Roul[10]; V Bataille[11]; N Naccache[11]
[1]AP-HP - Hospital Lariboisiere, Department of cardiology, Paris, France; *[2]University Hospital Henri Mondor, Creteil, France*; *[3]Hospital Pitie-Salpetriere, Paris, France*; *[4]University Hospital of Grenoble, Grenoble, France*; *[5]Cardiology Hospital of Lille, Lille, France*; *[6]University Hospital Arnaud de Villeneuve, Montpellier, France*; *[7]University Hospital of Amiens, Amiens, France*; *[8]University Hospital of Nantes Nord Laennec, Nantes, France*; *[9]Hospital Haut Leveque, Bordeaux-Pessac, France*; *[10]University Hospital of Strasbourg, Strasbourg, France*; *[11]French Society of Cardiology, Paris, France*

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New ESC guidelines pointed out the need to specify what are heart failure (HF) patients with mid-range left ventricular ejection fraction (mrLVEF) – defined by LVEF 40 to 49%- as compared to patients with preserved LVEF (pLVEF) and reduced LVEF (rLVEF). By using French Survey on Heart Failure (FRESH), we aim to compare characteristics of these 3 subgroups in acute HF.
Methods: FRESH is an on-going multicenter survey collecting exhaustive data in both acute and chronic HF (NCT01956539). Comparisons were performed using chi^2 or Fisher test for categorial variables and ANOVA or non-parametric Kruskal Wallis test for continuous variables. Multinomial logistic regression was performed.
Results: Among 595 chronic HF patients, 50% had rLVEF, 15% had mrLEVF and 35% had pLVEF.
There were significant differences across LVEF subgroups in clinical scenario at admission as well as age, gender, underlying cardiac disease, comorbidities, heart rate, arrhythmia, blood pressure, haemoglobin, natremia, BUN, natriuretic peptides, and use of medications during hospitalization and at discharge. The table shows significant results of the multivariate analysis.
Conclusion: Acute HF patients with mrLVEF exhibit some significant differences with both HF-rEF and HF-pEF, which deserves further investigations.

	Odd ratio	95%CI	p
HF-rEF versus HF-mrEF			
- Age(by 10y)	0.64	0.50-0.82	< 0.001
- Gender (female)	0.42	0.22-0.80	0.008
- Dilated cardiomyopathy	2.96	1.18-7.42	0.021
- Systolic blood pressure (by 10mmHg)	0.80	0.72-0.89	< 0.001
- Hemoglobin (by 1g/dL)	1.20	1.04-1.38	0.01
- Natriuretic peptides (BNP or NTproBNP)3rd vs 1st tertile	2.42	1.12-5.22	0.025
- Betablockers at discharge	2.00	1.04-3.82	0.037
HF-pEF versus HF-mrEF			
- Ischemic heart disease	0.38	0.19-0.75	0.005
- Heart rate (by 10bpm)	0.86	0.75-0.97	0.01
- Natriuretic peptides (BNP or NTproBNP)3rd vs 1st tertile	0.29	0.13-0.65	0.002
- Anti-aldosterone at discharge	0.23	0.12-0.44	< 0.001

P941

Hypercapnia in patients admitted in the emergency department for acute decompensated heart failure

D David Cabrita Roque[1]; J Augusto[1]; A Sachetti[1]; D Faria[1]; A Gaspar[1]; L Melo[1]; T Bernardo[1]; J Simoes[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal

Background: Blood gas assessment (BGA) is recommended in the evaluation of patients with acute heart failure only in those where oxygenation cannot be readily assessed by pulse oximetry, and when a precise measurement of O2 and CO2 partial pressures is needed. We aim to evaluate the prevalence and characteristic of hypercapnia in acute decompensated heart failure (ADHF).
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for acute decompensated heart failure. We included patients in whom a BGA was performed at admission. Hypercapnia was defined as pCO2 at admission > 45mmHg. The HF profile was assessed as according to the recent guidelines.
Results: 206 patients with ADHF as the primary reason for hospitalization performed BGA at the hospital admission (46.1% male, 74.7 ± 16.9 years). 201 (97.6%) patients were classified as profile B (wet and warm); of these 135 patients (65.5%) were classified as having acute pulmonary edema (APE). Profile C was less common (2.4%). Hypercapnia was observed in 70 patients (30.7%), more frequently in patients with APE (50.7% vs 25.9%, p = 0.001). Of the group of patients in APE, the use of bi-pressure airway ventilation was 55.9% for those with hypercapnia and 12.1% for those without hypercapnia (p < 0.001).
Conclusion: Hypercapnia is present in up to one third of the patients admitted with ADHF, more frequently in those with APE. The potential need for the use of bi-pressure airway ventilation and its prevalence in this population suggest that the knowledge of the CO2 level may be important in these patients.

P942

Chitotriosidase enzyme can be a negative acute phase protein in acute heart failure unlike coronary artery diseases

S Sara Cetin Sanlialp[1]; M Sanlialp[2]
[1]pamukkale university, cardiology, Denizli, Turkey; *[2]denizli government hospital, cardiology, denizli, Turkey*

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 (lysosomal storage diseases, sphingolipidoses, sarcoidosis, tuberculosis, thalassemia, multiple sclerosis etc.). Therewithal, it has been observed that CHIT activity in plasma is significantly high in ischemic heart diseases with arterial inflammation and ischemic strokes.There are no studies invastigating the relationship between conjestive heart failure and CHIT enzyme as much as day-to-day; this study 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) between 01.05.2014-01.11.2014, 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 highest CHIT activity in plasma (876,937 ± 820,938 ng/ml) is observed among chronic heart failure patients whereas the lowest CHIT activity in plasma (527,876 ± 323,04 ng/ml) is observed among 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 acute heart failure a negative correlation (p = 0,038 and r=-0,32) between plasma hs-CRP levels and CHIT activity occurred.
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.

Regression analyse of AHF vs Controls

Regression Analyse	Odd's Ratio	Confidence Interval	P Value
NT-proBNP	1,03	1,01-1,06	0,002
Hs-CRP	2,83	5,37-1,49	0,042
KIT	0,99	0,99-1	0,009
IL-6	1,7	1,12-2,6	0,012

P943

Advanced acute heart failure and ketogenic diet: a case series of a single centre initial experience

J Jonida Bejko[1]; T Bottio[1]; M Comisso[1]; M Carrozzini[1]; V Tarzia[1]; E Manzan[1]; D Gregori[1]; FP Francini[1]; G Gerosa[1]
[1]*University Hospital of Padova, Padua, Italy*

BACKGROUND: Ketogenic diet (KD) is an effective treatment for drug-resistant epilepsy. Recently, clinical indications have been increasing. Little is known on the contribution in cardiac metabolism.
Material and Methods: Seven adult pts affected by acute heart failure (HF), unresponsive to conventional medical and surgical therapy, were enrolled to observe the effects of KD as additional treatment. Pts demographics, diuresis, urine ketones, laboratory studies, diet duration, side effects and echocardiographic studies were recorded.
Results: Two pts presented biventricular failure after heart transplantation (HTx). Five pts presented right ventricular failure (RVF) after LVAD implantation. One pt was female (n = 1; 14%). Age range was 45-72 yrs. All pts were naïve to diet therapy. At 6 days of treatment pts responded to KD on: RVF (range 4-60% of TAPSE increase, p = 0.015); LV in two HTx (increase of 10-26% respectively,p = 1); glucose variability (GV) (p = 0.03). Hyperlipidemia was observed in 2 pts (28,6%, p = 0.015). Weight loss and increase in diuresis volume were common in all pts but not statistically significant (p = 0,4).
Conclusions: Perceived benefits of KD were improved RV function and reduced serum GV. These cases demonstrate that the use of KD for treatment of refractory HF can be undertaken safely and is well tolerated in different administration forms. Future research with proper numbers and identification of pts is necessary.

Outcomes

	N Pre-diet pts	Post-diet	Unadjusted p-value	Benjamini & Yekutieli adjusted p-value
	(N=7)	(N=7)		
TAPSE(mm)	7 7.85/ 8.8/ 9	12/13/13.35	0.015	0.19
FE (%)	2 51/52/53	58.25/61.5/64.75	0.5	1
Gluc.(mmol/L)	7 119.5/138.3/177.5	103/104.7/117.65	0.11	0.69
Gl.var	7 2.7/ 5.1/11.45	1.15/ 2.3/ 7.45	0.03	0.26
TG (mmol/L)	7 0.82/1.26/1.395	1.545/1.74/3.545	0.015	0.19
Na (mmol/L)	7 134.5/138/139.5	134.5/137/139	0.91	1
K (mmol/L)	7 3.6/4.1/4.35	3.65/4/4.3	0.53	1
Urea(mmol/L)	7 4.8/ 8.4/11.05	3.76/ 9.7/15.55	0.43	1
Creatinine(mg/dL)	7 65/ 73/125	66/103/154.5	0.84	1
Keto.ur ≤ 5mg/dL	7 0% (0)	100% (7)	-	-

Data are I quartile, Median, III quartile. P-values are reported both unadjusted and with Benjamini & Yekutieli correction. Test used: Shift-Algorithm using exact Wilcoxon Rank Test along with confidence intervals. Wilcoxon test has been shown to be more powerful in small sample situations.

P944

Frequency of etiological and precipitating factors in patients with acute de-compensated heart failure

M Muhammad Rauf[1]; KHAN Noman[1]; M Hafizullah[1]
[1]*Hayat abad Medical Complex , Cardiology, Peshawar, Pakistan*

Methodology: This cross sectional descriptive study was carried out at Cardiology Department, from October 2011 to April2012. Patients presented with ADHF were assessed and investigatedfor the causes and factors that precipitate heart failure (HF).
Results: Out of 291 patients, 153(52.5%) were males. Age ranged from 13-90 years with mean age 53.59 ± 18.98 years. The underlying etiology of HF was coronary artery disease (CAD) 29.2%, hypertension 18.5%, rheumatic heart disease (RHD) 13.7%, dilated cardiomyopathy (DCM) 11.0%, other cardiomyopathies 9%,multiple causes 12.4%, and others 6.1%. Most common precipitating factor for de-compensation was infections (28.2%) followed by poor compliance to medications (17.5%). Other precipitating factors include dietary indiscretion(11%), arrhythmias(13.7%), pregnancy(7.2%) and anemia(5.1%). No precipitating factor was found in 10% patients.
Conclusion: coronary artery disease, Hypertension, rheumatic heart disease and dilated cardiomyopathy are main etiological factors of ADHF. Infections, poor compliance to medications and arrhythmias are major precipitating factors.

P945

Is pulse pressure associated with short-term re-admission after index hospitalisation for acute heart failure syndrome?

L Cowie[1]; M Pang[1]; A Sultan[1]
[1]*Royal Albert Edward Infirmary, Cardiology, Wigan, United Kingdom*

Introduction: The prognostic value of pulse pressure has been investigated in chronic heart-failure patients, however, it's reliability as prognostic marker in patients with acute heart failure is unknown.
Hypothesis: We aimed to evaluate the effect of pulse pressure, at baseline and at discharge, on re-admission in 30-days after an index hospitalisation for unselected patients with acute heart failure (AHF) in the local population.
Patient selection and characteristics: We identified a total of 61 consecutive patients (mean age 78 years, 55.4% females) over three months period who were hospitalised for a mean of 7.6 days at a large district general hospital. 58.9% of patients were hypertensive, 34.1% were diabetics, 59% were known for previous chronic heart failure. 39.2% had myocardial infarctions, 55.7% had known atrial fibrillation and 16.0% had chronic obstructive pulmonary disease. Nearly 32.5% had acute kidney injury, but there was significant improvement in creatinine levels (123.7 mmol/l vs 113.1 mmol/L; p = 0.004) at the time of discharge. Interestingly, at discharge, a significant reduction in prescription for betablockers (87.1% vs 85.5% on discharge) was noted. Increasing number of patients received angiotensin converting enzyme-inhibitor (ACEi) or angiotensin receptor blockers (ARB) (66.2% vs 83.9%). Only 19.3% patients had aldosterone receptor inhibitors and 8% had Ivabadrine.
Results: Mean BP was reduced significantly from 138/78 mmHg to 123/68 mmHg (p < 0.01). Heart rate reduction was significant (88 beats per minute (bpm) to 74bpm; p < 0.0001), nonetheless it was still higher than the 70 bpm as suggested by SHIFT trial. 30-days all-cause mortality after an index admission was 9.6% and re-admission rate was 32.3%.
The mean pulse pressure drop was not significant (60.2 mmHg on admission vs 55.3mmHg at discharge, p = 0.09). Logistic regression analysis (MedCalc) showed pulse pressure on discharge (P < 0.0001) was significantly related to re-admission in 30 days after an index admission for AHF.
Conclusions: The results of this small study suggest that the prediction of re-admission after hospital discharge for acute heart failure could be improved based on pulse pressure at discharge. These results need confirmation in a larger study.

P946

Predictors of a longer lenght of stay in acute heart failure: a colombian experience

C I Clara Ines Saldarriaga[1]; JS Parada Zuluaga[2]; AM Quintero[1]; K Marisancen Carrasquilla[2]; AM Velez Granda[2]; EM Canas[2]; AM Agudelo[1]
[1]*Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia*; [2]*Universidad Pontificia Bolivariana, Cardiology, medellin, Colombia*

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Acute heart failure (AHF) is the leading cause of hospitalization for people aged 65 or older. Hospital length of stay (LOS) is a key determinant of higher hospitals costs.
Objective: To describe the clinical profile of patients admitted for AHF in a Colombian reference center and to identify the characteristics that predict a longer length of stay.
Methods: A prospective cohort study was performed
Results: 183 patients were hospitalized during a period of 5 months with diagnosis of AHF, the mean age was 67.6 +/- 15.3 years , 55.7% were males, the mean EF was 30.4% +/- 14,6 Most of the population had HFr EF. The clinical profile of the patients was : warm-dry: 3.8%, warm-wet: 78.7%, cold -dry: 3.8%, cold-wet 13.7%. Inotropes were prescribed in 15.8% and 5.5% presented new onset atrial fibrillation. the average LOS was 5 days and 53% of the population had a longer LOS. The 30 days mortality was 7%, 54.6% of the patients had at least one previous hospitalization. The most frequent comorbidities are presented in table 1. Multivariate and univariate analysis was performed and the presence of acute renal failure was the only predictor of a prolonged length of stay (Relative risk 1.66 CI 1.28 - 2.14)
Conclusion: Our population of AHF had a mean of stay of 5 days, were predominantly males, with reduce EF and a lot of comorbidities. Acute renal failure was the only predictor of a long stay.

Table 1

Comorbidities	Percentage
Hypertension	76.6%
Diabetes	32.2%
Atrial fibrillation	50.3%
COPD	21.9%
Coronary Artery disease	44.8%
Acute renal Failure	31.7%
Chronic renal failure	31.1%

Comorbidities

P947

Is tako-tsubo cardiomyopathy induced during dobutamine stress echocardiography a high-risk situation?

A Kassongo[1]; A Kone[1]; C Bensouda[2]; P Meimoun[3]; D De Zuttere[1]; H Lardoux[4]
[1]Institut Franco Britannique , LEVALLOIS PERRET, France; *[2]Clinique A.Paré, Neuilly sur Seine, France*; *[3]University Hospital of Compiegne, Compiegne, France*; *[4]Institut Mutualiste Montsouris , Cardiology , paris, France*

Background: Life-Threatening complications due to hemodynamic instability may occur early in Tako-Tsubo cardiomyopathy (TTC). Dobutamine Stress Echocardiography (DSE) is a non-invasive test to detect myocardial ischemia. TTC induced during DSE is a rare issue. Our purpose is the evaluate the frequency and severity of acute Left Ventricular (LV) dysfunction and its possible deleterious evolution in TTC induced during TSE

Patients and methods: From an exhaustive search and review, using key words "apical ballooning, stress cardiomyopathy and DSE", we identify 23 clinical reports of DSE induced TTC from 2008 to 2016, and we added one personal case.

Results: This cohort of 24 patients (pts) was homogenous as they all presented TTC during DSE. Collected observations came mostly from USA (n = 10) and Europe (n = 9). DSE tests, protocol and indications were conventional: thoracic pain (16/24) and pre-operative assessment (5/24). Symptoms occurred mostly at peak dose, 30 or 40 gammas/kg/mn (22/24) or rarely during recovery (3/25). Demographic and clinical data show: mean age= 63.5 ± 13 years - from 41 to 85; female=92%; female > 50 years = 84%. EKG ST elevation: 70.8%. All patients underwent emergency coro-angiography and all coronary angiogram were normal, with markedly depressed LV angio Ejection Fraction (LVEF): 33 ± 8% (not calculated for 10 pts). LV angiographic ballooning pattern was: apical n=15 (62%); mid n=5(20%), unknown (18%). Mean troponin peak was 3.87 (0.8 -9) ng/ml; Death occurs in one pt. (4.1%), at day 2, the eldest woman (85y) of the group because of cardiac failure. LVEF recovery was constant between day 2 and 30. New imaging techniques are still rarely added: Magnetic Resonance imaging (n = 4) and 2D longitudinal strain (n = 2)

Conclusions: TTC induced during DSE is a rare, but severe entity. It gives the rare opportunity to observe TTC at its very acute phase in all patients. Normal coronary arteries, acute LV dysfunction with apical or mid ballooning, low troponin levels, are typical markers of TTC. In this cohort, despite severe acute LV dysfunction, death remains rare. LV function normalizes rapidly and completely. Dobutamine infusion, psychological stress during DSE, may contribute to the occurrence of TTC during DSE but precise mechanism of this acute situation remains unknown.

P948

Persistent diastolic dysfunction following st elevation myocardial infarction

F Fathia Mghaieth Zghal[1]; F Azeiz[1]; B Rekik[1]; S Boudiche[1]; M Ben Halima[1]; N Khadher[1]; S Ouali[1]; A Farhati[1]; N Larbi[1]; MS Mourali[1]
[1]Rabta Hospital, Tunis, Tunisia

Objective: We performed serial Doppler echocardiography during hospitalization and at least one month following acute myocardial infarction (STEMI). The aim was to assess the correlation between persistent diastolic dysfunction and the infarct location, the peak of CPK and the left ventricular global longitudinal strain.

Design and method: In a prospective study, 127 consecutive patients (58.13 ± 11.92 years, 23 females, mean ejection fraction of left ventricle= 44.9 ± 9.9%) were enrolled. Echocardiography was performed several months (7.03 ± 6,70 months) after STEMI and the diastolic function was assessed according to the 2016 guidelines of the European Association of Cardiovascular Imaging.

Results: 65 patients (51%) sustained an anterior myocardial infarction. Only 25 patients (19%) had normal diastolic function (or a transient regressive dysfunction), 54 (42%) had grade 1 dysfunction, 11 (8%) had grade 2 dysfunction and 10 (7%) had grade 3 diastolic dysfunction. The diastolic function was indeterminate in 27 patients. The presence of diastolic dysfunction was associated with higher peak of CPK during the acute phase of myocardial infarction (938,40 ± 659,66 U/L vs 2060,95 ± 1348,17 U/L, p < 0,0001) and lower global longitudinal strain (-16,12 ± 2.73 vs -11,60 ± 5,29, p < 0,0001). There was no statistical significant correlation to the anterior infarct location (p = 0,18).

Conclusions: Left ventricular diastolic persistent dysfunction was present in the majority of STEMI patients. The extent of the infarction and the global longitudinal strain best identified patients with abnormal diastolic function.

CHRONIC HEART FAILURE

P949

Reliability of biomarkers (Nt-proBNP, Gal-3, NGAL, hsTnT, AVP, ST-2, MDA) in patients with HFrEF, HFpEF, diabetic nephropathy and arterial hypertension

S Litmeier[1]; F Weisrock[1]; M Fritschka[2]; S Beckmann[1]; D Djawid Hashemi[1]; J Wagner[1]; E Tahirovic[1]; S Radenovic[1]; A Busjahn[3]; B Pieske[1]; W Dinh[4]; HD Duengen[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; *[2]German Heart Institute of Berlin, Department of Cardiology, Berlin, Germany*; *[3]Health Twist, Berlin, Germany*; *[4]BAYER Pharma AG, Pharmaceutical Division, Wuppertal, Germany*

Background: Several biomarkers are available for the evaluation of diagnosis, supervision of therapy and risk prediction in various cardiovascular disease. Further, they may serve as a surrogate parameter in clinical trials. Although NT-proBNP, Gal-3, NGAL, hsTnT, MDA, ST-2 and AVP are well established, little is known about the test-retest reliability in patient cohorts with a high cardiovascular risk profile. The aim of the study was therefore to determine the biological reliability of biomarkers in different subgroups of cardiovascular disease.

Methods and Results: All biomarkers were measured in patients with heart failure with preserved ejection fraction heart failure with preserved ejection fraction (HFpEF) (n = 25), heart failure with reduced ejection (HFrEF) (n = 24), diabetic nephropathy (n = 20), and arterial hypertension (aHT) (n = 23). A second measurement took place about 7 days later (d4 to d14) combined with a physical examination, an extensive anamnesis, an initial echocardiography, a laboratory assessment and an electrocardiogram. Blood was taken from a venous puncture, stored at -80°C and biomarkers determined by the specific assay. Intraclass-Correlation for all biomarkers regarding all subgroups exceeded ICC > 0.80 (NT-proBNP=0.96, Gal-3=0.90, NGAL=0.91, hsTnT=0.95, ST-2=0.83, AVP=0.87) except for MDA (ICC=0.63). Gal-3 presented a strong reliability in aHT (ICC=0.93) and HFpEF (ICC=0.93), whereas there was a limited reliability in HFrEF (ICC=0.69). Regarding the subgroups the lowest reliability was achieved in aHT.

Conclusion: We confirm that the biological reliability of all examined biomarkers was strong, except for MDA. Our data suggests that Gal-3 is more reliable in HFpEF patients and should be considered more carefully in HFrEF patients. NGAL and AVP data showed the opposite pattern between the 2 heart failure entities. Hereby the study highlights the importance of selective use of biomarkers.

P950

Altered intestinal microflora in the progression of chronic heart failure

BI Bakhodir Narziev[1]; AG Gadaev[1]
[1]Tashkent Medical Academy, Cardiology, Tashkent, Uzbekistan

Background. An involvement of the gut in the progression and clinical evolution of heart failure has been discussed for years. Although the pathogenetic role of the gut microbiome and function have only recently started to be investigated in more detail in patients with chronic heart failure (CHF), data are accumulating to suggest that the gut plays an important pathophysiological role in both chronic inflammation and malnutrition in CHF.

Purpose: Identify changes in luminal and the wall microflora of the colon in patients with different heart failure functional classes (FC).

Methods: In total 34 CHF patients with were examined. 11 patients (32%) were in functional classes III-IV (NYHA) and others 23 (68%) were in functional classes I-II (NYHA). All patients were tested on bacteria in stool. Microbiological study of feces was carried out on the crop nutrient in the dilutions -1, -3, -5, and -7. After 48-hour incubation at 370C the estimation results. Microorganisms were identified by enzyme activity, as well as by microscopic examination of smears stained by Gram.

Results: The total number of Enterobacteriaceae level in patients with CHF FC I-II was -109 colony forming units (CFU)/g, and in patients with III-IV CHF FC - 106 CFU/g. The growth of enterobacteria marked mainly by E. coli - 106 CFU / g (I-II FC HF), against 109 CFU / g (III-IV CHF FC) (p < 0.0005), different types of Klebsiella - 104 CFU/g (I-II FC HF) and 107 CFU/g (III-IV CHF FC) (p < 0.001), citrate assimilating enterobacteria - 106 CFU/g (I-II FC HF) and 108 CFU/g (III- IV FC CHF)

($p < 0.001$). In addition, concentration of enterococci and fungi of the genus Candida were significantly differed. However, concentration of Bifidobacteria was 103 in FC III-IV against 107 in FC I-II ($p < 0,005$).
Conclusion: Gut microflora alternation is associated with clinical course of CHF, exactly, with increasing FC CHF occurs increase of Gram-negative microorganisms.

P951
Studying the relationship of endothelial NO synthase gene polymorphism and endothelial dysfunction in patients with chronic heart failure

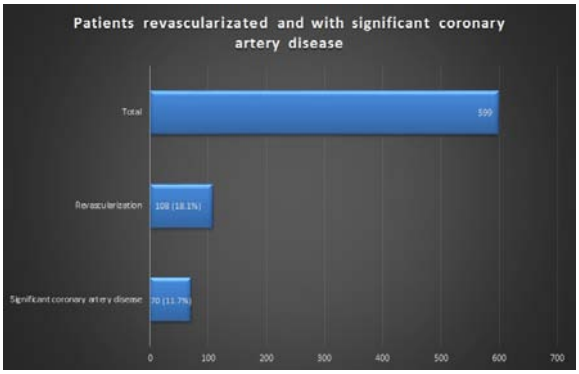
CH Abdullaeva[1]; G Yarmuhamedova[1]; U Kamilova[2]
[1]Tashkent Institute of doctors' improvement, Functional Diagnostics, Tashkent, Uzbekistan; *[2]Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, cardiology, Tashkent, Uzbekistan*

Purpose: Examination of influence of inducible gene NO synthase (iNOS) and endothelial gene NO synthase (eNOS) polymorphism on endothelial function at patient with CHF.
Material and 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 by functional class (FC) CHF in compliance with New York classification of cardiologists (NYHA) under conduction of test for 6 minutes walking (TSW): 1st group included 35 patients with CHF II FC and 2nd group included - 37 patients with CHF III FC by NYHA classification. Control group included 20 healthy volunteers. Vasomotion of brachial artery endothelium was assessed by D. S. Celemajer (1992) method on Acuson 128 apparatus (USA).
Results: Dysfunction of endothelium at CHF patients was connected with progressing of disease and characterized by reduce of endothelium-dependent vasoconstriction, which were more expressed at patients with III FC CHF. It was revealed that the amount of Glu polymorphous locus 298Asp eNOS gene in homozygous condition is associated with CHF severity. Homozygotes by Glu alleles of 298Asp eNOS gene showed more expressed failures of endothelium-dependent vasoconstriction in comparison with the same one at carriers of 298Asp alleles.
Conclusions: So, associative correlations of polymorphism of iNOS and eNOS genes with CHF severity flow have been established and polymorphism of eNOS (Glu298Asp) gene is associated with the failure of endothelium-dependent vasoconstriction.

P952
Asymptomatic left ventricular dysfunction, coronariography and significant coronary artery disease

D J Daniel Jorge Nascimento Matos[1]; S Madeira[1]; RC Teles[1]; J Brito[1]; N Vale[1]; M Castro[1]; P Freitas[1]; P Goncalves[1]; L Raposo[1]; H Mesquita Gabriel[1]; M Almeida[1]; M Mendes[1]
[1]Hospital Santa Cruz, Cardiology, Carnaxide, Portugal

Introduction: Coronary angiography is commonly performed to exclude coronary artery disease in the work-up of left ventricle dysfunction of unknown aetiology. The clinical yield of this approach is unclear in contemporary practice.
Purpose: We sought to determine the prevalence and predictors of clinically significant coronary artery disease in patients with left ventricle dysfunction of unknown aetiology referred for invasive diagnosis.
Methods: Single centre retrospective analysis including 599 patients with left ventricle dysfunction without angina or documented ischemia, who underwent coronary angiography, between 2005 and 2015. Clinically significant CAD was defined as left main stenosis >50%, left anterior descending artery (LAD) stenosis >70% or three vessel disease (proximal or middle LAD, circumflex and right coronary stenosis >70%). Predictors of clinically significant coronary artery disease were identified using binary logistic regression.
Results: The mean age of the studied population was 66 (±12) years old and 69% of the patients were males. The prevalence of diabetes, hypertension, dyslipidaemia and tobacco consumption was 35.4%, 66.1%, 43.7% and 40.2%, respectively. The most common presentations were fatigue in 53% and dyspnoea in 35% of the patients. Mild, moderate and severe depression of the ejection fraction was present in 31%, 37% and 32%, respectively. Forty-nine percent of the patient presented some degreed of coronary atherosclerosis and 18,1% had at least one lesion > 50%. Seventy patients (11,7%) had significant CAD. In univariate analysis, CAD population were older, had more syncope and less fatigue and COPD. After correction for other variables, age (OR 1,034 95%CI 1,009-1,06, $p = 0.008$) and tobacco use (OR 1,02 95%CI 1,009-3,1, $p = 0.044$) were independent predictors of significant CAD, on the other hand patients who presented with fatigue (OR 0,473 95%CI 0,273-0,82 $p = 0.008$) and with COPD (OR 0,22 95%CI 0,065-0,73 $p = 0.0138$) had less CAD.
Conclusion: The prevalence of significant CAD among patients with left ventricle dysfunction referred for coronary angiography for coronary disease exclusion is high and probably supports the use of this invasive approach in this setting.



P953
The role of galectin-3 in heart failure

F Federica Ricupati[1]; S Salvatore Novo[1]
[1]Università degli Studi di Palermo , Cardiology, Palermo, Italy

Aims: Biomarkers are increasingly being used in the management of patients with chronic heart failure (HF). Galectin-3 is implicated in the processes of fibrogenesis and ventricular remodeling in patients with heart failure. The objective of this study was to investigate the prognostic role of Galectin-3 in patients with reduced EF (< 50%) and preserved EF (> 50%).
Methods and Results: The study included 86 patients with clinical diagnosis of heart failure. The plasma levels of galectin-3 were measured in all patients at admission and at discharge.
The follow-up has had an average duration of 33 days.
At follow-up were recorded 19 cases of death from cardiovascular causes that involved 10 women and 9 men. The statistical analysis showed a strong correlation between the levels of Galectin-3 measured at admission and at discharge and adverse events at follow-up ($P < 0.001$).
These results were independent of the etiology of heart failure, the ejection fraction or the presence of cardiovascular risk factors.
Conclusions: High concentrations of galectin-3 correlate with a worse short-term prognosis in patients with heart failure regardless of etiology of heart failure and ejection fraction.
This biomarker thus looks promising as a prognostic factor in this set of patients, allowing the identification of patients at highest risk.

P954
Practical confirmation of the predictive accuracy of a 400 ng/L NTproBNP threshold for heart failure

A Abdallah Al-Mohammad[1]; D Rogers[1]; N Lewis[1]; A Charalampopoulos[1]; J Mant[2]
[1]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; *[2]University of Cambridge, Department of Public Health and Primary Care, Cambridge, United Kingdom*

Background and Purpose: Until 2012, both the European Society of Cardiology (ESC) and the National Institute of Health and Care Excellence (NICE) proposed that the diagnostic threshold for diagnosing heart failure (HF) using NTproBNP should be 400ng/l. A health technology assessment, published by one of the authors in 2009, calculated the predictive accuracy of that threshold in diagnosing HF to be 75%. We assessed the predictive value in a large cohort of patients attending our incident heart failure clinic
Methods: Consecutive patients referred to our institution with suspected new onset HF and NTproBNP > 400 ng/l were studied. Patients underwent detailed echocardiography and assessment by a HF consultant cardiologist. Patients were classified as having heart failure if the clinical and echocardiographic features supported the diagnosis of heart failure syndrome.
Results: 3939 patients were seen between 13th of April 2012 and 31st of December 2016. 935 patients (24%) did not have any evidence of heart failure. We assessed the stability of that percentage annually and found that the percentage of patients presenting to the diagnostic HF clinic with no evidence of heart failure was 20%, 25%, 23%, 23% and 27% in the years 2012, 2013, 2014, 2015 and 2016 , respectively.
Conclusions: The old threshold for NTproBNP of 400 ng/l predicted heart failure with 76% certainty, in a large consecutive cohort over a period of 5 years. This confirms previously published predicted values.

P955

Multi-layer longitudinal strain for noninvasive diagnosis of coronary allograft vasculopathy in heart transplant recipients: a comparative study ultrasound versus angiography.

N Nicolas Bonnet[1]; M Kerneis[1]; S Ouldamar[1]; F Huang[1]; F Laveau[1]; R Isnard[1]; P Leprince[1]; JP Collet[1]; S Varnous[1]; N Hammoudi[1]
[1]*Hospital Pitie-Salpetriere, Paris, France*

Background: Cardiac allograft vasculopathy (CAV) is associated with high morbidity in heart transplant (Htx) recipient. Coronary angiography is the reference method to diagnose CAV, however this procedure is invasive and requires the use of nephrotoxic contrast agents. The multi-layer strain is a new ultrasound technology allowing in particular the functional assessment of the sub endocardial left ventricular layer which is very sensitive to ischemia.
The aim of the study was to evaluate the value of multi-layer longitudinal strain to diagnose CAV in heart transplant patients as compared to angiography.
Methods: In this observational prospective study, 106 HTx patients (mean age, 53 ± 11.2 years; years since heart transplant = 7.0 ± 5.3 years) referred for routine coronary angiography were included. CAV was classified according to International Society of Heart and Lung Transplantation guidelines. In addition, all patients had an echocardiography within 24 hours before the angiography. The examinations were analyzed off-line by an independent operator, blinded to clinical history and coronary angiography results. The global longitudinal strain (GLS) of the different myocardial layers was measured. We included also 42 healthy subjects as control group.
Results: Compared to controls, sub-endocardial mid-myocardial and epicardial GLS were reduced in HTx patients (all p values=0.0001). Among 106 HTx patients, CAV was diagnosed in 47 (43 %) patients. Among CAV patients, 22 patients had grade 1 CAV (CAV 1) and 25 patients had higher CAV grade (CAV 2-3). There was no difference in sub-endocardial GLS between HTx patients with or without CAV (-19.94 ± 3.7% versus -19.43 ± 3.0% respectively, p = 0.45). The GLS of the other myocardial layers was also similar in both groups. Moreover, the GLS in HTx patients with CAV 2-3 was not different compared to patients without CAV or patients with CAV 1.
Conclusion: Compared with controls, multi- layer GLS is reduced in HTx patient. However, in HTx this technology appears not useful for the noninvasive diagnosis of CAV.

P956

Feseability and safety of right and left heart catheterization via an antecubital fossa vein and the radial artery in patients with heart failure: a single centre retrospective cohort study.

D Domenico D'amario[1]; F Burzotta[1]; AM Leone[1]; G Niccoli[1]; A Ruggio[1]; I Porto[1]; C Trani[1]; M Massetti[1]; F Crea[1]
[1]*Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy*

Background: Heart failure is the leading cause of hospitalization among patients older than 65 years of age. A significant proportion of patients require heart catheterization for diagnostic, therapeutic and prognostic purposes. To determine the feasibility and safety of full arm-arm catheterization access, we aimed to compare this approach with other established catheterization approaches.
Materials and Methods: In this retrospective cohort study, 493 consecutive patients with heart failure requiring right and LHC were studied and analyzed. Subsequently, all patients were divided into three groups based on the catheterization approach used: full arm-arm, hybrid arm-leg, and full femoral access.
Results: The three groups did not significantly differ in their baseline clinical, demographic or risk factor characteristics. The full arm-arm catheterization procedures were significantly longer when compared to hybrid arm-leg and full femoral approach (73 vs. 68 vs. 67 min., respectively, p = 0.039) but remarkably provided significantly less fluoroscopy radiation dose (40 337 ± 64799 vs. 62270 ± 120420 vs. 156077 ± 566495 cG/cm2, respectively, p = 0.039). Although the full arm catheterization group showed the lowest number of complications, their rates did not significantly differ among groups (p = 0.446). Finally, in patients in which the arm-arm approach was utilized, a significant earlier ambulation was achieved compared to the others groups (p = 0.021).
Conclusion: This is the first study to date that compared the safety and feasibility of full arm-arm access to femoral-femoral and hybrid arm-femoral approach in a population of HF patients that required simultaneous bilateral heart catheterization. Our results showed that a full catheterization access from the upper limb is a safe and feasible alternative to other catheterization approaches when accessing heart bilaterally. Moreover, this access provided significantly less radiation burden to patients and was associated with the lowest number of complications and shortest time to ambulation.

P957

The incremental shuttle walk test for the evaluation of people at risk of developing heart Failure: a HOMAGE sub-study.

B Beatrice Mariottoni[1]; P Pellicori[2]; JP Ferreira[3]; J Cuthbert[2]; J Verdonschot[4]; L Jacobs[5]; JG Cleland[6]; F Zannad[3]
[1]*Santa Margherita La Fratta Hospital, U.O.Cardiology, Cortona, Italy*; [2]*University of Hull, Hull, United Kingdom*; [3]*University of Lorraine, Nancy, France*; [4]*Maastricht University Medical Centre (MUMC), Maastricht, Netherlands*; [5]*University of Leuven, Leuven, Belgium*; [6]*Imperial College London, London, United Kingdom*

On behalf of: The HOMAGE investigators
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Background: - The six minute walk test is a potentially useful method for assessing functional capacity in most people with heart failure. It does not require specialized equipment but may not be a good test of cardiorespiratory limitation for those with good functional capacity. The incremental shuttle walk test (ISWT) may be a better method of assessing cardiorespiratory performance in people without severe limitation. There is extensive experience of this test in patients with lung disease (Singh et al 1992) but experience in heart failure is limited. The Heart 'OMics' in AGE-ing (HOMAGE) study aims to evaluate the effects of spironolactone on biomarkers in patients at risk of developing heart failure and includes an ISWT at screening.
Methods: This is an interim report on the first cohort of patients screened for HOMAGE, a trial evaluating spironolactone in patients at risk of developing heart failure; age >60 years with coronary artery disease or equivalent (eg:- long-standing type-2 diabetes mellitus and hypertension). Baseline treatments could include ACE inhibitors, calcium channel blockers and beta-blockers but neither MRA nor diuretics. Only patients in sinus rhythm with elevated plasma concentrations of natriuretic peptides (eg:- NT-proBNP >125ng/L) are included. The ISW is a standardised, progressive, incremental walking test for patients comprising up to 12 levels and 102 shuttles. Patients walk around a 10m shuttle course marked by cones, in time with a series of bleeps played from a CD. It produces a higher peak heart-rate and Borg Dyspnoea score as well as a more graded cardiorespiratory response to exercise compared to the 6 minute walk test (6MWD) (Singh et al., 1992). Changes of 50-70 metres are considered clinically significant (Singh et al., 2008). There is a learning effect. Results are reported according to quartiles (Q) of completed shuttles.
Results: Of 124 patients screened, mean age was 74 ± 6 years and 23% were women. The median (Q1-Q3) number of shuttles at screening was 45 (23 -61). Patients in each quartile were of similar age, had similar baseline heart rate (62 ± 10 bpm) and systolic blood pressure (146 ± 24mmHg) but patients in the lowest quartile of exercise capacity were more often women, had lower haemoglobin and tended to have higher plasma NT-proBNP [Q1: 298 (193-422) v Q4: 198 (147-305)ng/L; p = 0.16). Prior to exercise, patients reported a similar degree of breathlessness on moderate exertion during daily activity in each quartile. Immediately after exercise, perceived exertion was generally rated 'sort of hard' or 'hard' on a Borg scale for each quartile but post-exercise heart rate (Q1: 70 ± 14 v Q4: 88 ± 17 bpm; p = 0.0017) and systolic blood pressure (Q1: 158 ± 28 v Q4: 188 ± 34mmHg; p = 0.0012) were higher in those who completed more shuttles.
Conclusions: - Further experience with the ISWT is required.

P958

Echocardiographic diagnostic criteria for heart failure with preserved ejection fraction: does one-size fits all?

B Neves[1]; N Hammoudi[1]; F Pousset[1]; P Balagny[1]; L Legrand[1]; M Komajda[1]; R Isnard[1]
[1]*Hospital Pitie-Salpetriere, Cardiology Department, Paris, France*

Introduction: Heart Failure with preserved-ejection fraction (HFpEF) remains a diagnostic challenge in many situations as its symptoms can be confounded with other entities and no single exam has got perfect accuracy for the diagnosis. Echocardiography is an essential tool to identify signs that may support the diagnosis. Recent ESC guidelines propose structural and functional criteria in this setting. Our aim was to evaluate the different echocardiographic criteria sensitivity for HFpEF diagnosis on a cohort of patient hospitalized for HF decompensation and left ventricular ejection fraction (LVEF) ≥40%.
Methods: A cohort of patients admitted for HF decompensation between June 2015 and June 2016 on a tertiary HF center was analyzed. Electronic medical records and echocardiograms were retrieved. All patients with HF decompensation as a main diagnosis and echocardiographic evidence of EF ≥40% were included. Exclusion criteria included history of previously reduced EF, moderate valvular heart disease, constrictive pericarditis, congenital heart disease and previous cardiac transplantation.
Results: 225 patients had the clinical diagnosis of HFpEF decompensation as assessed by their attending physician. Among those with complete data, 82% had

indexed atrial volume ≥34ml/m2 and indexed-LV mass was elevated on 59%. Evidence of elevated filling pressure as assessed with E/E' ≥13 was noticed in 51% and average E' <9 cm/s in 67%. At least one structural criteria was abnormal in 90% and at least one functional criteria was abnormal in in 85% (sensitivity for either approach was not different, p = 0.199). When taking into account all the criteria, at least one structural or one functional criteria was abnormal in 99% of the patients.
Conclusions: HFpEF is a heterogeneous entity and single echocardiographic criteria may not be appropriate for every cases. We confirmed in our population that the strategy proposed in the last ESC HF guidelines of finding at least one structural or one functional criteria showed excellent sensitivity (99%) and good agreement with clinical diagnosis.

P959

Nurse-led cardiovascular disease management program impact of 30-day readmission in patients with heart failure

R Raed Odeh[1]; M Alkhateeb[1]; M Bdier[1]
[1]*King Abdulaziz Medical City, Riyadh, Saudi Arabia*

Background: Few studies have examined the potential benefits of nurse-led cardiovascular programs impact on readmission and outcomes in patients with heart failure (HF). However no studies have been conducted in this region to examine the benefits of such programs.
Objective: The purpose of this study was to evaluate the impact of nurse led cardiovascular disease management program (CVDMP) on 30-day readmission in patients with diagnosis of HF.
Methods: This is an observational retrospective cohort study included all admissions with the diagnosis of HF in 2014 and 2015 in a Cardiac center with the diagnosis of HF with reduced ejection fraction ≤ 45% or with symptoms of HF or with pulmonary edema during the time period of 2014 and 2015. All elective and planned admissions were excluded from the study. Patients were divided into two groups those with 30-day readmission and no readmission. As well as patients who have follow up in our nurse-led program and who are not. Data was extracted from the cardiac center electronic data-base included age, gender, diabetes mellitus, hypertension, date of admission, diagnosis of HF, history of cerebral vascular accident (CVA/stroke), length of stay, systolic and diastolic blood pressure (SBP and DBP) measurement, heart rate (HR), the use of guidelines medical therapy including, Ace Inhibitors/ Angiotensin Receptor Inhibitor (ACEi/ARBs), Beta blockers, Antiplatelet, Statins, potassium sparing diuretics, etiology of HF, creatinine clearance, and first creatinine.
Results: This study included the index admission of 786 patients (pts) who met the inclusion and exclusion criteria with 825 index admissions to the cardiac center with decompensated HF between January 1, 20014, and December 31, 2015. Of these admissions, 35 admissions (30 pts) (4.2%) and 790 admissions (756 pts) were categorized into 30-day readmission and no re-admission; respectively. 30-day readmission rate was 4.2%. Patients who are followed up in the nurse-led HF program had lower re-admission rate. Stroke and longer length of stay were associated with higher rate of 30-day readmission rate.
Conclusion: Our nurse-led program was associated with reduced 30-day readmission rate and with improved utilization of guidelines medical therapy. Further research is recommended to confirm these findings.

P960

Ranolazine alone or as an add-on to amiodarone for both prevention and cardioversion of atrial fibrillation in patients with or without chronic heart failure: a metaanalysis of the literature

R De Vecchis[1]; C Ariano[1]; A Cesaro[2]; A Giasi[1]; C Cioppa[1]
[1]*Cardiology Unit, Presidio Sanitario Intermedio "Elena d'Aosta", Naples, Italy*;
[2]*Department of Cardiology, Second University of Napoli, Monaldi Hospital, Naples, Italy*

Background: The possibility of using ranolazine as an antiarrhythmic drug active against atrial fibrillation (AF) has been investigated by several recent studies. In our meta-analysis, we provide an overview of these studies, taking into account also the efficacy demonstrated by ranolazine in the course of AF that occurs during chronic heart failure.
Methods: The rhythm control strategy was adopted by the studies that used the ranolazine as a therapeutical option against AF either alone or in combination with amiodarone in patients with or without heart failure. In this meta-analysis both randomized controlled trials (RCTs) and observational prospective cohort studies were admitted. The effect size was expressed using the risk ratio, with 95% confidence intervals.
Outcomes of interest: Efficacy endpoints. Five RCTs investigated the preventive effect exerted by ranolazine against AF occuring in the clinical setting of a recent coronary artery bypass graft (CABG) (post-operative AF: 3 studies) or, in alternative, against AF occurring in the absence of CABG(prophylaxis of non- postoperative AF: 2 studies). In addition, 4 RCTs investigated the therapeutic effect of ranolazine on the pharmacological cardioversion of recent-onset AF. Safety endpoints. The investigated safety endpoints were death, adverse events, QTc prolongation and hypotension.
Results: Eight studies(6 RCTs and 2 prospective cohort studies) were collected on the whole. Ranolazine was effective in preventing the occurrence of AF when compared to controls (RR= 0.60; 95% CI: 0.43–0.83; p = 0.002). Subgroup analysis showed a more pronounced prophylactic effect of ranolazine against post-operative AF (RR= 0.39; 95% CI: 0.18-0.84; p = 0.02) when compared to non- postoperative AF (RR= 0.76; 95% CI: 0.63-0.92; p = 0.04). Ranolazine increased the chances of successful cardioversion when added to amiodarone over amiodarone alone (RR 1.27; 95% CI: 1.08–1.50; p = 0.004) and significantly decreased the time to cardioversion(SMD= –2.83 h; 95% CI: –4.69 h to – 0.97 h; p < 0.001). Overall risks of death, adverse events, and QTc prolongation were similar when making a comparison between ranolazine and control group.
Conclusions: Ranolazine proved to be an useful and effective drug either for prophylaxis or conversion to sinus rhythm of AF that occurs in patients with or without chronic heart failure. Ranolazine use seems to be safe and associated with relatively few adverse events.

P961

Guideline-led prescribing among heart failure patients in the long-term care setting

S El Hadidi[1]; D O'sullivan[1]; D O'mahony[2]; E Darweesh[3]; S Byrne[1]; M Bermingham[1]
[1]*University College Cork, School of Pharmacy, Cork, Ireland*; [2]*Cork University Hospital, Department of Geriatric Medicine, Cork, Ireland*; [3]*Future University in Egypt , Faculty of Pharmaceutical Sciences and Pharmaceutical Industries, Cairo, Egypt*

Introduction: Heart failure (HF) may affect up to 45% of elderly residents in long term care (LTC) facilities. However, there are few data available describing such HF patients and the use of HF guideline-led therapy in the LTC setting.
Purpose: This study aims to describe HF care in LTC settings in terms of guideline-led prescribing using a validated tool.
Methods: This is an observational study of elderly patients in 14 LTC facilities in the Cork region of Ireland. Heart failure was documented on patient medical records or identified by prescription of a loop diuretic. Guideline-led prescribing was assessed using the Guideline Adherence Index (GAI) tool. The GAI considers prescription of loop diuretic, ACE-inhibitor/angiotensin receptor blocker (ACEI/ARB) and beta-blocker and it is adjusted to consider contraindications to therapy. High GAI was defined as prescription of ≥2 of these agents. Comparisons between patients were conducted using independent sample t-tests for continuous variables and chi-squared tests for categorical variables. A multivariable logistic regression model, adjusted for age and sex, was used to determine the associates of High GAI and the adjusted odds-ratio (OR) and 95% confidence interval (CI) were determined.
Results: The total number of residents was 732 (average age 83.9 ± 7.7; 30% male). The prevalence of HF was 36.2%. Patients with HF were older than those without HF (84.8 ± 7.4 vs. 83.4 ± 7.9 years, p = 0.024), were more likely to have coronary artery disease, CAD (32.5% vs. 16.1%, p < 0.001), atrial fibrillation, AF (31.3% vs. 16.9%, p < 0.001) and lung disease (23.0% vs. 11.1%, p < 0.001) but were less likely to have dementia (42.3% vs. 49.9%, p = 0.047). Patients with HF were prescribed more medicines than those without HF (12.7 ± 3.5 vs. 10.7 ± 3.7, p < 0.001). There was no significant difference in the rate of hypertension, stroke, diabetes or renal failure between those with HF and those without HF. Loop diuretics were prescribed to 87.5% of HF patients, ACEI/ARBs to 24.2% and beta-blockers to 22.6% while 17% of patients were prescribed all three of these medications. A loop diuretic was prescribed as monotherapy to 40% of HF patients while 5% of patients were not prescribed any HF medications. Average GAI was 56%. High GAI was achieved by 55% of patients. Patients with High GAI had greater number of comorbidities and greater number of prescribed medicines than those with did not achieve High GAI (both p < 0.05). In multivariate analysis, High GAI was associated with higher number of medications (OR=2.30, 95%CI 1.28-4.11), AF (OR=1.79, 95% CI 1.01–3.19) and CAD (OR=2.30, 95%CI 1.28–4.11). Dementia was not associated with High GAI.
Conclusion: In Irish LTC settings, utilisation of loop diuretic was high however there was a low utilisation rate of HF disease-modifying therapies. Presence of CAD and AF was associated with High GAI. However, there was no association between dementia and achievement of High GAI in HF.

P962

ExtraHF survey. The european survey on implementation of exercise training in heart failure patients: regional differences in structure and long term organisation

A Verde[1]; SM Binno[1]; U Corra'[2]; P Seferovic[3]; GQ Villani[1]; G Filippatos[4]; PP Ponikowski[5]; MF Piepoli[1]

[1]Guglielmo da Saliceto Hospital, Heart Failure Unit, Department of Cardiology, Piacenza, Italy; [2]Fondazione Maugeri, Department of Cardiology, IRCCS Scientific Institute of Veruno, Veruno, Italy; [3]University Belgrade Medical School, Department of Cardiology, Clinical Center of Serbia, Belgrade, Serbia; [4]Attikon University Hospital, Heart Failure Unit at the Department of Cardiology, Athens, Greece; [5]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland

On behalf of: Committee on Exercise Physiology & Training of the Heart Failure Association of the ESC

Background. In heart failure (HF), exercise training programmes [ETPs] are well-recognised intervention to improve symptoms, but still poorly implemented. The Heart Failure Association promoted a survey to investigate whether and how cardiac centres in Europe are using ETP in their HF patients. Aim of this study is to investigate the presence of geographical difference in ETP organisation and long term organisation.
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-EU.
Results: 173 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). Cardiologists, nurses, psychologists, exercise physiologist/therapists, dieticians, physiotherapists, are all figures involved, in all settings, in more than 50%, with the exception of the cardiologists that are involved in only 10% in the Northern regions. Consequently cardiologists is the leading figure, responsible for the ETP in all region, but in the Northern region, where nurses are playing this role. A structured long term follow-up programme was absent in most of the European regions, but in the Northern region where these programmes was described in more than 64%, mainly leaded by nurses.
Conclusions: A less expensive and more flexible structures of the organisation of the ETP may play a key roles in promote a larger implementation of this valuable tool.

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Treatment patterns in newly diagnosed patients with heart failure managed in the primary care and cardiology settings in France

S Eisenring[1]; C C Proenca[2]; B Balas[3]; F Calado[3]; C Thonnelier[4]; S Bruce Wirta[5]
[1]QuintilesIMS Switzerland, Basel, Switzerland; [2]Wellmera AG, Basel, Switzerland; [3]Novartis Pharma AG, Basel, Switzerland; [4]Novartis Pharma SAS, Rueil Malmaison, France; [5]Novartis Sweden AB, Stockholm, Sweden

Background and purpose: Heart failure (HF) is a progressive syndrome, and patients often receive empirical treatment. Knowledge of treatment patterns in patients newly diagnosed with HF in the primary care and cardiology settings in France will help to identify the unmet needs of patients.
Methods: Electronic medical records from two French databases (a general practitioner [GP] panel and a cardiologist panel) were used to identify patients. All patients (aged ≥18 years) who were newly diagnosed with HF from 1 January 2009 to 30 September 2013 were included. Patient histories available in the databases, from January 1994 (GP panel) or January 1998 (cardiologists) to December 2008, were used to exclude patients with a previous diagnosis of HF. Patient data were extracted for the 6 months before diagnosis and for the 12 months after the first prescription of a HF drug. Patients who were not prescribed a new treatment after diagnosis were excluded. Treatment periods were divided into quarterly windows. The dominant therapy for each patient was defined as that prescribed for the longest period over each quarter. Treatment discontinuation was defined as having no prescription for more than 3 months.
Results: The study population comprised 6566 patients with newly diagnosed HF (GP panel, 4940; cardiologists, 1626). In the 3 months after diagnosis, the most common dominant combination therapy was angiotensin converting enzyme inhibitor (ACEi)/angiotensin II receptor blocker (ARB) plus β-blocker (BB; 26.2%). The most common dominant monotherapies were ACEi/ARB (23.7%), diuretic (15.6%) or BB (12.7%). When treatment was stratified by New York Heart Association (NYHA) class, severe HF was associated with significantly increased use of ACEi/ARB + BB + mineralocorticoid receptor antagonist (MRA) or BB + MRA combination therapy, and ACEi or MRA monotherapy. Most patients had ≥1 treatment modification during the follow-up period (GP panel 63.2%; cardiologist panel 81.6%). Compared with patients treated by the GP panel, a greater proportion of those treated by cardiologists discontinued treatment (75.4% vs 51.2%). Treatment switches were more common in patients treated by cardiologists (14.8% vs 10.5%); treatment add-ons were more common in those treated by GPs (25.0% vs 21.8%). Patients with NYHA class III and IV HF were more likely to have ≥1 treatment modification than those with class I and II HF (71.8% vs 66.4%).
Conclusions: Combination therapies that included MRAs were prescribed to a greater proportion of patients with more severe HF based on NYHA class. Patients with more severe HF symptoms were more likely to experience ≥1 treatment modification than those with less severe symptoms. Treatment modification was more common in patients treated by cardiologists than in those treated by GPs, potentially owing to the greater proportion of treatment discontinuation in cardiology patients.

P964

Psychometric evaluation and health care provider feedback on a symptom tracker for use by patients with heart failure

EF Lewis[1]; T Theresa Coles[2]; S Lewis[2]; LM Nelson[2]; D Stull[3]; C Demuro[2]; S Turner[4]; C Chang[5]
[1]Brigham and Women's Hospital, Boston, United States of America; [2]RTI-HS, Patient-Centered Outcomes Assessment, Research Triangle Park, United States of America; [3]RTI-HS, Health Economics, Data Analytics and Design Strategy, Research Triangle Park, United States of America; [4]Novartis Pharmaceuticals Corporation, Critical Care, Portland, United States of America; [5]Novartis Pharmaceuticals Corporation, Cardiovascular US Health Economics & Outcomes Research, East Hanover, United States of America

Background: Failure to recognize worsening heart failure (HF) symptoms is associated with recurring hospitalization. Few communication tools are available to help patients recognize and communicate HF symptom changes with their health care providers (HCPs) in clinical practice. The HF Symptom Tracker (HFaST), a new patient-reported communication tool, was developed using a comprehensive process (literature review, expert clinician input, and qualitative interviews); patients evaluate symptom changes in 10 items over the previous 24 hours compared to what they usually experience on an 8-point scale (0 = did not experience, 1 = "much better" to 7 = "much worse").
Purpose: To evaluate the psychometric properties of the HFaST in adults with HF,collect feedback from HCPs on the feasibility and importance of the HFaST in clinical practice, and reduce the number of HFaST items to accommodate use in an out-patient setting.
Methods: The HFaST was administered for 7 consecutive days to individuals diagnosed with HF (n = 100 patients) during a multisite, cross-sectional, non-interventional study in the US. Additional patient-reported assessments included: a) Days 1-7: weight, 5 HF symptom severity items; b) Day 7: Kansas City Cardiomyopathy Questionnaire (KCCQ-12), patient global impression of change (PGIC). Test-retest reliability, construct validity, discriminating ability, and responsiveness of the HFaST items were evaluated. Ten HCPs completed a survey assessing the feasibility and importance of the HFaST in clinical practice.
Results: Patient response rate was excellent (98% participation in HFaST for >= 4 study days). Overall, HFaST measurement properties were satisfactory. Test-retest reliability was assessed with weighted kappa statistics (kappa = 0.71 to 0.97), supporting stability of HFaST item-level scores over time in stable patients with HF. Item-level HFaST response distributions were tabulated for subgroups of patients who indicated not experiencing a symptom on the KCCQ-12 (no fatigue, no shortness of breath, no swelling, no added pillows when sleeping). HFaST scores were generally consistent with KCCQ-12 responses, providing evidence for construct validity. The HFaST demonstrated discriminating ability between patients who reported improvement/no change vs. worsening based on the PGIC ($p < 0.05$ for 5 out of 6 items retained). HCPs rated the HFaST as a good (70%) or excellent (30%) means of assisting patients in tracking their HF symptoms. Based on previous qualitative work, the psychometric results, HCP feedback the 6 of the 10 HFaST items were retained, covering concepts such as fatigue, shortness of breath (3 items), swelling, and rapid weight gain.
Conclusions: The HFaST is unique among HF measures in its brevity (reduced to 6 items) and its ability to track symptom change by comparing current symptoms to "usual" state. This study provides evidence that the HFaST will be a useful communication tool in clinical practice.

P965

Identifying potentially inappropriate medicines use among heart failure patients in long term care using a disease-specific tool

S El Hadidi[1]; D O'sullivan[1]; D O'mahony[2]; E Darweesh[3]; S Byrne[1]; M Bermingham[1]
[1]University College Cork, School of Pharmacy, Cork, Ireland; [2]Cork University Hospital, Department of Geriatric Medicine, Cork, Ireland; [3]Future University in Egypt , Faculty of Pharmaceutical Sciences and Pharmaceutical Industries, Cairo, Egypt

Introduction: Heart failure (HF) may affect up to 45% of elderly patients in long-term care (LTC) settings and elderly LTC residents are at risk of potentially inappropriate prescribing. Furthermore, a number of medicines have been identified as contraindicated or cautioned in HF as their use may lead to worsening HF or poorer prognosis.
Purpose: To assess the prescription of potentially inappropriate medicines (PIMs) in

elderly HF patients in LTC using a disease-specific tool and to identify patient factors associated with the prescription of PIMs in these patients.
Methods: This is an observational study of 14 LTC facilities in the Cork region of Ireland. HF was identified when documented on the patient's medical chart or by prescription of a loop diuretic. PIMs were identified using the Potentially Inappropriate Medicines in Heart Failure (PIMHF) consensus tool. The PIMHF is a HF-specific tool that includes 11 medicines or medicine classes. Appropriate HF therapy refers to prescription of ≥2 HF recommended agents (loop diuretic, ACE inhibitor/angiotensin receptor blocker and beta-blocker). Poor renal function was defined as creatinine clearance <50mL/min. Comparisons between patients were conducted using independent sample t-tests for continuous variables and chi-squared tests for categorical variables. Univariable and multivariable logistic regression was used to determine the associates of PIMHF use. The model was adjusted for age and sex and the adjusted odds-ratio (OR) and 95% confidence interval (CI) were determined.
Results: The total number of residents was 732, of whom 265 (36.2%) had HF. Average age of HF patients was 84.8±7.4 years and 30% were male. A PIMHF item was identified in 115 HF patients (43.5%). Of these, 79 (29.8%) were prescribed ≥2 PIMHF items. The most commonly prescribed PIMHF items were non-steroidal anti-inflammatory drugs (n=26, 9.8%); oral corticosteroids (n=21, 7.9%); pregabalin (n=14, 5.2%) and metformin in patients with poor renal function (n=9, 3.3%). Patients prescribed a PIMHF were prescribed more medicines (13.2±3.3 vs.12.3±3.7, p=0.003) and had a greater number of comorbidities (12.4±3.4 vs. 11.1±3.4, p=0.03) than those who were not prescribed a PIMHF. Patients prescribed a PIMHF were also more likely to have diabetes (20.9% vs. 9.3%, p=0.008), be prescribed a beta-blocker (52.2% vs. 0.0%, p<0.001), and be prescribed appropriate HF therapy (68.7% vs. 44.0%, p<0.001). In univariable regression analysis the patient characteristics significantly associated with prescription of PIMHF were: higher number of comorbidities, higher number of medicines, diabetes and prescription of appropriate HF therapy. When adjusted, diabetes (OR=2.37, 95%CI 1.09-5.17) and appropriate HF therapy (OR=2.51, 95%CI 1.46-4.31) were associated with PIMHF prescription.
Conclusion: A disease-specific assessment tool may be of benefit in identifying opportunities to improve prescribing quality in HF patients residing LTC.

P966

OBLIC: a nationwide French prospective cohort of heart failure ambulatory patients managed in private practice

FM Mouquet[1]; D Guedj-Meynier[2]; G Godin[2]; T Beard[2]; M Raphael[2]; D Attias[2]; P Tessier[2]; P Gueranger[2]; L Brottier[2]; M Abi Chacra[2]; A Warembourg[2]; O Hoffman[2]; JP Huberman[2]; J Gauthier[2]; A Cohen Solal[3]
[1]Hopital prive Le Bois, Cardiology, Lille, France; *[2]College National des Cardiologues Francais, Paris, France*; *[3]Hospital Lariboisiere, Cardiology, Paris, France*

Background: Although private cardiologists manage the majority of patients with heart failure (HF) in France, no contemporary epidemiological data are available regarding the characteristics of these patients and the quality of care in private practice.
Purpose: Gathering epidemiological data and assessing the quality of care of HF patients managed in private practice.
Methods: A prospective cohort of HF patients was collected between January and March 2016. Private cardiologists gathered all ambulatory patients with a HF history during 2 consecutive weeks.
Results: A total of 1018 patients were included: 76% were managed for chronic HF with reduced ejection fraction (HFrEF) whereas 24% had history of HF with preserved ejection fraction (HFpEF). 77% had planned visits, 8% came for urgent unscheduled visits and 14% were seen after their hospitalization for decompensated HF. Mean age was 74 years (15-96). 63% among the patients were male. 61% had hypertension, 28% diabetes, 17% COPD, 14% sleep apnoea, 12% chronic renal failure and 8% anoemia. Each co-morbidity was more frequent among patients with HFpEF as compared to patients with HFrEF. Among patients with HFrEF, etiology was ischemic cardiomyopathy for 49%. 13%, 60%, 24% and 2% of patients were in NYHA I, II, II and IV respectively, and 71% had at least one hospitalization for decompensated heart failure. Among patients with an ejection fraction below 35% (n=253, 33%), 85% received a betablocker, 84% an ACEI or ARB, 28% received mineralo corticoid receptor antagonist. 6% received ivabradine. 18% were implanted with CRT and 30% with an ICD. At the end of the consultation, 11% were hospitalized for decompensated HF.
Conclusions: The OBLIC cohort provides epidemiological data from HF patients managed by private cardiologists in France. The patients' characteristics seem to be similar to those managed in hospital, and treatment is in adequation with the last European Society of Cardiology guidelines.

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Guidelines-recommended medications for heart failure in eight post-soviet countries: insights from the optimize heart failure care program

Y Lopatin[1]; A Grebennikova[1]; H Sisakyan[2]; H Hayrapetyan[3]; G Dadashova[4]; A Kurliandskaya[5]; Z Pagava[6]; Z Kipiani[7]; S Berkinbayev[8]; M Glezer[9]; A Chesnikova[10]; E Tarlovskaya[11]; L Voronkov[12]; V Tseluyko[13]; T Abdullaev[14]
[1]Volgograd State Medical University, Volgograd Regional Cardiology Centre, Volgograd, Russian Federation; *[2]University State Hospital 2, Yerevan, Armenia*; *[3]Erebouni Medical Center, Yerevan, Armenia*; *[4]Scientific Research Institute of Cardiology, Baku, Azerbaijan*; *[5]Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*; *[6]Centre of Vascular and Heart Diseases , Tbilisi, Georgia Republic of*; *[7]"New Hospital", Tbilisi, Georgia Republic of*; *[8]Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*; *[9]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*; *[10]State Medical University of Rostov-on-Don, Rostov-on-Don, Russian Federation*; *[11]Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russian Federation*; *[12]NSC Institute of Cardiology M.D. Strazhesko, Kiev, Ukraine*; *[13]Kharkiv National Academy of Postgraduate Education, Kharkiv, Ukraine*; *[14]Specialized Cardiology Center of the Republic of Uzbekistan, Tashkent, Uzbekistan*

Background: Several factors related to patients, physicians or non-medical reasons might be responsible for the slow implementation of guidelines on the management of patients with heart failure (HF) into clinical practice. This stimulates the search for clinician- and patient-focused tools that would improve evidence-based care in patients with HF. The aim of the study was to analyze the prescription of guideline-recommended medications to patients hospitalized due to worsening HF in Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Russia, Ukraine and Uzbekistan.
Methods: The Optimize Heart Failure Care program is a 12-month international, multi-center patient support program based on pre-discharge patient education, pre- and post-discharge check-lists, 'My HF Passport' and a smartphone application. 800 patients from the participating countries (mean age 62.4± 0.4 years, 69.6% male), NYHA II-IV (mean 2.71± 0.03), 78.7% in sinus rhythm, hospitalized due to worsening HF were included into this study.
Results: At discharge from the hospital, the prescription rates of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs), beta-blockers (BBs), mineralocorticoid receptor antagonists (MRAs) and ivabradine were 91.2%, 90.4%, 92.3% and 29.0%, respectively. The rate of prescription of these agents remained high throughout the 12 months of follow-up. Diuretics and digoxin were used in 72.2% and 7.2% of patients with HF, respectively. However, the proportion of patients at target dose and ≥50% of target dose was low (25.4% and 43.5% for ACEIs/ARBs, 21.1% and 47.2% for BBs, and 5.1% and 26.2% for ivabradine). Moreover, patients with HF treated with ≤50% of target doses of ACEIs/ARBs and BBs demonstrated a high rate of readmission for worsening HF (38% and 35.1%, respectively, vs. 19.3% and 20.3%, respectively, in patients on target doses, p<0.05 for both).
Conclusion: This is the first time such data on guideline-recommended medications in patients with heart failure has been collected in these eight post-Soviet countries. The rate of prescription of the heart failure medications was satisfactory; however, the dosage of guideline-recommended agents was usually suboptimal. Additional efforts are needed to improve the implementation of heart failure guidelines into clinical practice.

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Rationale and design of ARIADNE. assessment of real life care describing european heart failure management

U Uwe Zeymer[1]; AL Clark[2]; V Barrios[3]; T Damy[4]; J Drozdz[5]; C Fonseca[6]; LH Lund[7]; R Sabia[8]; S Hupfer[8]; G Di Comte[8]; A Maggioni[9]
[1]Institut für Herzinfarktforschung, Ludwigshafen Am Rhein, Germany; *[2]Hull York Medical School, Castle Hill Hospital, Department of Cardiology, Kingston upon Hull, United Kingdom*; *[3]University Hospital Ramon y Cajal de Madrid, Department of Cardiology, Madrid, Spain*; *[4]University Hospital Henri Mondor, Department of Cardiology, Creteil, France*; *[5]Medical University of Lodz, Department of Cardiology, Lodz, Poland*; *[6]Hospital de Sao Francisco Xavier, Lisbon, Portugal*; *[7]Karolinska Institute, Department of Medicine, Unit of Cardiology, Stockholm, Sweden*; *[8]Novartis Pharma AG, Basel, Switzerland*; *[9]Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy*

Background: Sacubitril/valsartan (LCZ696) reduced mortality and hospitalizations in the PARADIGM-HF trial as compared to enalapril in patients with chronic heart failure with reduced ejection fraction (HFrEF). The introduction of sacubitril/valsartan into real world practice is likely to have a significant impact on the epidemiology of HFrEF and clinical practice. Contemporary data on the epidemiology of CHF in Europe are scarce. Ongoing large registries, including the ESC Haert Failure Long-Term Registry and REPORT-HF sponsored by Novartis , are aimed at

describing the management of HF by hospital-based cardiologists. Here we report the rationale and design of ARIADNE, the first prospective registry describing the management of CHF and the way sacubitril/valsartan is introduced by office-based cardiologists (OBCs) and primary care physicians (PCPs) in a real world setting.
Purpose: The primary objective of ARIADNE is to describe the profile of HFrEF patients initiated on sacubitril/valsartan as compared with patients continued on standard of care (SoC) by OBCs and PCPs in terms of demographics, medical history, clinical status and to identify the baseline characteristics that are associated with the likelihood of reaching the target dose of sacubitril/valsartan 200 mg (97/103 mg) twice daily.
Additional objectives are to describe in these patients with HFrEF: 1) their demographics and medical history; 2) their treatment; 3) the pattern of administration of sacubitril/valsartan during titration and the final dose; 4) HF related outcomes; 5) healthcare resource utilization.
Methods: ARIADNE will enrol 12 000 patients over the age of 18 with HFrEF managed by OBCs and PCPs in 23 European countries. Enrollment will start in each country when sacubitril/valsartan is available for clinical use. The study will describe 6000 patients treated with SoC and 6000 patients started on sacubitril/valsartan.
Sacubitril/valsartan patients will be enrolled consecutively over an expected time of 12 months in each country, while enrolment of SoC patients will be split into 2 phases: the first 50% of SoC patients will be enrolled in parallel with the first sacubitril/valsartan patients; the second 50% of SoC patients in parallel with the last 10% of sacubitril/valsartan patients. By structuring the enrolment in this way, we will observe if the clinical criteria that drive the choice of the treatment change over the months following the introduction of sacubitril/valsartan into clinical practice.
Patients on sacubitril/valsartan and patients enrolled in the second wave of SoC will be followed for 12 months.
Conclusion: We report the rationale and design of the ARIADNE study, the first European-wide registry describing the management of HFrEF among OBCs and PCPs. Enrolment is expected to be completed by July 2018 and follow-up by July 2019. Baseline characteristics of the first 2000 patients will be available in May 2017.

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The role of body mass index on a n-terminal pro brain natriuretic peptide-guided versus a symptom-guided management in heart failure patients with reduced ejection fraction

N G H M Nick Marcks[1]; K Armas[2]; HP Brunner-La Rocca[3]
[1]Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands; *[2]National University of Colombia, Cardiology, Bogota, Colombia*; *[3]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*

On behalf of: TIME-CHF

Background/Introduction: Overweight and obesity has become an increasing problem in developed countries, affecting both children and adults. The absence of physical activity, diabetes and hypercholesterolemia are risk factors for developing obesity, which are also well known risk factors for developing congestive heart failure (CHF). Patients with obesity are known to have more persistent symptoms and NT-proBNP levels are lower, making it harder for the clinician to guide treatment. Therefore, we want to investigate the role of BMI on a NT-proBNP-guided versus a symptom-guided therapy in patients with heart failure with reduced ejection fraction (HFrEF) and the effect of BMI on NT-proBNP levels.
Methods: We performed a post-hoc analysis of the 'Trial of Intensified versus standard Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF)' trial. The TIME-CHF trial included 499 patients with HFrEF. Subjects were NYHA II or higher, aged 60 years or older and an age-adjusted NT-proBNP >400 ng/L (i.e. >800 ng/L depending on age) at the time of inclusion. Patients were included between January 2003 and June 2008. Follow-up was up to 5.5 years. For this analysis, patients were divided into three groups according to their BMI at baseline, i.e. normal weight or BMI <25, overweight or BMI 25-30 and obese or BMI >30.
Results: The main effect of BMI on outcome was a significantly better overall survival for patients with a BMI >25 ($p = 0.034$) and increased HF hospitalization free survival for patients with a BMI 25-30 ($p = 0.022$). Compared to the symptom-guided treatment strategy, a NT-proBNP-guided treatment strategy was beneficial in HFrEF patients with BMI >30 for overall survival (HR 0.426, $p = 0.048$, Wald 3.923), all cause hospitalization free survival (HR 0.406, $p = 0.002$, Wald 9.501) and HF hospitalization free survival (HR 0.311, $p = 0.002$, Wald 9.262). A NT-proBNP-guided treatment strategy was also found to improve HF-hospitalization free survival for HFrEF patients with a BMI between 25 and 30 (HR 0.570, $p = 0.012$, Wald 6.275). Furthermore, baseline NT-proBNP levels were significantly lower in patients with BMI >25 compared to BMI <25 (3144 pg/mL vs. 4845 pg/mL, $p < 0.001$) and remained significantly lower during follow-up (all $p < 0.001$) despite a decrease of NT-proBNP levels in both groups ($p < 0.001$).
Conclusion: We found the beneficial effect of a NT-proBNP-guided treatment strategy to be most positive in obese HFrEF patients (BMI>30) compared to a symptom-guided treatment strategy, whereas no effects were seen in patients with a normal weight (BMI <25). Therefore, a NT-proBNP-guided therapy should be considered to reduce overall mortality, all cause hospitalization free survival and HF hospitalization free survival in obese patients with HFrEF. Furthermore, the HF clinician should be aware of the lower NT-proBNP levels in obese patients.

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Ivabradine effect on outcomes in patients with systolic heart failure according to the duration of their disease: analysis from SHIFT

M Bohm[1]; K Swedberg[2]; M Komajda[3]; L Tavazzi[4]; JS Borer[5]; A Moyne[6]; I Ford[7]
[1]Klinik für Innere Medizin III, Universitatsklinikum des Saarlandes, Universität des Saarlandes, Homburg, Germany; *[2]Sahlgrenska Academy - University of Gothenburg, Department of Molecular and Clinical Medicine, Goteborg, Sweden*; *[3]Hospital Pitie-Salpetriere, Department of Cardiology, Université Pierre et Marie Curie Paris VI, Paris, France*; *[4]Maria Cecilia Hospital, GVM Care and Research, Ettore Sansavini Health Science Foundation, Cotignola, Italy*; *[5]State University of New York Downstate Medical Center, Howard Gilman and Schiavone Institutes, New York, United States of America*; *[6]Institut de Recherches Internationales Servier, Suresnes, France*; *[7]University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom*

On behalf of: SHIFT Investigators

Background and Purpose: In patients with chronic systolic heart failure (HF) and sinus rhythm, ivabradine reduces the composite of CV death and HF hospitalization. It is unclear whether the duration of HF prior to therapy affects survival or HF hospitalizations or whether the effect of ivabradine is modified by HF duration. We examined outcomes and the effects of ivabradine in patients with systolic HF with different durations of disease, incl. patients with relatively recent onset HF.
Methods: and results: In SHIFT, 6505 patients with CHF (LVEF ≤35%), in sinus rhythm, HR≥70 bpm, treated with guideline-recommended therapy were randomized to placebo or ivabradine. Prior to randomization, 1416 and 1459 patients had short HF duration (<1.5 years); 836 and 806 patients had HF duration from 1.5 to <4 years, and 989 and 999 patients had HF duration 4 years or longer in the ivabradine and placebo group respectively. Patients with longer duration of disease were older (62.5 years) compared with patients with recent HF (59.0 years, $p < 0.0001$), had greater disease severity (NYHA III/IV in 56% vs 44.9% in patients with recent HF, $p < 0.0001$), higher rate of comorbidities (MI: 62.9% vs 49.4%, $p < 0.0001$; renal dysfunction: 31.5% vs 21.5%, $p = 0.0008$; PAD: 7% vs 4.8%, $p = 0.0018$). Use of ACEI and BBs across groups was similar. However, dosages of BBs were lower in patients with recent HF (51% of patients were treated with ≥50% of recommended doses compared with 59% of patients with long duration of HF, $p < 0.0001$). Longer duration of disease was associated with poorer outcome. Ivabradine significantly reduced outcomes independently of duration of disease.
Conclusions: Our results show that duration of HF strongly predicts outcome. However, ivabradine improved clinical outcomes in patients with CHF independent of HF duration, including patients with recent onset HF.

HF duration	Ivabradine (N=3241)		Placebo (N=3264)		Adjusted HR, 95% CI	P	P interaction	
	n	%PY	n	%PY				
Primary composite endpoint of CV death or HF hospitalizations								
<1.5 years	267	10.68	333	13.47	0.83 [0.70;0.97]	0.0222		
1.5 to <4 years	217	15.32	244	19.01	0.80 [0.67;0.97]	0.0200		
≥4 years	309	19.78	360	23.32	0.83 [0.71;0.97]	0.0176	0.9597	
Hospitalization for worsening HF								
<1.5 years	163	6.52	230	9.31	0.73 [0.60;0.90]	0.0027		
1.5 to <4 years	142	10.03	176	13.71	0.73 [0.58;0.91]	0.0052		
≥4 years	209	13.38	266	17.23	0.76 [0.63;0.91]	0.0025	0.9632	

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A state-wide approach to multidisciplinary care: heart failure evaluation and reporting of outcomes (HERO)

A Annabel Hickey[1]; J Adsett[2]; JJ Atherton[2]; C Denaro[2]; T Nunan[3]; R Peters[4]
[1]*The Prince Charles Hospital, Advanced Heart Failure and Cardiac Transplant Unit, Brisbane, Australia*; [2]*Royal Brisbane and Women's Hospital, Brisbane, Australia*; [3]*Nambour Hospital, Nambour, Australia*; [4]*Princess Alexandra Hospital, Brisbane, Australia*

On behalf of: Queensland Heart Failure Services Steering Committee

Background: Collection and reporting of clinical indicators of chronic heart failure (CHF) care in Australia is frequently ad hoc, and difficult to verify or benchmark with other services.[1] Queensland has a CHF steering committee that oversees disease management programs (DMP) supported by a central coordinator. In 2014, the Queensland Cardiac Information Solutions Program agreed to develop systems to support the collection and reporting of clinical indicators.
Purpose: To evaluate the feasibility of the Heart Failure Evaluation and Reporting of Outcomes (HERO) clinical indicator reporting tool.
Methods: Consensus on the content and methods of collecting data was reached following a Delphi method involving all 24 CHF disease management programs in Queensland. Nine process indicators were agreed upon and included: referral follow-up time and review of left ventricular function for all newly referred patients; and prescribing and titration practices at hospital discharge, first outpatient visit and 6 months after referral. All indicators had detailed inclusion and exclusion criteria. Descriptive data included age, sex, indigenous status, referral source and type of heart failure. Outcomes for mortality, length of stay and readmissions is to be obtained by data linkage.
Results: Feasibility was assessed by comparing new referrals numbers with previous manually collected data; reviewing data completion, report quality and frequency. In 2015, the first year of data collection, 4,043 patients newly referred to heart failure DMPs were entered into HERO. This was consistent with manually collected data in the 2013 (n = 3951) and 2014 (n = 3900). Data was incomplete initially but improved to 90% with the introduction of monthly data quality reports sent to clinicians. Reports benchmark individual services to the state median, and provide details about exclusions and contraindications to inform clinical practice. For example statewide data for 2015 for beta-blocker titration not only shows those who have achieved target doses of beta blockers at 6 months post-hospital discharge (42%), but also includes those who are at maximally tolerated doses (31%) and who are still undergoing up-titration (18%), suggesting that the treatment variance statewide is relatively small (9%).
Conclusions: High completion rates suggest that HERO is sustainable and engages clinicians by providing routine reporting that highlights individual site performance benchmarked against state-wide performance with respect to patient follow-up, medication prescription and titration of doses. In the context of a coordinated state-wide approach to CHF-DMPs (which includes data collection and review, education and clinical mentoring) HERO is a powerful tool for achieving best practice.

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Pharmacological management of heart failure and device therapy in a british district general hospital

A Amrit Chowdhary[1]; A Whittingham[1]
[1]*Doncaster Royal Infirmary, Cardiology, Doncaster, United Kingdom*

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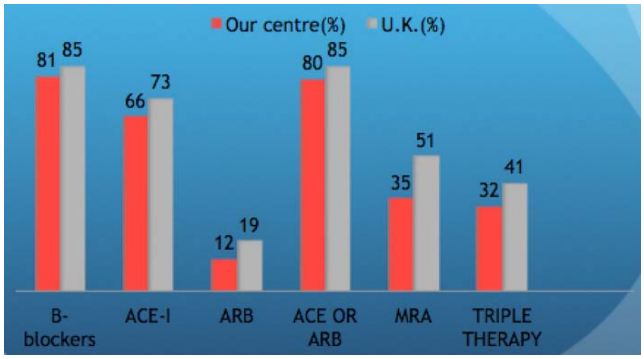
Background: Optimal pharmacological treatment and device therapy in Heart Failure (HF) is associated with a decrease in morbidity and mortality. We aimed to assess the rate of implantation of devices for heart failure and pharmacological therapy received by patients with a left ventricular ejection fraction (LVEF) of < 35% in a British District General Hospital.
Method: All trans-thoracic echocardiograms (TTE) done in our centre from 01/04/2015-30/10/2015 were scanned for patients having a LVEF of < 35%. Information regarding the demographics, pharmacological agents and doses along with existing device therapy was collected and analysed.
Results: A total of 7286 TTEs were reviewed of which 154 showed a LVEF of < 35%. In our sample population (LVEF < 35%), the average age was 71.4 years and 63% of the study population were male. A pacing device was already present in 9 patients (Cardiac Resynchronisation Therapy (CRT) -Defibrillator in 3 patients, CRT- Pacemaker in 1 patient and a permanent cardiac pacemaker in 3 patients). Based on the European Society of Cardiology (ESC) guidelines, a further 54 patients or 35% of the study population would have met the criteria for CRT device therapy. We found that 82% of the study population were on a beta-blocker. Most of these patients were on bisoprolol. However only 13% of the population were on the target dose of bisoprolol. In the population on the lower doses of bisoprolol, the average HR was 75 beats/min and average systolic blood pressure (SBP) was 130mmHg. It was also found that 102 patients were on an ACE-Inhibitor (ACE-I). Most of these patients were on ramipril. The target dose of ramipril was prescribed in only 33% of the population. In patients on less then the target dose of ramipril, the average SBP was 120mm Hg and the average serum creatinine was 98 umol/L. An angiotensin II receptor blocker (AIIRB) was prescribed in a further 19 patients.
It was noted that 53 patients were on a Mineralocorticoid Receptor Antagonist (MRA). Number of patients on triple therapy with a beta-blocker, ACE-I or AIIRB and MRA was 46.
Only a total of 4 patients were on Ivabradine. We identified 40 patients who would have potentially benefitted from addition of Ivabradine.
Conclusion: The rate of device implantation for heart failure in our centre was found to be low. Most of our patients were on appropriate pharmacological agents however, the doses of various agents was sub-optimal. Majority of patients were not on target doses of these medications despite a satisfactory, SBP, HR and serum creatinine.



Prescription of heart failure medication

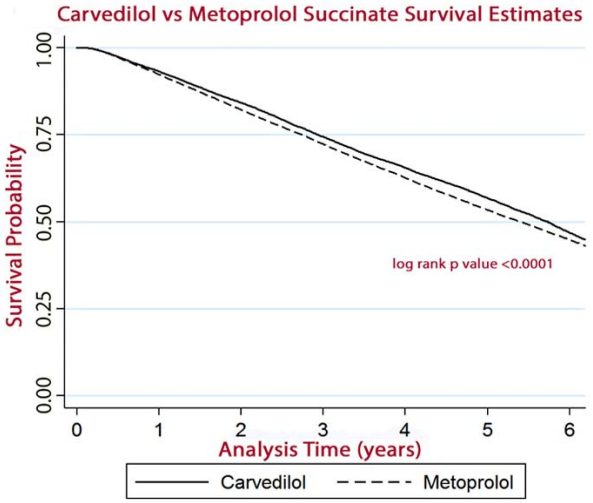
P973

Effect of carvedilol on metoprolol succinate on mortality in heart failure with reduced ejection fraction

T Tarek Ajam[1]; S Ajam[1]; S Devaraj[2]; S Sawada[1]; M Kamalesh[1]
[1]*Indiana University School of Medicine, Indianapolis, United States of America*; [2]*Ball State University, Indianapolis, United States of America*

Background: Beta-blocker therapy is indicated in all patients with heart failure (HF) due to reduced systolic function as per ACC/AHA guidelines. The relative benefit of carvedilol to metoprolol succinate remains unknown. We conducted a retrospective analysis of the survival benefit of carvedilol to metoprolol succinate in a large Veteran's Affairs (VA) database of patients with HF due to systolic dysfunction.
Methods: VA's databases were queried to identify all patients diagnosed with HF from 2007 to 2015 and treated with either metoprolol succinate or carvedilol. Carvedilol and metoprolol succinate were restricted by the VA pharmacy to patients with a diagnosis of HF and an ejection fraction of less than 40% at the time period of the database query. Study compared 114,745 veterans who were treated with metoprolol succinate matched to patients who were treated with carvedilol using propensity score matching with replacement techniques after adjusting for covariates. Sub-group analyses were performed separately for men, women, elderly, and duration of therapy more than 3 months and duration of therapy more than 6 months.
Results: The adjusted hazard ratio of mortality for metoprolol succinate compared to carvedilol is 1.04 (95% CI: 1.02-1.06, p value: < 0.0001). The sub-group analyses show that the results hold true separately for male, female, over or under 65 years old, therapy duration more than 3 months and more than 6 months, high heart rate, and low heart rate.
Conclusion: Beta-blocker therapy with carvedilol is superior to metoprolol succinate in patients with HF due to systolic dysfunction in terms of mortality.

Hazard Ratio fo Metoprolol v. Carvedilol			
MODELS	Metoprolol as Treatment Relative to Carvedilol	Matched SampleN=87,882	
Model A	Unadjusted	Hazard Ratio	1.05
p value			
	< 0.01		
95% CI	1.03-1.07		
Model B	Adjusted with Patient Characteristics and Comorbidities	Hazard Ratio	1.04
p value			
	< 0.01		
95% CI	1.02-1.06		
Model C (Preferred Cox model)	Adjusted with Patient Characteristics, Comorbidities, and Medications	Hazard Ratio	1.04
p value			
	< 0.01		
95% CI	1.02-1.06		



Survival Estimates

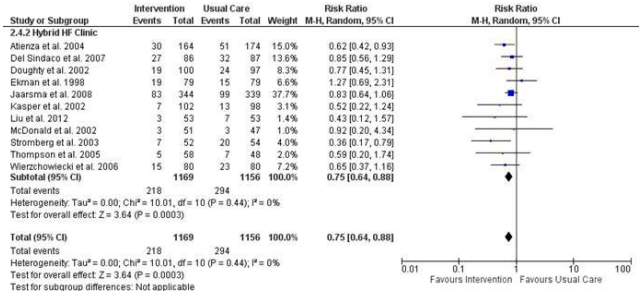
P974

Impact of mode of delivery of disease management programmes on clinical outcomes among patients following hospitalised heart failure: a systematic review and meta-analysis

I O'neill[1]; CP Gale[2]; A Mccallum[3]; H Mcintyre[4]; I Squire[5]; M Cherif[6]
[1]Ionic Reports Ltd, London, United Kingdom; *[2]Leeds Institute of Cardiovascular and Metabolic Medicine, Leeds, United Kingdom*; *[3]Gloucestershire Care Services NHS Trust, Gloucestershire, United Kingdom*; *[4]East Sussex Healthcare NHS Trust, St Leonards-on-Sea, United Kingdom*; *[5]Glenfield Hospital & University of Leicester, Leicester, United Kingdom*; *[6]Novartis Pharmaceuticals UK Ltd, Frimley, United Kingdom*

Funding Acknowledgements: Novartis Pharmaceuticals UK Ltd

Background: Disease management programmes (DMPs) for heart failure (HF) are associated with improved clinical outcomes. We investigated whether the benefit of HF DMPs were associated with their mode of delivery.
Methods: Systematic review and random effects meta-analysis of randomised controlled trials (RCTs) examining outcomes after hospitalisation for HF in patients randomised to scheduled DMPs or usual care. DMPs were categorised as: outpatient HF clinic visits alone (standard HF clinic), clinics with home visits (hybrid HF clinic) or home visits alone without clinic attendance (home visits). The primary outcomes were HF re-admissions, all-cause re-admissions, cardiovascular mortality and all-cause mortality.
Results: We identified 33 RCTs (n = 6,547 patients) evaluating standard HF clinics (n = 6), hybrid HF clinics (n = 12) and nurse-led home visits (n = 17). There was no statistically significant difference between standard HF clinics and usual care for the primary outcomes. Compared with usual care, hybrid HF clinics were associated with a reduced risk of HF re-admission (RR 0.74, 95% CI 0.57–0.95; P=0.02), all-cause re-admission (0.75, 0.60–0.94; P=0.01), cardiovascular mortality (0.57, 0.34–0.97; P=0.04) and all-cause mortality (0.75 0.64–0.88; P=0.0003). Nurse home visits without clinic attendance was associated with a lower risk of HF re-admission (RR 0.64, 95% CI 0.51–0.81; P=0.0002), all-cause re-admission (0.84, 0.76–0.93; P=0.0008) and all-cause mortality (0.83, 0.70–0.99; P=0.04). Significant heterogeneity in study outcome was evident (I2, 0%-78%).
Conclusion: Following hospitalisation for with HF, follow-up with home visits or a combination of home visits and HF clinic attendance were associated with significantly reduced mortality and morbidity. HF disease management programmes should include nurse-led home visits to improve outcomes.



Hybrid HF clinics: All-cause mortality

P975

Effectiveness of the 'heartfailurematters.org' website in patients with stable HF

KP Wagenaar[1]; KP Dickstein[2]; BD Broekhuizen[1]; T Jaarsma[3]; AW Hoes[1]; F H Frans Hendrik Rutten[1]
[1]University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands; *[2]University of Bergen, Cardiology, Bergen, Norway*; *[3]Linkoping University Hospital, Cardiology, Linkoping, Sweden*

On behalf of: e-Vita heart failure study group
Funding Acknowledgements: Unrestricted grant from "Care Within Reach"

Background: The ESC/HFA website heartfailurematters.org (HFM website) is widely used, but its effectiveness has never been formally evaluated.
Aim: To assess the effect on self-care of the HFM website on top of usual care provided by heart failure (HF) nurses in outpatient clinics.
Methods: In a randomized controlled we compared usual care + HFM website to usual care in stable HF patients from nine Dutch HF outpatient clinics. The primary outcome was self-care measured with the European Heart Failure Self-care Behaviour Scale (EHFScB scale). Secondary outcomes were health status, and cost-effectiveness.
Results: In total, 300 (150 per group) patients were included. The mean age was 66.8 (SD 11.0) years, 74.2% were male, and 78.8% was classified as NYHA I or II at baseline. Participants had on average three face-to-face contacts per year with the HF nurse. After 3 months follow-up, the mean score on the self-care scale was significantly higher in the usual care + HFM website group compared to usual care: 73.5 vs. 70.8 (difference 2.7, 95%CI 0.6 – 6.2). This effect attenuated during the following 9 months until no difference after one year (difference -0.6, 95%CI -3.7 – 3.4). Quality of life and HF knowledge had a similar pattern as was observed in self-care.
The mean costs per patient were €4,865 and €5,741 per quality-adjusted life years for HFM website + usual care and usual care, respectively. The net monetary benefit was positive (larger than 0) for HFM versus usual care.
Conclusion: The heartfailurematters.org website helps improve self-care in stable HF patient on the short-term when provided in addition to rather intensive usual care provided at HF outpatient clinics, but this effect seems to attenuate over time. Nevertheless, it is cost-effective considering its effects on quality-adjusted life years.

P976

Impact of different therapeutic targets on the prognosis of heart failure patients include in a cardiac rehabilitation program

L Lamia Kesri-Tartiere[1]; MN Bartholomei[1]; M Duport[1]; S Timpone[1]; P Percet-Marrone[1]; L Poirette[1]; JM Tartiere[2]
[1]LEON BERARD HOSPITAL, 83400, HYERES, France; *[2]Hospital Center of Toulon-La Seyne Sur Mer, 83000, Toulon, France*

Aim: Rehabilitation of chronic heart failure(HF) patients is associated with different actions that may affect prognosis. Physical activity, adaptation of drugs and screening of patients requiring defibrillator and/or biventricular pacing (CRT/CRT-D) are all possible modifiable factors during this period.
Method: 88 consecutives HF patients were recruited during a cardiac rehabilitation program. Participation in the entire rehabilitation program (REHAB), maintain or increase of beta-blocker doses(BB), presence of ACE inhibitors/angiotensin receptor blocker(ACEI/ARB) or mineralo-receptor-blocker(MRB), ivabradine, maintain or decrease of diuretics doses and implantation during this period of CRT/CRT-D were studied as univariate and multivariate factors associated with the risk of occurrence(mean follow up 971 ± 343 days) of death or heart transplant(N=19).
Results: Patients were: male(84%), 62 ± 13 years, ischemic cause(56%), NYHA class 3/4(50%), and LVEF 30 ± 9%. REHAB was possible for 86% of patients. Maintain or increase of BB(82%), ACEI/ARB(88%), MRB(56%), ivabradine(13%), maintain or decrease of diuretics(72%), CRT/CRT-D(15%). Adaptation of at least 3 drugs was possible in 78%. Factors associated with a lower occurrence of events were(OR (95% CI)): maintain or increase BB doses(0.41 (0.16-1.09)), ACEI/ARB(0.22 (0.08-0.59)), maintain or decrease diuretics(0.49 (0.20-1.21)), REHAB(0.25 (0.10-0.66)). In multivariate analysis, only ACEI/ARB was significant(0.30 (0.10-0.89)). When each modification of drugs was replaced by the favorable modification of at least three of the five drugs, this parameter was significantly related to survival in multivariate analysis(0.33 (0.13-0.85)), as for REHAB multivariate analysis(0.34 (0.12-0.93)).
Conclusion: During the outpatient rehabilitation for heart failure patients, maintenance or increase of therapeutic and especially for ACEI/ARB with participation in the entire rehabilitation program are associated with better prognosis.

P977

Utilization and outcomes following initiation of sacubitril/valsartan in a newly established heart failure disease management program

B Bassam Atallah[1]; ZG Sadik[1]; R Ferrer[2]; J Stapleton[2]; M Khalil[3]; F Bader[3]
[1]Cleveland Clinic Abu Dhabi, Pharmacy Services, Abnu Dhabi, United Arab Emirates; *[2]Cleveland Clinic Abu Dhabi, Nursing, Abu Dhabi, United Arab Emirates*; *[3]Cleveland Clinic Abu Dhabi, Cardiovascular Medicine, Abu Dhabi, United Arab Emirates*

Background: Sacubitril/valsartan is a combination medication of a neprilysin inhibitor and angiotensin receptor blocker. It was FDA approved in July 2015 to reduce the risk of cardiovascular death and hospitalization for HF in patients with chronic heart failure (NYHA class II–IV) and reduced ejection fraction. At our institution, sacubitril/valsartan was added to the formulary in February, 2016.
Purpose: To evaluate the appropriateness of the prescribing of sacubitril/valsartan and the success in reaching target dose based on our institution set criteria and the PARADIGM-HF trial.
Methodology: This is a retrospective chart review of patients that received a prescription for sacubitril/valsartan between February 1st and December 31st 2016. Data collected included demographics, initial dose, indication, adverse reactions, readmissions, titration or discontinuation. Descriptive statistics were used for analysis.
Results: A total of 61 patients were identified for a mean follow-up period of 126.5 days (SD ± 92.6) with 25% followed for at least 208 days. A total of 48 patients (78.7%) were appropriately initiated, 90.2% were on ACEI/ARB (30.9% of which on target dose) prior to the switch (table 1). Moreover, 41 patients (75.9%) were switched to an appropriate starting dose (figure 1). Four patients (6.6%) experienced adverse drug reactions, including hypotension leading to discontinuation in 3 of them. Overall, 60.7% had sacubitril/valsartan titrated up and 31 patients (50.8%) achieved the target dose by the end of our follow-up period; 6 patients were re-admitted, of which 5 were for elective purposes.
Conclusion: At our institution, sacubitril/valsartan is prescribed for the appropriate indication in most cases. While utilizing our extensive initiation criteria, most patients continued on this medication and many reached target dose. The overall adverse reactions and readmission rate were lower in this cohort of patients when compared to the PARADIGM-HF trial; however our mean follow-up period was significantly shorter.

Table 1

Characteristic	All patients on sacubitril/valsartan
Age (years)	57 ± 13.7
Gender - Male	65.6%
Systolic BP > 100mmHg	95.1%
Prior ACEI/ARB	90.2%
Target Dose ACEI/ARB	30.9%
Recent MI, CVA, cardiac surgery or CRT (within 3 months)	4.9%
Creatinine clearance ≤ 30 mL/min or SrCr increase ≥ 30% baseline	3.4%

Table 1. Baseline characteristics of patients initiated on sacubitril/valsartan

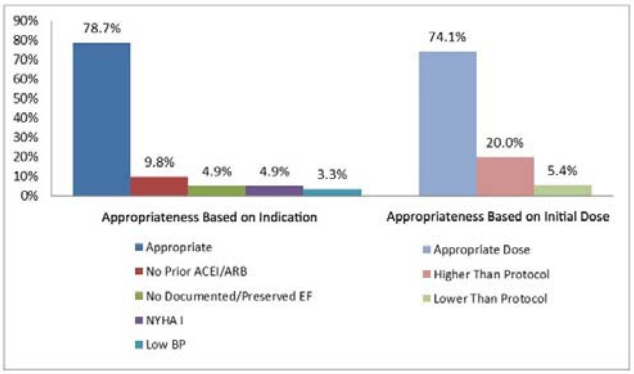


Figure 1

P978

Do we treat heart failure differently according to the ejection fraction?

JR Beramendi Calero[1]; I Irene Rilo Miranda[1]; S Garcia Gutierrez[2]; A Anton Ladislao[2]; C Goena Vives[3]; L Quintas Ovejero[3]; M Morillas Bueno[2]; F De La Cuesta Arzamendi[1]
[1]Hospital Donostia, San Sebastian, Spain; *[2]Hospital Galdakao-Usansolo, Bilbao, Spain*; *[3]Hospital Comarcal de Mendaro, Cardiology, Mendaro, Spain*

Objetive: Regarding the treatment of heart failure, the evidence we have is very different depending on whether the systolic function is preserved or depressed. We have proposed to assess IF we treat heart failure differently according to the ejection fraction.
Methods: A prospective observational cohort study involving a total of 582 patients who come to our hospital for acute decompensated heart failure (acute heart failure and decompensated chronic heart failure). The following variables were collected: sociodemographic, CV risk factors, comorbidities, history of heart disease (ischemic, cardiomyopathy, valvular, arrhythmia) and analytical and echocardiographic data of the emergency department and hospital admission.We compared the treatment to the discharge of 582 patients diagnosed with heart failure admitted to 3 hospitals of the Basque Health Service between 2011 and 2013. We established 3 groups according to the ejection fraction: 188 patients had EF < 40 (Group A) , 101 patient FE between 40 - 49% (Group B) and 193 patients FE> 49% (Group C)
Results: 31.38% of patients in group A, 26.73% in Group B and 28.42% in Group C were treated with ACE inhibitors (p 0.66). 23.40% of Group A, 26.73% of Group B and 23.97% of Group C were treated with ARA II (p 0.80). 38.83% of patients in Group A, 34.65% of Group B and 30.14% of Group C were treated with beta-blockers (p. 14). 48.40% of Group A, 51.49% of Group B and 52.74% of Group C were treated with loop diuretics (p. 64). 31.38% of Group A, 35.64% of Group B and 30.82% of Group C received antiaggregant treatment (p 0.66). 15.43% of Group A, 9.90% of Group B and 13.01% of Group C received antialdosteronic treatment (p. 41). 15.96% of Group A, 25.74% of Group B and 31.16% of Group C were treated with calcium antagonists (p. 0009). Prevalence of hypertension with respect to groups A, B, C: 77.59% vs 79.17% vs 89.47% p 0.0013. Prevalence of Atrial Fibrillation with respect to groups A, B, C: 43.62% vs 55.00% vs 59.66% p 0.0026.Ischemic etiology of heart failure compared to groups A, B, C: 42.55% vs 31.68% vs 25.94% p 0.0007.
Conclusions: 1. Despite the different evidence that we have in the pharmacological treatment of heart failure depending on whether the systolic function is preserved

or depressed, we did not find significant differences in the treatment with respect to ACE inhibitors, ARBs, Beta-blockers, diuretics or anti-aldosteronics.
2. There are a greater number of patients with preserved EF treated with Calcium Antagonists in relation to the higher prevalence of hypertension in these patients.
3. However, we found no difference in antiplatelet or anticoagulant therapy, despite the higher prevalence of ischemic heart disease in the group with depressed EF and atrial fibrillation in the group with preserved EF.

P979
Zero admissions for heart failure

JL Bonilla Palomas[1]; AL Gamez Lopez[1]; M Moreno Conde[1]; MC Lopez Ibanez[1]; CJ Raez Ruiz[1]; R Cruz Arandiga[1]; JP Batres Sicilia[1]; R Ruiz Quero[1]; B Herrador Fuentes[1]; S Gomez Cano[1]; J Leal Helmling[1]; E Ramiro Ortega[1]; A Raez Ruiz[1]
[1]*Hospital San Juan de la Cruz, Úbeda, Spain*

Introduction: Heart failure provoques high number of hospital admissions and is a major cause of mortality and hospital readmissions. The benefits of heart failure units or heart failure programs have been amply demostrated in both observational and randomized studies. The application of a universal model is not feasible because of differences in organizational structures and the available resources. In fact, local conditions are the main determinants of the final model.
Purpose: The main aim of this study was to evaluate the impact of the implementation of the Zero admissions for heart failure project, with which we have tried to optimize the structure of the heart failure unit of our center and improve the coordination of multidisciplinary team.
Methods: Within the Zero admissions for heart failure project we have improved collaboration with primary care, internal medicine and emergency service (training workshops for physicians and nurses, regular meetings with family physicians, provision of interconsultation by telephone), we have redefined integrated care pathways and the work of the expert nurse, day hospital and home care have been strengthened. To evaluate de impact of the project we have compared the number of admissions and the readmission rates at 30 days and 6 months of patients included in our heart failure unit before (2015) and after (2016) the development of the Zero admissions for heart failure project.
Results: 150 patients were hospitalized because of heart failure in our center in 2015 and 115 in 2016 (admission rate decreased by 23,3%). The admission rate at 30 days was 3% in 2015 and 0% in 2016, and at 6 months was 6% in 2015 and 3% in 2016. Between patients with new onset heart failure, the readmission rate at 6 months was 4% in 2015 and 0% in 2016.
Conclusion: Due to the development of the Zero admissions for heart failure project, the complexity of our heart failure unit has grown remarkably in the last year. This has resulted in a reduction of the admission and the readmission rates at 30 days and 6 months with respect the previos year.

P980
The long term protective role of mediterranean diet in first diagnosed acute coronary syndrome patients with heart failure with preserved ejection fraction; results from hellenic heart failure study.

M Kouvari[1]; C Christina Chrysohoou[2]; H Kosyfa[1]; G Kalogirou[1]; P Aggelopoulos[1]; A Filippou[3]; S Iosifidis[3]; E Tsiamis[1]; D Tousoulis[1]
[1]*University of Athens, First Cardiology Clinic, School of Medicine, Athens, Greece*; [2]*University of Athens, Athens, Greece*; [3]*Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

On behalf of: Hellenic Heart Failure study

Background/Introduction: Heart failure with preserved ejection fraction (HFpEF) seems to be associated with similar or even higher morbidity and mortality rates compared with their lower EF counterparts, yet their management remains enigmatic, demanding differential approach. In this context, nutrition has been scarcely investigated. Purpose: The role of Mediterranean diet in first diagnosed Acute Coronary Syndrome (ACS) patients with HFpEF prognosis was examined.
Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiology Clinic in Athens with ACS diagnosis were enrolled in the study. For the purposes of the present work only n=690 first diagnosed ACS patients were included in the analysis. Follow up was performed in 1, 2 and 10 years. Adherence to Mediterranean diet was assessed through MedDietScore (range 1-55) and categorized in tertiles (i.e. low (0-16), moderate (17-20), high (21-55)). Heart failure phenotype was defined according to baseline EF; heart failure with reduced EF (i.e. < 40%) (HFrEF), preserved EF (i.e ≥50%) (HFpEF) and mid range EF (i.e. 40-49%) (HFmrEF). Results: Ranking from low to high MedDietScore tertile (i.e. 1st to 3rd) 1y, 2y and 10y fatal/non fatal ACS prognosis was significantly lower (all ps < 0.05). Multivariate logistic regression analysis revealed a significant inverse association between MedDietScore and fatal/non ACS incidence in 1y (OR=0.84, 95%CI (0.71, 1.00)), 2y (OR=0.91, 95%CI (0.82, 1.00)) and 10y (OR=0.93, 95%CI (0.85, 1.00)), after adjusting for potential confounders. When EF was included in the analysis MedDietScore lost its significance. Then, analysis was oriented towards heart failure phenotypes. After adjusting for HFpEF phenotype, MedDietScore retained its significance in 1y (OR=0.85, 95%CI (0.95, 0.97)), 2y (OR=0.92, 95%CI (0.84, 1.00)) and 10y (OR=0.96, 95%CI (0.88, 1.00)). Additionally, their prognosis-advantage over their lower EF counterparts was highlighted in long term follow up period only after adjusting for MedDietScore (OR=0.36, 95%CI (0.17, 0.76)). Conclusion: Mediterranean dietary pattern seemed to ameliorate both short and long term ACS prognosis of HFpEF patients. Hence, healthy dietary habits in accordance with this pattern may possess a cost effective supplementary-to-medical rehabilitation approach.

P981
Ivabradine use in patients with HFrEF in the heart failure multidisciplinary program (PIC) in a private hospital: first registration and 3-years follow up, Central American (CA) region.

MOS Speranza[1]; JPD Diaz[1]
[1]*Hospital Clinica Biblica, Cardiology, San Jose, Costa Rica*

Funding Acknowledgements: Fundings for research Hospital Clinica Biblica, Novartis grant

Introduction and objectives: Heart rate (HR) elevation in patients (p) with heart failure with reduced ejection fraction (HFrEF) is related to increased mortality and hospitalization for HF; its reduction improves the filling of the left ventricle, increases the myocardial oxygen supply and reduces its consumption, all of which is beneficial in p with impaired left ventricular systolic function.
Use of ivabradine (IBRA) in p with HFrEF, in sinus rhythm (SR) and HR > 70 beats per minute (bpm), reduces hospitalizations for HF and mortality for HF.
The management of p with advanced HF in PIC ensures a morbidity and mortality reduction with the highest levels of evidence.
The first retrospective analysis in a PIC at a private hospital in CA, during 3 years of all case p with HFrEF who received treatments (tx) recommended by International Guidelines and maintained HR > 70 bpm at rest in SR, with the purpose of reducing it. The use of baseline clinical data, natriuretic peptides (NP) and LVEF at rest, compared with same variables in follow up, in a region where these PICs are borning.
Methods: 26 p with HFrEF for 3 years of PIC. General data, tx, baseline clinical condition, BP, pulse, NYHA, quality of life (QoL), NP, LVEF by Doppler Echocardiography were registered, and IBRA tx response was compared baseline and end. 18 p completed data; 8 incomplete (baseline or follow-up data).
Results: Ambulatory p, with HFrEF (<35%) and SR HR > 70 bpm; age 78 years, 17 men. Tx average time with IBRA 11 months, 53.5% more than 1 year. Baseline medications, 93% ACEIs or ARAs II; 85% beta-blockers and 74% MRA, maximum tolerated doses. No patient used IBRA prior baseline. 20% CRT. Variables behavior assessed: HR (baseline 89 bpm vs 62 bpm after IBRA 2 months); BP (baseline systolic 100 mmHg vs 123 mmHg end; baseline diastolic 55 mmHg vs 65 mmHg end); LVEF (baseline 29% vs 35% end); BNP baseline 7,550 pg/ml vs 1,935 pg/ml end. 5 p improved NYHA III to NYHA I, 5 p improved NYHA III to NYHA II, 3 had deterioration NYHA III; rest remained unchanged. 77% p no dose adjustment required (HR below 70 bpm). 6 p began with 2.5 mg every 12 hours and increased to 5 mg every 12 hours after 15 days. By KCCQ-12 increase 42 to 59 points. 1 discontinuation case of IBRA due to bradycardia (HR < 50 bpm). 2 p were hospitalized, one pneumonia and one HF decompensation. 3 dead: 1 myocardial infarction, 2 HF progression.
Conclusions: 26 p studied, registered and treated with IBRA in the PIC at private hospital in CA, most of them registered metric improvements identified as prognosis factors (HR, BP, LVEF, NP, NYHA and QoL). This assessment, registration and follow up of p with HFrEF with use of IBRA in a PIC, is the first one carried out in CA. Results reflect the usual clinical practice in a PIC, with cardiologists and nurses trained to support and follow-up p, and evidence the importance of PIC when using and prescribing drugs like IBRA, in a region where these PICs are rare.

P982
The role of the crossover of the using the ranolazine and trimetazidine in dynamics of reduced left ventricular function in patients after anterior or lateral myocardial infarction without myocardial

J Jafar Ramazanov[1]; I Pershukov[2]; T Batyraliyev[3]; Z Karben[3]; A Kotvitskiy[4]; N Bosak[5]; L Shulzhenko[5]; A Omarov[6]; B Sidorenko[2]
[1]*Central Hospital of Oil Workers, Cardiology, Baku, Azerbaijan*; [2]*Presidential Medical Centre, Moscow, Russian Federation*; [3]*Sani Konukoglu Medical Center, Gaziantep, Turkey*; [4]*Pirogov Russian National Research Medical University , Moscow, Russian Federation*; [5]*Regional Clinical Hospital, Krasnodar, Russian Federation*; [6]*Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*

Background: A significant proportion of patients (pts) with myocardial infarction (MI) with ST elevation in different countries remains without primary revascularization

currently. Lack of reperfusion in many cases leads to a decrease in left ventricular (LV) systolic function. A lot of the patients with reduced left ventricular ejection fraction (LVEF) refuses of planned revascularization in spite of the severe symptoms of angina and heart failure. For these patients, optimal pharmacotherapy remains the only option for improving quality of life.

Methods: All pts suffered anterior or lateral MI with ST elevation within 2-4 months prior to study. All pts had a LVEF less than 40%. On sonography there were no dyskinesis zones, were hypokinesis and akinesis of LV wall only. Patients hadn't a significant defeat heart valves or severe LV hypertrophy (more than 15 mm). All patients were treated with beta-blockers, ACE inhibitors, statins, ASA and clopidogrel. Design of cross-appointment of trimetazidine (TR) and ranolazine (RN) was as follows: half of the patients (group TR) randomly first administered to TR 70 mg/d bid for 3 months, then follow the control sonography and TR replaced by RN 1000 mg/d bid, which is also used for next 3 months with sonographic control at the end of 6 months. The other half of the patients (RN group) gets back scheme - the first 3 months pts were used RN 1000 mg/d bid, after sonography at 3 months RN was replaced by TR 70 mg/d bid, and after the next 3 months pts get a new sonografic control. In total, 276 pts was included and observed up to 6 months in the study.

Results: Both groups (TR and RN) were includes 138 patients. Women were 20% (TR) and 21% (RN). DM rates were 24% and 22%, respectively, arterial hypertension was 73% (TR) and 78% (RN). Anterior MI was in 56% and 49%, respectively. LVEF at baseline was 34 ± 4% (TR) and 33 ± 4% (RN). After 3 months of therapy LVEF were increased on 3% in the TR group (to 37%), and grew on 8% (to 41%) in RN group. Disposal of observation to 3 months was similar in both groups at 4%. In secondary control after 6 months LVEF increased to 41% in TR group, while it rose up 44% in the RN group. In general, LVEF grew for 6 months by 7% (TR) and 11% (RN). Disposal of 6 months was similar in both groups, amount to 6%.

Conclusions: The use of ranolazine for 3 months gives a significant increase in LVEF (8% vs. 3%, $p < 0.05$ at initial appointment of trimetazidine). After crossing over the subsequent appointment of ranolazine and trimetazidine expressed similar second increase of LVEF (4% and 3%).

P983

Evaluation of an integrated group education program on quality of life for family members of patients living with heart failure

V Vida Sadeghzadeh[1]
[1]*Islamic Azad University- Zanjan Branch, Zanjan, Iran (Islamic Republic of)*

Background: Educational interventions for family members of patients with health problems, leads to reduced distress and discomfort they cause.

Purpose: This study aimed to determine the effect of integrated group education program on quality of life of family members of patients with heart failure.

Methods: This study is a randomized controlled trial. 96 family members of patients were eligible to participate in the study. Before randomization, participants completed initial questionnaire and then were divided in six groups of 16. Hospital anxiety and depression questionnaires were used to measure anxiety and depression and Nottingham Health Profile questionnaire was used to measure quality of life. To determine the reliability of the questionnaire was used test retest and with using correlation test, reliability of the questionnaire was 85%. The internal reliability for anxiety and depression was calculated separately by Cronbach's Alpha. Descriptive and inferential statistics were used for the analysis of data. To examine the differences in the level of anxiety, depression and quality of life with classification variables was used ANOVA. Data was analyzed by SPSS 17 statistical software.

Results: There were significant differences between the education and quality of life and of 6 dimensions in both groups before and after. The results showed that the integrated learning program on quality of life in family members of patients with heart failure in the intervention group was more effective than the control group. The results showed a higher significant correlation between anxiety and depression and quality of life. Results showed that there is a significant correlation between the age of family members of the patients and quality of life ($p < 0.01$).

Conclusions: Nurses are a contributing factor in health promotion and public education to individuals and communities, especially the family members of patients can play an important role to healthy and sustainable behavior change and to identify risk factors, support and provide training to help clients improve their health.

P984

Clnical, hemodynamic and neyrohumoral effects of switching patients with chronic heart failure from angiotensin II reseptor blocker valsartan to azilsartan.

K Kamala Zahidova[1]; FA Guliyev[1]
[1]*The Azerbaijan State Advanced Training Institute for Doctors , Baku, Azerbaijan*

On behalf of: CHFA

Purpose. At present angiotensin II receptor blockers are highly effective and safe drugs that reduce the activity of RAAS.Therefore we have conducted this study in order to accses efficacy of switching patients from therapy with valsartan in dose 40-80 mg/day to azilsartan in dose 20-40 mg/day.

Methods: We studed from therapy 196 patients with CHF II-III NYHA class on standard therapy which included ARB valsartan in dose 40 -80 mg/day.In all patients at baseline and after 6 months of therapy we assessed clinical status,quality of life with Minnesota questionnaire and visual -analog scale, performed 6-min walk test and echocardiography for evaluation of LVEF and measured level of N-terminal fragment of pro-barin natriuretic peptide(NT pro BNP) in blood serum.

Results: Switching patients from valsartan in dose 40-80 mg/day to ARB azilsartan in dose 20-40 mg was associated with significant improvement of clinical status with increase of 6 min walk distance, betterment of parameters of quality of life, and significant rise of LVEF combined with lowering of mean CHF class NYHA (all $p < 0,01$ compared baseline).There was no significant dynamics NT pro BNP level in the whole group but in the subgroup with NT pro BNP values above median significant lowering we noted its significant lowering ($p < 0,05$). No significant association between dynamics of main clinic and laboratory parameters and decrease of sistolic blood presure (SBP) and diastolic blood presure (DBP) was observed.

Conclusion: Therefore, switch of patients with CHF II-III NYHA class from APB valsartan to azilsartan in this disease was associated with improvement of quality of life, clinical status, and LV systolic function. This was combined with lowering of initially elevated NT pro BNP level irrespective of changes of SBP ana DBP.

Effects valsartan and azilsartan in CHF

Parameters	Baseline	After 6 months	p
SBP,mmHg	132±12	128±10	p = 0,1
DBP ,mmHg	75±4	73±5	p = 0,3
NYHA class	2,3±0,2	1,6±0,5	p < 0,01
6-min walk test,m	350±34	401±19	p < 0,001
QL,by MLHFQ, Score	35±16	27±8	p < 0,05
LVEF,%	37±5	42±8	p < 0,001
NT pro BNP, pg/ml 1890±85 1200±36	p = 0,3		

P985

Impact of early tolvaptan treatment for very elderly patients with heart failure and chronic kidney disease

K Kei Yoshioka[1]; M Yokoi[1]; M Otagaki[1]; T Yoshio[1]; K Matsumura[1]; T Noda[1]; T Sakuma[1]; T Ueyama[1]; Y Iharada[1]; H Park[1]; Y Yamamoto[1]; I Shiojima[1]
[1]*Kansai Medical University, Moriguchi, Japan*

Introduction: Tolvaptan (TVP) was approved in Japan for the treatment of congestive heart failure 5 years ago.Recent years, very elderly patients with heart failure (HF) are increasing in number. Treatment of very elderly patients with HF is relatively difficult since those patients tend to be resistant to conventional treatment regimen including loop diuretics and diuretics therapy is frequently associated with further reduction in kidney function. TVP was used as a final weapon for those patients,and it was very effective. However, it is unclear whether it should be administered TVP from the early stage or late stage for the very elderly patients with HF and CKD.

Hypothesis: To investigate whether TVP administration to the those patients are much better at early stage or late stage.

Methods: Among very elderly patients (defined as aged 80 or older) with HF and CKD, those who were resistant to conventional treatment (including loop diuretics, carperitide (hANP), and vasodilators) or who exhibited impaired kidney function following initial treatment (more than 30% increase in the serum creatinine compared to baseline) were enrolled. Subjects were additionally given oral TVP (7.5-15mg/day). And it was divided into two groups of the early treatment group to which TVP was administered within three days after the start of treatment and the late treatment group to be administered on after that

Results: Forty patients (mean age:86 ± 4.3) were enlored in this study. There were no significant differences in the baseline clinical parameters between the early and late tolvaptan treatment groups. However, the early use of tolvaptan was associated with shorter hospital stay, lower rate of in-hospital death, higher urine volume in 24hours.

Conclusions: Our results suggest that be beneficial to consider administering tolvaptan earlier in very elderly patients with HF and CKD.

P986

Single centre audit of Right Heart study in patients with decompensated heart failure.

WA Ashram[1]; BM Mcadam[1]; KA Alharbi[1]
[1]*Beaumont Hospital, cardiology, Dublin, Ireland*

Background: Recent clinical studies have questioned the routine use of right heart catheterization for the hemodynamic assessment of patient with heart failure to guide therapeutic intervention. The AIM of our audit was to review the use of this procedure in our center to study the impact in patients with advanced heart failure in terms of clinical outcomes, therapeutic interventions and complications.
Methods: and results: We reviewed 137 consecutive patients who underwent 70 right heart studies in our Hospital in 20 months period of time. The age range was between 25 and 92 years with median age of 58 years, with 53 males and 84 females. The main indications for the procedure were heart failure, with either worsening renal function, hypotension and/or low output state with serum creatinine of 137 umol/L +2.7 and interestingly 36 patients (26%) had cardio-renal syndrome and Nt-Pro BNP was elevated in almost all patients with a mean level of 4387pg/ml. 87% had an ECHOs. 32% of them had LVEF > 55% , 45% had LVEF of 35 -55% and 23% had LVEF less than 35%. At least 34% had moderate MR. 45% of the patients had almost normal RV function and 39% had severely reduced RV function. The inpatient mortality rate was high with 44% of this cohort died.
Right femoral vein access was the most common site of assess with 7Fr. system used in three quarters of the patients. Right Brachial Vein access was used in 37 cases (27%) and a 6Fr. catheter was use in most of these cases. There was two immediate complications occurred over this period. One of the patients had a pulmonary hemorrhage and the other had a hematoma at the excess site at the groin. Data obtained from 101patients (73%) showed an elevated PAWP, with median of 17 mmHg. Furthermore, the majority of patients had pulmonary hypertension (57%). Only 42 (30%) cases had cardiac output assessment using TD method with a mean value of 4.5L/min. PVR was greater than 2 Wood units in the 50% of patient who have Cardiac output measures.
Invasive measurement of mean PAWP was 17mmHg indicating volume overload state and mean PA pressure was 27 mmHg + 11.39, this correlated poorly with PA pressure estimation by echo Doppler. One patient was septic with elevated CO and low PVR and required pressors. Another 18 patients had confirmed low output state with elevated PAWP and low cardiac output and were commenced on vasodilator therapies, pressors (Milrinone) and infusion of frusemide in CCU.
Summary/Conclusion: In this selected cohort of patients with heart failure, a significant proportion had heart failure but with preserved systolic function with associated renal dysfunction pulmonary hypertension and RHC was an excellent diagnostic tool with improvement in short term clinical status with positive impact on clinical decision making and therapeutic intervention. Right brachial vein as an access to perform RHS was very convenient for both the operator and the patient without any immediate or late complication.

P987

Effect of ivabradine in the vulnerable phase: results from de optimize Colombia project

C I Clara Ines Saldarriaga[1]; G Gonzalez[2]; S Navarrete[3]; LE Echeverria[4]; M Novoa[5]; N Murillo[6]; A Rivera[7]; MJ Rodriguez[4]; B Rolong[8]; G Trout[9]; C Martinez[1]; CV Arguello[10]; L Semanche[11]; E Contreras[12]; J Vanegas[13]
[1]*Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia*; [2]*Fundacion Santa Fe de Bogota , Cardiology - heart failure, Bogota, Colombia*; [3]*clinica fundadores, medicos asociados, cardiology, Bogota, Colombia*; [4]*Fundacion cardiovascular, cardiology, Bucaramanga, Colombia*; [5]*clinica del norte, cardiology, medelin, Colombia*; [6]*Angiografia de occidente, cardiology, Cali, Colombia*; [7]*Clinica los Rosales, universidad tecnologica de Pereira, cardiology, Pereira, Colombia*; [8]*fundacion cardiotoracica, cardiology, barranquillla, Colombia*; [9]*Universidad del Magdalena, cardiology, santa Marta, Colombia*; [10]*clínica leon xiii, cardioloy, medellin, Colombia*; [11]*clinica general del norte, cardiology, barranquilla, Colombia*; [12]*clinica de occidente, cardiology, cali, Colombia*; [13]*fundación cardiovascular - instituto del corazón , cardiology, manizales, Colombia*

On behalf of: Optimize Colombia project
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Hospitalization for heart failure is a strong predictor of mortality and new admissions to the hospital especially in the first three months after discharge; this is the "vulnerable phase" of the disease.
Objective: To identify the efficacy of implementation of OPTIMIZE program at hospital discharge in Colombian population of heart failure patients in the vulnerable phase of disease in terms of clinical outcomes: Left ventricular (LV) ejection fraction, functional class and the composite endpoint of decompensation + readmissions to the hospital after 30 days of follow up. The program included education, material to enhance adherence and early initiation of ivabradine to obtain a goal heart rate of 60 – 70 bpm.
Methodology: Prospective cohort study.
Results: 436 patients were included, 68% were male and 32% were females, the mean age was 66 years with a mean ejection fraction of 32%. Ischemic cardiomyopathy was the cause of heart failure in 40.8% of the patients. 94% of the population was on beta blockers and 42% also received Ivabradine. Only 61.4% of the patients were followed in an outpatient service after 30 days. The impact on clinical outcomes is reported in table 1.
Conclusion: The implementation of OPTIMIZE program and early initiation of ivabradine in the vulnerable phase, from hospital discharge; improve LV function and the NYHA functional class with a reduction in the composite end point of decompensation + hospitalization for heart failure.

Table 1

30-day outcomesN= 268	WithIvabradine N=131	Without Ivabradine N=137	P value
Change in LV ejection fraction	5%	0%	0.005
Improvement in at least 1 NYHA class	42%	12%	0.000
Decompensation + hospitalization	1,53 %	8,57%	0.009

Clinical outcomes

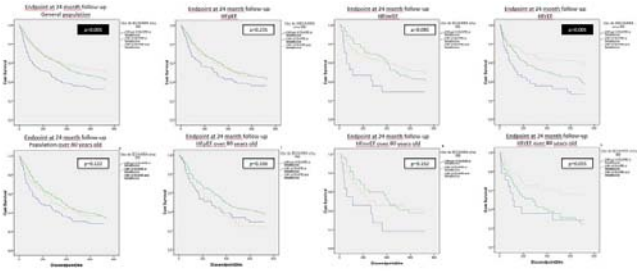
P988

Heart failure: what impact does age have on betablockage and renin-angiotensin inhibition?

J G Julio Gil Goncalves Pereira[1]; L Abreu[1]; H Antunes[1]; ML Goncalves[1]; B Marmelo[1]; I Pires[1]; I Cunha[1]; R Silverio[2]; LF Santos[1]; J Costa Cabral[1]
[1]*Hospital Sao Teotonio, Cardiology, Viseu, Portugal*; [2]*Hospital Sao Teotonio, Internal Medicine, Viseu, Portugal*

Introduction: In heart failure (HF), treatment with Betablocker (BB) and Angiotensin-converting-enzyme Inhibitors (ACE-I) or Angiotensin II receptor antagonists (ARB) are invaluable in the reduction of mortality and re-admission rates.
Purpose: The objective of this study is to evaluate the impact of treatment with BB and/or ACE-I/ARB in patients admitted for HF. The goal is to ascertain if the treatment has the same impact on prognosis in patients older than 80 years old.
Methods: Retrospective study of patients admitted for the first time with the diagnosis of HF. Clinical, analytical and echocardiographical parameters were evaluated. The sample was divide into 3 groups depending on left ventricular ejection fraction (LVEF): HFpEF group with LVEF>50%; HFmrEF with LVEF 40-50%; HFrEF with LVEF < 40%. The patients were further divided based on their medication at discharge: patients without BB or ACE-I/ARB; patients with BB or ACE-I/ARB; patients medicated with both BB and ACE-I/ARB. Kaplan-Meier curves were created to evaluate the occurrence of the combined endpoint of death and/or re-admission for HF at 24month follow-up.
Results: The study was comprised of 1052 patients, 50.8% male, of which 47.5% were older than 80 years old.
In the following table, the percentage of patients in which the combined endpoint occurred is described based on treatment approaches.
In the first row of images, the Kaplan-Meier curves are displayed according to the medication and HF category. In the second row, the same is displayed but for patients over 80 years old.
Conclusion: In the general population, treatment with the combination of BB and ACE-I/ARB has shown to impact prognosis. There was a significant reduction of mortality and re-admission rate in the treatment group. This impact is due to the effect of medication in patients with HF and reduced LVEF (HFrEF). However, that protective effect does not occur in patients over 80 years old, despite LVEF.

	Without BB or ACE-I/ARB	with BB or ACE-I/ARB	with the combination of BB and ACE-I/ARB	P
General Population	67.4%	57.8%	50.7%	0.012
HFpEF	63.9%	56.7%	56.1%	0.513
HFmrEF	70.6%	60.0%	51.3%	0.472
HFrEF	73.5%	62.1%	43.2%	0.002
General Population over 80 years old	71.8%	65.0%	66.7%	0.547
HFpEFover 80 years old	70.7%	61.9%	77.8%	0.133
HFmrEFover 80 years old	81.8%	64.9%	63.6%	0.526
HFrEFover 80 years old	71.4%	75.6%	47.8%	0.066

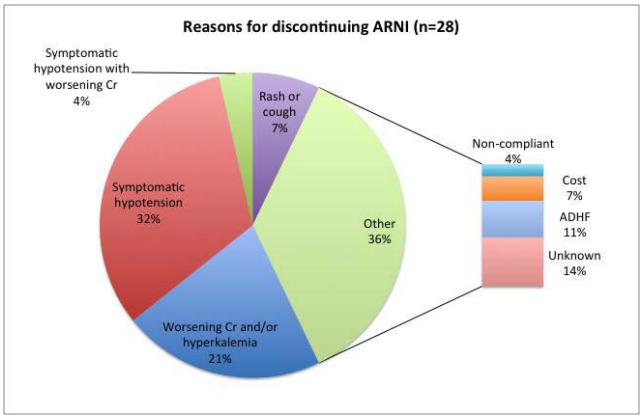


P989

Tolerability and short-term outcomes of angiotensin receptor-neprilysin inhibitor (ARNI) use in a Singaporean cohort

N Natalie Koh[1]; VJ Goh[2]; CK Teoh[1]; LY Teo[1]; CP Lim[1]; D Sim[1]
[1]National Heart Centre Singapore, Singapore, Singapore; [2]Duke-NUS Graduate Medical School Singapore, Singapore, Singapore

Introduction: Following positive outcomes data from the PARADIGM-HF trial, the first-in-class angiotensin II receptor blocker neprilysin inhibitor (ARNI), LCZ696, has entered heart failure pharmacotherapy guidelines as an acceptable substitute for angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in heart failure with reduced ejection fraction (HFrEF). Use of ARNI was associated with hypotension, renal insufficiency, and angioedema in PARADIGM-HF. Information on the tolerability and outcomes of ARNI use in our local Asian HFrEF population is lacking. We retrospectively studied the baseline characteristics, adverse event rates, and short-term outcomes in a pilot Singaporean HFrEF cohort started on ARNI.
Purpose: We aimed to ascertain the safety, tolerability and efficacy of ARNI in our Singaporean population.
Methods: We reviewed data from 179 patients receiving ARNI up to July 2016, from a single tertiary hospital. Data collected included demographic variables, laboratory investigations, clinical symptoms, and comorbidities. Patients were followed up until they reached either end points of death or LVAD implantation.
Results: The mean age of the study population was 60 years. 78% of the patients were male. The average left ventricular ejection fraction (LVEF) was 23%, with 60% of heart failure due to an ischaemic etiology. Overall, ARNI was discontinued in 28 (16%) patients and dose reduced in 7 (4%) patients due to adverse events. Patients who discontinued ARNI were older (age 65 vs 59 years, $p = 0.026$). There were no other significant baseline differences between the groups such as gender, NYHA functional class, comorbidities, heart failure medications, and other clinical attributes. 5.6% of patients had ARNI discontinued due to symptomatic hypotension, 2.2% due to worsening creatinine, and 1.7% due to hyperkalemia. Other reasons for discontinuation are described in the figure below. Patients who discontinued ARNI had higher rates of all-cause (18% vs 2%, $p = 0.003$) and cardiovascular (15% vs 1%, $p = 0.002$) mortality but no difference in rate of heart failure hospitalizations. Overall, there was no difference in serum creatinine and potassium at baseline and three months. A significant decrease in NT-proBNP was observed at three months compared to baseline (median 3614 vs 1328pg/mL, $p < 0.001$). Finally, more patients were in NYHA class I, and fewer patients in NYHA class III (19% vs 5% and 8% vs 23% respectively, $p < 0.001$), after three months on an ARNI than at baseline.
Conclusion(s): ARNI use is well-tolerated in our Singaporean cohort. The most common reason for discontinuation of ARNI was symptomatic hypotension. Patients who discontinued ARNI tended to be older, and had higher all-cause and cardiovascular mortality. While ARNI seemed to improve NT-proBNP and NYHA functional class in this short-term study, a longer duration of study and larger cohort are needed to further support these findings.



Reasons for discontinuing ARNI

P990

Vasopressin receptor antagonist shortens the lengh of stay and reduces the risk of worsening renal function in hospitalized chronic heart failure patient with hyponatremia : a prospective cohort study

DIAN Y Hasanah[1]; RARSAR Soerarso[1]; NANI Hersunarti[1]; BAMBAN Siswanto[1]
[1]Harapan Kita Hospital, Cardiology, Jakarta, Indonesia

Background: Acute decompensated heart failure (ADHF) is one of the leading causes of hospital admission in the whole world. The primary aim of therapy for ADHF is reduction of the congestive state and diuretics are the corner stone of primary therapy in ADHF. Although this strategy is effective in the acute care setting, diuretics therapy has been associated with adverse effects, including electrolyte abnormality, neurohormonal activation, and renal dysfunction, so called, worsening of renal function. WRF coexisting with ADHF is a common situation, and this complicates the treatment course of heart failure , because WRF leads to diuretics refractoriness , longer length of hospital stay , and increase in mortality and additional hospitalizations during follow-up. Tolvaptan is an oral selective V2 receptor antagonist, and some studies have shown the preferable effects for renal function with tolvaptan which shorten lengh of stay when it is used in heart failure patients with hyponatremia combine with diuretic. This study aims to identify the impact of Tolvaptan for acute heart failure patients with hyponatremia.
Methods: This study was conducted in our Cardiovascular Center. We analyzed 62 hospiltalized chronic heart failure patients with hyponatremia and decrease renal function from 2015-2016, 31 patients were treated with Tolvaptan and furosemide (IV), while the other 31 patients received furosemide (IV) only. The indicators used to measure the impact of Tolvaptan are Creatinin value and Length of Stay (LOS).
Results : Using paired sample t-sample t test, we compare the Cr rate before and after consuming Tolvaptan, the analysis shows that p-value=0.080, less than α=5%. Therefore, we can conclude that there is statistically significant difference in the improvement of renal function. In the first group treated with furosemide (IV) and tolvaptan, creatinine level dropped farther than those in the second group with furosemide only (average delta Cr 0.58 vs 0.18) with p value 0.06 in favor for furosemide (IV) + tolvaptan treatment. Moreover in the second indicator, Based on t-test results, p-value is 0.001 less than α=5% so that we can conclude that there is statistically difference in LOS between the two groups. Patients with furosemide (IV) and Tolvaptan are associated with shorter LOS (average: 3.6 days) compared to patients with furosemide (IV) only (average LOS: 4.9 days).
Conclusion: : Tolvaptan has a significant effect in the improvement of renal function

and shorter LOS in hospitalized heart failure patients with hyponatremia treated with intravenous furosemide.

P991

Ivabradine reduces myocardial hibernation in patients with acute coronary syndrome

GAYANE Gayane Chngryan[1]; TM Solomenchuk[1]; LM Kopchak[1]
[1]*Lviv national medical university n.a. Danylo Halytsky , Lviv, Ukraine*

Methods: The study involved 112 patients with acute coronary syndrome who were divided into 2 groups: group I - 73 patients with viable (hibernating) myocardium , the group II of 39 patients with non-viable myocardium , and each - 2 subgroups. The criterion of myocardial viability was improved left ventricular (LV) ejection fraction (EF) of ≥ 5% in dynamics between the first observation and 21 day. Double performed echocardiography in M-, B- modes and calculated: end - systolic size (ESS), end - systolic volume (ESV), stroke volume (SV), LVEF, wall motion score index (WMSI) was derived as the sum of individual scores divided by the total number of segments analyzed and asynergy index (AInd) (total score segments/16). The patients included in the subgroup IA (n = 34) and II A (n = 14), on the background of standard therapy they received additionally ivabradine, the patients in subgroup I B (n = 39) and II B (n = 25) - did not take ivabradine.
Results: When analyzing received data was observed following dynamics, which are presented in the table.
Conclusions: Ivabradine in patients with myocardial hibernation improves the systolic function (decreasing the ESS, ESV, increasing the SV, LV EF) and improves recovery of regional abnormalities myocardium (WMSI, AInd). In patients with nonviability myocardium admission ivabradine enables not impair this parameters.

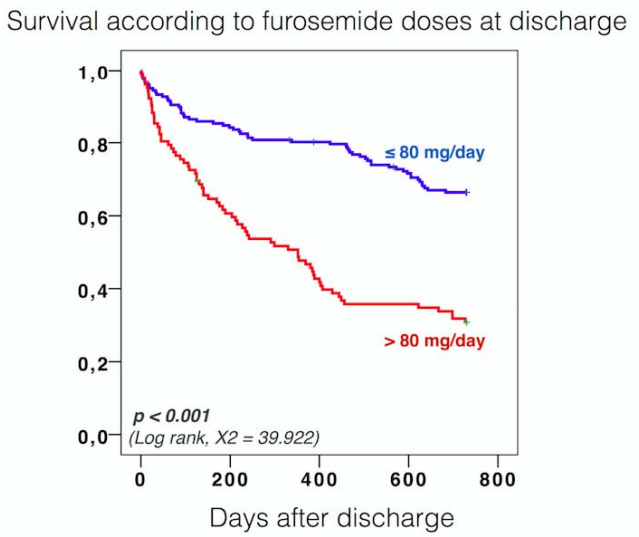
P992

Furosemide doses and long-term mortality after discharge from heart failure episode

J Jerome Costa[1]; L Simone[1]; P Nazeyrollas[1]; D Metz[1]
[1]*University Hospital of Reims, Cardiology, Reims, France*

Background: Heart failure causes congestion, treated by loop diuretics. While there is a lack of evidence supporting the positive impact of these drugs on survival, previous studies suggested that high loop-diuretic doses could be associated with impaired survival of heart failure patients.
Purpose: To determine if furosemide doses > 80 mg/day are associated with higher long-term mortality.
Methods: Clinical, biological and echocardiographic datas were retrospectively analyzed from the electronic medical record of patients discharged after acute heart failure hospitalization in a general cardiology department between January and December 2013, including treatment prescriptions at discharge and time of death within the two-years follow-up.
Results: Among 313 patients discharged (163 men and 150 women, mean age 78.3 years), 132 died within the two-years follow-up (42%). Furosemide was the first treatment on prescription (96%) with daily doses ≤ 80 mg/day for 196 patients (63%, group 1) and doses > 80 mg/day for 114 patients (37%, group 2). In univariate analysis 730 days after discharge, 68.9% patients in group 1 were still alive whereas they were 33.3% in group 2 (OR 4.44 [2.63–7.47], p < 0.001]. After Cox-regression, furosemide doses > 80 mg/day, chronic obstructive pulmonary disease or asthma, impaired left-ventricle ejection fraction, renine system antagonists, dyskaliemia, inflammation and anemia impacted the two-years global survival, with respective OR of 2.39 [1.60–3.57] (p < 0.001), 2.02 [1.28–3.18] (p = 0.002), 1.69 [1.10–2.59] (p = 0.016), 0.60 [0.39–0.90] (p = 0.016), 3.58 [1.80–7.11] (p < 0.001), 2.04 [1.21–3.47] (p = 0.008) and 1.87 [1.17–2.98] (p = 0.008).

Conclusion: At hospital discharge after an episode of acute heart failure, furosemide doses > 80 mg/day is an independent predictive marker of two-years global mortality.



Survival according to furosemide doses

P993

Long-term sacubitril/valsartan therapy is associated with decrease of arterial elastance in stable patients with heart failure with reduced ejection fraction

Z Kobalava[1]; S Villevalde[1]; O Lukina[1]; L Babaeva[1]; I Meray[1]
[1]*RUDN University, Moscow, Russian Federation*

Objective: Angiotensin receptor-neprilysin inhibitor (ARNI) is recommended to further reduce the morbidity and mortality for patients with chronic symptomatic heart failure with reduced ejection fraction (HFrEF) according to the 2016 ESC Guidelines. The aim of the study was to assess the effects of long-term sacubitril/valsartan therapy 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 16 patients with stable HFrEF (14 male, 69 ± 9 years (M ± SD), arterial hypertension 88%, previous myocardial infarction 88%, diabetes mellitus 43%, dyslipidemia 63%, LV EF 32 ± 6%, serum creatinine 122 ± 23 μmol/l, eGFR 55 ± 13 ml/min/1.73m2, serum potassium 4.43 ± 0.38 mmol/l) were enrolled. Patients received a stable background treatment for at least a month (ACEI 94%, beta-blockers 100%, aldosterone receptor antagonists 81%, loop diuretics 75%). ACEI treatment was interrupted for 36 h and replaced with sacubitril/valsartan 50, 100 or 200 mg 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 12 month sacubitril/valsartan therapy. VAC was assessed as the ratio Ea/Ees, optimal range was considered as 0.5-1.2. Wilcoxon test was considered significant if p < 0.05.
Results: Sacubitril/valsartan therapy was associated with significant decrease of Ea (2.20 ± 0.84 vs 1.79 ± 0.63 mmHg/ml/m2, p = 0.005). Ees remained unchanged

P991 Data of echocardiography

I group ((n = 73)	II group(n = 39)							
Data	I Asubgroup (n = 34)		I Bsubgroup (n = 39)		II Asubgroup (n = 14)		II Bsubgroup (n = 25)	
	1st day	21st day	1st day	21st day	1st day	21st day	1st day	21st day
ESS (sm)	4,26 ± 0,13	4,07 ± 0,13*	4,07 ± 0,13*	4,56 ± 0,14#	4,27 ± 0,19	4,25 ± 0,15	4,30 ± 0,16	4,31 ± 0,15
ESV (ml)	87,38 ±6,88	76,97 ±6,13*	102,71 ±7,45	93,48 ±6,88*#	85,21 ±8,18	82,85 ±7,00	87,08 ±7,71	87,32 ±7,40
SV (ml)	60,11 ±4,8	73,82 ±5,28*	54,33 ±2,40	63,10 ±2,56*	55,14 ±3,51	57,57 ±4,04	70,40 ±3,29	69,40 ±3,05
LV EF (%)	39,44 ± 1,60	48,30 ± 1,59*	36,61 ± 1,30	43,82 ± 1,20*#	41,07 ± 2,80	41,78 ± 2,10	40,40 ± 2,17	40,08 ± 1,29
WMSI	1,36 ± 0,08	1,04 ± 0,11*	1,45 ± 0,09	1,37 ± 0,08#	1,64 ± 0,20	1,48 ± 0,18	1,29 ± 0,10	1,50 ± 0,13
AInd	1,65 ± 0,07	1,38 ± 0,06*	1,79 ± 0,07	1,61 ± 0,07#	1,90 ± 0,15	1,64 ± 0,11	1,54 ± 0,08	1,61 ± 0,13

* - significant differences in dynamics through 21 day (p < 0.05) # significant differences between subgroups I A and I B in 21 day (p < 0.05)

(1.00 ± 0.34 vs 1.01 ± 0.44 mmHg/ml/m2 and, p>.05). VAC tended to decrease (2.26 ± 0.77 vs 1.86 ± 0.34). Central systolic blood pressure (BP) decreased from 116 ± 19 to 106 ± 10 mmHg (p = 0.001) and central pulse pressure - from 44 ± 15 to 38 ± 7 mmHg (p < 0.05). Parameters of LV work efficiency did not change significantly; although potential energy tended to decrease (5038 ± 1437 vs 4489 ± 2118 mmHg*ml/m2), LV efficacy (ratio stroke work/ pressure-volume area) tended to increase (0.57 ± 0.07 vs 0.62 ± 0.04). Correlation between decrease of Ea and brachial BP decrease was not found. Sacubitril/valsartan was well tolerated and there were no BP-related adverse events.

Conclusion: In stable patients with HFrEF long-term sacubitril/valsartan therapy was associated with decrease of Ea rather than Ees changes. Changes of Ea did not correlate with systolic BP decrease.

P994

How improve quality of medication management in cardiology? Benefit of clinical pharmacist assistance in cardiology units.

Y Yohan Audurier[1]; N Chapet[1]; B Mathieu[1]; F Leclercq[2]; JL Pasquie[2]; F Roubille[2]; A Jalabert[1]; G De Barry[1]; C Breuker[1]; A Castet-Nicolas[1]

[1]University Hospital Arnaud de Villeneuve, Pharmacy department, Montpellier, France; *[2]University Hospital Arnaud de Villeneuve, Cardiology department, Montpellier, France*

Several previous studies have shown that medication management was ofen incomplete for patients with heart failure (HF) or acute coronary syndrom (ACS). In the same time, other studies had reported that clinical pharmacists improved medication quality and safety. So, a pharmacy team was relocated in cardiology units. 1 senior pharmacist, 1 junior pharmacist and 7 student pharmacists were deployed in intensive care of cardiology and complete hospitalization (79 beds).

The aim of this study is to evaluate the impact of clinical pharmacist in cardiology department.

This prospective experience was realized during one year (december 2015-december 2016). Pharmacy team used several clinical pharmacy activities to improve medication management of patients : medication reconciliation, pharmaceutical intervention (PI) during medical examination and medical staff, prescription revision. Pharmacist's interventions were directly classified with ACP-IP, a national tool edited by The French Society of Clinical Pharmacy. This check-list had permitted the analysis of number and type of PI, drugs and cardiovascular diseases involved, and the physicians' acceptance rate.

828 PI were registred for 507 patients. The mean age was 71,6 years. Most frequent type of PI were overdosage (150 ; 18,1%), underdosage (127 ; 15,3%), missed drug (158 ; 19,1%), inappropriate form of administration (74 ; 8,9%) and contraindications (56 ; 6,8%). The physician's acceptance rate was 96,9%. Concerning drugs involved, medications of cardiovascular system were the most important (231 ; 27,9%) followed by medication of alimentary tract and metabolism (152 ; 18,4%) and nervous system (108 ; 13,0%). More precisely for cardiovascular system, Statines were the most important therapeutic class implicated (57 ; 24,7%), followed by ACE inhibitors/Angiotensin II receptor antagonist (53 ; 22,9%) and Beta-blockers (32 ; 13,9%). 51 PI concerned optimization of ACS pharmacotherapy and 52 PI were about management of HF pharmacotherapy.

These results reflect the importance of collaboration between physicians and pharmacists on the medication management of cardiovascular diseases and comorbidities. Others studies about improvement were begun especialy for the medication management of HF patients.

This experience is a complete success, physicians and pharmacists will continue this collaboration to perpetuate works in progress and optimize medication management in cardiology.

P995

Is diuretic resistance a lost battle?

R Rocio Eiros[1]; I Baraibar[1]; A Hernandez[1]; A De La Fuente[1]; E Iglesias[1]; M Palacio[1]; J Ibero[1]; I Garcia Bolao[1]; JJ Gavira[1]

[1]University Clinic of Navarra, Cardiology, Navarra, Spain

Background: Data from a variety of sources have raised concerns about the overall safety profile of diuretics in heart failure (HF). A frequently mentioned complication of diuretic therapy in acute decompensated HF(ADHF) is diuretic resistance(DR), which consists in poor response to diuretic treatment with loop diuretics (LD), although the exact frequency is unknown due to the lack of a single definition. One of the most difficult challenge to face is the presence of chronic kidney disease. We hypothesized that the combination of hydroclorotiazyde(HTZ) and amiloride(A), would be a safe and effective strategy despite renal function, notwithstanding his controversial use in this scenario.

Methods: This retrospective cohort study all patients with DR admitted for ADHF treated with the combination of A(5 mg) and HTZ(50 mg) was made in addition to treatment with LD. Two groups were created according to their basal glomerular filtration rate: (Group A < 60 mL/min/1,73m2, and group B >60 mL/min/1,73m2).The primary efficacy endpoint were first change in net urine output(UOP) at 24 and 48 h from after iniciating treatment and change in body weight at 24 h and discharge. Secondary efficacy endpoint was length of stay, 30-day readmission rate, and in-hospital mortality. Evaluation of sodium, potassium, creatinine(Cr) (mg/dL) and glomerular filtration rate by MDRD in plasma was made at 24 h and at discharge.

Results: 107 patients were included (68 male) with a mean age of 74 ± 12. Ischemic and valvular heart disease were the most prevalent cause of HF (34% vs 30%). Most patients had NYHA class III or IV. Group A was composed by 54 patients and group B with 53 patients. UOP improved more at 24 h in group A (p = 0,022) compared to group B, but on both groups increased statistically significant at 24 h and 48 h. Change in body weight at 24 h and discharge was also statistically significant. Secondary efficacy outcomes were also similar, as there were no significant differences (Table 1). Not statistically significant changes of Cr at 24 h were found neither of MDRD. None of them developed electrolytic disturbances.

Discussion: To our knowledge, this is the first and largest study to demonstrate the efficacy and the safety use of the HTZ/A diuretic despite renal function in patients with ADHF and DR to date. This results give clinicians an attractive option, safe, effective and available worldwide, to overcome such a frequent situation in daily practice as DR.

Table1: Primary and secondary outcomes

Diuresis (mL)BasalAt 24 hoursAt 48 Hours	Group A2000(294-5380) 2525(33-7200) 2455(920 - 7550)	Group B2400(350-5800) 3000(1040-9300) 2450(800-6100)	P0. 04*0.019*
Weight (kg)BasalAt 24 hoursAt 48 Hours	67.2(52.2-98) 67.6(48.9-96.4) 64,3(48.-99.3)	69.3(41-129,9)68.2(41-128.5) 66.3(42.6-127)	0.01*0.01*
Length of stay Hospital readmissionIn-hospital mortality	22(3-39)12(22%) 3(5%)	13(3-26)12(22%) 3(5%)	0.60.90.6

* statistically significant

P996

IVC analysis - a reproducible and clinically relevant metric which deserves greater prominence in heart failure management

M J Barrett[1]; M Iacoviello[2]; F Monitillo[2]; D Grande[2]; C Rizzo[2]; C Hanley[3]; A Kent[3]; J Britton[3]; A Fitzgerald[4]; P Campbell[1]; R O'hanlon[5]; K Mcdonald[1]

[1]St Vincent's University Hospital, Cardiology, Dublin, Ireland; *[2]Polyclinic Hospital of Bari, Bari, Italy*; *[3]Fire1, Dublin, Ireland*; *[4]Heartbeat Trust, Dublin, Ireland*; *[5]St. Michael's Hospital, Heart Failure Unit, Dublin, Ireland*

Background/Introduction: Heart Failure (HF) management has advanced significantly, however hospitalisation rates and mortality remain high. Maintaining euvolaemia is key to preventing decompensation but this is challenging. The Inferior Vena Cava (IVC) represents a pliable reservoir for circulating volume, and changes in its' shape during respiratory cycles are recognized as markers of intravascular volume status – albeit not routinely used in HF management.

PURPOSE: To assess the reproducibility and test the clinical utility of using the IVC as a marker of volume status in a chronic HF population.

Methods: This was a multicentre study conducted between University Hospital in Ireland and A.O.U. Consorziale-Policlinico, Italy. Stable outpatients were enrolled in prospective fashion during routine scheduled heart failure visits. Patients with a HF admission or unscheduled contact with the HF service in the preceding 6 months were excluded.

Reproducibility was measured by three measurements of maximal IVC diameter (IVCd) and collapsibility index (CI) at 0, 1 and 24 hours. Interobserver agreement was measured by two independent physicians analysing recorded 2-D IVC images. IVCd and CI were compared against other indicators of volume status including symptoms, examination and serum natriuretic peptides (NP).

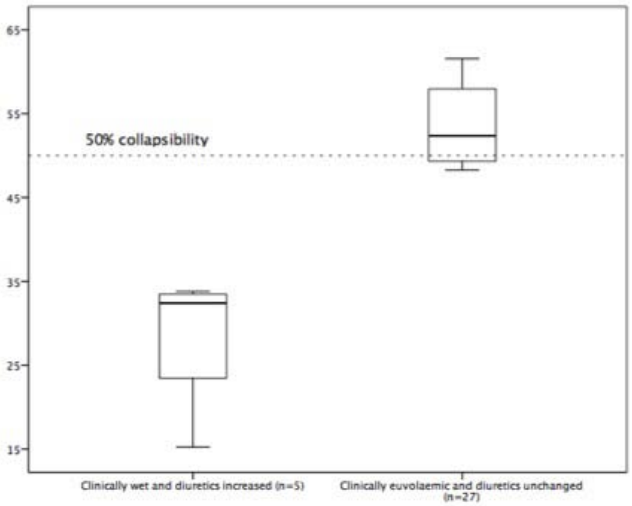
Results: A total of 60 patients were included – 31 from Ireland and 29 from Italy. Mean age was 69.6 years. 71.7% were male and 75% had a diagnosis of heart failure with reduced ejection fraction (HFrEF).

IVCd as measured by independent operators in both centres displayed excellent interobserver agreement with an r2 value of 0.818 (p < 0.001).

Serial IVC measurements over 24 hours showed excellent reproducibility, with an overall average standard deviation around the mean of 1.3mm for maximum diameter and 7% for CI.

Patients were managed according to standard care by an experienced HF physician blinded to the IVC analysis. Five patients of the cohort had intensification of diuretic

therapy based on clinical symptoms and/or signs. The CI of these patients was found to be significantly lower , indicating potential volume overload, than those without clinical congestion (31.1% vs 50.2%, p = 0.022).
When comparing IVC metrics to other markers of volume overload, patients with a dilated or poorly collapsible IVC had a significantly higher N-terminal pro B-type NP (3682 pg/mL vs 490 pg/mL, p = 0.015) and poorer estimated glomerular filtration rate (55 ml/kg/min vs 69 ml/kg/min p = 0.029).
Conclusion(s): Measurement of IVC metrics in stable outpatient HF populations in two international tertiary HF centres appears to be a reliable and reproducible test. Preliminary data suggests clinically relevant correlation with volume status. Use of these measurements may provide a novel treatment target for HF optimisation in the future. Further analyses and extension of the dataset continues at both sites



P997

Un-suggested prescriptions of non-cardio-selective beta-blockers for heart failure in patients with concurrent chronic obstructive pulmonary disease: a danish nationwide retrospective cohort study.

M Maurizio Sessa[1]; A Mascolo[1]; RN Mortensen[2]; MP Andersen[3]; G Rosano[4]; A Capuano[1]; F Rossi[1]; G Gislason[5]; H Enghusen-Poulsen[6]; C Torp-Pedersen[3]
[1]Second University of Naples, Department of Experimental Medicine, Naples, Italy; *[2]Aalborg University Hospital, Department of Clinical Epidemiology, Aalborg, Denmark*; *[3]Aalborg University, Department of Health, Science and Technology, Aalborg, Denmark*; *[4]San Raffaele Pisana Hospital IRCCS, Rome, Italy*; *[5]The Danish Heart Foundation, Copenhagen, Denmark*; *[6]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*

Background: Since 2008, European Society of Cardiology (ESC) clinical management guidelines for acute and chronic heart failure has discouraged the use of non-cardio-selective beta-blockers for heart failure in patients with the chronic obstructive pulmonary disease. Although the pulmonary consequences of beta-2-blockade are well known, it is not known to which extent the international guidelines have been followed. It is important to know whether adherence to guidelines needs to be reinforced. Therefore we conducted a Danish nationwide study of beta-blockers use in patients with obstructive pulmonary disease and heart failure in the period from 2009-2012.
Methods: The study population was followed from index date to death or censoring on 31 December 2012. The index date was defined as the date of co-diagnosis of heart failure and chronic obstructive pulmonary disease and co-treatment with beta-blockers with an indication of heart failure or 1 January 2009 for those patients that fulfill these requirements prior to 1 January 2009. The first primary outcome was the proportion of patients with obstructive pulmonary disease and heart failure that received carvedilol as opposed to beta-1-selective blockers with an indication of heart failure. Also examined were factors important for selection of carvedilol.
Results: In total, 3902 patients received carvedilol in the study period with a restricted mean time persistence of 507 days, of which 1156 (29.6%) were naïve for carvedilol. In total, 5272 hospitalizations for chronic obstructive pulmonary disease occurred during treatment with carvedilol, involving 1729 (44.4%) out of 3902 patients. The hospitalization rate was in average one hospitalization each 165 days. Naïve patients had during exposure to carvedilol an odd of being hospitalized due to worsening of the lung function of 13.14 (95% Confidence Interval [CI] 10.03-17.56) times higher if compared to themselves in an equivalent period prior to carvedilol administration. Patients with heart failure, chronic obstructive pulmonary disease, and concurrent chronic kidney disease had a higher probability of receiving carvedilol (Odds ratio [OR] 1.16; 95%CI 1.04-1.29). Contrarily those with concurrent hypertension (OR 0.75; 95%CI 0.69-0.81), atrial fibrillation (OR 0.62; 95%CI 0.57-0.67), inhalator glucocorticoids (OR 0.75; 95%CI 0.67-0.85), anticholinergics/selective beta-2-adrenoreceptor agonists inhalants (OR 0.80; 95%CI 0.71-0.90) or selective beta-2-adrenoreceptor agonists inhalants short acting (OR 0.88; 95%CI 0.81-0.96) had lower probability of receiving carvedilol.
Conclusion: An increased awareness of administering non-cardio-selective beta-blockers for heart failure in patients with chronic obstructive pulmonary disease and concurrent heart failure should be warranted.

P998

Tolvaptan for heart failure in chronic kidney disease patients: a systematic review and meta-analysis

J Jonathan Sen[1]; E Chung[2]; D Mcgill[3]
[1]Austin Health Hospital, Melbourne, Australia; *[2]University of Toronto, Toronto, Canada*; *[3]Canberra Hospital, Canberra, Australia*

Background: Heart failure (HF) is frequently associated with renal impairment. Tolvaptan, a vasopressin type 2 receptor antagonist is reported to be effective in treating congestion in HF management without significant electrolyte loss compared to conventional diuretics. However, there is a lack of evidence guiding its use in patients with chronic kidney disease (CKD).
Purpose: This systematic review and meta-analysis aimed to evaluate the efficacy and safety outcomes of tolvaptan for HF management in patients with CKD.
Methods: We searched Medline, Embase, PubMed, Cochrane databases, Google Scholar, the New York Academy of Medicine Grey Literature Database, and hand-searched reference lists of articles for observational studies and randomized clinical trials that assessed the efficacy and safety outcomes of tolvaptan against placebo or standard care in adult patients with HF and CKD. Study screening, data collection, quality assessment of included studies were performed independently. Meta-analysis was performed using Comprehensive Meta Analysis, version 2.2.064. Our protocol was registered with PROSPERO
Results: 19 studies were included in the qualitative review and 5 studies were included in the meta-analysis involving 1597 patients. Compared to baseline, tolvaptan appeared to increase serum sodium concentration (5 studies; mean change of 0.58 mmol/L [95% CI: 0.05-1.11]; p = 0.03) and increase urine flow rate (3 studies; 1.36 mL/h [95%=0.76-1.96]; p = 0.00). However, no significant differences in glomerular filtration rate (GFR) (4 studies, 0.06 mL/min/1.73 m2 [95% CI: -0.13 to 0.24]; p = 0.52), serum creatinine (5 studies, -0.04 mg/dL [95% CI: -0.25 to 0.16]; p = 0.68) vs. baseline. Tolvaptan was also associated with a greater change of sodium concentration (3 studies; 0.37 mmol/L [95% CI: 0.04 to 0.70]; p = 0.03) compared to placebo or standard care. No significant difference in change of eGFR (3 studies; 0.13 mL/min/1.73m2 [95% CI: -0.08 to 0.35]; p = 0.23) and serum creatinine (4 studies; 0.13 mg/dL [95% CI: -0.08 to 0.34]; p = 0.21) compared to placebo or standard care. There was also very low heterogeneity. No significant difference in mortality rates were reported in studies. A lower percentage of worsening renal function was found in patients receiving tolvaptan compared to control group (29% vs. 33%, respectively).
Conclusion: Our review offers reasonable support in the use of tolvaptan in patients with CKD. Tolvaptan may offer an improvement in serum sodium without significant change in renal function compared to placebo or standard care in managing HF in CKD patients. However, further research with high quality randomized controlled trials is needed to establish the effect of tolvaptan on long-term efficacy and safety outcomes.

P999

Effect of short daily versus conventional dialysis on cardiac structure and function in patients with diuretic-resistant congestive heart failure.

TH Bampali[1]; CD Gouva[2]; V Foulidis[3]; A Bechlioulis[1]; K Naka[1]; KP Katopodis[2]
[1]University Hospital of Ioannina, 2nd Cardiology Department, Ioannina, Greece; *[2]General Hospital of Artas, Nephrology Department, Arta, Greece*; *[3]General Hospital of Artas, Cardiology Department, Arta, Greece*

Background: Heart Failure (HF) is a problem of growing significance worldwide. Although the efficacy of conventional therapies has been established, an increasing number of patients suffer from frequent re-hospitalizations due to persistent congestion, resistant to high doses of loop diuretics. This diuretic-resistant congestive HF (DR-CHF) is associated with poor prognosis. Alternative non-pharmacological strategies aiming to better control of overhydration based on hemodialysis have been previously considered.
Purpose: The aim of our study was to estimate the effect of short daily hemodialysis (sdHD) versus conventional hemodialysis (cHD) on left ventricular structure and

function indices, blood pressure (BP) and total water homeostasis in patients with DR-CHF and chronic kidney disease stage III-IV.
Methods: Twenty patients (12 males, mean age 65.8 ± 10.3 years) with DR-CHF and chronic kidney disease stage III-IV were enrolled. We performed a non-randomized, controlled study of sdHD (group 1; n=11 patients, 6 sessions/week, 2 hours/session) vs cHD (group 2; n=9 patients, 3 sessions/week, 4 hours/session) with a follow-up period of 6 months. Conventional echocardiography with assessment of left ventricular mass (LVM) and left ventricular ejection fraction (LVEF) was performed and the total water homeostasis was determined in all patients at baseline and follow-up.
Results: The 2 groups did not differ in baseline characteristics. The total weekly ultrafiltrated removed volume did not differ between groups; 6.2 ± 0.6 vs 5.9 ± 0.8 L in groups 1 and 2 respectively (p = ns). Renal function, estimated by creatinine clearance, remained unchanged in both groups at 6 months (45.4 ± 21.3 vs 42.1 ± 18.9 ml/min, p = ns in the sdHD, and 43.6 ± 19.5 vs 37.7 ± 11.2 ml/min, p = ns in the cHD group). In the sdHD group, a significant improvement in BP (systolic / diastolic) was observed at 6 months (150.7 ± 10.7 vs 130.6 ± 9.7 mmHg, p < 0.01 / 88.2 ± 7.6 vs 68.7 ± 10.5 mmHg, p < 0.01) resulting in a reduction in anti-hypertensive drug use, whereas no difference was noted in the cHD group (154.6 ± 9.7 vs 148.3 ± 11.5 mmHg, p = ns / 90.1 ± 5.4 vs 82.7 ± 6.2 mmHg, p = ns). At the end of follow-up, a significant decrease in LVM was observed only in the sdHD group (147.9 ± 47.3 vs 122.6 ± 38.9 g, p < 0.01), but not in the cHD group (152.7 ± 36.9 vs 145.6 ± 31.7 g, p = ns). Similarly, LVEF improved only in the sdHD group (22.5 ± 4.3 vs 38.7 ± 9.6%, p < 0.01),whereas not in the cHD (24.1 ± 3.8 vs 26.9 ± 10.8%, p = ns).
Conclusions: In DR-CHF patients with advanced kidney dysfunction sdHD sessions , in contrast to cHD sessions, were associated with improved BP control and cardiovascular structure and function (reduction in LVM and improvement in EF), despite a similar decongestion effect. None of these therapies improved the renal function. Further larger studies are needed to establish the clinical value of short daily hemodialysis as a potential novel therapeutic tool in the management of this challenging clinical entity.

P1000
Determinants and prognostic value of peak oxygen uptake in the current era of heart failure disease modifying therapy

J Roibal-Pravio[1]; E Barge-Caballero[2]; MJ Paniagua-Martin[2]; G Barge-Caballero[2]; D Couto-Mallon[2]; D Martinez-Ruiz[2]; R Fabregas-Casal[2]; P Blanco-Canosa[2]; C Naya-Leira[2]; CM Riveiro-Rodriguez[2]; Z Grille-Cancela[2]; CM Costa-Grana[2]; R Perez-Fernandez[2]; JM Vazquez-Rodriguez[2]; MG Crespo-Leiro[2]
[1]Universidad de A Coruña (UDC), A Coruña, Spain; *[2]Complexo Hospitalario Universitario A Coruña (CHUAC), A Coruña, Spain*

Purpose: To study the determinants and accuracy of peak oxygen uptake (VO2) to predict the outcome of patients with heart failure (HF) in the current era of disease modifying therapy.
Methods: We studied 282 patients with HF who consecutively underwent ergospirometry for prognostic stratification from 2009 to 2015 in a single center. Baseline variables independently associated with peak VO2 were identified by means of lineal regression. Survival was assessed by means of the Kaplan-Meier method and Cox´s regression.
Results: Mean age of studied patients was 52.7 years; 24% were women, 42% had ischemic heart disease and 74% had reduced LVEF (<0.40). NYHA III or IV class was present in 36% cases. 92% patients were on beta-blockers, 79% on ACEI/ARBs and 70% on MRAs. Mean VO2 was 19.6 ± 5.2 ml/kg/min. In multivariable linear regression, age (p < 0.001), NT-pro-BNP (p < 0.001), body mass index (p < 0.001), and female sex (p = 0.027) were independently associated with lower VO2, while TAPSE (p < 0.001) was independently associated with higher VO2. A peak VO2 < 14 ml/kg/min was associated with significantly higher risk of the composite outcome death, heart transplantation or need for mechanical circulatory support during follow-up (HR 2.38, 95% CI 1.10−5.26, p = 0.027).
Conclusions: Peak VO2 retains a significant prognostic value in the current era of HF disease modifying therapy. In our study, age, female gender, body mass index, NTproBNP and TAPSE were identified as independent clinical determinants of peak VO2.

P1001
Pulsatile hemodynamics in heart failure with reduced ejection fraction - determinants and prognostic value

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

Background: The findings relating pulse pressure (PP) and outcome in heart failure with reduced ejection fraction (HFrEF) have been controversial.
Purpose: We aimed to clarify the determinants and prognostic value of brachial PP in HFrEF.
Methods: We measured pulsatile hemodynamics (brachial blood pressure (BP), central BP, wave reflections, pulse wave velocity), using radial tonometry, a transfer function and dedicated algorithms, in 81 patients (mean age 61 years, 90% men) with HFrEF, and followed them for 4.1 years. Patients were divided into quartiles (Qu), according to brachial PP. Main outcome was all-cause mortality.
Results: As compared to Qu 2 + 3, patients in Qu1 had lower BP, lower values for antegrade pressure wave, larger left atrium, larger enddiastolic and endsystolic left ventricular volumes, lower EF, and higher nt-proBNPs. The predominant cause of HFrEF in Qu1 was dilated cardiomyopathy.
As compared to Qu 2 + 3, patients in Qu4 were older, had a higher prevalence of hypertension, diabetes and coronary artery disease, had higher blood pressures and higher values for antegrade and reflected waves and pulse wave velocity. Enddiastolic and endsystolic volumes were smaller, and filling pressures were lower, but nt-proBNP levels were higher in Qu4.
In survival analysis (logrank test, p = 0.0009), patients in Qu1 as well as Qu4 had a higher mortality (Qu 1 vs Qu 2 + 3: HR 3.1 (95% CI 1.2-8.1); Qu 4 vs Qu 2 + 3: HR 4.4 (95% CI 1.7 - 11.2)) - Figure. In a multivariate Cox proportional hazards model predicting all-cause mortality, Qu4 (HR 4.65 (CI 1.69-12.80), p = .003), and, of borderline significance, Qu 1 (HR 2.93 (0.96-8.88), p = 0.059), and log nt-proBNP (HR 2.27 (0.94-5.5), p = 0.07), were the independent predictors. Age, gender, presence of ischemic cardiomyopathy, EF, and SBP did not enter the final model.
Conclusion: Lower as well as higher PP is associated with impaired survival in HFrEF. In the first case, the lower PP likely is the expression of a very poor cardiac function. In the latter case, the higher PP stems from an increased pulsatile afterload. Both conditions can be detrimental.

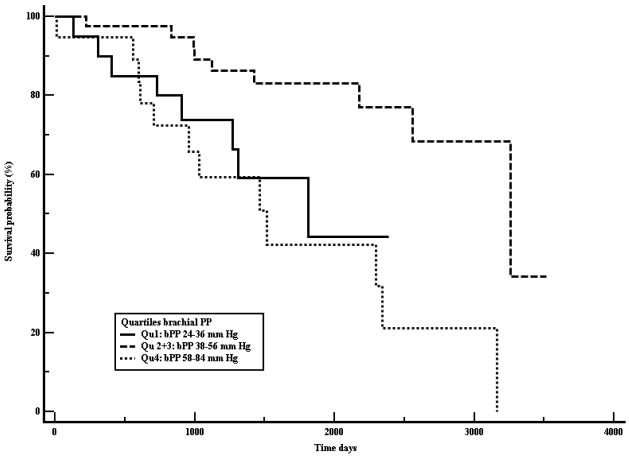


Fig 1

P1002
Mathematical prediction of unfavorable course of chronic heart failure

Z D Zulfya Rasulova[1]; UK Kamilova[1]
[1]Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, Cardiology, Tashkent, Uzbekistan

Purpose. Identification of predictive factors of an adverse course of the chronic heart failure (CHF).
Methods: In total were inspected 120 patients with the coronary heart disease with the I-III functional class (FC) of CHF. To all patients carried out: echocardiography with assessment of final diastolic and systolic volumes and sizes of left ventricle (FDV, FSV and FDS, FSS LV), the fraction of emission (FE) of LV, index of systolic and diastolic sphericity (ISs and ISd); when carrying out doppler echocardiography of carotid and cephalic arteries arteries and renal arteries estimated indicator of the thickness of intim of mussel (TIM) at the level of the general carotid artery (GCA), resistive and pulsation index (RI and PI) at the level of the right and left renal artery; determined the level of serumal creatinine (Kr), calculation method of glomerular filtration rate (GFR) by formula MDRD (Modification of Diet in Renal Disease Study) in ml/min/1,73m2.
Results: To assess the significance of the parameters in predicting the course of CHF based on renal function is used method of non-homogeneous sequential procedure with the development of differential diagnostic tables (DT) in three stages is used: the first - research of probability of sign at CHF depending on severity, calculation of the diagnostic coefficients (DC) and determination of informational content (J) of each sign; the second stage - drawing up DT, with inclusion of

the signs which had high J (≥0,5), determination of their sensitivity (Se), the predictive importance (PI); the third stage - choice of diagnostic thresholds (the recreation center sum) which have allowed to make the correct decision. The following diagnostic indicators have been selected: the LV structural and geometrical parameters (FDS, FDV and FSS LV, FE LV, ICs and ICd), parameters of vascular remodeling (TIM at the level of the right and left general carotid artery, RI and PI at the level of the right and left renal arteries) and GFR MDRD.
To study the PI for signs of progression of heart failure symptoms were selected DC which had informative: GFR MDRD less than 60 ml/min/1,73m2, FE LV less than 50%, FDV more than 137 ml, FSS more than 43 mm, ISd, TIM of general carotid artery, more than 1,1 mm.
At the threshold value of DC = +15 and over is predicted unfavorable course of CHF, with the values of DC = - 20 or less it is concluded that a stable flow of CHF. Results of research have shown that the most sensitive signs for definition of the forecast of CHF at patients: availability of FE less than 50% (Se = 1), TIM thickening general carotid artery (Se = 0,96), increase in FDV more than 137 ml (Se = 0,95) and FSS more than 43 mm (Se = 0,95). Conclusions: The analysis of the carried-out mathematical forecasting of adverse current of CHF has shown that the most precursory adverse predictive symptoms are: FE less than 50%, FDV more than 137 ml, FSS more than 43 mm and GFR less than 60 ml/min/1,73m2.

P1003

A white-coat effect for heart rate in heart failure? Characteristics and prognostic implications in idiopathic dilated cardiomyopathy

A Bisson[1]; B Lequeux[2]; N Clementy[1]; M Boyer[1]; C Andre[1]; F Ivanes[1]; D Angoulvant[1]; D Babuty[1]; L Laurent Fauchier[1]
[1]*Tours Regional University Hospital, Hospital Trousseau, Tours, France*; [2]*University Hospital of Poitiers, Poitiers, France*

White coat-effect for blood pressure is defined as temporary increase in blood pressure before and during visit in the clinic, regardless what the average daily ambulatory blood pressure values are. We hypothesized that such a phenomenon may also exist for heart rate (HR) in patients with heart failure (HF) whilst HF guidelines advocate a more aggressive drug management when HR in sinus rhythm is ≥70 bpm, and that white-coat effect on HR (WCHR) might be associated with a different prognosis in patients with idiopathic dilated cardiomyopathy (IDC).
Methods: Among 117 IDC patients (WHO criteria) in sinus rhythm, 24-hour Holter monitoring was performed at enrolment to assess heart rate (HR) and heart rate variability (HRV) parameters. The HR and HRV were measured automatically over 24 hours, during daytime and nighttime periods. We considered mean HR measured during the first hour of recording (HRH1) as possibly being affected by WCHR. The endpoint of cardiac events included cardiac death, heart transplantation and major arrhythmic event (sustained VT/VF).
Results: Among 117 patients with IDC (age 51 ± 12, LVEF 33 ± 12%), 36 (31%) had WCHR ≥5 bpm for HRH1 compared to mean daily HR, and 12 (10%) had WCHR ≥10 bpm. There were 6 patients (5%) with HRH1≥70 bpm whilst daily HR was < 70 bpm. Patients with WCHR ≥5bpm had lower LVEF than those with WCHR < 5 bpm (30 ± 12% vs 35 ± 11%, p = 0.02) and those with WCHR ≥10 bpm were younger than those with WCHR < 10 bpm (42 ± 12 vs 52 ± 11, p = 0.006). With a follow-up of 62 ± 44 months, there were 41 events in 39 patients: 24 cardiac deaths including 12 sudden deaths, 5 sustained VT/VF and 12 heart transplantation. In univariate analysis, HRH1 was a predictor of cardiac events (Hazard Ratio 1.028, 95%CI 1.007-1.049, p = 0.01; C statistic 0.653, 95%CI 0.559-0.738, p = 0.006). However, HRH1 was not an independent predictor after adjustment on age, LVEF, NSVT, NYHA functional class, HR, HRV and QRS duration. Neither WCHR ≥5 bpm nor WCHR ≥10 bpm was an independent predictor of cardiac event.
Conclusions: In patients with IDC, a phenomenon of WCHR is a common finding and may misclassify HR for adaptation of drug therapy according to current HF guidelines in 5% of the cases. Since WCHR was not independently associated with a worse prognosis, we suggest that HR would be better assessed in very stable conditions. Ambulatory monitoring or home HR measurement could result in more accurate evaluation of HR and hence more appropriate treatment.

P1004

Impact of tricuspid regurgitation on survival in patients with chronic heart failure

K Kaoutar Kharbouche[1]; K Kharbouche[1]; I Elhaddad[1]; L Azouzi[1]; R Habbal[1]
[1]*chu ibn rochd, cardiology, casablanca, Morocco*

Purpose: Tricuspid regurgitation (TR) is common in patients with chronic heart failure (CHF). However, data about the prognostic value of significant TR in CHF patients are sparse.
Methods: 1600 consecutive patients with CHF were included between 2009 and 2014. Patients represented an unscreened contemporary cohort of CHR patients treated according to current guidelines in a tertiary heart failure clinic. At study entry detailed clinical and echocardiographic data were collected. The prognostic impact of significant TR was assessed and compared with established risk factors.
Results: TR was common in the study population. 10.6% of patients had severe, 24.0% moderate, and 65.4% of patients had no or mild TR. Kaplan Meier analysis showed a considerably increased mortality rate of patients with moderate and severe TR (p , 0.0001). However, by multivariable analysis NTpro-BNP (p ¼ 0.0054), systolic blood pressure (p ¼ 0.0012), heart rate (p ¼ 0.0152), age (p , 0.0001), serum creatinine, (p , 0.0001), serum sodium (p ¼ 0.0449) and left ventricular function (p ¼ 0.0130), but not TR independently predicted mortality. These independent predictors of mortality were used to define disease severity to analyse the predictive value of TR at different stages of CHF. In patients with mild and moderate CHF, characterized by NT-proBNP concentrations ,500 mg/pg, serumcreatinine levels ,1.5mg/dl, sustained systolic blood-pressure. 100mmHg, heart rate ,90/min, severe TR was highly predictive of mortality (p , 0.0001 for all, except NTproBNP p ¼ 0.00175). In patients with advanced disease, however, significant TR did not add additional information.
Conclusion: The prognostic impact of TR strongly depends on the severity of heart failure. Whereas TR excellently predicts excess mortality in mild to moderate CHF, it has no additive value in advanced CHF when compared with established risk factors. Since it is only in mild to moderate CHF that severe TR is associated with adverse outcome it is this group of patients that might benefit from tailored pharmacological or surgical interventions

P1005

Low incidence of overt heart failure in south italy centenaries is linked with good life style: preliminary data from the ciao study

R Marino[1]; S Navarin[1]; C Bartoli[1]; M Guariglia[1]; R Di Rienzo[1]; A Maisel[2]; L Daniels[2]; S Di Somma[1]
[1]*S. Andrea Hospital - II Faculty of Medicine University La Sapienza., rome, Italy*; [2]*Veterans Affairs San Diego Health Care System, San Diego, United States of America*

On behalf of: GREAT NETWORK

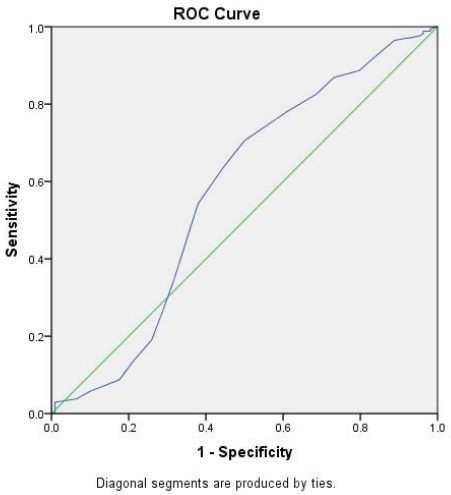
Background: In south of Italy there is a a longer life expectancy compared to the other italian regions and the number of centenaries is exstimate to be of 4-5% of whole in habitants.
Purpose: Aim of our study(Cilento Initiative Aging Outcome(CIAO) was to perform a preliminary evaluation of all reasons of the longevity in this region people. A complete cardiological assessment in order to evaluate the incidence of Heart failure in centenarian from Cilento region compared to their cohabitants of the age between 50 to 70 years old and to link the results with their life-style.
Materials and Methods: 26 centenarians(Cen) and two of their cohabitants (coh) were enrolled in their houses. The centenarians were reached at their home by mean of fully equipped car with cardiological instruments. Clinical assessment was performed including medical history, clinical exam to check signs of congestions, collection of Weight, Height, Blood pressure(BP), Heart rate (HR), respiratory rate (RR), oxigen saturation (SaO2) partial fraction of oxygen (FiO2). Moreover the partecipants underwent: electrocardiogram (EKG) , bioimpedance vector analisys (BIVA), Lung ultrasound test (LUS), ecocardiography to evaluate the heart function and structure and the collapsability of inferior cava vein. Life style of centenarians (including diet and physical activity)were also recorded. A six months later a phone call Follow up was also performed.
Results: 26% of Cen had a diagnosis of chronic heart failure (CHF)but were. Ischemic cardiopathy (CHD) was 4% in Cen and 6% in Coh. Risk factors for heart failure were less present in Cen compared to Coh. Diabetes was present in 8% of Cen compared to 23% in Coh. Hypertension was detected in 48% of Cen and 51 % of Coh. High Colesterol level was 16% in Cen compared to 26 % in Coh. Dispnea at rest was present in only 8% of Cen . The hydration score mean was 76,8 ± 4,36 inCen and 73,9 ± 1,9 in Coh (ns). At Lung ultrasound (LUS) no pleural effusion was detected in both groups. At echocardiography the percentage mean of ejection fraction(EF) and inferior vein cava diameter (IVC) were in the normal ranges for both groups :EF 52 ± 1,9, ad 55 ± 5,63 respectively and IVC: 15 ± 5,51 in Cen compared 15 ± 3,38 in Coh. Regarding life style we found out that compared to Coh Cen had more adherence to strictly mediterranean diet and physical activity. At Follow up no death occurred in Cen but one hospitalization between Cen and two in Coh.
Conclusions: The centenarians of Cilentum, despite of the presence of all typical cardiovascular risk factors, present low incidence of symptoms and signs of overt heart failure probably because of the adherence to mediterranean diet and acvitve life style.

P1006

The role of sodium level and in-hospital mortality in patients with acute, or acute worsening chronic heart failure

M Marija Vavlukis[1]; B Pocesta[1]; H Taravari[1]; E Shehu[1]; D Kitanoski[1]; I Bojovski[1]; I Kotlar[1]; S Kedev[1]
[1]*University Clinic for Cardiology, Skopje, Macedonia The Former Yugoslav Republic of*

AIM of the study: to determine the role of low sodium level (sNa) as a predictor of in-hospital mortality (IHM) in acute and acute worsening chronic heart failure.
DESIGN: observational retrospective study. Included patents admitted to ICU because of AHF. Analyzed variables: demographics: age, gender; co-morbidities, Biochemical: hemoglobin, anemia, renal failure, sodium, creatinine, BUN; Hemodynamic parameters: heart rate, systolic and diastolic BP, LV ejection fraction (based on what patients were divided in PEF-HF and REF-HF), Statistical analyze: descriptive, t-test, Chi square, uni and multivariate logistic regression, ROC Curve. Significance determined at the level of 0.05.
Results: 451pts. at mean age 69,9 ± 10.8, 201(44,6%) females and 250 (55,4%) males were included. Presence of co-morbidities: Afib 41,0%; COPD 23,5%; DM 41,5%; HTA 71,6%; carotid artery disease (CAD) 41,2%; previous symptomatic HF 34,8%; renal failure 12,0%, anemia 31.9%; mean EF 42,9 ± 10,3% (21.3% with PEF-HF (≥50%); HR 109 ± 29 BPM; SBP 143 ± 44, DBP 86 ± 24mmHg; Hgb 13 ± 3.8, BUN 26.8 ± 21.5; creatinine 128.9 ± 124.9mikromol/L; sodium 138 ± 6mmol/L.Pts were divided in two groups reduced sNa < 135 (115 -25.5%), and normal sNa ≤ 135 mmol/L. A total of 108 (23,9%) cardiac deaths were registered (IHD group), with the highest mortality rate during the first 48 hours (68.5%).
Univariate predictors: HLP: beta -.662; p = 0.011, exp(B). 516; HTA: beta -0.751, p = 0.001, exp(B) 0.472; CAD: beta. 931; p = 0.005, exp(B) 2.536; renal failure: beta 0.819, p = 0.007, exp(B) 2.268; sNa < 135: beta 0.743, p = 0.002, exp(B) 2.102; anemia: beta. 930, p = 0.000, exp(B) 2.533; EF categorical: beta 0.746, p = 0.017, exp(B) 2.109; EF (%): beta -.167, p = 0.000; DBP: beta -.299, p = 0.000; SBP: beta -.281, p = 0.000; sodium: beta -.105, p = 0.025; Hgb: -.034, p = 0.000; creatinine: beta. 199, p = 0.000; BUN: beta. 165, p = 0.000. In multivariate analyze as independent predictors for IHM were identified: HLP (p 0.011), high DBP (p 0.000) as negative predictors; CAD (p 0.002), anemia p = 0.042, EF (%) p = 0.005 and sNa < 135mmol/L p = 0.039 as positive predictors. But when we entered low sodium as selection variable, three independent predictors were identified: HTA (p 0.039), DBP (p 0.009) and creatinine (p 0.002).
Variables independently significantly positively associated with low sodium level were low SBP (p 0.002), high BUN (p 0.000), and CAD (p 0.002), while HTA (p 0.025) was independently negatively associated. When we entered IHM as selection variable there were three independently associated predictors added to low sNa: high BUN (p 0.006), creatinine (p 0.026) and presence of CAD (p 0.006). Normal sNa level had good discriminate function (ROC Curve: Area under the Curve. 572, p < 0.024 (CI. 503-.641) (image 1), in predicting absence of IHM.
Conclusion: low sodium is one of the significant independent predictor of in-hospital mortality in patients treated because of acute or acute worsening chronic heart failure.



ROC curve for sNa and IHM

P1007

The beneficial effect of the management of heart failure patients with reduced ejection fraction at an outpatient clinic after hospitalization and applying guideline recommended therapy on mortality

N Nyolczas[1]; B Szabo[2]; M Dekany[1]; D Vagany[1]; T Borsanyi[1]; B Muk[1]; ZS Majoros[1]; M Szabo[1]; RG Kiss[1]
[1]*Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary*; [2]*Orebro University Hospital, Cardiology, Orebro, Sweden*

Background: Mortality of heart failure (HF) is high despite the significant recent advances in pharmacological and device therapy. National data published a few years ago showed nearly 30% annual mortality. The data of European Society of Cardiology Heart Failure Long-Term Registry revealed 23.6% 1-year mortality in patients hospitalized with a diagnosis of HF and 6.4% among patients with chronic stable HF.
Purpose: The aim of the study was to assess the survival data of patients suffering from heart failure with reduced ejection fraction (HFrEF) managed at our HF outpatient clinic after HF hospitalization in the last 15 years.
Patients and methods: We assessed the data of 513 patients with severe HFrEF (LVEF≤40%, NYHA III-IV) managed at our HF outpatient clinic after HF hospitalisation between June of 2001 and June of 2016. At the beginning of the management the patients' characteristics were as follows: mean age 62.6 ± 12.5 years, mean NYHA functional class 3.56 ± 0.45, mean LVEF 27.5 ± 6.9, proportion of men 75.6% and ischemic aetiology 49.8%. We made every effort to achieve the optimal medical and device therapy in all patients. Mean follow-up time was 5.6 ± 4.3 years. Survival was estimated by Kaplan-Meier method.
Results: After optimization of pharmacological therapy 95.6% of patients received ACEi/ARB, 96.8% of them BB and 86.1% MRA. 32.7% of patients on ACEi/ARB therapy got target dose (equivalent to 40 mg enalapril), 80.6% of them received at least the half of the target dose, and mean of the individual value of the ACEi/ARB dose expressed as percent of the target dose was 66.1 ± 33.1%. The target dose of BB was applied in 50.2% of patients, 89.2% of them were treated with at least the half dose, and mean of the individual value of the BB dose expressed as percent of the target dose was 82.2 ± 42.0%. CRTP implantation was performed in 57 patients, CRTD in 64 and ICD in 47 cases. After treatment optimization LVEF (36.4 ± 10.5; p < 0.001) and NYHA functional class (1.75 ± 0.77; p < 0.001) improved significantly. The 1-year mortality was 89.7% and 5-year mortality was 55.0% in this studied patient group.
Conclusion: The mortality rate of severe HFrEF patients managed at an outpatient heart failure clinic after hospitalization and treated with guideline recommended optimal pharmacological and device therapy can be decreased by one third to half compared to the general HF patient population.

P1008

Mortality rate of patients with heart failure with preserved ejection fraction on carvedilol therapy; results from the Croatian heart failure registry

D Markovic[1]; B Jurcevic Zidar[2]; J Macanovic[1]; D Milicic[3]; D Glavas[1]
[1]*University Hospital Center Split, Clinic for heart and cardiovascular diseases, Split, Croatia*; [2]*Public health institute of Split-Dalmatia county, Split, Croatia*; [3]*University Hospital Centre Zagreb, Zagreb, Croatia*

On behalf of: CRO-HF group

Background. The mortality of heart failure (HF) patients is still high in majority countries, despite the quality treatments, new guidelines and continuosly education of medical staff. Treatment for heart failure with reduced ejection fraction (HF-REF) is widely well known and used in medical practice. The treatment approach for heart failure patients with preserved systolic function (HF-PEF), according to recent guidelines and scientific papers, is still not defined.
Purpose: The aim of this study was to analyze mortality rate of HF patients and to investigate how carvedilol therapy in HF-PEF patients influenced on mortality rate after ten-year follow-up from Croatian heart failure (CRO-HF) registry.
Methods: A group of 2203 in-hospital patients with diagnosis of HF (median age 76, 53.3% males, 46.7% females) who were hospitalized at University Hospital Split were analysed. Particularly, after ten-year follow-up, HF-PEF patients on carvedilol therapy were analysed and HF-PEF patients without any beta-blocker on discharge letter were enrolled as control group (119 vs 218, respectively); the data were part of CRO-HF Registry. HF-PEF was classified as EF≥40%. After follow-up, the mortality rate was analysed in the carvedilol and control group.
Results: In-hospital mortality rate of 2203 patients was 13.8%. In-hospital mortality rate was higher in females than in males (females=14.4%, males=12.6%). HF-PEF with EF ≥50% had 37.8% and HF-PEF with EF 40-49% had 24.9% patients. We found significant difference in mortality rate when we compared patients with EF < 50% and EF≥50% (Hi2=4.652; P=0.037; CI=0.069). Patients with EF < 50% had 2.5 higher mortality rate. In the group of patients with EF < 50% mortality rate was 4.2%, and 1.6% in the group of patients with EF ≥50%.

When we compared group on carvedilol therapy with control group we analyzed 337 patients; 159 men and 178 women. The mean age of patients was 77.29 ± 10.2 years. After ten-year follow-up, in carvedilol group 76 patients died and mortality rate was 63%. In the control group 167 patients died and mortality rate was 76%. For comparing these two groups we used chi square test and mortality rate in carvedilol group was significantly lower chi-square=6.212, p = 0.0212.
Conclusion: Ten-year mortality rate of HF patients from CHO-HF registry is still high. We should try to reduce the mortality with quality implementation of guidelines, with better involvement of Heart Failure Association and all society. Carvedilol therapy appears to be associated with lower mortaliy rate in patients with heart failure with preserved systolic function.

P1009
Soluble ST2-receptor (sST2) is more powerful predictor of long-term prognosis in patients with acute decompensated heart failure, compared with copeptin

A Skvortsov[1]; V Protasov[1]; O Narusov[1]; S Nasonova[1]; T Kuznetzova[1]; V Masenko[1]; S Tereschenko[1]
[1]*Russian Cardiology Research and Production Complex, Moscow, Russian Federation*

Background: novel biomarkers sST2 and copeptin are known as powerful predictors of CHF patients (pts) long-term prognosis.Purpose: to evaluate head to head significance of copeptin and soluble ST2 (sST2) in heart failure pts risk stratification in one year follow-up period after acute decompensation (ADHF).
Methods: In the prospective single-center study were included 159 pts with ADHF III-IV FC NYHA. Blood samples to determine NT-proBNP, sST2, copeptin, hsTnT concentration were collected at the admission and at discharge from the hospital, and after 3, 6 and 12 months of follow-up. The combined primary end point of the trial included cardiovascular (CV) death, hospitalization due to HF, episodes of HF deterioration needed additional i/v diuretics and CV death with successful resuscitation.
Results: During 1-year follow-up 56 pts (35,2 %) had 78 (49,1%) cardiovascular events. Biomarker concentrations in low risk pts (without CV events) were significantly lower compared with high risk pts (who have CV events). At the discharge from the hospital sST2 concentrations had the best predictive capacity compared with copeptin and NT-proBNP for the primary end point at 1-year follow-up: AUC=0,768 (95% CI 0,682-0,854) vs 0,735 (95% CI 0,64-0,83) and AUC=0,727 (95% CI 0,637-0,816), respectively, p < 0,001 for all. Lack of copeptin concentration decrease below 28,3 pmol/l and sST2 concentration below 37,8 ng/ml were associated with the highest risk of CV events: respectively HR[95% CI] = 5,14(2,204-11,98), p < 0,0001 and HR[95% CI] = 6,755 [3,026- 15,082], p < 0,0001. Cutting value for NT-proBNP was 1696,0 pg/ml, HR[95% CI] = 4,41 [1,41-9,624], p < 0,0001. Values of sST2 at the discharge additionally to standard clinical model and NT-proBNP levels were the most significant predictor of CV events in long-term follow-up (beta=0,519, p < 0.0001), copeptin was less powerful (beta=0,32, h=0,019). Moreover, in multimarker model, which included all biomarkers only sST2 values had additional significant prognostic information (p = 0,007).
Conclusion: sST2 is more powerful predictor of long-term prognosis in patients with acute decompensated heart failure, compared with copeptin. Discharge values of sST2 from the hospital combined with NT-proBNP have the best predictive capacity to reflect the adverse long term prognosis in patients with ADHF.

P1010
Heart failure and comorbidities in acute coronary syndrome prognosis; a hierarchical analysis of clinical and lifestyle factors per heart failure phenotype, from hellenic heart failure study.

M Kouvari[1]; C Christina Chrysohoou[2]; H Kosyfa[1]; G Kalogirou[1]; P Aggelopoulos[1]; S Iosifidis[3]; A Filippou[3]; E Tsiamis[1]; D Tousoulis[1]
[1]*University of Athens, First Cardiology Clinic, School of Medicine, Athens, Greece*; [2]*University of Athens, Athens, Greece*; [3]*Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

On behalf of: Hellenic Heart Failure study

Background/Introduction: comorbidities in the context of secondary cardiovascular disease prevention highly determines patients' prognosis. Focusing on heart failure and the differential pathophysiology behind its phenotype the "comorbidities" hypothesis remains a scientific field of much interest in the treatment spectrum. Purpose: to investigate the comorbidities in each heart failure phenotype and to classify these clinical as well as lifestyle factors in relation to Acute Coronary Syndrome (ACS) prognosis.
Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, the 10y follow-up (2006-2016) was performed in 745 participants. Heart failure phenotype was defined according to baseline EF; heart failure with reduced EF (i.e. < 40%) (HFrEF), preserved EF (i.e ≥50%) (HFpEF) and mid range EF (i.e. 40-49%) (HFmrEF). Age, sex, overweight/obesity, current smoking, MedDietScore, physical activity, hypertension, hypercholesterolemia and diabetes mellitus were evaluated in relation to 10y ACS prognosis, in each heart failure phenotype, based on hierarchical classification analysis using Fisher linear discriminant function. Results: The 10y fatal/non fatal ACS incidence was 68%, 53% and 45% in HFrEF, HFmrEF and HFpEF respectively. Crude analysis revealed that ranking from the lowest to the highest EF values (i.e. from HFrEF to HFpEF) patients had higher likelihood to suffer from hypertension (from 62% to 55%, p = 0.04), hypercholesterolemia (from 82% to 73%, p = 0.01) and overweight/obesity (from 32% to 25%, p = 0.10); yet no significant differences were observed as regards diabetes mellitus. In discriminant analysis, in HFpEF patients the predominant predictors associated with 10y ACS prognosis were overweight/obesity (Wilks'Lamda=0.962), current smoking (Wilks'Lamda=0.965), MedDietScore (Wilks'Lamda=0.987) and physical activity (Wilks'Lamda=0.992) (all ps < 0.05). In HFrEF, only hypertension came on the top of the list (Wilks'Lamda=0.954, p = 0.02) whilst the remained factors were not highlighted as important in the classification. In case of HFmrEF results seemed to be closer to their HFpEF counterparts with inconclusive outcomes. Conclusion: ACS prognosis seemed to be highly determined by metabolic comorbidities, namely in HFpEF patients; whilst lifestyle modifications may possess an important supplementary recommendation in the rehabilitation process in this heart failure phenotype.

P1011
Heart failure with reduced LV ejection fraction and atrial fibrillation/flutter, what predicts LV ejection fraction recovery?

D Damon Jackson[1]; P Mottram[1]; C Bowman[1]; J Cameron[1]; E Quine[1]; S Lockwood[1]
[1]*Monash University, Monash Heart, Melbourne, Australia*

Introduction: Heart failure with reduced left ventricular ejection fraction (HFREF) and atrial arrhythmias (Atrial Fibrillation/Flutter) often co-exist, and the relationship between reduced ejection fraction (LVEF) and the uncontrolled heart rate (HR) is unclear.
Objective: To explore the factors associated with recovery of LVEF in patients presenting with both atrial arrhythmia and reduced LVEF (< 45%).
Methods: Patients with HFREF and atrial arrhythmia admitted to a specialist HFREF clinic were included. Treatment was according to Heart Failure guidelines; atrial arrhythmias were managed at physician's discretion. Demographic, clinical and echocardiographic data were collected at baseline and follow up. Patients with improved LVEF (>10% increase) were compared to patients with unchanged LVEF.
Results: 45 patients (64 ± 12 years, 24% female, baseline LVEF 25 ± 9%) were included. At 9 ± 5 months follow-up 47% (n = 21) demonstrated improved LVEF (repeat EF 48 ± 8%, p < 0.01). Improved LVEF pts had greater reduction in HR compared with unchanged LVEF pts (-42 ± 24 vs −8 ± 16 bpm, p < 0.01). Increase in LVEF correlated with reduction in HR (r -0.59) regardless of rhythm. Pts with improved LVEF were less likely to have hypertension, documented IHD or diabetes (all p < 0.01). Left atrial size was similar between groups (p = 0.51) but improved LVEF had smaller LVEDD (p = 0.04) and higher mitral annular velocities (p = 0.01) at baseline.
Conclusions: In patients presenting with HFREF and atrial arrhythmias, improved heart rate control was associated with improvement in LVEF, regardless of rhythm. LVEF was also more likely to improve in those without coronary artery disease, hypertension or diabetes.

P1012
Red blood cell distribution width predicts the risk of heart failure exacerbations but not death in stable patients with chronic heart failure in a short-term observation

A M Anna Maryla Kowalczys[1]; M Bohdan[1]; M Gruchala[1]
[1]*Medical University of Gdansk, 1st Department of Cardiology, Gdansk, Poland*

Introduction: Chronic heart failure (CHF) is one of the most challenging problems in cardiology nowadays. Although many patients are treated optimally, the prognosis still remains poor. There are many biomarkers valuable in predicting the outcome of patients with CHF. Some authors have reported that RDW may be useful for risk stratification in patients hospitalized with acute heart failure. Nevertheless, its role in stable CHF still remains unclear.
PURPOSE: The aim of the study was to assess the relationship between RDW and major adverse cardiac events (MACEs) in stable patients suffering from CHF.
Methods: There were 75 patients: 70 (93%) men and 5 (7%) women (mean age: 59 ± 12 years) with stable CHF, NYHA class 2,1 ± 0,57, with reduced left ventricular ejection fraction (LVEF) recruited for the study. All patients underwent following

examinations: medical history, physical examination, laboratory tests including blood morphology with RDW and BNP, 12-lead electrocardiogram, chest X-ray, echocardiogram, six-minute walk test (6MWT). All patients recruited for the study were treated according to ESC guidelines. The follow-up period was 6 months. MACEs were defined as: death of all causes, cardiovascular death, hospitalization due to the heart failure exacerbation. In order to establish the link strength and direction between variables, the correlation analysis was used in calculating the Pearson and/or Spearman correlation coefficients. In all the calculations the level of significance was set at $P = 0.05$.

Results: The LVEF ≤35% (mean 23 ± 7%) was confirmed in all patients as well as elevated BNP level (762 ± 717 pg/ml). The RDW was increased in the majority of patients and achieved 15 ± 1.8%. The percentage of patients with heart failure exacerbation was 13% at 3 months and 24% at 6-month follow-up. The mortality rate was 4% at 3 months and 6% at 6-month follow-up. We found that RDW value was significantly higher in patients with CHF decompensation during the 6-month observation (16.7 ± 1.5% vs. 15 ± 1.7%, $P < 0.0001$). There was no relationship between RDW value and death during 6-month follow-up in stable patients with CHF.

Conclusions: Red blood cell distribution width may be a potential predictor of subsequent hospitalizations due to heart failure decompensation in stable patients with CHF with reduced left ventricular ejection fraction in short-term observation. No other correlations between RDW and MACEs were found.

P1013

Heart failure in patients with acute coronary syndrome: characterization of population and impact on prognosis.

J Pais[1]; B Picarra[1]; RA Guerreiro[1]; D Bras[1]; J Carvalho[1]; K Congo[1]; AR Santos[1]; M Carrington[1]; J Aguiar[1]
[1]*Hospital Espirito Santo de Evora, Departement of Cardiology, Evora, Portugal*

Introduction: Patients (P) with chronic heart failure (CHF) usually have multiple co-morbidities, so their approach in the context of Acute Coronary Syndrome (ACS) can be an important challenge.

Purpose: To characterize the P with ACS and previous CHF and to evaluate the impact of the presence of CHF on the therapeutic approach, complications and in-hospital mortality.

Methods: We studied 745 P admitted in our Cardiac Intensive Care Unit with the diagnosis of ACS. We considered 2 groups: P with prior CHF and P without previous CHF. The patient's age, gender, personal history, clinical and electrocardiographic presentation of ACS, in-hospital therapy, left ventricular ejection fraction, coronary angiography and angioplasty were recorded. During hospitalization the following complications were defined: heart failure, cardiogenic shock, need of invasive mechanical ventilation, re-infarction, mechanical complications, aborted sudden death, stroke and major haemorrhage. In-hospital mortality was compared between both groups.

Results: P with previous CHF constituted 7.1% (53 P) of the study population. These patients were older (77.3 ± 8.9 vs 66.6 ± 13.6, $p < 0.001$), had higher prevalence of history of arterial hypertension (88.7% vs 76.2%, $p = 0.03$), myocardial infarction (50.9% vs 24.3%, $p < 0.001$), coronary surgical revascularization (18.9% vs 5.2%, $p < 0.001$), valvular disease 22.6% vs 1.4%, ($P < 0.001$), peripheral arterial disease (22.6% vs 5.1%, $p < 0.001$), chronic renal failure (41.5% vs 10.1%, $p < 0.001$), chronic lung disease (22.6% vs 4.2%, $p < 0.001$) and haemorrhage (9.6% vs 1.8%, $p < 0.001$). P with previous CHF presented more frequently with NSTEMI (62.3% vs 45.7%, $p < 0.001$) and indeterminate location myocardial infarction (26.4% vs 4.6%, $p = 0.02$).At admission they also presented Killip-Kimbal class ≥ 2 more frequently (64.2% vs 16.8%, $p < 0.001$) and less frequently with chest pain (58.5% vs 87.7%, $p < 0.001$).

During hospitalization, P with prior CHF underwent less coronary angiography (56.6% vs 86.7%, $p < 0.001$), less radial artery access for coronary angiography (53.6% vs 79.0%, $p = 0.001$), and fewer angioplasties (32.1% vs 68.7%, $p < 0.001$). The presence of prior CHF was associated with lower left ventricular ejection fraction (40.9 ± 10.4% vs 48.2 ± 9.9%, $p = 0.004$), with development of acute decompensated heart failure (47.2% vs 12, 4%, $p < 0.001$), need for non-invasive ventilation (17.0% vs 2.2%, $p < 0.001$) and higher in-hospital mortality (13.7% vs 4.8%, $p = 0.008$). There is no significant statistically differences on re-infarction, mechanical complications, aborted sudden death and stroke.

Conclusion: The clinical and electrocardiographic presentation of ACS seems to be influenced by the presence CHF. The presence of prior CHF was associated with development of acute decompensated heart failure and higher in-hospital mortality.

P1014

Body composition as a risk of prolonged hospitalisations in patients with heart failure and / or respiratory distress

L Leslie Verdeja Vendrell[1]; D Gonzalez-Islas[2]; A Navarrete-Penaloza[2]; A Jimenez-Cepeda[2]; G Perez-Cortes[2]; A Orea-Tejeda[2]; R Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; B Robles-Uribe[2]; A Figueroa-Herrera[2]; S Torres-Montiel[2]
[1]*Autonomous University of Puebla, Puebla, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Distress Clinic , Mexico City, Mexico*

Background: The muscle mass of the skeletal muscle decreases around 0.1 - 0.5% per year at the age of 30, and this loss increases starting from the age of 65. Body composition has been identified as a predictor of longer hospital stays on different populations. Malnutrition in patients delays the total hospitalization days, and this results will affect the morbidity and mortality patients. However, in patients with Heart Failure (HF) and Respiratory Distress (RD), it is unknown what type of body changes can prolong hospitalizations days. Objective: To determine if body composition is a predictor of prolonged hospital staying.

Methods: A cross-sectional study involving patients older than 18 years hospitalized with confirmed diagnosis of HF and / or RD. Prolonged hospital staying were defined as more than 7 days. Body composition analysis was performed using electrical impedance by vector analysis (BIVA) and was classified into normal composition, obesity and cachexia. A logistic regression was performed to determine the risk of hospitalization accordingly. Results: 71.7% of the population were women (mean age: 54.6 ± 21.18), of which 68.4% had a hospital stay> 7 days. Those with prolonged hospital staying had a higher prevalence of COPD (56.5% vs 18.2%, $p = 0.008$), HF (45.8% vs 22.7%, $p = 0.100$). Subjects with obesity (OR: 4.68, CI 95%, 1.04 - 21.03, $p = 0.044$) and cachexia (OR: 5.85, CI 95%, 1.22-27.99, $p = 0.027$) had greater risk of prolonged hospital staying compared to subjects with normal body composition. Conclusions: Obesity or cachexia increase the risk of prolonged hospitalization staying in patients with HF and / or RD.

P1015

Genetic predictors of acute and chronic heart failure in patients with acute acute coronary events

NG Lozhkina[1]; V Kozik[1]; EA Glebchenko[1]; MK Khasanova[1]; MI Voevoda[2]; YI Ragino[2]; VN Maksimov[2]; AD Kuimov[1]
[1]*Novosibirsk State Medical University, department of faculty therapy, Novosibirsk, Russian Federation*; [2]*Institute of Internal Medicine, Laboratory of Molecular Genetics, Novosibirsk, Russian Federation*

The purpose of the research is to test SNPs for association with the severity of acute heart failure and decreased ejection fractions in patients with acute coronary syndromes (ACS). Materials and methods. 280 patients with acute coronary syndrome (ACS) admitted to the intensive care unit of Novosibirsk Municipal Clinical Hospital No. 1, of whom 175 were men (mean age, 56.2 ± 5.2 years) and 105 were women (mean age, 62.1 ± 5.3 years). ACS was diagnosed based on criteria developed by the European Society of Cardiology and the American College of Cardiology (2000). Cardiac ventriculography and coronary angiography were performed on day 1–3 following the onset of ACS symptoms. SNPs were detected and identified in real-time PCR assays. The following SNPs were retained for further consideration: rs499818, rs619203, rs10757278, rs1333049, rs1376251, rs2549513, rs4804611, and rs17465637. Results. It has been found that some of the SNPs found quite differently contribute to ACS prognosis. Reliable differences of LVEF average level at carriers of different genotypes both in the general group, and at gender separation were not revealed in the analysis of association of left ventricular ejection fraction (LVEF) with rs1376251, rs17465637, rs619203, rs2549513. Statistically significant differences were not revealed in the analysis of frequencies of genotypes and alleles of studied polymorphisms in groups with the different Killip index without gender separation and separately at men and women.

Conclusions: The genetic markers rs480461, rs499818, rs1333049 and rs10757278 can be used in the prognostic assessment of patients with acute and chronic heart failure at acute coronary syndromes.

P1016

Polimorphism of cyp7a1 gene as marker of cardiovascular complications for hypertensive patients with 2 type diabetes and nephropathy

O Chernatskaya[1]; N Demikhova[1]
[1]*Sumy State University, Medical Institute, Sumy, Ukraine*

Cholesterol 7-alpha-hydroxylase (CYP7A1) is a microsomal cytochrome P450 that catalyzes the first step in bile acid synthesis. CYP7A1 gene encoding CYP7A1 enzyme is located on the 8q11-12 chromosome and it consists of 6 exons and 5

introns. The CYP7A1 genetic variants influenced serum levels of low density lipoproteins and triacylglycerols. Bile acid metabolism was reported to be involved in glucose metabolism homeostasis. However, the exact relationship between bile acid and glucose metabolism as well as insulin sensitivity is not clarified. Participants with insulin resistance had significantly higher risk of hyperbileacidemia.

Aim of study: the determination of interconnection between the level of glycated hemoglobin (HbA1c) and three genotypes of CYP7a1 gene for prevention cardiovascular complications in patients with type 2 diabetes mellitus (DM) and concomitant arterial hypertension (AH).

Methods: We examined 130 patients during our clinical trial. There are 80 patients with type 2 DM and AH in the first (I) group and 50 persons with AH in the second (II). The middle age are (57 ± 0.23) and (69 ± 0.57), t=19.52, p < 0.001 years.

The method for diagnostic different allele variants is polymerase chain reaction.

Results: The genotypes AA, AC and CC are determined in 5 (6.25%), 22 (27.5%), 53 (66.25%)patients respectively in the I group and 20 (40%), 19 (38%), 11 (22%) in the II group. The levels of HbA1c are (6 ± 0.25) % and (4.9 ± 0.31) %, t=2.76, p < 0.01 for AA genotype, (7.3 ± 0.6) % and (5.7 ± 0.42) %, t=2.18, p < 0.05 for AC genotype, (8.2 ± 0.59) % and (6.1 ± 0.45) %, t=2.83, p < 0.01 for CC genotype.

The mean levels of HbA1c were (6.8 ± 0.21)%, (4.2 ± 0.43)%, t=5.43, p < 0,001 for participants from the I,II groups respectively. The mean levels of AI were (3.8 ± 0.04), (3.1 ± 0.02), t=15.65, p < 0,001 for participants from the I,II groups respectively. The levels of systolic BP were (156 ± 0.45)mmHg, (143 ± 0.66)mmHg, t = 16.27, p < 0.001 and of diastolic – (105.3 ± 0.6)mmHg, (94 ± 0.43)mmHg respectively for patients with combination of AH and type 2 DM and for persons with AH. The higher levels of BP, HbA1c and more severe dyslipidemia are the characteristics of patients with AH and type 2 DM in comparing with persons had only AH.

Conclusions: CC allele of CYP7a1 gene is more popular for patients with type 2 DM and concomitant AH. CC genotype is associated with higher levels of HbA1c which is a risk factor of cardiovascular and cerebrovascular events. As a result the combined therapy is necessary for prevention severe complication of DM and AH especially with CC allele of CYP7a1 gene. There is the connection between factors of CVC such as AI, HbA1c, systolic and diastolic BP for patients with AH and type 2 DM. It is very important to define these markers for preventing end points and for improving treatment.

P1017

The relation between the low triiodothyronine syndrome and plasma selenium concentration in HFrEF - Pilot study.

MM Magdalena Maria Fraczek-Jucha[1]; K Zbierska-Rubinkiewicz[1]; KA Plens[2]; R Rychlak[1]; J Nessler[1]; A Gackowski[1]

[1]Jagiellonian University Medical College, Department of Coronary Disease and Heart Failure, John Paul II Hospital, Krakow, Poland; *[2]KCRI, Krakow, Poland*

Background/Introduction: The function of deiodinases - selenoproteins converting tetraiodothyronine (T4) to triiodothyronine (T3) may be disturbed by oxidative stress accompanying heart failure. It is hypothesized that selenium (Se) is used by glutathione peroxidase to eliminate reactive oxygen species. Selenium deficiency causes lack of deiodinase resulting in decreased T4 to T3 conversion.

Purpose: To evaluate prevalence of low T3 syndrome in chronic heart failure and to assess its clinical significance.

Methods: Research conform to the principles of the Declaration of Helsinki of the World Medical Association. The study group consisted of 43 consecutive patients with HFrEF, NYHA III-IV. Exclusion criteria: thyroid dysfunction, severe systemic disease, treatment with amiodarone, steroids or propranolol. Patients with low T3 formed Group 1 and remaining ones - control Group 2.

Results: Group 1 consisted of 6 patients and Group 2 consisted of 37 patients - the prevalence of low T3 was 14%. Patients with low T3 concentration presented higher levels of NT-proBNP (19106.00 vs. 3617.43 pg/ml, p = 0.0004), hsCRP (29.31 vs. 5.17 mg/l, p = 0.0227) and RVSP (55.67 vs 40.64 mmHg, p = 0.0184) but lower Se levels (38.75 vs 57.54 μg/l, p = 0.0078) and LVEF (13.14 vs 27.68 %, p < .0001). Group 1 had higher in-hospital mortality (50% vs 0%), p = 0.0017. Results presented in Table 1 indicate that inflammatory status and Se deficiency may be associated not only with low fT3 levels but also with the poor prognosis in heart failure.

Conclusion(s): Further research concerning coexistence of low T3 syndrome, Se deficiency, deiodinase malfunction and progression of heart failure should be conducted. If the influence of low T3 on prognosis is confirmed, supplementation of T3 and/or Se may become a therapeutic option in selected patients with HFrEF.

Table 1. fT3 and Se - correlations.

Variable	By variable	Correlation	p-value
fT3	hsCRP	-0.4484	0.0026
fT3	selenium	0.4295	0.0045
fT3	NT-proBNP	-0.5348	0.0002
fT3	LVEF	0.4877	0.0009
Se	NT-proBNP	-0.4018	0.0084
Se	LVEDV	-0.3242	0.0362
Se	LVEF	0.4593	0.0022
Se	+ dP/dt	0.3724	0.0427
Se	TAPSE	0.4825	0.0012

P1018

Significance of novel biomarkers for short-term and long-term prognosis in patients after acute heart failure decompensation

V N Protasov[1]; AA Skvortsov[1]; OY Narusov[1]; D E Protasova[2]; TV Kuznetcova[1]; GA Tkachev[1]; VP Masenko[1]; SN Tereshchenko[1]

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

Background: novel biomarkers are powerful predictors of CHF patients (pts) prognosis.Purpose: to evaluate significance of soluble ST2 receptor, copeptin, galectin-3, hs Troponin-T (hsTn-T), NT-proBNP and NGAL for short-term and long-term prognosis in patients after acute heart failure decompensation (ADHF).

Methods: In the prospective single-center study were included 159 pts with ADHF III-IV FC NYHA. Blood samples to determine NT-proBNP, sST2, copeptin, hsTnT, NGAL, Gal-3 were collected at the admission and at discharge from the hospital. The combined primary end point of the trial included cardiovascular (CV) death, hospitalization due to HF, episodes of HF deterioration needed additional i/v diuretics and CV death with successful resuscitation.Results: During 1-year follow-up 56 pts (35,2 %) had 78 (49,1%) cardiovascular events. Biomarker concentrations in low risk pts (without CV events) were significantly lower compared with high risk pts (who have CV events). The positive predictive values were found for all tested biomarkers. For short-term pts prognosis (90 days) admission hsTn-T values were the best compared with other biomarkers: AUC=0,811 (95% CI 0,707-0,916), p < 0,0001. Cutting value for admission hsTn-T was 33,3pg/ml, OR[95% CI]=9,319 (1,996-43,521), p = 0,001. In long-term period hsTn-T's predictive capacity decreased and at 12 months pts follow-up AUC for end point was only 0,663 (95% CI 0,567-0,758), p = 0.001. For long-term prognosis (1 year) sST2 at the discharge from the hospital had the best predictive capacity compared with NT-proBNP, copeptin and other biomarkers: AUC = 0,768 (95% CI 0,682-0,854) vs 0,727 (95% CI 0,637-0,816) and 0,735 (95% CI 0,64-0,83) respectively, p < 0,0001 for all. Lack of sST2 concentration decrease below 37,8 ng/ml, copeptin concentration below 28,3 pmol/l and NT-proBNP bellow 1696,0 pg/ml, were associated with the highest risk of CV events: respectively OR[95% CI] = 6,755 [3,026-15,082], 5,14[2,204-11,98] and 4,41[1,41-9,624], p < 0,0001 for all. Only one combined biomarkers model in our study significantly increases opportunities in patients long-term risk stratification. The model with combined concentrations of sST2 and NT-proBNP at the discharge had the best predictive value in the medium (180 days), and long-term (365 days) pts prognosis: AUC 0,821 (0,74-0,901), p < 0.0001; HR[95% CI] = 3,33 (1,726-6,434) p < 0.0001 and AUC 0,802 (0,72-0,884), p < 0.0001; HR[95% CI] = 3,54 (2,078-6,035), p < 0.0001, respectively. The highest risk of CV events [OR=11,8 (95% CI 3,16-43,77) p < 0,0001] had pts with discharge and sST2 and NT-proBNP concentrations ≥ cutting values (respectively ≥37,8 ng/ml and ≥1696,0 pg/ml).Conclusion: Admission hsTn-T concentrations are the best predictor of adverse short-term prognosis in pts with ADHF. Combined sST2 and NT-proBNP values at the discharge are more powerful predictor of medium and long-term prognosis in patients after ADHF, compared with other novel biomarkers.

P1019

Evaluation of NT-proBNP role in risk stratification of patients with heart failure in 12 and 18 months follow-up

A Curti Gialdino[1]; FA Immordino[1]; S Novo[1]

[1]University Hospital Paolo Giaccone, Department of Sciences for Promoting Health (PROSAMI), Chair and post-graduate School of Cardiovascu, Palermo, Italy

Background: Patients affected by heart failure (HF) commonly undergo multiple hospitalizations.

Aim: This study want to verify the prognostic role of NT-proBNP levels during hospitalization in a 12 and 18 months follow-up.
Methods: We enrolled 170 patients, 85 with preserved (HFpEF) and 85 with reduced ejection fraction (HFrEF), collecting samples for the evaluation of NT-proBNP levels at baseline and at discharge from hospital. We assessed rates of mortality, new MACE, new hospital admission because of HF and fatal/not fatal events.
Results: In HFrEF patients we found higher predictive values for mortality in both our controls (all $p < 0{,}0001$) while the area under the ROC curve values were always higher at discharge (AUC >0,82). A predictive value of NT-proBNP for MACE and for fatal/not fatal events was also found (all $p < 0{,}002$), with a stronger relationship with discharge assays (all $p < 0{,}0001$). On the contrary, in HFpEF patients only discharge assay seems to have a prognostic role for all outcomes in both our two controls ($p < 0{,}01$) but with lowers predictive values. To assess the independence of our NT-proBNP evaluations we add consecutively our titrations in a multivariate Cox regression models founding the ones with the higher hazard ratio (HR) for all outcomes we evaluated except for new hospitalization because of HF both within 12 and 18 month compared to others variables evaluated (age, sex, haemoglobin, serum creatinine and troponin, systolic blood pressure, heart rate and ischemic etiology). NT-proBNP at discharge always are the one with higer HR compared to admission ones both in HRrEF patients and HFpEF patients.
Conclusions: NT-proBNP titrations during hospitalization are predictive of mortality, MACE and fatal/not fatal events but not for new hospitalization because HF after 12 and 18 month from hospitalization. Discharge assay seems to have the most predictive value compared to admission one.

P1020

Choice of an anticoagulant affects endothelial function but not long-term prognosis in patients with acute decompensated chronic heart failure

IV Shevchenko[1]; AA Shavarov[1]; GK Kiyakbaev[1]; VS Moiseev[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Objective: to estimate the effect of unfractionated heparin (UFH), enoxaparin or fondaparinux on long-term prognosis in patients, hospitalized with acute decompensated chronic heart failure (ADCHF).
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. The control group included 20 patients with compensated CHF (NYHA class II or III), mean age 68 ± 9 years, 11 (55%) women, who also received standard CHF therapy. On admission and after anticoagulant treatment had been finished, 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%. Twelve months after the admission all ADCHF patients were contacted by phone for end-points (rehospitalization and/or death).
Results: All ADCHF patients had severe endothelial dysfunction (ED), compared with controls, with baseline FMD ratio of -2.15 ± 2.86 and $9.00 \pm 1.47\%$ ($p < 0{,}001$), respectively. In all three anticoagulant groups there was significant difference between the baseline and 'after treatment' measurements: with -1.5 ± 1.8 and $5.72 \pm 2.03\%$ ($p = 0.0001$) in the UFH group ($n = 20$), -3.1 ± 2.0 and $6.75 \pm 1.47\%$ ($p = 0.0009$) in the enoxaparin group ($n = 20$) and -3.3 ± 2.1 and $7.02 \pm 1.67\%$ ($p = 0.0001$) in UFH group ($n = 20$). Delta FMD ratios were the lowest in the heparin group and the highest in the fondaparinux group, though not statistically significant: 6.70 ± 2.30 vs 9.53 ± 1.45 vs $9.90 \pm 2.07\%$, respectively ($p = 0.06$). Despite the received treatment, within 12 months after hospitalization due to ADCHF, 38 (63%) patients had combined end points: 15 patients in the UFH group, 12 in the enoxaparin and 11 in the fondaparinux group ($p = 0.07$). Thirteen (22%) of them died: 6, 4 and 3 patients, respectively ($p = 0.16$). No significant correlation was found between the chosen anticoagulant: UFH (R=0,17, $p = 0{,}44$), enoxaparin (R=0,13, $p = 0{,}81$) or fondaparinux (R=0,14, $p = 0{,}32$) and long-term prognosis.
Conclusion: In ADCHF patients and sinus rhythm, despite standard treatment, long-term prognosis is still poor. Though the choice of an anticoagulant can affect endothelial function, it does not improve their long-term prognosis by lowering the risk of rehospitalisation or/and death within 12 months. Key words: acute decompensated chronic heart failure, sinus rhythm, endothelial dysfunction, flow-mediated endothelium-dependent vasodilation

P1021

Heart failure with recovered ejection fraction in malaysian cohort

GSK Lau[1]; MH Tan[1]; WH Han[1]; P Thomas[1]; K Raja[1]; S Nayar[1]; CJ Yap[1]; M Vijayan[1]; K Mohd Fadhli[1]; TR Noel[1]; YY Ngau[1]; S Jeyaindran[1]
[1]*Hospital Kuala Lumpur, General Medicine, Kuala Lumpur, Malaysia*

Introduction: Heart failure with recovered ejection fraction (HFrecEF) has been recognised as a new classification with distinct clinical characteristics and prognosis. Data on Asian patients remained limited. This study aimed to characterise the HRrecEF population and compare it with those with persistently reduced left ventricular ejection fraction (LVEF).
Methods: This was a retrospective study looking at patients who were followed up in Heart Failure Clinic Hospital from April 2013 to December 2016. HRrecEF was defined as current LVEF ≥40% with previous documented LVEF <40%; those with reduced LVEF (HFrEF) had current and previous LVEF <40%.
Results: Due to limitation of resources, only 74 clinic patients had repeat echocardiograms. From this, 35 patients had HFrecEF and 26 patients had HFrEF. Median age was 62 (IQR 52 - 67). Males ($n = 40$; 65.6%) and Malay race ($n = 33$; 54%) predominated in both groups. Hypertension ($p = 0.006$) and COPD ($p = 0.029$) appeared to be common co-morbidities in the HFrecEF group. Systolic blood pressure <130mmHg ($p = 0.008$) and lower baseline alanine transaminase (ALT) ($p = 0.034$) have been associated with recovery of LVEF. There was also improvement of NYHA class noted in patients with HRrecEF. Hospital readmission rates were significantly lower in the HFrecEF group ($p = 0.029$). No mortality was recorded in both groups.
Discussion: The results highlighted the importance of risk factor control, especially hypertension and smoking, as part of heart failure management. The significance of ALT as a biomarker of recovery is yet to be determined; but this serves as precursor to future studies.
Conclusion: In this cohort of patients with HFrecEF, patients have better outcomes with fewer admissions, however future studies need to be conducted to understand further the nature of this subset of patients.

P1022

Heart failure: an open door for infections?

J Azevedo Duarte[1]; J Almeida[1]; R Ribeiro[1]; C Henriques[1]; J Delgado Alves[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Internal Medicine 4, Amadora, Portugal*

Background: Chronic heart failure (CHF) is the most common cause of hospitalization in people over 65 years old, carrying a severe impact on life quality and expectancy. Patients with CHF remain at a systemic inflammatory state, frequently presenting high levels of ferritin, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as well as inflammatory cytokines (IL-6, IL-8, TNF alpha). Previous studies have suggested that patients with CHF have a higher incidence of infections. One of the proposed underlying mechanisms is the peripheral tissue hypoxia, which leads to suppression of the cellular immunity and activation of the anti-inflammatory pathways.
Methods: Retrospective analysis of the patients with heart failure admitted to an Internal Medicine ward in the period of one year (between August of 2015 and August of 2016).
Purpose: Clinical audit of a cohort of patients admitted with heart failure to evaluate the relationship between CHF and the incidence of infections.
Results: 225 patients were included. The average age was 78 years old, the majority was female ($n = 125$, 55%) and the average length of hospital stay was 16 days. The most common HF etiologies were hypertensive (33%) and ischemic (26%), being HF with preserved ejection fraction predominant ($n = 124$, 55%). The most frequent causes for HF decompensation were infection, disease progression and anemia. Of the total of 225 patients, 201 (89%) presented with decompensated HF and from these 133 (66%) had an infection, whereas 24 (11%) had no signs or symptoms of decompensated HF and within these 13 (54%) had an infectious illness at admission or during hospital stay. Respiratory and genitourinary infections were the most common identified infections in both groups of patients, being the causative pathogen only identified in 36% of the totality of cases. There was no relationship between CHF decompensation and the occurrence of infection, ($p = 0{,}263$, two-tailed Fisher's exact test, Cramer's V=0,078).
Conclusion: According to literature, patients with CHF are likely to have a higher risk of infection, being this one of the most frequent causes of HF decompensation. However, in our study, there's no evidence of a statistically significant relationship between decompensated HF and frequency of infection.

P1023

Polysomnographic respiratory parameters and left ventricular function in heart failure patients with predominant central sleep apnea

K Simionescu[1]; M Adamek[2]; J Biernat[3]; A Mlynarska[4]; A Drzewiecka[3]; KS Golba[1]
[1]Medical University of Silesia, Department of Electrocardiology and Heart Failure, Katowice, Poland; *[2]Medical University of Silesia, Chair and Department of Thoracic Surgery, Faculty of Medicine and Dentistry, Katowice, Poland*; *[3]7th University Hospital, Department of Electrocardiology and Heart Failure, Katowice, Poland*; *[4]Medical University of Silesia, Department of Internal Nursing, Chair of Internal Medicine, School of Health Sciences, Katowice, Poland*

Introduction: Sleep breathing disorders, including obstructive sleep apnea (OSA) and Cheyne-Stokes respiration with central sleep apnea (CSR-CSA), commonly occur in patients with heart failure (HF). OSA may lead to development or progression of left ventricular (LV) dysfunction whereas CSA is likely a consequence rather than a cause of HF. Therefore CSA in HF with reduced ejection fraction (HFrEF) is highly prevalent and associated with more severe forms of heart dysfunction. There is only few data concerning respiratory parameters of central apnea/hypopnea events and ventricular function in these patients.
Methods: 27 consecutive patients (20 males and 7 females, 63.7 ± 9.7 years) with HFrEF (LVEF < 35%) were enrolled. In 17 cases HErEF 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 LV ejection fraction (LVEF) was 25 ± 3% (Simpson EF) with mean end diastolic (EDD) and end systolic (ESD) diameters of 69.5 ± 2mm and 59.1 ± 2.5mm respectively and average LV diastolic and systolic volumes of 279 ± 63.5 and 210.6 ± 33.5 respectively. Sleep apnea with predominant CSA was diagnosed in 20 patients, in 3 patients CSA coexisted with OSA and 4 patients had no sleep-breathing disorders. In subjects diagnosed with predominant CSA in 6 cases HF resulted from previous coronary ischemic disease and in 14 was related to non-ischemic cardiomyopathy. In these patients LVEF was 22.1 ± 8.6% with EDD and ESD of 71.15 ± 8.2 mm and 61.2 ± 10.1mm respectively and LV diastolic and systolic volumes of 288.4 ± 94.1ml and 223.35 ± 72.24ml respectively what resulted in stroke volume of 65 ± 35.76 ml. The apnea/hypopnea index (AHI) in CSA patients was 24.88 ± 1.4 compare to AHI of 20.6 ± 2.3 in those without predominant CSA. The total duration of apnea/hypopnea (Total A/H) lasted between 18,9 and 232,1 min and this parameter exhibited no statistically significant correlation to LVEF (r = -0.11; p = 0.64) as well as no correlation to SV was observed (r = -0.06; p = 0.82). Surprisingly, no association was noted between LVEF and minimal oxygen saturation (SO2) during sleep (r = 0.035; p = 0.88) and percentage of SO2 below 90% in total sleep time (SO2 < 90%TST) (r = 0.01; p = 0.68). However, polysomnographic features revealed negative correlation to maximal duration of apnea/hypopnea event (Tmax A/H) and EF (r = -0.51, p = 0.021). No correlation was observed between Tmax A/H and LV diameters as well as LV volumes.
Conclusion: Although central sleep apnea is highly prevalent in more serve forms of systolic heart failure the polysomnographic oxygen saturation parameters has not showed significant association with deterioration of LV function. The maximal duration of apnea/hypopnea event however proofed to be parameter affiliated with progressive retrogression of systolic LV function.

P1024

Clinical outcomes in atrial fibrillation patients with non-vitamin K antagonist oral anticoagulants and heart failure

C Goena Vives[1]; L Quintas Ovejero[1]; R Garcia Martin[1]; I Lluis Serret[1]; J Taboada Gomez[1]; I Rilo Miranda[2]; JR Beramendi Calero[2]; M Telleria Arrieta[2]
[1]Mendaro's Hospital, Cardiology, Mendaro, Spain; *[2]Donostia University Hospital, Cardiology, Donostia, Spain*

Introduction: The efficacy and safety of non-vitamin K antagonist oral anticoagulants (NOACs) in non-valvular atrial fibrillation (NVAF) patients has not been established in a real-world setting, particularly in special patient population.
Purpose: We aimed to evaluate the efficacy and safety of NOACs in Heart Failure.
Methods: A total of 195 consecutive patients with NVAF who had taken NOACs with Heart Failure (HF) (53 cases, 27.2 %) or without (no-HF) (142 cases, 72.8%) were retrospectively reviewed. The efficacy outcome was stroke or systemic embolism. The safety outcome was bleeding or death.
Results: The follow-up days were 498.The mean age, gender and prevalence of renal dysfunction was similar between the two groups. HF patients have a higher predicted stroke and bleeding risks compared with no-HF patients (see table 1). The NOACs used were Dabigatran, Apixaban and Rivaroxaban. Despite differences between groups were not statistically significant, in the HF patients, Apixaban was the most used (59.6%) followed by Dabigatran 25% and Rivaroxaban 15.4 (see table 1). The global incidence of death (10.3 %), systemic embolism (2.5%) and major (3.33%) and minor (6.6%) bleeding was higher comparing the pivotal trials due to de higher predicted risk of our population in the study but there were no differences statistically significant between two groups.
Conclusion: The benefit of NOACs was similar in NVAF patients with and without heart failure, despite the heart failure group has an additional risk for adverse effects. Further study is required on the optimal anticoagulant regimen in HF but these results suggest that NOACs may be a first line treatment option in NVAF and heart failure.

Table 1

	No-HF	HF	p
Gender (Female %)	46.42	37.73	NS
Mean age (years)	75.09 ± 9.90	76.17 ± 9.59	NS
CHA2DS2VASC	3.49 ± 1.6	4.81 ± 1.52	< 0.001
HASBLED	2.96 ± 1.37	3.72 ± 1.3	< 0.001
Glomerular filtration rate	71.00 ± 18.43	67.91 ± 21.83	NS
NOAC (N and %)			
Dabigatran	57 (41.0 %)	13 (25.0 %)	NS
Apixaban	65 (46.8 %)	31 (59.6 %)	NS
Rivaroxaban	17 (12.2 %)	8 (15.5%)	NS

P1025

Sexual dysfunction: a reality in the patient with heart failure

T Tatiana Duarte[1]; S Goncalves[1]; A Lourenco[1]; S Correia[1]; D Ferreira[1]; C Sa[1]; R Rodrigues[1]; M Fonseca[1]; R Marinheiro[1]; F Seixo[1]; R Caria[1]
[1]Hospital Center of Setubal, Cardiology, Setubal, Portugal

Introduction: Sexual dysfunction (SD) is a frequent comorbidity in patients (pts) with cardiovascular disease, being the association with coronary artery disease (CAD) and peripheral arterial disease (PAD) well established. The prevalence in pts with heart failure (HF) is unclear, especially in females. This comorbidity is still underestimated by the doctors, despite their impact on quality of life. Aim: To determine the prevalence of SD in a population with HF and to characterize this population. To evaluate the impact of SD on quality of life.
Methods: Anonymous questionnaires for evaluation of sexual function (Female Sexual Function Index: FSFI; International índex of erectile function) were applied, prospectively, to pts followed in a HF clinic. Patients aged > 70 years were excluded, taking into account the high prevalence of SD in this age group. The population was divided in two groups - Group A: with SD; Group B: without SD - and characterized according to baseline characteristics, comorbidities, degree of systolic dysfunction, NYHA class and therapy. The prevalence of SD and the impact on quality of life were evaluated (degrees: none, slight, moderate, very high). Results: Were studied 38 pts (76% (n = 29) male, mean age 59 ± 9 years). SD was diagnosed in 79% (n = 30-Group A) of the pts, with a prevalence of 79% (n = 23) in males and 78% (n = 7) in females. The age and CAD were associated with the prevalence of sexual dysfunction. (Figure 1) There was no difference between the two groups in relation to the others comorbidities (Hypertension, atrial fibrillation, Diabetes mellitus, Dyslipidemia, PAD) as well as to therapeutics, namely betablockers and BNP level. The severity of HF, in terms of ejection fraction and NHYA class, were not associated with a higher prevalence of SD. Sixty percent of the pts (n = 18) of Group A considered that SD had a "moderate" impact on their quality of life.
Conclusion: Sexual dysfunction is a frequent comorbidity in pts with HF and should be valued by the doctors. By the importance in quality of life and prognosis, the evaluation of sexual function should be part of the rehabilitation program for pts with cardiovascular disease. The continuation of the study, including more pts will allow more conclusions.

Variables	Group A (n=30)	Group B (n=8)	p-value
Age (years)	61 ± 9	53 ± 5	0,003
CAD	22	2	0,0012
Hemoglobin (mg/dl)	14 ± 2	15 ± 1	0,058
BNP (pg/mL)	436 ± 635	343 ± 501	ns
Betablocker	29	7	ns

Variables according sexual dysfunction

P1026

Use of the minnesota living with heart failure quality of life questionnaire in kosovo

A Artan Ahmeti[1]; A Poniku[1]; E Haliti[1]; P Ibrahimi[1]; S Elezi[1]; MY Henein[2]; G Bajraktari[1]
[1]University Clinical Centre of Kosovo (UCC), Department of Cardiology, Pristina, Kosovo Republic of; *[2]Umea University Hospital, Umea, Sweden*

Background and Aim: Quality of life is one of the most important end-points in heart failure (HF) patients. The Minnesota Living with HF Questionnaire (MLHFQ) is the most widely used measurement for assessing the quality of life (QoL) in HF patients. This questionnaire had been translated and validated into the Albanian language. We used this questionnaire to evaluate the QoL in HF patients in Kosovo.
Methods: The study subjects were 103consecutive HF patients (63 ± 10 years, 56 female, 48% hypertensive and 26% ischaemic etiology, classified as NYHA I-III) admitted in outpatient or in-patient clinics at our University Clinical Centre. At the moment of evaluation the patients were clinically stable and on optimized drug therapy. Relationships were tested between questionnaire score and different clinical and demographic factors.
Results: There was no difficulty in the administration of the Albanian version of MLHFQ or in the patient's understanding of the questions. The overall median score of MLHFQ was 51 (mean 50 ± 18). A strong correlation was found between MLHFQ and NYHA functional class (p = 0.002), and it was with a higher score in female patients (p = 0.015). The other biochemical and clinical indices did not correlate with MLHFQ. The MLHFQ did not differ between different etiologies of HF patients.
Conclusions: The Albanian version of the MLHFQ proposed in this study proved to be valid for HF patients and served as a new and important instrument for assessing QoL in Kosovo's patients. The MLHFQ was mildly higher in our patients compared with previous studies. The questionnaire score correlate with functional NYHA class, reflecting the severity of the disease, and is higher in female gender.

P1027

Chronic systolic heart failure rehospitalization rates study from OPTIMIZE HF program: data from two centers

H Hamayak Sisakian[1]; H Hayrapetyan[2]; L Sahakyan[1]; M Hovhanisyan[1]; H Petrosyan[2]
[1]Yerevan State Medical University Hospital 1: University Cardiology Clinic, Department of General and Invasive Cardiology, Yerevan, Armenia; *[2]Erebouni Medical Center, Cardiovascular Center, Yerevan, Armenia*

Heart failure (HF) hospitalization rates considerably decreased in western Europe , but little is known about trends in eastern European countries. OPTIMIZE HF program is a prospective study aiming to assess rehospitalization rates of decompensated chronic systolic heart failure patients after discharge from hospital during 12 month period in eastern European countries. A total of 177 patients from two University affiliated hospitals with HF hospitalization were recorded. (median age -63 years, 36 % female). Mean NYHA functional class on admission was 2,7 and on discharge 2,2. During hospital period patient education programs were conducted for lifestyle and self monitoring of key measurements. Patients were on ambulatory follow up after 15, 30, 90, 180 days from discharge. After a first HF hospitalization any HF readmission rates within 90 , 180 and 1 year were 17.5 , 27.1 and 34,4 % respectively. The most common comorbidities were arterial hypertension (57,6 %) and chronic kidney disease (40,6 %). Permanent atrial fibrillation was found in 16,4 % patients on admission. In 72,3 % of cases, coronary artery disease was the main etiology of HF. Mortality after 1 year period was 22,5 %. 77,4% of patients were on beta blocker, 88,1 % - on RAAS inhibitors and 33 % -on ivabradine.
Conclusions: Rehospitalization trends and mortality may be comparable with western European mataanalysis data due to adherence to guideline based pharmacotherapy , education programes for patients , frequent outpatient monitoring visits.I

P1028

Gender-specific descriptions of chronic heart failure

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

Aim: To evaluate gender-specific etiology, clinical presentation and treatment of chronic heart failure (CHF).
Methods: 200 hospitalized patients with CHF (100 men and 100 women) were included in a retrospective cross-sectional study conducted in our Regional Clinical Hospital. Statistical criteria such as Mann-Whitney, chi-square and Fisher's exact tests were used.
Results: Women with CHF were older than men (61,9 ± 9,8 vs 58,1 ± 12,8 years, p = 0.019), had higher heart rate at admission (83 ± 16,9 vs 77,1 ± 15,3 beats per minute, p = 0.005) and lower glomerular filtration rate calculated by Cockcroft-Gault (77,2 ± 29,9 vs 91,5 ± 30,9 ml/min, p < 0.001). Coronary heart disease was the main reason of CHF, in men it was more common than in women (77% vs 63%, p = 0.045). The frequency of hypertension (20% vs 30%), chronic rheumatic heart disease (2% vs 5%) was the same. Clinical manifestations of heart failure depending on sex have not been identified. The most frequently clinical symptoms were dyspnea (89% men and 91% women), fatigue (49% men and 57% women), tachycardia (48% men and 53% women). Such symptoms as decreased ability to work (30% of men and 25% women) and edema (9% of men and 13% women) were less common. Women more often demonstrated class 3 NYHA (46% vs 29% of men, p = 0.019). The prevalence of heart failure class 2 NYHA was high regardless of gender (56% men and 48% women, p = 0.322). The prevalence of left ventricular diastolic dysfunction was independent of sex (57% of men and 62% of women). Ejection fraction (EF) of the left ventricle in women was somewhat higher than in men (65,2 ± 10,4% vs 61,5 ± 9,8%, p = 0.010), while the number of patients with a reduced EF was similar in men (12%) and women (8%). Pulmonary hypertension was found in 60% of men and 43%of women, p = 0.024. Diabetes mellitus was more common in women (18% vs 7% in men, p = 0.033). In men and women equally often were used β-blockers (82% and 83%), antiplatelet agents (78% and 80%), ACE inhibitors (23% and 22%), ARBs (35% and 41%), aldosterone antagonists (19% and 28%), cardiac glycosides (5% and 7%); while in women diuretics more often were prescribed (51% vs 32% of men, p = 0.010).
Conclusions: Gender-specific descriptions of chronic heart failure are higher age of female patients, more frequent formation of functional class 3 disease in women, more prevalent in women cohort of diabetes mellitus and lower – pulmonary hypertension. Differences in treatment depending on gender practically not observed, and the attention is drawn to the incomplete line therapy to current clinical guidelines for chronic heart failure, necessitating ongoing optimization of therapeutic measures.

P1029

Cognitive function in chronic heart failure: relation to clinical variables

A Alina Lyashenko[1]; L Voronkov[1]; A Solonovych[1]
[1]NSC Institute of Cardiology M.D. Strazhesko, department of heart failure, Kiev, Ukraine

Background: Cognitive impairment is observed in 30-80% of chronic heart failure (CHF) patients (pts) and closely correlates with age and severity of disease. Nevertheless, evidence of association between cognitive function (CF) and other clinical characteristics in CHF is still lacking.
Objective: To establish the relationship between CF and clinical variables and comorbidities in CHF.
Methods: 45 stable CHF pts, NYHA II-IV, with left ventricular ejection fraction (LVEF) < 40% were examined. CF was evaluated with standard MMSE and Shulte tests. Besides routine examination, the 6-minute walk test and interview on the HADS depression questionnaire were performed.
Results: Cognitive dysfunction (abnormal MMSE and Shulte tests) was observed in 68.8% of patients. There were no impact of sex, LVEF, hemoglobin level, diabetes, and, surprisingly, of atrial fibrillation on the results of CF tests. Simultaneously, CF testing results were significantly worse in NYHA III-IV vs NYHA II patients (p = 0.042 for MMSE and p = 0.002 for Shulte test), at age < 60 vs ≥60 years (p = 0.010 for MMSE and p = 0.003 for Shulte) and in hypertensives vs non-hypertensives (p = 0.0027 for MMSE, p = 0.020 for Shulte).
Both MMSE and Shulte tests significantly correlated with the 6-min walk test distance (r=0,30, p = 0.021 and r = -0.21, p = 0.044, respectively) and with the HADS depression score (r = -0.45, p = 0.003 and r=0.44, p = 0.003, respectively).
Conclusion: In stable CHF patients, besides high NYHA class and age ≥60 years, cognitive impairment is associated with history of hypertension, worse exercise tolerance and highest depression score.

P1030

Microalbuminuria and glomerular filtration rate in chronic heart failure: relation to clinical variables

A Alina Lyashenko[1]; L Voronkov[1]; A Dudnik[1]; L Mkhitaryan[1]
[1]NSC Institute of Cardiology M.D. Strazhesko, department of heart failure, Kiev, Ukraine

Background. In contrast to glomerular filtration rate (GFR), the place of microalbuminuria (MAU) in chronic heart failure is not still clear.
Objective: To evaluate the relation of MAU compared to GFR to clinical and laboratory variables in CHF.
Methods: 45 stable patients with CHF (NYHA II-IV, with left ventricular systolic dysfunction (ejection fraction < 40 %) were examined. MAU was detected by immunoturbidimetric method. GFR was calculated by CKD EPI equation.
Results: MAU (albumin 30-299 mg/24 hours) was observed in 100 % of pts. There was no impact of age, sex, hypertension, diabetes or atrial fibrillation on MAU level. MAU was higher in NYHA III-IV vs NYHA II patients: 66 (52-120) vs 158 (50-260) mg/24 hours respectively, (p < 0,001). Moreover, MAU level directly correlated with uric acid (r=0,34, p = 0,024) and myeloperoxidase activity (r=0,37, p = 0,012). Clinically relevant renal dysfunction (GFR < 60 ml/min/1,73 m^2) was observed in 18 (40%) pts. In contrast to MAU, GFR was significantly lower at age ≥ 60 vs < 60 (p = 0,001), in pts with diabetes vs non-diabetes pts (p = 0,012), in pts with hypertension vs normotensives (p = 0,024). GGR was higher in NYHA II vs NYHA III-IV pts

(p = 0,026). Direct correlation was observed between GFR and Minnisota quality of life score (r=0,45, p = 0,004), and between GFR and LVEF (r=0,28, p = 0,06).
Conclusion: Compared to MAU, GFR more closely correlated with variables which reflect both CHF severity and co-morbidities. Simultaneously, direct link between MAU and plasma UA and with myelopeuoxidase activity may reflect possible oxidative stress involvement in MAU mechanism in CHF. In our CHF pts, MAU was the obligate finding.

P1031

Oral iron therapy improves functional capacity of heart failure patients with iron deficiency anemia

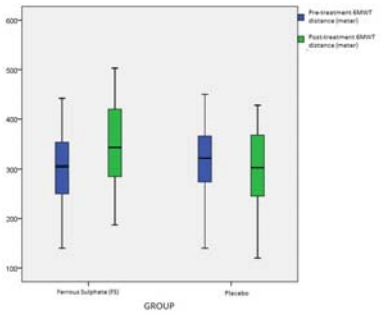
L Lita Suryani[1]; BB Siswanto[1]; SB Raharjo[1]; N Hersunarti[1]; R Soerarso[1]; H Angkasa[2]
[1]National Cardiovascular Center Harapan Kita, Cardiology and Vascular Medicine, Jakarta, Indonesia; *[2]University of Indonesia, Faculty of Medicine, Jakarta, Indonesia*

On behalf of: Clinical Cardiology and Critical Care Division of National Cardiovascular Center Harapan Kita

Background: Anemia is a common morbidity in heart failure (HF). Intravenous iron is known to improve patient's condition. However, it is expensive and invasive. This study investigated the effectiveness and safety of oral iron therapy in improving ferritin, transferrin saturation (Tsat), haemoglobin (Hb) and functional capacity in systolic HF patients with iron-deficiency anemia (IDA).
Methods: Double blind randomized controlled trial was conducted in National Cardiac Centre. Fifty-four subjects (age 18-75 y.o) suffering from HF (EF < 50%) and IDA with eGFR>30ml/min/1.73m2 were enrolled and randomized to placebo(n = 27) or oral Ferrous Sulphate (FS;n=27) for 12 weeks. Primary outcome was functional capacity measured by 6-minute walk test distance (6MWT). Ferritin, Tsat,Hb, NT-proBNP and side effects were documented.
Results: Forty-one subjects (placebo n=19;FS n=22) completed the study. Over 12 weeks, against baseline : Hb: -0.0263 ± 0.743g/dl (placebo;p = 0.879) and 1.0591 ± 1.432g/dl (FS;p = 0.002); Ferritin: -11.64 ± 52.42ng/ml (placebo;p = 0.346) and 102.78 ± 74.93ng/ml (FS;p = 0.000); Tsat: 2,99 ± 11,99% (placebo;p = 0,575) and 14,13 ± 9,66% (FS;p = 0,000); 6MWT: -16.84 ± 40.05m (placebo;p = 0.083) and 46.23 ± 35.93m (FS;p = 0.000). Between groups: Hb: 1.085 ± 0.365 (p = 0.005); Ferritin: 114.42 ± 20.52ng/ml (p = 0.000); Tsat: 11,14 ± 3,38% (p = 0,002); 6MWT: 63.07 ± 11.87m (p = 0.000). Little change were seen in NT-proBNP. Adverse effects (2 vs 1, placebo vs FS;p = 0.588) and gastrointestinal side effects were experienced by both groups (9 vs 6, placebo vs FS;p = 0.211).
Conclusion: Oral FS therapy for 12 weeks increased ferritin, Tsat, Hb levels and improved functional capacity of HF patients with acceptable minimal side effects. Oral FS might be a cheaper alternative to intravenous iron for low-to-middle income countries.

Comparison of 6MWT between Groups

Variables	Group	Pre	Post	p Value
Ferritin (ng/mL)	FS	110,36 ± 71,58	213,14 ± 73,93	0,000
Placebo	123,37 ± 68,0	111,74 ± 81,39	0,345	
Tsat (%)	FS	15,34 ± 4,95	29,48 ± 10,61	0,000
	Placebo	17,00 ± 6,70	20,03 ± 10,9	0,575
Hb (gr/dL)	FS	11,63 ± 0,81	12,69 ± 1,81	0,002
	Placebo	11,34 ± 0,88	11,32 ± 1,03	0,321
6MWT (meter)	FS	300,14± 85,25	346,36 ± 85,22	0,000
	Placebo	309,26 ± 75,60	295,53 ± 93,07	0,083



Comparison of 6MWT between groups

P1032

Common polymorphism RS10519210, RS1739843, RS6787362 in patients of Russian Federation with HFrEF AFTER myocardial infarction

VM Tishkova[1]; MY Sitnikova[1]; AA Kostareva[1]; LV Prokopova[1]
[1]Federal Almazov North-West research centre, heart failure, saint-petersburg, Russian Federation

Introduction: Conducting research of genome-wide studies (GWAS) in patients after MI may identify a group of patients with increased risk of HF and contribute to the development prevention measures.
PURPOSE: of the study: Explore the inhabitants of the North-West Federal District of Russia occurrence of polymorphic alleles HSPB7 (rs1739843), FRMD4B (rs6787362) and locus 15q22 (rs10519210), whose connection with the syndrome of heart failure has been established in the course of GWAS.
Materials and Methods: To study men 30 - 65 years old MI 3 months ago. The main group included 260 patients with HF I-IV functional class, LVEF (Simpson) < 40%, in reference group - 246 patients, without HF and LVEF (Simpson)> 50%. The group of healthy people made 96 donors.
We assessed anthropometric indices, clinical status, ECG, echocardiography, ECG monitoring. Genotyping by PCR was performed in "real time" (Applied Biosystems thermocycler 7500 Real Time PCR System).
Results: Two groups were comparable by prescription of hypertension (11.4 years versus 11.2 years), but different in its prevalence (68.5% and 83.3%, p < 0.01). In the main group there were more patients with heredity (34.23% and 22.88%, p < 0.01), more frequent AF (31.2% and 14.4%, p < 0.001), pulmonary embolism (12.5% and 0.4%, p < 0.001), left ventricular aneurysm (20.6% and 0.9%, p < 0.001). In the group with HFrEF was a wide range of QRS (124.6 ± 259.4 ms and 96.9 ± 53.1 ms, p < 0.001), higher the pressure in the pulmonary artery (46,3 ± 48,7 mm Hg and 30.2 ± 24.8 mmHg, p < 0.001).
There was significant difference between the occurrence of polymorphism rs1736843 of HSPB7 gene depending on the HF and EF: CC genotype was detected in 48.1% of the patients, CT - 10.4% of the patients in the main group, in 80.9% and 7.3% in reference group, and in 80.2% and 4.2% in healthy group, accordingly (p1-2, 1-3 < 0,001). FRMD4B gene exceeded the threshold of significance and prevalence. Genotype AA was detected in the main group in 83.5% of the patients, GG – none, in 87.8% and 2.9% in the reference group , in 89.6% and 0% in healthy group, respectively (p1- 2, 3-2 < 0.01). Prevalence of USP3 gene in groups did not differ between individuals.
Conclusions: The data of the prevalence of the studied genotypes after MI are similar with those in European studies: polymorphisms HSPB7 (rs1739843) and FRMD4B (rs6787362) was significantly associated with development of CHrEF.

P1033

Recurrent heart failure-related hospitalizations in patients with mid-range ejection fraction

M Domingo[1]; P Moliner[1]; J Lupon[1]; M De Antonio[1]; J Nunez-Villota[2]; E Zamora[1]; J Santesmases[1]; B Gonzalez[1]; M Rodriguez[1]; S Altimir[1]; V Diaz[1]; MI Troya[1]; M Boldo[1]; C Diez-Quevedo[1]; A Bayes-Genis[1]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; *[2]University Hospital Clinic of Valencia, Valencia, Spain*

Introduction: 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. Long-term re-hospitalizations of patients with HF and left ventricular ejection fraction (EF) mildly reduced (HFmrEF) is not well known
Objective: To assess HF-related recurrent hospitalizations in ambulatory patients with HFmrEF of different aetiologies attended in a multidisciplinary HF Unit
Patients and methods: 124 patients with HFmrEF were evaluated (89 men and 35 women). Mean age was 65.2 ± 12 years. Median duration of HF was 10.5 months [Q1-Q3 1–46.5]. Ischemic aetiology was present in 57.3%. Eighty-seven (70.2%) and 31 (25%) patients were in NYHA class II and III respectively). We compared HF-related recurrent hospitalizations with those occurred in patients with reduced (HFrEF) and preserved (HFpEF) patients (836 and 92 respectively). Worsening HF-related death was also assessed.
Results: At a mean follow-up of 5 ± 3.3 years, 72 HF-related hospitalizations in 28 patients with HFmrEF (22.6%) were registered. The crude incidence of HF-related recurrent hospitalizations was 1.15 (95%CI 0.90-1.45) per every 10 person-years. This number was significantly lower than that observed in 836 patients with HFrEF followed during 4.7 ± 3.1 years: 1.60 (95%CI 1.48-1.73) per every 10 person-years, p = 0.007; and than that observed in 97 patients with HFrEF followed during 3.9 ± 2.8 years: 2.97 (95%CI 2.44-3.58) per every 10 person-years, p < 0.001. Age- and sex- adjusted Cox regression survival curves for worsening HF-related cause of death showed significant better outcome in HFmrEF patients with in regard to HFpEF patients (HR 0.33 [95%CI 0.13-0.82], p = 0.02), but only a better trend regarding to HFrEF patients (HR 0.56 [95%CI 0.29-1.11], p = 0.1).
Conclusions: While worsening HF-related death was only slightly and non-significantly lower in HFmrEF patients than in HFrEF patients, HF-related

recurrent hospitalizations were significantly lower in the former. Patients with HFpEF showed the worse prognosis, broth from the HF-related morbidity and mortality point of view.

P1034

Androgen status in non-diabetic elderly men with heart failure

G Loncar[1]; B Bozic[2]; A Neskovic[3]; N Cvetinovic[4]; M Lainscak[5]; N Prodanovic[6]; HD Dungen[7]; S Von Haehling[8]; Z Radojicic[9]; T Trippel[7]; B Putnikovic[3]; V Popovic[10]
[1]Zvezdara University Medical Center, Faculty of medicine University of Belgrade, Cardiology Department, Belgrade, Serbia; *[2]Military Medical Academy, University of Belgrade, Belgrade, Serbia, Institute for Medical Research, Institute for Physiology and Biochemistry, Belgrade, Serbia*; *[3]University hospital Zemun, Faculty of Medicine University of Belgrade, Department of Cardiology, Belgrade, Serbia*; *[4]Zvezdara University Medical Center, Cardiology Department, Belgrade, Serbia*; *[5]General Hospital Celje, Faculty of Medicine University of Ljubljana, Departments of Cardiology & Research & Education, Celje, Ljubljana, Slovenia*; *[6]Military Medical Academy, Clinic for Rheumatology and Clinical Immunology , Belgrade, Serbia*; *[7]Charité Universitätsmedizin Berlin, Department of Cardiology, Campus Virchow, , Berlin, Germany*; *[8] University of Medicine Göttingen, Campus Virchow, Charité Universitätsmedizin Berlin, Innovative Clinical Trials, Department of Cardiology and Pneumology, Department of Cardiology, Gottingen, Berlin, Germany*; *[9]Faculty of Organizational Sciences, University of Belgrade, Institute for Statistics, Belgrade, Serbia*; *[10]Clinical Center of Serbia, Faculty of medicine, University of Belgrade, Institute of Endocrinology,, Belgrade, Serbia*

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Purpose: We aimed to evaluate androgen status (serum testosterone (TT) and estimated free testosterone (eFT)) and its determinants in non-diabetic elderly men with heart failure (HF). Additionally, we investigated its associations with body composition, muscle strength, and long-term survival.
Methods: 73 non-diabetic men with HF and 20 healthy men aged over 55 years were studied. Echocardiography, 6-min walk test, grip strength, body composition measurement by DEXA method were performed. TT, sex hormone binding globulin, NT-proBNP, and adipokines (adiponectin and leptin) were measured. All-cause mortality was evaluated at 6-years of follow-up.
Results: Patients with HF and healthy controls were similar of age (67 ± 7 vs. 67 ± 7) and body mass index (28 ± 5 vs. 28 ± 3 kg/m2). Androgen status (TT, eFT) was similar in elderly men with HF compared to healthy controls (4.79 ± 1.65 vs. 4.45 ± 1.68 ng/ml and 0.409 ± 0.277 vs. 0.350 ± 0.204 nmol/l, respectively). In HF patients, TT was positively associated with NT-proBNP ($r = 0.371$, $p = 0.001$) and adiponectin levels ($r = 0.349$, $p = 0.002$), while inverse association was noted with fat mass ($r = -0.413$, $p < 0.001$). TT and eFT were independently determined by age, total fat mass and adiponectin levels in elderly men with HF ($p < 0.05$ for all). There was no correlation between androgen status with skeletal muscle mass and muscle strength. In a multivariate model, androgen status was not predictor for all-cause mortality at 6-years of follow-up.
Conclusion: In non-diabetic men with HF, androgen status is not altered and is not predictive of long-term outcome.

P1035

Clinical characteristics and management of hospitalized patients with heart failure, results from Mongolia

G Ulziisaikhan[1]; O Tsogbadrakh[1]; B Namsrainaidan[2]; B Norpil[1]; M Dagva[3]; DAVID Sim[4]
[1]Third State Central Hospital, Cardiovascular Center, Cardiology, Ulaanbaatar, Mongolia; *[2]National University of Medical Science, Cardiology, Ulaanbaatar, Mongolia*; *[3]Third State Central Hospital, Cardiovascular Center, Ulaanbaatar, Mongolia*; *[4]National Heart Centre Singapore, Heart failure programme, Singapore, Singapore*

Background: Heart failure is a major and growing public health concern in Mongolia. However, there is insufficient information of heart failure locally.
Purpose: The aim of the study is to describe the clinical characteristics and management of hospitalized patients with heart failure in Mongolia.
Methods: Total of 5325 patients case notes were analyzed from general hospitals of 18 out of 21 provinces (rural areas) and 3 out of 9 districts of the capital city, and also The Third State Central Hospital, the national reference hospital for cardiovascular disease. Patients were admitted during January 2013 to December 2015.
Results: 3515 patients (66%) were males, 1810 (34%) were females. The number of patients with heart failure was increasing, 1555, 1810 and 1960 patients in 2013, 2014 and 2015 respectively ($p < 0.0001$). Ischemic heart disease (41.1%), arterial hypertension (19.4%) and valvular heart disease (15.7%) were main causes of heart failure in Mongolian patients. The main co-existing risk factors were hypertension (50%), obesity (46%), atrial fibrillation (35%), smoking (26.5%), excessive alcohol consumption (16.7%) and diabetes mellitus (12.7%).
HFrEF was present in 57.9%, HFmrEF in 20.8% and HFpEF was present in 21.3% of all participants. The mean age of the patients 58.2 ± 12.88 in males and 59.1 ± 14.9 in females. The mean length of hospitalization was 9.03 ± 2.7 days. ACEI/ARBs , MRA and beta blocker usage was 71%, 69% and 46% respectively.
Conclusion: Heart failure poses a significant burden on the healthcare system in Mongolia. Major public health program targeting at improvement of general public education and heart failure management among medical professionals is needed.

P1036

Ambulatory blood pressure monitoring in heart failure with preserved ejection fraction patients

V Vitalina Yarosh[1]; L Yena[1]; I Mudruk[1]
[1]D. F. Chebotarev State Institute of Gerontology NAMS of Ukraine, cardiology, Kyiv, Ukraine

Inadequate control of blood pressure (BP) is an important factor in the development of chronic heart failure (CHF) with preserved ejection fraction (HFpEF). There is evidence that the level of mean ambulatory systolic blood pressure (BP), unlike the office systolic BP (SBP), is independently associated with the development of HFpEF.
Purpose: to study 24-h profile of blood pressure in elderly hypertensive patients with HFpEF.
Methods: 120 patients (mean age $67,8 \pm 1,2$ years), 30 pts with essential hypertension (EH) with no signs of heart failure and 90 pts with EH complicated by HFpEF underwent ambulatory blood pressure monitoring (ABPM), Doppler echocardiography, 6-minute walk test.
Results and discussion The increased values of office SBP were determined in both group patients , but mean 24-h, daytime and nighttime BP values were significantly higher in HFpEF patients compared to hypertensive patients. Office diastolic BP (DBP) values were comparable in two groups and did not exceed the recommended range. Therefore, mean 24-h DBP values slightly exceeded the upper limits in both groups. The distance of 6-minute walk test does not correlate with office BP levels. There is no limiting impact of high blood pressure (in the range up to $154,3 \pm 1,4$ mm Hg) on physical activity in patients with initial stages of CHF.
The 24-h pulse BP was higher in HFpEF pts ($63,2 \pm 0,9$ mm Hg compared with $54,9 \pm 1,4$ mm Hg in EH pts, $p < 0,05$) confirmed the increased risk of cardiovascular events in HFpEF patients.
The normal BP circadian rhythm was recorded significantly more frequent in EH pts (40,0 %) compared with 17,8 % HFpEF pts. 54 HFpEF pts (60,0%) demonstrated abnormal pattern of day/night SBP dynamics and 37 pts (41,1%) - abnormal pattern of DBP, in contrast to patients with uncomplicated EH (13 pts (43,3 %) and 6 pts (20,0 %), respectively).
Conclusions: HFpEF patients demonstrated insufficient control of both office and 24-h BP. 82,2% of HFpEF pts were characterized by pathological types of BP circadian rhythm with dominating non- dipper type.

P1037

A comparison of non-invasive methods of measuring body composition in patients with heart failure, a report from SICA-HF.

V Vennela Boyalla[1]; P Shah[1]; P Pellicori[1]; R Dierckx[1]; J Cuthbert[1]; A Bennett[1]; A Clark[1]; J Cleland[1]
[1]Castle Hill Hospital, Cardiology, Hull, United Kingdom

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Background: Cachexia is common in patients with chronic heart failure (CHF) and is associated with a poor prognosis. How best to measure body composition is not clear.
Methods: We characterized body composition in 120 patients [mean age $70 + 10$ years, mean left ventricular ejection fraction (LVEF) $44 + 10\%$, and median N-terminal pro B-type natriuretic peptide (NTproBNP) 845 (interquartile range: 355-1368ng/l) with CHF enrolled in the "Studies Investigating Co-morbidities Aggravating Heart Failure" (SICA-HF). We measured body composition using a multi-frequency segmental body composition analyser (BCA) and dual-energy X-ray absorptiometry scan (DEXA) on the same day.
Results: Mean fat mass (FM) was 27.2 + 11.6 kg by BCA and 31.2 + 12.1 kg by DEXA (mean difference -4.0 kg (95% limits of agreement: -10.2, 2.2; 5% of values outside limit of agreement)); mean muscle mass (MM) was 56.6 + 10.9 kg by BCA and 47.7 + 9.5 kg by DEXA (mean difference of 8.9 kg (95% limits of agreement: 1.9, 15.9; 3% of values outside limit of agreement)). Mean bone mass (BM) was 3.0 + 0.5 kg by BCA and 2.3 + 0.7 kg by DEXA (mean difference of 0.65 kg (95% limits of agreement: -0.15, 1.4; 1% of values outside limit of agreement)). There was

a good correlation for both MM and FM between DEXA and BCA (MM: r = 0.95, p < 0.001; FM: r= 0.97, p < 0.001) but worse correlation for BM between DEXA and BCA (r = 0.79, p < 0.001). Both DEXA and BCA body composition measurements correlated well with other measures of cachexia.
Conclusions: There are differences in the measurements of FM, MM and BM between the two techniques and should not be used interchangeably.

P1038
The quality of life and level of depression of patients with heart failure and comorbid diabetes mellitus type 2

O Afanasiuk[1]; V Shmaliy[1]; V Maslovskyi[1]
[1]*National Pirogov Memorial Medical University, Internal medicine #3, Vinnitsa, Ukraine*

Purpose - to study the QL and level of depression in patients with different stages of HF and comorbid diabetes mellitus (DM) type 2.
Materials and methods: Were examined 62 patients with HF and comorbid DM type 2, mean age 62.5 ± 0.08 years. The patients were divided into three groups depending on left ventricle ejection fraction(LVEF). The first group included 20 patients with LVEF≥50%, the second group – 22 patients with LVEF 40-49%, the third group – 20 patients with LVEF < 40%. Patients themselves filled out the Minnesota questionnaire quality of life with HF (MLHFQ) and the depression scale of Beck (BDI). All studies conformed to the principles of the Declaration of Helsinki of the World Medical Association.
Results: In the analysis of questionnaires MLHFQ was observed that every patient noted a worsening of QL including due to the presence of depression, and were asked to fill the BDI. The dates presented in Table 1.
According to the presented dates, it should be noted that the QL and depression level of patients is much worse depending on the progression of symptoms of HF. Indicators of blood glucose were consistent with the state of compensation and subcompensation and didn't significantly affect the QL and depression level in patients of each group. The level of depression ranged from mild in the first group to moderate in the second and third groups. Patients were offered a psychiatric consultation for the correction of depressive states, but agreed to counseling only 6,45% (n = 4) patients of the third group. Most patients argued the rejection of consultation by psychiatrist worsening of symptoms of HF, but not the manifestations of depression.
Conclusions: Violation of the QL and increase in level of depression in patients with HF and comorbid DM type 2 significantly depends on the symptoms of HF. Contributes to incorrect assessment of their condition by patients, which significantly impairs the compliance between doctor and patient. The influence of depression on the violation of QL in this category of patients requires further study.

Table 1.

Questionnaire	LVEF≥50% (n=20)	LVEF 40-49% (n=22)	LVEF < 40% (n=20)
MLHFQ,scores	53.3±2.83	63.6±2.44*	78.4±2.5***###
BDI,scores	14.3±1.13	16.1±1.56	19.4±1.91*
Note:The probability of indicators difference to the value ofLVEF≥50%*- (p < 0,05);***- (p < 0,001);The probability of indicators difference to the value ofLVEF 40-49%;###- (p < 0,001).			

P1039
Duration of heart failure, hospitalization rate and treatment compliance in elderly heart failure patients with anemia of chronic diseases.

NI Solomakhina[1]; D Shchekochihin[1]; ES Nakhodnova[1]; ZV Taranova[2]; SV Pavlushina[2]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*; [2]*First Veterans Hospital, Moscow, Russian Federation*

Background. Anemia is a common comorbidity in heart failure (HF) patients. It can be attributed to heart failure by itself, iron deficiency conditions and other comorbidities. The aim of present study in to analyze HF duration, rate of hospitalizations and treatment compliance in old and very old patients, presented with HF decompensation and criteria of anemia of chronic diseases.
Materials and methods: 35 patients, aged 76-97 (average 87 ± 10,5 years, 20 women (57,1%)) with decompensated heart failure and anemia of chronic diseases were analyzed. Controls were 35 age and sex-matched patients with decompensated HF without anemia. Criteria of anemia of chronic diseases were decreased hemoglobin (< 12 g/dl) with normal or increased serum ferritin level and normal transferrin saturation.
Results: Patients with anemia and without anemia did not differ significantly in HF presentation, NYHA IV had 46% of anemic patients and 42% of patients without anemia (p = 0,8). More patients with HF and anemia had HF durations of 5-10 years (78 %) versus 34% of non-anemic patients (p = 0,0003). Average HF duration in anemic patients was 6,5 years compared to 4,5 years in non-anemic ones. Anemic patients required more hospitalizations due to HF decompensation than non-anemic. 61% of anemic HF patients were admitted to the hospital 4-5 times during previous year versus 17% of non-anemic HF patients (p = 0,0002). However, anemic HF patients seems to be undertreated by HF medications. Only 5,7% of HF anemic patients received MRAs to the date of current hospitalization compared to 14,3% of non-anemic patients (p = 0,42). The same is true for beta-blockers (31% vs 60%, p = 0,03) and ACEi/ARB (23% vs 46%, p = 0,07).
Conclusions: Old and very old patient with HF and anemia of chronic diseases have longer duration of heart failure compare to non-anemic HF patients. These patients require frequent hospitalization for HF decompensation, probably due to undertreatment by main HF medication. Old and very old patients with HF and anemia of chronic diseases is a high risk group that require special attention in daily clinical practice.

P1040
The study psychological state of patients with chronic heart failure

U Umida Kamilova[1]; SH Kadirova[2]
[1]*Republican specialized scientific-practical Medical Center Therapy and Medical Rehabilitation, Tashkent, Uzbekistan*; [2]*Buhara medical institute, Therapy, Buhara, Uzbekistan*

Purpose. To study the psychological state of patients with postinfarction cardiosclerosis complicated FC I-II chronic heart failure (CHF).
Methods: The study included 42 men with CHF CHD. Assessment of psychological status was performed using Zung Self-Rating Depression Scale and the scale of reactive and personal anxiety Spielberger-Hanin. To assess the psychological protection technique was used "index lifestyle' - Plutchik-Kellerman LSI.
Results: For patients with heart failure has been characterized by an increased degree of denial of existing problems, displacement (with the exception of the idea of consciousness and related emotions), projection, conjugated with aggression and intellectualization, the control of different emotions and excessive dependence on a rational interpretation of the situation. Affective disorders such as anxiety and depression appeared closely linked (r = 0,50; P < 0.001) and were typical of younger patients (r = -0,46; p < 0.05 and r = -0.66; P < 0.001, respectively). The emergence of depression was proportional to the severity of clinical symptoms (r = 0,46; P < 0.05). With the denial of the existence of compensation were associated severity: the higher the show turned out to be the negation of patients with CHF, the expressions were anxiety and depressive disorders.
Conclusions: Thus, there was an association between the severity of depression and the severity of disease in patients with CHF.

P1041
Global analysis of survival of patients of the study remadhe randomized prospective submitted to the DMP with follow-up of 16 years

FDC Fatima Das Dores Cruz[1]; VS Issa[1]; PR Chizzola[1]; GE Conceicao[1]; SF Ayub[1]; EA Bocchi[1]
[1]*Heart Institut, São Paulo, Brazil*

Introduction: The survival of patients with a diagnosis of heart failure is limited around 50% in five years survive, and may present a worse prognosis for most types of cancer.
Objectives: This investigation includes extension of the prospective, randomized, REMADHE study with intervention group, submitted to a telephone education and monitoring program, with analysis of the survival of both groups (control and intervention) from October 1999 to December 2016
Results: 412 patients, 60.5% (MG), with mean left ventricle ejection fraction of 34.7 ± 10.5% and mean age of 50.8 ± 11.7 years, etiology (%): 23.5 ischemia, 18.4 idiopathic, 14.6 chagasic, 13.3 hypertensive, with mean left ventricle ejection fraction of 34.7 ± 10.5% and mean age of 50.8 ± 11.7 years , 4 alcohol, 26.2 others. The survival was 5.5 ± 4.6 years.
Conclusion: Despite the technological and pharmacological advances, heart failure still presents as a syndrome of high mortality.

ADVANCED HEART FAILURE

P1042

Ways of reducing mortality in waiting list of heart transplant

PA Fedotov[1]; MYU Sitnikova[1]; MA Bortsova[1]; YV Sazonova[2]; VE Rubinchik[2]; AE Bautin[2]; AS Yakovlev[2]; GV Nikolaev[2]; ML Gordeev[2]; MA Simonenko[2]; MA Karpenko[2]

[1]Federal Almazov North-West Medical Research Centre, Heart Failure, Saint-Petersburg, Russian Federation; *[2]Federal Almazov North-West Medical Research Centre, Saint-Petersburg, Russian Federation*

From 2010 to 10.2016 in Federal Almazov North-West Medical Research Centre in waiting list of heart transplant (WLHTx) included 151 patients (pts). Heart Transplantation (HTx) was performed in 79 pts, 6 pts refused to transplantation, 19 pts out of the WLHTx (due to the improvement of the appearance or contraindications to HTx), 35 pts died and 12 pts continue to expect a HTx. From 2010 to 2015, the mortality on the waiting list decreased from 33% to 7.5% per year. Purpose: To identify predictors of death in patients WLHTx.

Methods: The mean age of patients was 46 ± 13 years, men - 72% (n = 108). The etiology of heart failure in patients WLHTx: coronary artery disease in 48% of patients (n = 72), DCM - 39% (n = 59), non-compact myocardium - 7% (n = 11), others the Commission - 6% (n = 9). CHF 4[3,4] FC, LVEF 21 ± 10%, VO2peak 11.4 ± 2.9 ml/kg/min, PCWP - 19[14,24] mmHg, TPG - 9[8,14] mmHg, cardiac index (CI) 1.9 ± 0.5 l/min/m2, pulmonary vascular resistance (PVR) of 3.0[2.3; 4.2] Wood units. Duration in WLHTx 107[44;1923] days. In WLHTx received therapy: combined diuretic therapy - 100%, spironolactone - 100%, beta-blockers - 82% (n = 124), ACEI/ARA 52% (n = 78), ivabradine - 15% Amiodaron - 60%, inotropes - 49% (n = 74), 12 pts (10%) implanted CRT-D, 48 pts (32%) – ICD, BiVAD (EXCOR) - 9 patients (6%), physical therapy - 100%. All patients were divided into 2 groups: 1 group (n = 116) patients survived in WLHTx, 2 group (n = 35) - patients who died. Since 2010 it received 378 proposals of potential heart donors. After further examination of the donor, perform coronary angiography and echocardiography evaluation of visiting medical team of our Center the number of effective donors was 79. Results: deceased patients compared with surviving patients at the time of inclusion in WLHTx possessed higher CHF FC (4 [4;4], and 3 [3;4], respectively; p = 0.004), low GFR (64 ± 19 and 81 ± 24, respectively, p = 0.008) greater frequency of use of inotropic support (71% and 42%, p = 0.04), high bilirubin (TBIL) level (34[23; 47] and 17[14;28], p = 0.01), ALT (52[22;502] and 22[14;31], p = 0.008), low-sodium (129 ± 8 and 139 ± 5; p = 0.03), shorter duration before the outcome (29[10; 45] and 106[63; 204], p = 0.0001). Thus, the dead patients for inclusion in WLHTx were initially more severe group of patients. From the selected predictors (CHF FC, GFR, RLA, Hb, TBIL, 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), CHF 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: 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 required increase in the frequency of implantation of MCS, increasing the number of effective donors, including from donors with expanded criteria (single-vessel coronary disease with the technical possibilities revascularization).

P1043

Influence of cytomegalovirus infection on long-term mortality and cardiac allograft vasculopathy risk after heart transplant

E Elizabet Mendez Eirin[1]; E Barge-Caballero[1]; MJ Paniagua-Martin[1]; R Marzoa-Rivas[1]; D Couto-Mallon[1]; G Barge-Caballero[1]; A Canizares[1]; JM Vazquez-Rodriguez[1]; MG Crespo-Leiro[1]

[1]University Hospital A Coruna, Cardiology, Corunna, Spain

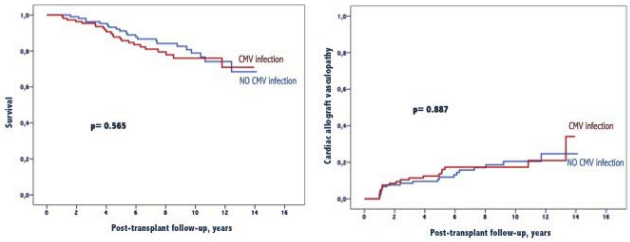
BACKGROUND: Cytomegalovirus (CMV) infection is a major concern in heart transplant (HTx). There is conflicting evidence of the effect of CMV infection on survival and the risk of cardiac allograft vasculopathy (CAV) after HTx.

PURPOSE: The purpose of this study was to evaluate the impact of CMV infection during the first year after HTx on long-term follow-up.

Methods: A retrospective, single-centre study analyzed 222 HTx recipients (mean age 54 ± 12 years, 80 % men) who underwent transplantation between February 2001 and December 2011. The impact of CMV infection during de first year on survival and CAV incidence was assessed. Graft vascular disease was defined as the presence of stenosis > 50% of the luminal diameter of any of the 3 main epicardial coronary vessels or their branches visualized on coronary angiography.

Results: During a mean follow-up of 7.8 ± 3.5 years, 45 (20.9%) patients died and 3 (1.4%) received a second HT [death was of cardiac origin in 20 (44.4%) patients and was noncardiac in 25 (55.6%)] and 38 patients (17.7%) had CAV. No statistically significant differences were observed in the cumulative incidence of death or CAV between recipients with CMV infection during the first year after HTx and patients without CMV infection (figure 1).

Conclusions: The results from this study demonstrate that CMV infection during the first year after HTx is not associated with worse transplant outcomes.



P1044

Long term outcome in patients with cardiac resynchronization therapy

LJ Ljilja Music[1]; N Bulatovic[1]; M Music[1]

[1]Clinical Center of Montenegro, Podgorica, Montenegro

Although cardiac resynchronization therapy (CRT) improves left ventricle (LV) function and short -term prognosis, long -term effect of CRT remains unclear.

55 patients with LV ejection fraction (EF) less than 35% with available pre-CRT and follow up echocardiogram were included in this study. Median follow up interval was 36.9 months. Patients with improvement of LVEF more than 5-10% were categorized as responders. Primary endpoint was cardiac death or heart failure hospitalization. 50 patients (90%) were classified as responders and 5 (10%) patients as non responder. LVEF of responders before CRT was 25,8 ± 9.8% and increased to 38 ± 3.1% after CRT. LVEF of non-responders was 27.7 ± 5.9% and increased to 31.0 ± 1.1% after CRT. Responders showed better survival from cardiac death and heart failure hospitalizations (90% vs. 33%, log rank p = 0.01). In univariate analysis, B-type natriuretic peptide, hemoglobin, serum sodium, serum creatinine, serum albumin, LVEF before CRT and CRT responder were significantly associated with survival free from cardiac death and heart failure hospitalization. In multivariate analysis, CRT responders (HR 0.28 ,95% CI 0.06-0.09, p = 0.03) and BNP (HR 41.1, 95%CI 6.1-327, p = 0.0001) remained significant.

Improvement of LV function in patients undergoing CRT is associated with better survival free from cardiac death or heart failure hospitalization.

P1045

Patient selection for heart transplantation: a survival benefit index accounting for both waiting-list and post-transplantation mortality

L S Lee Son Nguyen[1]; S Varnous[2]; G Coutance[2]; S Ouldamar[2]; N Zahr[3]; P Leprince[2]

[1]Hospital Pitie-Salpetriere, Cardiologie médicale, Paris, France; *[2]Hospital Pitie-Salpetriere, Cardio-Thoracic Surgery Unit and Pathology Department, Paris, France*; *[3]Hospital Pitie-Salpetriere, Department of Pharmacology and CIC-1421,, Paris, France*

Background: Graft shortage requires recipient selection for heart transplantation (HTx). Risk models that can predict mortality on waiting list and post-HTx exist but only separately. We aim to design a survival benefit index (SBI) to assess the benefit expected from HTx on 1-year mortality.

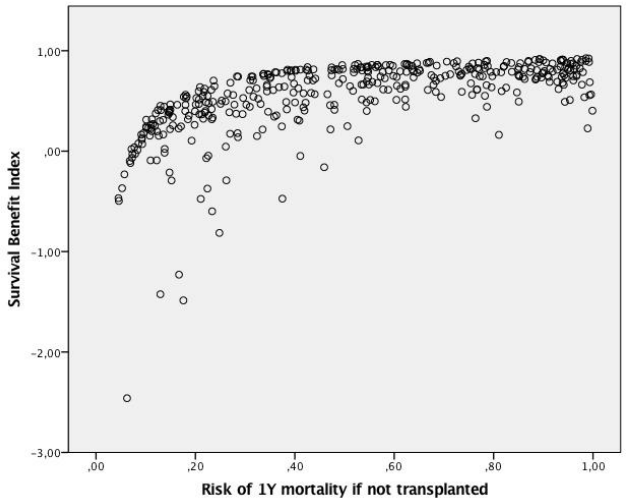
Methods: Patients listed for HTx (2009 to 2014) were included. We assessed 1-year mortality after listing without HTx ("no-HTx mortality") and after HTx ("post-HTx mortality"). We evaluated the discrimination of existing models: 2 for no-HTx, 2 for post-HTx mortality. We then computed 2 new models by logistic regression. The SBI was defined as the relative risk reduction of 1-year mortality.

Results: All existing no-HTx models were discriminative (all p < 0.0001) while none of those for post-HTx were. Derived models from our cohort had discriminative properties of ROC AUC 0.82 (p < 0.0001) for no-HTx and 0.67 (p < 0.0001) for post-HTx mortality, validated with ROC AUC 0.83 (p < 0.0001) and 0.69 (p = 0.002) respectively. The SBI increased with the risk of no-HTx mortality; higher risk patients benefited more than low risk patients (+78% vs. +8%; p < 0.0001).

Conclusion: The SBI may help physicians with heart allocation providing the expected benefit from HTx at one year from data available on the day of listing.

Derived risk models for one-year mortali				
	Coefficient	OR	95% CI	p-value
no-HTx mortality model				
Critical care setting at listing	1.631	5.11	[1.33 - 19.7]	0.018
Urea (per mmol above 7)	0.154	1.17	[1.04 - 1.31]	0.01
Age (per year above 50)	0.056	1.06	[1.01 - 1.11]	0.011
Total bilirubin (per μmol/l above 17)	0.051	1.05	[1.01 - 1.10]	0.022
Intercept	-1.672	-	-	-
post-HTx mortality model				
Age (per year above 50)	0.069	1.071	[1.02 - 1.13]	0.012
Listing urea (per mmol above 7)	0.052	1.054	[1.00 - 1.11]	0.0034
Pulmonary comorbidity	1.208	3.346	[1.12 - 10.0]	0.031
Intercept	-2.388	-	-	-

OR: odd-ratio



Survival Benefit Index

P1046

Is sidenafil treatment associated with higher rate of vasoplegic syndrome after heart transplantation?

E Sole-Gonzalez[1]; H Capellades-Olivella[1]; S Mirabet[1]; V Brossa[1]; L Lopez[1]; A Sionis[1]; M Rivas-Lasarte[1]; J Alvarez-Garcia[1]; M Gomis-Pastor[2]; MT Rivilla[3]; M Tauron[4]; E Roig[1]

[1]Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain; *[2]Hospital de la Santa Creu i Sant Pau, Farmacology Department, Barcelona, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Anesthesiology Department, Barcelona, Spain*; *[4]Hospital de la Santa Creu i Sant Pau, Cardiac Surgery Department, Barcelona, Spain*

BACKGROUND. Pulmonary hypertension (PH) prior to heart transplantation (HTx) increases the risk of right ventricular dysfunction after HTx. Sildenafil has been postulate as a non-invasive treatment to reduce PH in candidates to HTx. Due to its systemic effects, sildenafil could induce bleeding and vasoplegia in the acute post-HTx and increase mortality.

Purpose: To assess the effect of sildenafil on vasoplegia at 24h after HTx. A composite endpoint (vasoplegia and haemorrhagic shock) was also evaluated.

Methods: We analysed a retrospective cohort of 63 HTx since 2012 to 2016. Patients were classified according to their haemodynamic situation at 24h post-HTx in: 1)Stable haemodynamic; 2)Cardiogenic shock; 3)Hypovolemic status; 4)Haemorrhagic shock; 5)Vasoplegia. Vasoplegia was defined as: mean arterial pressure >60 mmHg with vasoconstrictors or ≤60 mmHg despite them, with cardiac index ≥2.5 l/min/m2 and central venous pressure ≥10 mmHg.

Results: Sixteen patients (25%) were treated with a mean dose of 88 mg/24h of sildenafil prior to HTx. Receptor age and sex, donor age, proportion of urgent HTx and ischaemic time were similar in the two groups. Other important variables are showed in Table. Comparing the haemodynamic status of the two groups at 24h post-HTx, sildenafil group presented non-significant tendencies of less incidence of cardiogenic shock (6 vs13%;p = 0.7), higher rate of haemorrhagic shock (19 vs 8%;p = 0.4), and vasoplegia (37 vs 21%;p = 0,2). The composite endpoint was significantly higher in the sildenafil group (56 v. 29%;p = 0.05). However, both groups had similar acute mortality (12.5 vs 12.8%;p = 0.97). Regression analysis identified a tendency of sildenafil treatment as predictor of vasoplegia (OR 3.2 [CI95% 0.84-12.47]p = 0.08).

Conclusions: 1)Treatment with sildenafil prior to HTx was associated with higher rate of bleeding and vasoplegia in the first 24h after-HTx. 2)However, sildenafil was not associated with increased acute mortality.

Table. Characteristics of two groups.			
	Sildenafil group (n = 16, 25%)	Control group (n = 47, 75%)	p value
Previous cardiac surgery, n (%)	5 (31.3)	6 (12.8)	0.093
Ischaemic aetiology, n (%)	11 (68.8)	14 (29.8)	0.006
Baseline mean pulmonary pressure (mmHg),x (SD)	38.7 (9.3)	28.9 (7.9)	< 0.001
Baseline transpulmonary gradient (mmHg), median (Q1-Q3)	9.8 (7.8-17.5)	7.3 (4.0-9.8)	0.005
Baseline Woods units, median (Q1-Q3)	2.8 (2.3-4.7)	1.8 (1.1-2.5)	0.002
Treatment with ACEI or ARB, n (%)	11 (68.8)	27 (57.4)	0.425
Systemic vascular resistence index at 24h, median (Q1-Q3)	1258 (1029-1802)	1361 (1196-1647)	0.657
Use of noradrenalin at 24h, n (%)	11 (68.8)	26 (55.3)	0.346

P1047

Identification and treatment of iron deficiency in advanced heart failure patients listed for heart transplantation

A Soltan[1]; J Evans[2]; S Pettit[2]

[1]University of Cambridge, School of Clinical Medicine, Cambridge, United Kingdom; *[2]Papworth Hospital NHS Trust, Cambridge, United Kingdom*

Background. Iron Deficiency (ID) is common in patients with advanced heart failure (HF) and is associated with a worse prognosis. Treatment of ID with intravenous Ferric Carboxymaltose (FCM) has been shown to improve symptoms, quality of life and exercise capacity, receiving a class IIa recommendation in the 2016 European Society of Cardiology guidelines. FCM may be particularly beneficial in patients listed for heart transplantation by reducing the likelihood of blood transfusion and the associated risk of Human Leukocyte Antigen (HLA) sensitisation.

Purpose: The aim of this study was to assess the prevalence of anaemia and ID among patients on the waiting list for heart transplantation, and to describe the response of ID patients to treatment with FCM.

Methods: All outpatients listed for heart transplantation between 01/02/2014 and 01/02/2016 at Papworth Hospital were included in a retrospective, observational study. The results of screening for ID were obtained from hospital records. Anaemia was defined as haemoglobin (Hb) concentration < 13 g/dL (males) and < 12 g/dL (females). ID was defined as Ferritin < 100mg/L, or 100-300mg/L where Transferrin Saturation (TSAT) < 20%. Patients treated with FCM were identified from pharmacy records. Efficacy of FCM was evaluated by comparison of Hb concentration, Ferritin level and TSAT before and after treatment. Data were summarised as mean ± standard error and compared with paired, two-tailed t-tests.

Results: 71 patients were listed for heart transplantation during the study period. All patients were screened for anaemia, but only 57 (80%) were screened for ID. Overall, the prevalence of anaemia was 59% and the prevalence of ID was 51%. Of the 29 patients with iron deficiency, 72% were anaemic and 28% were not anaemic. Use of FCM was sub-optimal during the study period. Only 38% of ID patients were treated with FCM. There were no adverse reactions during administration of FCM. When used, FCM appeared to be highly effective. A single dose of FCM was associated with an increase from baseline in Hb concentration (1.27 ± 0.27 g/dL, p = 0.0001), Ferritin level (225 ± 83 mg/L, p = 0.0187) and TSAT (8.5 ± 2.4 %, p = 0.0043).

Conclusions: ID was present in more than half of advanced heart failure patients who were listed for heart transplantation at a single UK centre. Over a quarter of iron deficient patients were not anaemic. Use of intravenous FCM was associated with an increase in Hb concentration, Ferritin levels and TSAT. Screening for ID and treatment with FCM should be encouraged in this population. Future work should assess the impact of FCM on quality of life and outcomes.

P1048

Value of cTnT-hs and sAXL for coronary allograft vasculopathy diagnosis after heart transplantation

S Sonia Mirabet Perez[1]; J Ordonez Llanos[1]; P Garcia De Frutos[2]; L Lopez Lopez[1]; V Brossa Loidi[1]; R Leta Petrarca[1]; E Sole[1]; J Garcia Picart[1]; A Ferrero[1]; M Tauron[1]; E Roig Minguell[1]

[1]Hospital de Sant Pau, Barcelona, Spain; [2]Department of Cell Death and Proliferation, IIBB-CSIC, IDIBAPS , Barcelona, Spain

Cardiac allograft vasculopathy (CAV) is one of the main limiting factors for long-term survival after heart transplantation (HTx). CAV is usually a silent phenomenon, being sudden death or heart failure the first manifestation of the disease. So, invasive monitoring with routine coronary angiography is recommended to detect CAV. The aim of the present study was to evaluate the usefulness of several biomarkers to detect CAV in HTx recipients.

Methods: This is a single center cross-sectional study in HTx patients who had undergone routine CAV assessment by coronary angiography or by coronary multi-slice computed tomography (MSCT) between January 2012 and April 2015. Blood samples were collected at the time that angiography or MSCT were perfomed. sAxl (protein involved in vascular remodeling) , Lp-PLA2 (marker of atherosclerosis), cTnT-hs (biomarker for myocardial necrosis) and GDF 15 (biomaker associated with cardiovascular events) were assessed and correlated with the presence of CAV. CAV was classified according the ISHLT recommendations.

Results: 96 HTx patients were included. Mean time after HTx was 9 ± 7 years. 49 patients had CAV (CAV1 in 26, CAV2 in 6, and CAV3 in 17 patients). In the univariate analysis patients with CAV had significantly higher cTnT-hs values (33 + 33,9 ng/l vs 18 +16,9 ng/l ;p = 0,008) and sAXL values (79 + 42 ng/l vs 65 + 24 ng/l; p = 0,036) than patients without CAV. Patients with severe CAV 2-3 had also higher cTnT-hs and sAXL values (43 ± 39 vs 20 ± 19 ng/L ;p < 001 and 92 ± 54 vs 66 ± 23 ng/L ;p < .001, respectively) than patients without CAV or mild CAV. After adjusting for clinical variables related to CAV, multivariate analysis identified hs-TnT values as the only biomarker associated with CAV, along with younger age at HTx. The ROC curve identified cTnT-hs>21 ng/L as the best cut-off value associated with the presence of CAV2-3, with an area under the curve 0.733 (p < 0.001) and a sensitivity of 65%, specificity 79%, positive predictive value 50%, negative predicted value 88%. There were no significant differences in Lp-PLA2 and GDF15 values between patients with and without CAV.

Conclusion: Monitoring sAXL and cTnT-hs could be usefull for identifying heart transplantation patients with CAV development. In our study, cTnT-hs values < 21 ng/L identify a group of HTx patients with low risk of CAV.

P1049

Quality of life in advanced heart failure- disconnect between patients' and clinicians' perceptions, independent of clinician experience.

R Roslyn Prichard[1]; PJ Newton[2]; PM Davidson[3]; S Goodall[4]; PS Macdonald[1]; FL Zhao[4]; CS Hayward[1]

[1]St Vincent's Hospital, Heart Lung Clinic, Sydney, Australia; [2]University of Technology, Sydney, Faculty of Health, Sydney, Australia; [3]Johns Hopkins University of Baltimore, Nursing, Baltimore, United States of America; [4]University of Technology, Sydney, Centre for Health Economic Research and Evaluation, Sydney, Australia

Background: Quality of life (QoL) is an important consideration for advanced heart failure (AHF) patients and clinicians making decisions about complex therapies, as well as policy makers seeking to fund cost effective treatments. But it is rarely formally assessed outside clinical trial settings. This initial data from a prospective study of frailty and QoL in a pre heart transplant cohort, explores how well clinicians treating AHF patients in a quaternary transplant centre predicted patient reported QoL.

Methods: Patients undergoing frailty assessment (including cognitive and depression screening) completed the EQ5D 5L questionnaire. Clinicians interacting with those patients were asked to complete a proxy-patient version of the EQ5D 5L within 72 hours of assessment. Utility scores were applied and paired proxy/patient results compared. Bland Altman plots, of all 110 pairs stratified by clinician experience (< 10years, >10 years) and presence of ventricular assist device (VAD), were used to determine bias and agreement limits. Spearman r coefficients comparing the clinician estimates and patient reported scores were assessed for correlation.

Results: Only mild to moderate correlations between proxy and patient reported utility scores were observed in 110 pairs (Minimum r = 0.21 for anxiety/depression and Maximum r=0.47 for overall utility) [Table 1]. These did not improve in a sub analysis of 52 pairs where the clinicians had greater than 10 years experience. Bland Altman plots revealed a potential trend to underestimation of patient reported pain and discomfort particularly at higher/ more disabling scores.

Conclusion: There remains a disconnect between patient and proxy clinician assessment of QoL, independent of clinician experience. Introducing a brief QoL questionnaire to routine patient assessments, may help to identify the outcomes that matter most to the patients.

Correlation bias and agreement

	r	95% conf. interval	P	Bias	SD of bias	95% limits of agreement From	To
Mobility all	0.34	0.16 to 0.50	0.00	-0.28	1.21	-2.66	2.10
self care	0.41	0.24 to 0.56	< 0.0001	0.00	0.91	-1.78	1.78
usual activities	0.26	0.07 to 0.43	0.01	-0.03	1.30	-2.57	2.51
pain / discomfort	0.30	0.11 to 0.47	0.00	-0.35	1.05	-2.41	1.72
Anxiety /depression	0.21	0.02 to 0.38	0.03	0.05	0.96	-1.82	1.93
Overall Utility index	0.47	0.30 to 0.61	< 0.0001	0.05	0.22	-0.38	0.49

Paired data points for each QoL domain and overall utility score generated the following correlation, bias and agreement data. (Spearman and Bland Altman analyses)

ATRIAL FIBRILLATION

P1050

Predictive ability of pulse wave velocity for arrhythmia recurrence in hypertensive patients with atrial fibrillation

A Shavarov[1]; GK Kiyakbaev[1]; VS Moiseev[1]

[1]RUDN University, Moscow, Russian Federation

Background: Aortic stiffness promotes to adverse left atrial (LA) remodeling that result in the development and persistence of atrial fibrillation (AF).

Purpose: We investigated whether aortic stiffness could predict AF recurrence in patients (pts) with arterial hypertension (AH) and persistent AF.

Methods: The study included 55 pts (40% men) aged 66 (62; 73) years with AH short-term recurrent AF treated with metoprolol (n = 31) and diltiazem (n = 24). All patients underwent clinical and echocardiographic examination, 24-hour (hr) ambulatory blood pressure (BP) monitoring, pulse wave analysis using the SphygmoCor system before and 3 months after treatment. LA structure abnormalities were defined as LA volume index ≥34 mL/m2. LA empting fraction ≤45% and LA expansion index ≤90% were categorized as LA phasic dysfunction.

Results: LA structural and/or functional abnormalities were found in 44 (80%) pts. AF recurrences were documented in 36 (65%) pts during follow-up period. To compare with AF-free group pts with AF recurrence had significantly higher age, CHA2-DS2-VASc score, peripheral and central pulse pressure (PP), PP amplification, time to return of reflected pressure wave (Tr), and carotid-femoral pulse wave velocity (PWV) [p < 0,001 for all cases]; 24-hr mean SBP, peripheral systolic BP, systolic pressure-time integral and augmentation index [p = 0,01 for all cases]; 24-hr mean heart rate, central systolic BP and ejection fraction [p = 0,02 for all cases]. Arrhythmia anamnesis was longer in AF-free group (12 vs 10 month, p = 0,01). Age [odds ratio (OR) 1,07; 95% CI 1,01-1,13; p = 0,02] and PWV [OR 1,46; 95% CI 1,18-1,80; p = 0,0004] were associated with increased risk of AF recurrence in nonlinear regression analysis.

Conclusion: Pulse wave velocity and age could be significantly associated with arrhythmia recurrence in hypertensive patients with short-term anamnesis of atrial fibrillation.

P1051

HsC-reactive protein as a predictor of mortality in patients with atrial fibrillation in heart failure

S Sadat Kurtalic[1]; N Kurtalic[1]; E Jahic[1]; E Malkic[1]

[1]Cantonal Hospital "Dr. Irfan Ljubijankic", Department of Internal Medicine, Bihac, Bosnia and Herzegovina

Background: To determine the predictive value of HSC-reactive protein level in mortality for patients in heart failure with atrial fibrillation.

Respondents and methods: Cross-section study analysed the predictive value of C-reactive protein in 200 patients with heart failure of all ages, both sexes. The study was conducted in the period from January 1, 2012, to January 31, 2014, at the Department of Internal Medicine of Hospital. Considering the leaders of the heart rate, respondents were divided into two equal groups: the first group were patients in heart failure with atrial fibrillation, and the second group were patients in heart failure with sinus rhythm. All patients with heart failure were clinically examined, with electrocardiogram, ultrasound of the heart, and the value of HsCRP in serum was determined. In the study, the value of HsCRP considered normal if < 5.0 mg / l.

Results: The average age of patients in the first group was 65.0 (8.6) years, and in the second group 65.3 (9.1) (t = 0.215, df = 198, p = 0.83). The first group consisted of 47/100 (47%), while the second group had 41/100 (41%) of female respondents, (X 2 = 0.73, df = 1, p = 0.48). There were more male respondents in both groups. The average value of HsCRP in the entire sample was 5.75 (5.68) mg / L (range 0.0 to 28.0 mg / l). The frequency of respondents with elevated HsCRP in the first group was 40 (40%), while the second group was 44 (44%), (X2 = 0.18; df = 1; p = 0.67). In the first group there were 21 (21%) mortality, and 15 (15%) in the second group (X 2 = 0.85, df = 1, p = 0.36). Univariate regression analysis of the first group of respondents HsCRP shown the relation of chances (odds ratio - OR) of 1.13 (95% CI = 1.04 to 1.22; p = 0.003), and when a function of time (hazard ratio - HR) was taken into account, HsCRP as a predictor was 1.10 (95% CI = 1.04 to 1.17; p = 0.001). In the second group of respondents HsCRP showed OR = 1.07 (95% CI = 0.98 to 1.17; p = 0.13), and HR value was 1.06 (95% CI = 0.99 to 1, 14; p = 0.11).
Conclusion: HsC-reactive protein is a significant predictor of mortality in patients with atrial fibrillation in heart failure.

P1052
Atrial fibrillation in patients with heart failure

CC Diaconu[1]; D Berceanu[2]; D Bucur[2]; GN Dediu[3]; MA Iancu[4]
[1]University of Medicine and Pharmacy Carol Davila, Emergency Clinical Hospital Floreasca, Bucharest, Romania; *[2]Emergency Clinical Hospital Floreasca, Bucharest, Romania*; *[3]University of Medicine and Pharmacy Carol Davila, Emergency Clinical Hospital Sf. Ioan, Bucharest, Romania*; *[4]University of Medicine and Pharmacy Carol Davila, Family Medicine, Bucharest, Romania*

Introduction. Atrial fibrillation is a frequent companion of heart failure. Heart failure patients with atrial fibrillation may have some particularities as compared to those with sinus rhythm. The purpose of the study was to analyze the frequency and particularities of patients with chronic heart failure and atrial fibrillation, hospitalized in the Internal Medicine clinic of a University Clinical Emergency Hospital.
Methods: The study included 980 patients with chronic heart failure, consecutively admitted between January 1st, 2016-November 30, 2016. We have retrospectively analyzed the frequency of atrial fibrillation and the clinical correlations in patients with chronic heart failure, using data from the hospital record database and SPSS software. Results. The distribution by sex in the group of study: 49.8% men, 50.2% women. The mean age of the whole group was 74 ± 11.6 years. 39.9% of the patients with chronic heart failure had permanent atrial fibrillation. We have found a statistically significant correlation between the presence of atrial fibrillation and anemia: 27.68% of pts with atrial fibrillation had anemia, as compared to 16.20% (p < 0.001). 85.20% of pts with heart failure and atrial fibrillation had hypertension, versus 54.76% of those without atrial fibrillation (p = 0.001). We have found also a statistically significant correlation between the presence of atrial fibrillation and dyselectrolytemias (p < 0.001), and also between atrial fibrillation and coronary heart disease (p < 0.001). Dysthyroidism was diagnosed in 13.77% of pts with atrial fibrillation versus 4.93% in those without atrial fibrillation (p = 0.001). We have found a weak correlation (p = 0.003) between atrial fibrillation and chronic kidney disease or between atrial fibrillation and pulmonary hypertension (p = 0.029). Conclusions: Atrial fibrillation is a frequent comorbidity in heart failure (40% in our study). Patients with heart failure and atrial fibrillation have a higher frequency of anemia, arterial hypertension, dyselectrolytemias, coronary heart disease and dysthyroidism.

P1053
Antithrombotic treatment differences among hospitalized patients with atrial fibrillation and heart failure

A Samaras[1]; E Michou[1]; G Fotos[1]; G Dividis[1]; D Vasdeki[1]; E Kotsi[1]; P Tsoukra[1]; E Forozidou[1]; T Panagiotidis[1]; A Kartas[1]; I Doundoulakis[1]; G George Giannakoulas[1]; H Karvounis[1]; A Tzikas[1]
[1]AHEPA General Hospital, Thessaloniki, Greece

On behalf of: MISOAC Investigators

BACKGROUND Appropriate anticoagulation therapy should be prescribed in all patients with atrial fibrillation (AF) and heart failure (HF) at risk of stroke. According to the 2016 ESC AF guidelines non-vitamin K oral anticoagulants (NOACs) are recommended in preference to Vitamin K antagonists (VKAs) in patients with non-valvular AF who are eligible for NOACs, while antiplatelet monotherapy is not recommended for stroke prevention in AF patients regardless of stroke risk.
PURPOSE: To determine the type of antithrombotic treatment [oral anticoagulation (OAC) and antiplatelet (OAP)] in a "real-world" contemporary observational dataset of patients with AF and to highlight the differences in patients with a history of HF versus no HF and also amongst the three subtypes of HF [heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF)].
Methods: We studied consecutive patients who were hospitalized to the cardiology department of a tertiary hospital with any diagnosis and coexisting non-valvular AF. Subjects with HF were classified in three groups according to their LVEF (HFrEF, HFmrEF, HFpEF). Comparisons were made between patients with and without HF, and among HF subtypes.
Results: A total of 510 patients were enrolled between December 2015 - December 2016, of whom 232 (45.5%) had documented HF (HFpEF: 63%, HFrEF: 21%, HFmrEF: 16%). Monotherapy with an OAC was prescribed in 73% and OAP monotherapy in 10% of patients, while 17% were under combination therapy with OAC and OAP. There was a preference for NOACs over VKAs in patients without HF (65% vs 35% respectively, p < 0.05), while NOACs and VKAs were equally prescribed in patients with HF (48% vs 52% respectively). At discharge, there was a trend (p = 0.10) for administration of NOACs over VKAs in HFpEF patients (58% vs 42%) compared to HFrEF (37% vs 63%) and HFmrEF (41% vs 59%). There was a common co-administration of OACs and OAPs in the HFmrEF subgroup (36%), which was significantly higher compared to the HFpEF patients (9%, p < 0.05) but not significantly higher compared to the HFrEF subgroup (12%).
Conclusions: In the "real life" clinical setting, one tenth of hospitalized patients with AF were under OAP, which is not supported by the current ESC Guidelines, while a significant number of patients received combination therapy with OACs and OAPs. Patients with a history of HF were less likely to receive NOAC therapy at discharge compared to patients without HF. Patients with HFmrEF were more likely to be under co-administration of OACs and OAPs in comparison to HFpEF patients.

P1054
Clinical implications from the interdependence between heart failure and atrial fibrillation

D Daniel Seabra[1]; H Guedes[1]; P Silva[1]; L Marques[1]; A Andrade[1]; J Azevedo[1]; P Pinto[1]
[1]Hospital Centre do Tamega e Sousa, Cardiology Department, Penafiel, Portugal

Background/Introduction: Heart failure (HF) and atrial fibrillation (AF) represent two relevant diseases that are growing in cardiovascular medicine. They share common risk factors and aspects of pathophysiology instilling challenge in their clinical approach. When both are present, patients (pts) have a worse prognosis, with a significant impact in healthcare.
Purpose: To assess the clinical impact of AF in pts with heart failure with reduced ejection fraction (EF) and the prognostic implications.
Methods: We conducted a retrospective study based on a cohort of pts from a HF clinic of a single hospital center. Included pts with reduced EF and previous diagnosis for, at least, six months; they were divided in two groups: with permanent AF (G1) and without AF (G2). Evaluated clinical characteristics and major cardiac events – hospitalization from HF (hospHF) or acute coronary syndrome (hospACS) and death from cardiovascular cause (CVm) and non-cardiovascular cause (nCVm). Assessed the relationship with recovery of left ventricle systolic function (LVSF) (defined as EF increase > 10% with respect to the initial value) and size (Q) (defined by quotient between the follow-up [FU] and the initial value of the indexed left ventricle end-diastolic diameter).
Results: Included 290 pts, with a mean age of 60.56 ± 13.25 years and male predominance (75.2%). The prevalence of ischemic etiology was 41%. The mean initial EF was 29.2 ± 10.8%. The FU was 39.9 ± 18.5 months, with a mean EF during FU of 34.9 ± 12.5%.
G1 consisting of 99 pts and 191 in G2. There was a more advanced age in G1 (64.2 vs 58.7 years, p < 0.001) and a predominance of males in both groups (p 0.01). Appreciably higher prevalence of chronic renal dysfunction (glomerular filtration rate ≤ 60mL/min/1.73m2) was observed in G1 (40.4 vs 27.2%, p 0.02). There were no significant differences regarding the etiology of HF and the prevalence of other cardiovascular risk factors between the groups.
The presence of AF correlated negatively with the recovery of the LVEF (21 vs 65 pts; p 0.023). Observed a significant higher Q in G1 (0.98 vs 0.94 ± 0,02, p 0.002). During the FU, G1 had a greater number of clinical events - hospIC (p < 0.001), CVm (p 0.003) and nCVm (p < 0.001); without meaningful differences in hospACS (p 0.552). The presence of AF was associated with worse functional class (p < 0.001) and greater use of diuretic therapy (p 0.002); In the pts with AF, there is predominance of hypocoagulation with vitamin K antagonists (p < 0.001).
Conclusion(s): In this study, the presence of AF has a important influence on HF since it is a limiting element for the recovery of the LVEF and is associated with higher end-diastolic ventricle size. As consequence, it has a close relate relation with worse clinical prognosis and functional class. In pts with AF, the higher prevalence of chronic kidney disease influences the hypocoagulation strategy.

P1055

Increased left atrial volume predicts atrial fibrillation recurrence after transcatheter ablation: a systematic review and meta-analysis

I Ibadete Bytyci[1]; G Bajraktari[1]; MY Henein[2]
[1]*University Clinical Centre of Kosova, Clinic of Cardiology, Pristina, Kosovo Republic of*; [2]*Umea University, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background and Aim: Left atrial (LA) enlargement is associated with atrial fibrillation (AF) incidence and outcome. Trans-catheter ablation has become an established treatment for symptomatic atrial fibrillation (AF) patients who are refractory to drug therapy. However, AF recurrence and the need for repeat procedure are common in these patients. Although a number of predictors of AF recurrence have already been proposed, patient selection remains controversial. The aim of this meta-analysis was to analyze the potential association between LA volumes and AF recurrence after ablation.

Methods: We systematically searched PubMed-Medline, EMBASE, Scopus, Google Scholar and the Cochrane Central Registry, up to December 2016 in order to select clinical trials and observational studies, which reported the predictive role of LA maximal volume (LAVmax) and LAVmax indexed (LAVI) for AF recurrence after catheter-ablation. 3259 patients from 31 studies with paroxysmal AF (PAF), persistent (PeAF) or longstanding persistent AF (L-PeAF) were included.

Results: The pooled analysis showed that after 16.8 ± 10.7 months follow-up, patients with AF recurrence had larger LAVmax and LAVI in comparison with those without AF recurrence, with a weighted mean difference (WMD) of 16.21 ([95% CI 11.70 to 20.73], P < 0.0001) and 4.19 ([95% CI 2.97 to 5.42], P < 0.0001). In subgroup analysis, the difference in LAVI was present according to the type of AF; in PAF WMD was 2.08 ([95% CI 0.48 to 3.55], P < 0.01), in PeAF/L-PeAF was 3.55 ([95% CI 0.68 to 6.43], P=0.0007), with no significant difference between the two subgroups (Chi2=0.85, I2 = 0.0%, p = 0.36).

Conclusions: Left atrial maximal volume and indexed volume correlate with atrial fibrillation recurrence after catheter ablation.

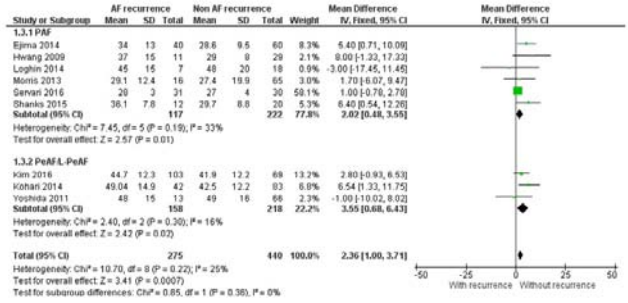


Figure 3. Comparison of LAVI with weight

CARDIOMYOPATHY

P1056

The molecular defect in hypertrophic cardiomyopathy and drugs that correct the defect

S Steven B Marston[1]; A Choudry[1]; V Kren[2]; M Papadaki[1]; J Zamora[1]; I Gould[1]; AE Messer[1]
[1]*Imperial College London, London, United Kingdom*; [2]*Academy of Sciences of the Czech Republic, Prague, Czech Republic*

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Mutations in contractile proteins have been found to be the cause of a number of common cardiomyopathies including familial hypertrophic cardiomyopathy (HCM) and familial dilated cardiomyopathy (DCM). In most cases the mechanism proposed for causing the disease is derangement of the thin filament-based Ca2 + -regulatory system of the muscle. HCM has been linked to a higher myofilament Ca2 + -sensitivity. In addition we have identified a molecular level dysfunction common to both HCM and DCM-causing mutations. This is an uncoupling of the relationship between troponin I (TnI) phosphorylation and modulation of myofilament Ca2 + -sensitivity, essential for normal responses to adrenaline. We have identified compounds that can specifically reverse these abnormalities in vitro and therefore have potential for treatment.

The first compound studied was Epigallocatechin-3-Gallate (EGCG). We found that this is capable of both Ca2 + desensitisation and re-coupling of HCM mutant myofilaments so as to restore function to the same as native myofilaments, both by quantitative in vitro motility of single filaments and in single myofibrils.

100μM EGCG can restore normal function to troponin from samples with mutations in all the sarcomeric proteins tested including TnI, TnT, TnC, tropomyosin, actin, β-MHC and MyBP-C and in myectomy samples where no mutation has been identified. The restorative effect is species independent, being the same in both human and cat myofilaments.

We have recently identified a number of similar compounds that can also re-couple and/or desensitise HCM mutant myofilaments; moreover we have found that the properties of desensitisation and re-coupling can be separated and that these effects show a preference of one stereoisomer over another. Thus Epicatechin gallate (ECG) is a desensitiser that does not re-couple. In contrast Silybin B, dehydrosilybin B, taxifolin, quercetin and novobiocin are re-couplers that do not have any desensitising activity, whilst Silybin A and dehydrosilybin A are neither desensitisers nor re-couplers.

We propose that the activity of desensitising and re-coupling compounds depends upon their preferential binding to wild-type and mutant, phosphorylated and unphosphorylated troponin. Thus a pure re-coupler may only bind to mutant dephosphorylated troponin. We have mapped EGCG binding to whole troponin by molecular dynamics simulations and find that it is located between the N-terminal phosphorylatable peptide of TnI and the N-terminal Ca2 + regulatory domain of unphosphorylated TnC. In this position it could stabilise and influence the N-terminal TnI interaction with TnC that is involved in modulation of Ca2 + -sensitivity by phosphorylation. Interestingly, Silybin A and B that are not desensitisers, do not bind to unphosphorylated wild-type troponin in MD simulations

P1057

Genetic spectrum of diseases underlying diffuse generalyzed form of hypertrophic cardiomyopathy

E Elena V Zaklyazminskaya[1]; M Polyak[1]; ANNA Bukaeva[1]; O Blagova[2]; YU Frolova[1]; M Malikova[1]; S Dzemeshkevich[1]
[1]*B.V. Petrovsky Russian Scientific Center of Surgery of the Russian Academy of Medical Sciences, Moscow, Russian Federation*; [2]*I.M. Sechenov First Moscow Medical Academy, Clinic of Cardiology, Moscow, Russian Federation*

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Background: As many as 65% of primary hypertrophic cardiomyopathy (HCM) cases are associated with mutations in sarcomeric genes. The diffuse generalized form of HCM is a specific anatomical phenotype characterized by diffuse hypertrophy of the interventricular septum and significant hypertrophy of the papillary muscles, with their displacement towards the left ventricular (LV) apex.

Aim: This study also aims to analyze the genetic spectrum of the diseases associated with the diffuse generalized form of HCM.

Methods: From 2009 to 2015, 31 patients with diffuse generalized HCM were examined. Genetic screening of the 10 genes encoding sarcomeric proteins (MYBPC3, TAZ, TPM1, LDB3, MYL2, ACTC1, MYL3, MYH7, TNNI3, and TNNT2) was performed, followed by additional Sanger resequencing of the low-covered regions in order to confirm all detected variants. Mutational testing in additional genes causing some particular genetic syndromes was performed by bidirectional Sanger sequencing.

Results: Mutations in the sarcomeric-encoding genes were detected in 4 cases (13%) what is a low prevalence as compared to the overall prevalence of all of the mutations (60-65%) in the HCM cohort. Multisystemic inherited diseases (progressive myopathies - 2 patients, lysosomal storage diseases - 4 patients, and RASopathies - 4 patients) accounted for 32% of the index cases.

A new reconstructive surgical technique was developed and implemented, allowing for the normalization of both the intraventricular pressure gradient and LV diastolic filling. 26 patients of them underwent the following reconstructive surgery: transaortic extended septal myectomy, longitudinal resection of the papillary muscles with preservation of annulo-papillary contact, mitral valve replacement through the left atrium, and ICD implantation.

Significant normalization of intracardiac hemodynamics was observed in 1, 3 and 5 year follow-ups in 24 patients. Morphological evaluation of the removed mitral valve leaflets showed connective tissue dysplasia. Five patients (19%) experienced appropriate ICD shocks.

Conclusion: The prevalence of classic 'sarcomeric' mutations was less frequent than expected in patients with diffuse generalized HCM. "Non-sarcomeric" genetic

mutations associated with LV hypertrophy were detected in 10 cases (32%). An excessive level of fibrosis may explain the high risk of ventricular fibrillation, and stresses the need for early reconstructive surgery as a primary prevention of sudden cardiac death (SCD).

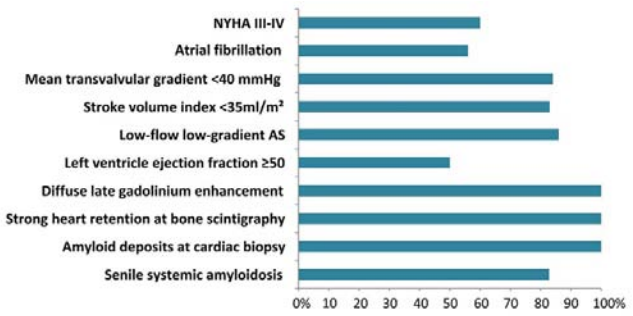
P1058

Aortic stenosis and transthyretin cardiac amyloidosis: the chicken or the egg?

A Arnault Galat[1]; AG Guellich[1]; DB Bodez[1]; MS Slama[2]; MD Dijos[3]; DMZ Zeitoun[4]; OM Milleron[4]; DA Attias[5]; JLDR Dubois-Rande[1]; DM Mohty[6]; EA Audureau[7]; JLM Monin[7]; TD Damy[1]

[1]University Hospital Henri Mondor, Cardiology, Creteil, France; *[2]Hospital Antoine Beclere, Clamart, France*; *[3]University Hospital of Bordeaux, Bordeaux, France*; *[4]Hospital Bichat-Claude Bernard, Paris, France*; *[5]Centre Cardiologique du Nord, Saint Denis, France*; *[6]University Hospital of Poitiers, Poitiers, France*; *[7]University Hospital Henri Mondor, Creteil, France*

Background: Aortic stenosis (AS) and transthyretin-cardiac amyloidosis (TTR-CA) are both frequent in elderly. The combination of these two diseases has never been investigated.
Aims: To describe patients with concomitant AS and TTR-CA.
Methods: Six cardiologic French centers identified retrospectively cases of patients with severe or moderate AS associated with TTR-CA hospitalized during the last six years.
Results: Sixteen patients were included. Mean ± SD age was 79 ± 6 years, 81% were men. 60% were NYHA III-IV, 31% had carpal tunnel syndrome and 56% had atrial fibrillation. Median (Q1;Q4) NTproBNP was 4382 (2425;4730) pg/mL and 91% had elevated cardiac troponin level. 88% had severe AS (n = 14/16), of whom 86% (n = 12) had low gradient AS. Mean ± SD interventricular septum thickness was 18 ± 4 mm. Mean left ventricular ejection fraction and global longitudinal strain were 50 ± 13% and -7 ± 4% respectively. Diagnosis of TTR-CA was histologically proven in 38%, and was based on strong cardiac uptake of bone tracer at scintigraphy in the rest. 81% had wild-type TTR-CA (n = 13), one had mutated Val122I and 19% did not had genetic test (n = 3). Valve replacement was surgical in 63% and via transcatheter in 13%. Median follow-up in survivors was 33 (16;65) months. Mortality was of 44% (n = 7) during the whole follow-up period.
Conclusions: Combination of AS and TTR-CA may occur in elderly patients particularly those with a low-flow low-gradient AS pattern and carries bad prognosis. Diagnosis of TTR-CA in AS is relevant to discuss specific treatment and management.



characteristics of AS/CA patients

P1059

Hypertrophic cardiomyopathy in the pediatric stage: clinical, electrical and echocardiographic characteristics.

MA Lopez Garrido[1]; N Abdeselam-Mohamed[1]; HN Orellana-Figueroa[1]; V Cuenca-Peiro[2]; B Picazo-Angelin[2]; L Conejo-Munoz[2]; M De Mora-Martin[2]; JI Zabala-Arguelles[2]

[1]University Hospital Virgen de la Victoria , Department of Cardiology, Malaga, Spain; *[2]Regional University Hospital of Malaga, Department of Cardiology, Malaga, Spain*

Background: Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden death in adolescence, appearing generally at that age, and being less frequent in the pediatric stage. The aim of our study was to know the characteristics of HCM patients diagnosed in the pediatric age.
Methods: We studied a sample of patients with MCH from our consultation of Pediatric Cardiology, recording clinical, electrocardiographic, echocardiographic and adverse events during follow-up (death, functional class worsening, cardiac transplantation and / or arrhythmic events). Patients with diagnosis of any metabolopathies or polymorphic syndromes were excluded.
Results: Nineteen patients were studied (mean age 7 years, 16% women). The mean age at diagnosis was 4.5 years old. The most frequent reason for being diagnosed was the family screening (31.6%). The 42.1% had a history of HCM and the 10.5% of sudden death. The 26.3% presented symptoms at the time of diagnosis, being the syncope the most frequent (60%). The 73.7% had signs of left ventricular hypertrophy on the electrocardiogram and 47.4% had alterations in the repolarization. In the echocardiographic study, 15 (78.9%) had an asymmetric distribution of hypertrophy and in 4 (21.1%) was concentric. Anterior mitral systolic movement was observed in 26.3% and a significant dynamic gradient in 36.8%, which was severe in 3 patients (15.8%). The 100% of the patients with the dynamic gradient received beta-blocker treatment, but only 30% achieve an improvement with them. The median follow-up was 14 months (RIC 7-24), without having registered any adverse event.
Conclusions: 1. The most frequent cause of diagnosis of HCM in the pediatric stage was family screening.
2. A quarter part of the patients had symptoms at the time of diagnosis.
3. In a low percentage it was possible to reduce the dynamic gradient after the beta-blocker treatment.
4. There were no adverse events in the follow-up in our series.

P1060

Quality of life in outpatients with hypertrophic cardiomyopathy.

M Jacquelinet[1]; A Duva Pentiah[2]; A Coisne[1]; P Lapierre[3]; E Hebbar[2]; M Fertin[2]; H Ridon[2]; D Montaigne[1]; N Lamblin[4]; P De Groote[2]

[1]CHRU Lille, Service d'Explorations Fonctionnelles CardioVasculaires, Lille, France; *[2]CHRU Lille, Service de Cardiologie, Lille, France*; *[3]CHRU Lille, Service d'Addictologie, pôle de Psychiatrie, Lille, France*; *[4]CHRU Lille, Unité de Soins Intensifs Cardiologiques, Lille, France*

Background: Hypertrophic cardiomyopathy (HCM) is a relatively common genetically transmitted heart disease associated with sudden cardiac death, heart failure and atrial fibrillation (AF). Quality of life (QoL) provides subjective information completing traditional measures of health. Very few studies have assessed QoL in HCM patients.
Purpose: To assess QoL in HCM patients and to identity factors associated with QoL.
Methods: A single-center prospective observational study was conducted in HCM outpatients referred to a University Hospital between March 2015 and March 2016. QoL was assessed with the Short-Form 36 Health Survey (SF36) and psychological well-being with the Hospital Anxiety and Depression (HAD) questionnaire. Sociodemographic, clinical, biological, and echocardiographic data were collected.
Results: 78 questionnaires were analyzed. Physical component score (PCS) and mental component score (MCS) of the SF36 were significantly lower in patients with HCM compared to French population (PCS = 44.4 ± 10.3 versus 50.4 ± 9.9, p < 10-4; MCS = 45.8 ± 9.9 versus 48.8 ± 9.9, p = 0.017). Impaired physical QoL was independently predicted by 6 variables that accounted for 60% of the variance: low education level (p < 0.006), impact of disease on a child project, (p < 10-4), AF (p < 0.011), palpitations (p < 10-4), high NYHA functional class (p < 10-4) and high score at the HAD depression subscale (p < 0.032). Impaired mental QoL was independently predicted by 5 variables that accounted for 54% of the variance: family history of HCM (p < 0.012), syncope or presyncopal symptoms (p < 0.013), high number of medications (p = 0.005), and high score at the HAD anxiety (p < 10-4) and depression subscale (p < 10-4).
Conclusion: Physical and psychological QoL are clinically and statistically impaired in patients with HCM. Identification of QoL predictors suggest potential targets to provide more comprehensive health-care strategies for HCM patients.

P1061

Feasibility and benefits and of exercise training in patients with amyloid cardiomyopathy

B Gellen[1]; M Wuliya[2]; H Ben Elhaj[2]; S Guendouz[3]; D Bodez[3]; S Peyrot[2]; T Damy[3]

[1]ELSAN, Polyclinique de Poitiers, Cardiology, Poitiers, France; *[2]Henri Mondor University Hospital Group, Cardiac Rehabilitation, Créteil, France*; *[3]Henri Mondor University Hospital Group, Cardiology, Créteil, France*

Introduction: Cardiac amyloidosis (CA) is a common cause of hypertrophic cardiomyopathy (HCM). Data about the feasibility and benefits of cardiac rehabilitation (CR) in these patients are lacking.
Methods: Consecutive heart failure (HF) patients with confirmed CA addressed for CR were prospectively included in this single centre cohort from 2011 to 2015.

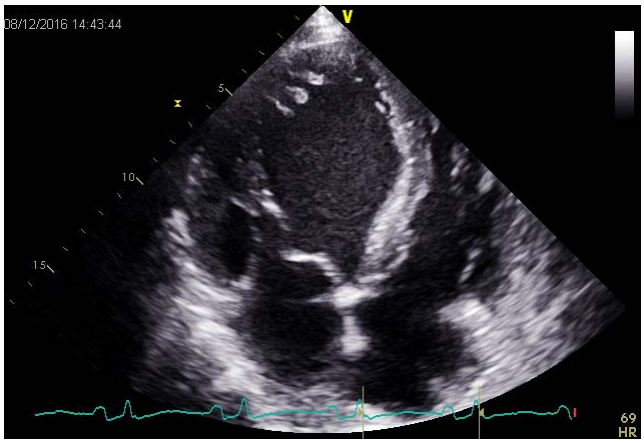
Patients underwent exercise testing on a cycle ergometer before and after participation to a standard group-based CR program. The CR program was considered as feasible if the patient could participate in ≥10 training units without adverse events. The CR program was considered as beneficial in case of a relative increase in peak oxygen consumption (VO2) and/or in maximal workload after CR of ≥16%.
Results: Twenty-seven patients were included (68 ± 12 years, 81% male). Mean left ventricular (LV) ejection fraction was 49.8 ± 12.8%, and mean LV wall thickness was 17 ± 3 mm. The majority of the patients had AL amyloidosis (N=16; 59%). Two-third of the patients had a pacemaker. The maximum workload at the initial exercise test was 49 ± 40 W.
Cardiac rehabilitation was feasible in 19 patients (70%). Patients with feasible CR as compared to patients with CR failure had more pacemaker (84% vs. 25%; p = 0.0061), lower NT-proBNP (2239 ± 8600 vs. 8600 ± 8613 ng/l; p = 0.045), and a longer initial exercise test (360 ± 263 vs. 134 ± 62 sec.; p = 0.0190). Age and type of amyloidosis were not significantly associated with CR feasibility.
Among the patients with feasible CR, nine (47%) showed significant functional benefit, with a 36 ± 23% (25 ± 20W) increase in maximal workload after CR, as compared to 0 ± 17% (2 ± 10W) among those without benefit. Benefit was not significantly associated with the number of training units (27 ± 16 vs. 22 ± 14, n.s.). Benefit was associated with age (63 ± 13 vs. 73 ± 11 years, p < 0.05), NT-proBNP (1080 ± 851 vs. 10516 ± 9810 ng/l, P < 0.05), creatininemia (92 ± 36 vs. 158 ± 83 μmol/l, p < 0.05), and LVEF (57 ± 10 vs. 42 ± 10%, p < 0.05), but not with the type of amyloidosis neither with the degree of LV hypertrophy.
Conclusions: The presence of a pace-maker seems to facilitate cardiac rehabilitation in CA. Elderly CA patients with impaired LVEF seem not to benefit from CR with respect to functional capacity. The type of amyloidosis and the degree of LV thickening are neither associated with CR feasibility nor with functional benefit.

P1062

Surprise after a successful fibrinolytic therapy in acute stroke

R Roland Gal[1]; L Szapary[2]; L Toth[3]; S Szukits[3]; K Toth[1]; T Habon[1]
[1]*1st. Department of Medicine, University of Pécs, Medical Center, Pécs, Hungary*; [2]*University of Pecs, Stroke Center, Department of Neurology, Pecs, Hungary*; [3]*University of Pecs, Department of Radiology, Medical Center, University of Pécs, Pecs, Hungary*

Introduction: Stroke is the third leading cause of death worldwide, and almost 80% of the total cases of strokes are ischemic strokes. Cardiogenic embolism accounts for approximately 20% of ischemic strokes. The most frequent source of cardioembolic stroke is the nonvalvular atrial fibrillation, but many other pathological heart conditions can be an etiological factor. Noncompaction cardiomyopathy is a rare, genetic disease, caused by intrauterine arrest of compaction of the myocardial fibres, resulting in multiple trabeculations, typically the apex in the LV myocardium.
Case report: A 56-year-old regular alcohol drinker patient without significant medical history was admitted, 1-1,5 hours after the onset of symptoms, with ictal left-sided mild hemiparesis and dysarthria. Urgent brain CT scan didn't identify bleeding or early signs of stroke. Thrombolysis was performed within 2 hours. Control CT scan at 24 hours showed extensive lesions in the territory of the right middle cerebral artery. Patient's hemiparesis was completely resolved 2 days after intervention. Echocardiography revealed previously unknown severe left ventricle dysfunction (EF: 24%), diffuse hypo-kinesis of the apex, and extended apical trabeculation with intratrabecular thrombi. The cardiac MRI showed typical morphological pattern of non-compaction cardiomyopathy, but it also supposed ischemic etiology, based on extended, irreversible damaged areas of myocardium (delayed contrast enhancement). With regard to the recent neurological event coronary CT angiography was performed, which identified significant stenosis of LAD and Cx, with extensive calcification. Besides of the tailored, evidence-based heart failure and secondary prevention therapy, we introduced oral anticoagulant therapy as well. The patient was discharged in stable condition (NYHA I-II.), and scheduled for a follow-up MRI and elective revascularization.
Conclusion: Close cooperation between neurologist and cardiologist is crucial during stroke care. In the background of the stroke severe cardiological diseases can often be found. Fast cardiological diagnosis can improve the survival of the patient, can change the treatment or, as in our case, also requires a complex approach.



Trabeculation with thromi

P1063

A new de novo mutation in the MYH7 gene causing dilated cardiomyopathy with mild myopathy in pediatric patient

Y Yulia Rogozhina[1]; M Polyak[1]; E Zaklyazminskaya[1]
[1]*Russian Research Center of Surgery, Moscow, Russian Federation*

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Introduction: Dilated cardiomyopathy (DCM) is characterized by left ventricular enlargement and systolic dysfunction. The estimated prevalence of DCM is 1:3,000 and about 35% of patients will have familial disease. For children it is much rare condition and its annual incidence is estimated to be 0.58 cases/100,000 children. Early-onset sporadic DCM is usually considered as a recessive form of disease with 25% risk of recurrence.
Patient and methods: The patient is Russian boy 2 y.o. with dilated cardiomyopathy and primary weaknesses of axial muscles. The proband was examined by pediatrist, neurologist, and geneticist. The clinical evaluation included medical history taking, echocardiogram, creatine phosphokinase (CK) measurement and electromyography. The genetic evaluation included whole genome sequencing (WGS) for the patient, with following confirmation by the Sanger sequencing ofthe findings, cascade familial screening, and predictive in silico analysis of possible clinical impact. Proband's mRNA was extracted from the muscle sample and converted into cDNA using standard molecular methods.
Results: WGS revealed a novel genetic variant c.5655 + 5G>C in the MYH7 gene. Splice site damage was predicted by Netgene2 and SpliceSite Predictor tools. Analysis of cDNA shows the skipping of exon 38 without frameshift (p.1854_1885del). Diagnosis of the MYH7-related myopathy was established based on the clinical evaluation and genetic finding. De novo origin of c.5655 + 5G>C variant was confirmed after the testing of parent's DNA samples. We consider the genetic variant c.5655 + 5G>C as a pathogenic mutation causing dilated cardiomyopathy and myopathy.
Conclusion: Mutation c.5655 + 5G>C in the MYH7 gene causes MYH7-related myopathy with unusually early manifestation. Severe de novo mutations in the MYH7 gene could be responsible for some early-onset DCM with myopathy. It is important to clarify de novo status, because those mutations have a benign prognosis for following family planning.

P1064

The effect of the CHF optimal medical treatment on clinical and functional parameters in pts with peripartum and idiopathic dilated cardiomyopathies

NA Kurbanov[1]; TA Abdullaev[1]; ST Mirzarakhimova[1]; I A Igor Tsoy[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

The aim: To study the effect of six-month CHF optimal medical treatment (OMT) clinical and hemodynamic parameters of pts with idiopathic (IDCM) and peripartum (PPCM), dilated cardiomyopathies (DCM).
Materials and methods: The study included 93 pts with dilated cardiomyopathy. It were conducted ECG EchoCG, X-ray cardiometry, 6-minute walk (6MWT) and the

assessment of the clinical condition (ACC) by Mareev for CHF pts before and after treatment. All pts received the standard treatment of heart failure and were randomized into two grs: the first gr included 50 pts with peripartum cardiomyopathy (mean age 28,2 ± 0,8 years.), In the second - 43 pts with idiopathic dilated cardiomyopathy (mean age 38. 1 ± 2,1 years; $p < 0.001$).

Results: At the time of study entry, all pts were stabilized on the CHF OMT. By the end of the treatment of the dynamics of reduction of heart rate in both grs was significantly (respectively 32.3% versus 29.7%, both $p < 0,01$), which was accompanied by improved performance of 6MWT in 2.1 times (from 194 ± 10,1 to 412, 5 ± 12m; $p < 0,001$) in pts with PPCM and 2.2 times (from 186 ± 12 to 412 ± 12.6 m; $p < 0,01$) for pts with idiopathic forms of the disease, which are accompanied by an improvement of the clinical condition by ACC (10 ± 0,3 to 3,4 ± 0,3 points and 9,9 ± 0,3 to 3,8 ± 0,2 points, both $p < 0,01$), a decrease FC HF (with 3,4 ± 0,1 to 1,7 ± 0,1 and 3,3 ± 0,1 to 1,6 ± 0,1; are both $p < 0.01$), respectively PPCM and IDCM. Basic therapy HF exerted similar effect on intracardiac hemodynamics, but reliable results were obtained in PPCM pts, increased on 23.2% (from 37 ± 1,3 to 45,6 ± 2% in particular left ventricular (LV) ejection fraction; $p < 0.001$) reduction in the EDD on 4.8% (from 6.5 ± 0.1 cm to 6,2 ± 0,1 cm; $p < 0.05$), the ESD on 15.2% (from 5,3 ± 0,1 to 4,6 ± 0,1 cm; $p < 0.001$) in comparison with idiopathic forms of DCM pts, LVEF increased only on 11.7% (from 34 ± 1,5 to 38 ± 1.6%, $p > 0.05$) with decreasing of ESD on 3.5% (from 5.8 ± 0.1 to 5.6 ± 0.1 cm; $p > 0.05$), while EDD LV practically unchanged. It should be noted that in 19 (38%) pts during treatment with PPCM fully normalized LVEF, which was not observed in the control gr.

Conclusions: Standard therapy for heart failure in 6 months have unidirectional impact on clinical and hemodynamic parameters in both grs, but pts suffering from PPCM showed a significant improvement in myocardial contractility and reduced linear size of the heart.

P1065

Cardiac troponinT in patients with dilated cardiomyopathy

E Martins[1]; A Sousa[1]; P Canedo[2]; L Lopes[3]; M Campelo[4]; B Moura[5]; S Amorim[4]; F Rocha Goncalves[1]; JC Machado[2]; J Silva Cardoso[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; *[2]Institute of Investigation and Innovation in Health of University of Porto, Porto, Portugal*; *[3]Garcia de Orta Hospital, Lisbon, Portugal*; *[4]H. São João, Porto, Portugal*; *[5]Regional Military Hospital n°1, Porto, Porto, Portugal*

On behalf of: FATIMA investigators

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Background: Dilated cardiomyopathy (DCM) is a genetic heterogeneous entity, with variants described in more than 40 genes, including cardiac troponin T gene (TNNT2) in approximately 3% of the cases. As next generation sequencing becomes more widely available, establishing causality for genetic variants becomes increasingly relevant.

Purpose: We aimed to determine the genetic variations in TNNT2 in DCM patients.

Methods: We evaluated 107 unrelated patients with idiopathic DCM (iDCM) or familial DCM (fDCM). 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. Patients with mutations in TNNT2 gene were comprehensively analyzed.

Results: Six variants in TNNT2 gene were found in 7 (6.5%) patients (5 men, men age 42 ± 13, 4 cases of fDCM). One variant has been previously described in a DCM family (Arg173Trp) and another in association with increased left ventricular (LV) thickness (Ala28Val). One variant (His109Tyr) was present in two patients. Two patients presented 2 genetic variants (TCAP Glu105Gln + TNNT2 His109Tyr and MYBPC3 Arg44His + TNNT2 Ser275Phe). Arg173Trp was classified as likely pathogenic and the remaining of uncertain significance.

Mean age at diagnosis was 31 ± 17 years (vs 39 ± 13 of the remaining patients, $p = 0.221$) and they were mildly symptomatic (5 in NYHA class I and 2 in class II). One had previous hospitalization from HF, one received an ICD and another had had previous heart transplant. Mean LVEDD was 60 ± 7mm (vs 64 ± 9m, $p = 0.257$), LV ejection fraction 40 ± 9% (vs 30 ± 11%, $p = 0.018$) and one patient presented right ventricular (RV) impairment. All were in sinus rhythm and one had left bundle branch block (LBBB). At a median follow-up of 20 months (IQR 13) none presented adverse events.

The patient with the likely pathogenic variant was a 53 year-old man, with fDCM, in NYHA class II that presented LBBB, RV dysfunction and underwent ICD implantation.

Patients with double variants, TCAP + TNNT2 (iDCM) and MYBPC3 + TNNT2 (fDCM), were both in NYHA class I; LVEF/LVEDD were 39%/61mm and 49%/61mm and neither had RV impairment; the latter presented noncompaction criteria and family history of death from HF.

Conclusions: In our series, variants in TNNT2 were more common than previously published. Our patients presented an early onset but, contrasting to the literature, they had higher LVEF and the clinical course was not very aggressive in most instances. This illustrates the uncertainties related to specific genotype/phenotype association and genetic causality in DCM.

P1066

Markers of fibrosis in patients with nonischemic dilated cardiomyopathy and ventricular arrhythmia.

MV Marina Kostyukevich[1]; LH Yeghiazaryan[1]; KA Zykov[2]; NA Mironova[1]; OV Stukalova[3]; SP Golitsyn[1]
[1]Russian Cardiology Research and Production Complex, Department of clinical electrophysiology and endovascular treatment of cardiac rhythm disorders, Moscow, Russian Federation; *[2]Russian Cardiology Research and Production Complex, Department of immunopathology, Moscow, Russian Federation*; *[3]Russian Cardiology Research and Production Complex, Depatment of radiology, Moscow, Russian Federation*

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Introduction: Decompensated heart failure and ventricular arrhythmias account for majority of sudden cardiac death cases in patients with heart failure due to nonischemic dilated cardiomyopathy (DCM). Myocardial fibrosis among other factors, such as inflammation, may substantially contribute to the development of life-threatening ventricular arrhythmias.

Purpose: The aim of the study was to evaluate the level of fibrosis biomarkers in patients with DCM and healthy controls, amount of myocardial fibrosis according to magnetic resonance imaging (MRI) and its relation to ventricular arrhythmias.

Methods: The study enrolled 35 patients with nonischemic DCM, NYHA class I-II (age 43.2 ± 13.6) and 19 healthy controls (age 29.2 ± 2.6). Heart rhythm disorders were assessed by 24-hour ECG monitoring in all patients. Markers of fibrosis - transforming growth factor $\beta 1$ (TGF-$\beta 1$) and matrix metalloproteinase 9 (MMP-9) were studied in all patients. High-resolution MRI was applied for 15 patients with an assessment of late gadolinium enhancement (LGE; 15-18 min after gadolinium introduction, dose 0.15 mmol/kg), scar zone volume percentage and its ratio to the grey zone.

Results: Total number of ventricular ectopic beats during Holter monitoring in DCM patients was 627 [35; 5246] beats/day. There was no significant difference in MMP-9 level between two groups: 944.3 [557.4; 1506] in DCM patients and 786.2 [434.8; 1331] ng/ml in healthy controls. Although insignificant, there was tendency to a lower level of TGF-$\beta 1$ in DCM patients: 100.2 [47.44; 141.3] ng/ml vs. 148[50.9; 160.4] ng/ml in healthy controls ($p = 0.11$). In DCM patients level of TGF-$\beta 1$ was associated with more frequent ventricular bigeminy and episodes of ventricular tachycardia ($r = 0.47$ and 0.36 respectively; $p < 0.05$). The presence of LGE in patients with DCM was accompanied by a higher level of MMP-9 ($p = 0.076$). According to high resolution MRI volume percentage of the scar zone was 2.7% [0.8; 10.8]. Its association with higher level of MMP-9 was also observed ($r = 0.55$; $p < 0.05$). Volume percentage of the scar zone and it's ratio to the grey zone correlated with the more frequent ventricular pairs ($r = 0.66$; 0.46 respectively; $p < 0.05$).

Conclusion: In the present study we showed association between the extent of fibrosis according to high resolution MRI and the laboratory markers of fibrosis. Both of them were connected to ventricular arrhythmia prevalence. Received data support the concept of myocardial fibrosis importance in ventricular arrhythmia development. Described parameters may be useful for risk stratification of sudden cardiac death in this group of patients and require further investigation.

P1068

Dilated cardiomyopathy with midrange ejection fraction at diagnosis: characterization and natural history

M Merlo[1]; P Gentile[1]; M Marco Gobbo[1]; B Pinamonti[1]; F Ramani[1]; G Barbati[1]; M Gigli[1]; D Stolfo[1]; G Sinagra[1]
[1]University Hospital Riuniti, Cardiovascular department, Trieste, Italy

Background: Heart Failure comprises a wide range of patients classified according to the Ejection Fraction (EF). Patients with a Left Ventricular EF (LVEF) in the range of 40–49% represent a 'grey area', defined as mid–range EF (HFmrEF). Few data on the characteristics and outcomes of HFmrEF patients are available, mostly in the specific group of dilated cardiomyopathy (DCM).

Aims: To define characteristics, evolution and prognosis of DCM patients with HFmrEF at diagnosis.

Methods and results: From 1988 to 2013 we analysed 959 idiopathic DCM patients consecutively enrolled. One hundred and seventy–five (18%) fulfilled the criteria for HFmrEF, while 637 patients had a EF'40%. At baseline, compared with patients

with reduced EF (HFrEF), HFmrEF presented features of a less advanced disease: lower NYHA III–IV classes (5 vs. 29% in HFmrEF vs. HFrEF group respectively, p<0.001), lower left bundle brach block (20 vs. 35%, p = 0.001), less left ventricular end–diastolic volume (69(59;82) vs. 100(81;123) ml/m2, p<0.001), lower rate of right ventricular dysfunction (9 vs. 21%, p = 0.003), of moderate–severe mitral regurgitation (13 vs. 42%, p<0.001), and of restrictive pattern (5 vs. 37%, p<0.001). Furthermore, during a median follow–up of 50(10;118) months, HFmrEF group presented a lower rate of all–cause mortality/heart transplantation (9.1% vs. 36% in HFrEF, p<0.001) and of sudden cardiac death or malignant ventricular arrhthmias (4.5% vs.15.2%, p<0.001). Finally 29 out of 175 HFmrEF patients (17%) evolved to HFrEF after a median follow–up of 70(25;43) months, consistently worsening their long–term prognosis.

Conclusions: HFmrEF identifies a consistent subgroup of DCMs diagnosed in an earlier stage and presenting an apparent better evolution. However, some HFmrEF DCMs patients evolve into HFrEF despite medical therapy and this evolutions leads a worse prognosis.

P1069

Continuous positive airway pressure (CPAP) effect on blood pressure in patients with obstructive sleep apnea syndrome (OSAS)

G Giorgiana Dediu[1]; A Balaceanu[1]; A Iancu[2]; G Aron[1]; S Rujinski[3]; M Bogdan[3]; I Dina[1]; C Diaconu[4]

[1]Emergency Clinical Hospital St John, Internal Medicine, Bucharest, Romania; *[2]University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*; *[3]"Marius Nasta" Institute Of Pneumology, Bucharest, Romania*; *[4]Emergency Clinical Hospital Floreasca, Internal Medicine, Bucharest, Romania*

Introduction: Hypertension is present in 50% of patients with OSAS, many cardiologists claiming the need to evaluate the dipper / nondipper profile of patients. Currently several case-control studies showed the antihypertensive effect of CPAP therapy on hypertensive patients with OSAS.

Objectives: To assess the effect of CPAP on blood pressure in patients with OSAS.

Materials and methods: Interventional prospective study that enrolled 52 patients with OSAS. In all these patients, blood pressure was measured at the moment of inclusion in the study. From these 52 patients, 20 were hypertensive. Patients were divided into 2 groups: group A who received CPAP (24 patients) and group B without CPAP (28 patients). Patients were foloowed up at 3 and 6 months.

Results: 32 patients with OSAS had no hypertension, 20 patients were hypertensive. 7 patients with grade 3 hypertension had severe OSAS. From the group of hypertensive patients, 10 patients received CPAP (from group A) (from those 5 have severe OSAS and grade 3 hypertension) and 10 did not receive CPAP (from group B). 3 months after enrollment we observed that no patient from the CPAP group had grade 3 hypertension, from those with grade 2 hypertension one moved in the normal high blood pressure class. At six months, we observed that normotensive patients who received CPAP had the mean systolic blood pressures value decreased by 2 mm Hg.

Conclusion: In our study, 38,46% from the patients with OSAS were hypertensives. CPAP decreased the blood pressure values in hypertensive patients with severe OSAS. Even normotensive patients with OSAS had a reduction of blood pressure values with CPAP.

P1070

Features of left ventricular remodeling in patients with hypertensive cardiomyopathy with and without metabolic syndrome

K Chernyshova[1]; V Bondar[1]; E Yakimenko[1]; V Tbileli[1]

[1]Odessa National Medical University, Department of internal medicine, Odessa, Ukraine

Left ventricular remodeling (LVR) is the most characteristic cardiac damage in patients with hypertensive cardiomyopathy (HC) and influences on the course and prognosis. Left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular complications. However, the structural and functional features of cardiac remodeling in patients with HC and concomitant metabolic syndrome (MS) have been insufficiently studied. The purpose of our research was to study the characteristics of cardioremodeling processes in patients with arterial hypertension and hypertensive cardiomyopathy in the presence and absence of metabolic syndrome. We examined 128 hypertensive patients with HC and MS, which formed the basic group, and 112 hypertensive patients with HC without MS, which formed the control group. Patients in both groups were performed echocardiography with assessment of basic indicators and types of LV remodeling. Assessment of left ventricular diastolic function was performed in pulsed mode doplerEchoCG. Statistical significance of differences was determined using T-test and Fisher's criteria (φ). The results obtained exhibit more expressed signs of LVH by echocardiography data in the basic group compared to control ($p < 0,01$), the main indicators of LVH in hypertensive patients with HC and MS were: interventricular septum thickness was ($1,30 \pm 0,01$) cm, thickness of left ventricular posterior wall - ($1,26 \pm 0,01$) cm, left ventricular mass index - ($144,3 \pm 5,23$) g/m2. These results are related to chronic increasing of blood pressure, hormonal and metabolic disorders in MS. In hypertensive patients with HC and MS violations of left ventricular geometry were absent in 8 patients (6 %) compared with 15 patients in the control group (13 %) ($\varphi = 1,72$, $p < 0,05$). In patients of control group the incidence of concentric LVH was significantly higher compared to hypertensive patients with HC and MS, 67 people (60 %) compared with 60 patients (47 %), respectively ($\varphi = 1,85$, $p < 0,05$). However, eccentric LVH significantly was more frequent in basic group compared with the control, 56 (44 %) and 19 (17 %) patients, respectively ($\varphi = 4,25$, $p < 0,01$). Concentric left ventricular remodeling most rarely encountered in both groups: 11 patients (10 %) versus 4 (3 %), respectively ($\varphi = 2,09$, $p < 0,05$). Hypertensive cardiomyopathy in combination with metabolic syndrome is accompanied by more expressed cardioremodeling processes. Violation of LV geometry was significantly more frequent in hypertensive cardiomyopathy with metabolic syndrome. In the structure of violations as eccentric and concentric type of hypertrophy are equally often found. In addition, the presence of concomitant metabolic syndrome causes a more expressed diastolic dysfunction.

P1071

Plasma microRNA-155 as biomarker of left ventricular hypertrophy in chronic kidney disease patients. Preliminary study.

D Klimczak[1]; T Pilecki[2]; D Zochowska[2]; A Wirkowska[2]; M Kuch[3]; L Paczek[2]

[1]Medical University of Warsaw, Division of Heart Failure and Cardiac Rehabilitation , Warsaw, Poland; *[2]Medical University of Warsaw, Department of Immunology, Transplant Medicine and Internal Diseases. Transplantation Institute, Warsaw, Poland*; *[3]Medical University of Warsaw, Department of Cardiology, Hypertension and Internal Medicine, Warsaw, Poland*

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Introduction: Emerging evidence indicates that microRNA play important role in regulation of myocardial growth and repair. Chronic kidney disease (CKD) patients are at increased risk of hypertension and left ventricular hypertrophy compared to the rest of population and may benefit from early diagnosis and interventions. One of prohypertrophic pathways includes angiotensin II acting via angiotensin II receptor type 1 (AGTR1). It has been observed that miR-155 negatively regulates the expression of that receptor. Therefore miR-155 expression level may vary depending on the presence of myocardial hypertrophy.

Aim: To assess the expression of microRNA-155 in plasma of chronic kidney disease patients and evaluate its relationship with left ventricular hypertrophy (LVH).

Material and Methods: We have enrolled 26 patients with stable CKD stage 2-5 (age:60,12 males) and 26 healthy age-matched control subjects (age 54,10 males) in the study. Quantification of plasma miRNA was performed with the use of real time quantitative polymerase chain reaction (RT-qPCR). Relative expression of investigated miRNAs compared with healthy volunteers was calculated using the delta delta Ct method. As the endogenous control we have chosen U6 snRNA. In every patient the left ventricular mass index (LVMI) was calculated based on the transthoracic echocardiography measurements. As LVH we have defined LVMI above 95 g/m2 in women and 115 g/m2 in men. Additionally, we performed 24-hour ambulatory blood pressure measurement in every participant.

Results: The expression of miRNA-155 was upregulated in CKD patients compared to control group (median expression relative to U6 snRNA was 3,39 (Q1-Q3=1.81-6.64). CKD patients had higher LVMI than control subjects (mean 133vs104 g/m2, p = 0.002), higher serum creatinine (1,9 vs 0,8 mg/dl, p = 0.0001), higher average day and night systolic blood pressure, SBP (129vs120, p = 0.008). The groups did not differ significantly in terms of age (p = 0,13) and sex. None of the patients had symptomatic heart failure. Due to non-normal distribution of miRNA-155 expression, we have performed a log transformation of its values. We have observed a trend towards positive correlation between log miR-155 and LVMI (r=0.18) but with no statistical significance (p = 0.37). Patients with LVH were older (62vs 8, p = 0.004) had lower GFR (51vs79 ml/min/BSA, p = 0.003), higher average SBP (127vs120 mmHg, p = 0.04), lower HDL (56vs71 mg/dl, p = 0.02), higher triglycerides level (145vs89 mg/dl, p = 0.001). The LVMI correlated significantly with GFR (r= -0.46,p = 0.001), and age (r=0.32, p = 0.023).

Conclusion: In this preliminary study plasma miR-155 was not associated with LVMI. This may be due to pleiotropic action of miR-155 and heterogenicity of CKD patients. As the study group is relatively small, further studies are necessary to confirm that results. Traditional risk factors seem to be more reliable indicators of LVH in CKD patients so far.

P1072

Circulationg fibrosis biomarkers and transcriptome profile in patients with hypertrophic cardiomyopathy

V Zaitsev[1]; A Runov[2]; M Vonsky[2]; A Gurshchenkov[1]; A Ryzhkov[1]; O Moiseeva[1]; L Mitrofanova[1]

[1]Almazov Federal Heart Centre, Saint Petersburg, Russian Federation; *[2]Institute of Cytology RAS, Saint Petersburg, Russian Federation*

Introduction: There are limited data on the prognostic significance of fibrosis in patients (pts) with hypertrophic cardiomyopathy (HCM). The aim of the study was to evaluate profile of circulating fibrosis biomarkers and candidate gene expression in myocardial tissues depending on the severity of myocardial remodeling in pts with obstructive HCM.

Materials and Methods: 15 pts (56,1 ± 9,7 yrs m:f 6:9). with obstructive HCM after septal myectomy were included. 10 pts without heart pathology were examined as control group (57.6 ± 0.8 yrs). ECHO, cardiac MRI with contrast enhancement, histological and immunohistochemical biopsy analysis, circulating fibrosis biomarkers (TGFß1, MMP-2,9, TIMP-1, galectin-3, sST2, CITP, PICP, PIIINP, NT-proBNP) were performed for all pts. Six candidate genes (MMP2, MMP9, TIMP1, TGFβ1, Gal3, SSTR2) were selected for the study. mRNA content was determined by quantitative PCR after RT-qPCR.

Results: Pts with HCM have max LVOT gradient (85 ± 20 mm Hg), max wall thickness (23 ± 6 mm), IMMLV (169 ± 72 g/m2) and late gadolinium enhancement (LGE) according MRI data. Increased serum PICP, PIIINP levels were revealed in pts with HCM in comparison with the controls. A positive correlation was found between NT-proBNP, galectin-3 and sST2 serum levels. Upregulated expression of MMP2, TIMP1, TGFß1, Gal3 genes was detected, while MMP9 and SSTR2 gene expression was downregulated in HCM myocardial tissue. We also found that downregulated MMP9 mRNA expression was associated with elevated serum MMP-9 level.

Conclusions: Better understanding of pathological processes in the myocardial tissue leading to fibrosis development might provide a clue for novel arrhythmia and heart failure outcomes biomarker discovery.

Clinical characteristics of patients

	Patients with HCMM± n=15	The control groupM± n=10
Galectin-3, ng/ml	8,70±1,28	6,54±2,14
MMP-2,ng/ml	275 (228;369)	306(255;323)
MMP-9,ng/ml	1483(1054;1827)	531(227;647)
TIMP-1, ng/ml	153,5±38,3	148,6±41,2
The ratio MMP-9/ TIMP-1	9,8(7,9;11,3)	5,2(3,2;9,9)
CITP, ng/ml	0,635±0,365	0,444±0,138
PICP, ng/ml	39(28;62)	15(14;20)
PIIINP,ng/ml	11,9(11,0;13,4)	6,6(2,5;8,5)
TGF-β1, ng/ml	20,2±9,3	15,8±5,1
sST2, ng/ml	26,2±4,8	20,3±3,7

P1073

Pregnancy hypertension is alternative pathway for the development of heart failure.

S Bele[1]; A Rrugia[2]; E Petrela[3]; A Abazaj[2]

[1]University Hospital"Queen Geraldine" Tirana, Tirana, Albania; *[2]University Hospital"Koco Glozheni" , Tirana, Albania*; *[3]University Hospital Centre "Mother Theresa",Tirana, Tirana, Albania*

Background. The combination of increased pressure and volume in pregnancy hypertension explains may be the tendency to eccentric hypertrophy of the LV but it may represent the early manifestation of a cardiomyopathic process

Purpose: To assess heart's structural effects of pregnancy hypertension in the third trimester of pregnancy.

Methods: The study involved 250 pregnant women in the third trimester of pregnancy without hypertension and another disease before pregnancy. ECG, BP, weight gain, BMI, laboratory analyses have all been carried out. Echocardiographic evaluations were performed. Results: From the analysis of echocardiographic data resulted that in pregnancy hypertension eccentric and concentric ventricular remodelling occur with diastolic dysfunction and left atrial size is increased. Women with hypertension during pregnancy had significant altered diastolic function compared to normotensive, We found lower E/A ratio (p = 0,046),longer DTE (p = 0,003) and significantly longer IVRT (p < 0.001) lower Vp(p = 0.012) ,increase E/e′s ratio (p < 0.001). and E/e′l ratio (p < 0.001). LV end-diastolic(168 ± 29) and end-systolic(69 ± 1) volume increased during hypertensive pregnancy to normotensive (151 ± 16/ 58 ± 9); p < 0.001) but these women had normal systolic function. A significant statistical relation was found between LAV and geometric remodulation (r = -0.215, p = 00001) as well as between LAV and diastolic dysfunction (r = -0.267, p < 0.001).

Conclusions: In the present study, the EH of the LV may represent the early manifestation of a cardiomyopathic process. This alternative pathway for the development of heart failure is supported by studies that have demonstrated eccentric hypertrophy to be associated with more severe systolic dysfunction compared with concentric hypertrophy. In spite of the fact that this has not been observed in our cases, the possibility cannot be excluded that this form of the geometric remodeling might cover up a mute form of LV's contractile insufficiency.

P1074

Polymorphism of aldosterone synthase gene and left ventricular hypertrophy in patients with arterial hypertension and hypertensive cardiomyopathy

V Vadym Bondar[1]; K Chernyshova[1]; D Oliynyk[1]; V Vasilets[1]; N Chumachenko[1]; E Kobeleva[1]; V Tbileli[1]

[1]Odessa National Medical University, Department of internal medicine, Odessa, Ukraine

The activation and remodeling of renin-angiotensin-aldosterone system is very important in the pathogenesis of development and progression of hypertensive cardiomyopathy (HC) in patients with arterial hypertension (AH). The influence of polymorphisms of aldosterone synthase gene on aldosterone synthesis and degree of left ventricular hypertrophy (LVH) at the present time is actively studied.

The purpose of the study: the analysis of genotype distribution of the polymorphism C-344T of aldosterone synthase gene and assessment of degree of left ventricular hypertrophy depending on the presence of "normal" or "pathological" genotypes of this polymorphism in patients with arterial hypertension and hypertensive cardiomyopathy in Ukrainian population.

Materials and Methods: we examined 240 patients with AH and HC (ESC/ESH 2013). The analysis of polymorphism C-344T aldosterone synthase gene was determined by PCR. Subsequently, the patients were divided into two subgroups depending on the presence of "normal" (CC) or "pathological" (CT + TT) genotypes. In each subgroup we additionally studied the degree of LVH by echocardiography.

Results: and discussion: in the surveyed group of patients with AH and HC the frequency of "normal genotype" (CC) was (47,5%/114) patients, "pathological genotype" (CT + TT) – (52,5%/126), (p = 0,35). Subgroup 1 (CC) included 114 patients, subgroup 2 (CT + TT) - 126 patients. According to echocardiographic data, in subgroup 2 ("pathological genotype" CT + TT) IMMLV was (142,2 ± 3,4) g/m2, in subgroup 1 ("normal genotype" CC) IMMLV was (130,4 ± 3,2) g/m2, (p = 0,015). The presence of "pathological" genotype was accompanied by significantly more expressed left ventricular hypertrophy and high IMMLV.

Thus, in the surveyed group of patients with arterial hypertension and hypertensive cardiomyopathy in Ukrainian population the "normal" and "pathological" genotypes of polymorphisms C-344T of aldosterone synthase gene were observed with almost equal frequency. The presence of "pathological" genotype is associated with more expressed left ventricular hypertrophy and can be used to predict the severity of hypertensive cardiomyopathy in patients with arterial hypertension.

P1075

Acute left heart failure on pic hypertensive: impact afterload contractile function parameters left ventricular

NABILA Taleb Bendiab[1]; M Boucif Ghomri[1]; A Meziane Tani[1]

[1]University Hospital of Tlemcen, cardiologie, faculty of medicine, University of Tlemcen, Tlemcen, Algeria

Introduction: The appearance of a hypertensive acute pulmonary edema is often sudden , dramatic, and life-threatening. In acute heart failure with hypertensive crisis , signs and symptoms of heart failure are accompanied by high blood pressure and left ventricular systolic function is often preserved.

Materials and Methods: Prospective descriptive study of making a complete echo cardiographic analysis of systolic diastolic function in a total of 35 patients admitted for USIC crisis of acute pulmonary edema in hypertensive origin with a systolic blood pressure greater than 16mmHG and this during and after the crisis.

Results: Of the total , 22 were men and 13 women and the mean age was 65 + / - 12 years. Systolic blood pressure during the was 196 + / - 18 mmHg and after treatment 132 + / - 11.l. Pulse pressure was 70 mm Hg in sup 75% of our population. LVEF during the acute pulmonary edema was 49 % + / - 10 and after the disappearance of symptoms and pulmonary congestion it was 48 % + / - 8. Filling pressures were elevated in almost all patients during the crisis, the calculation of LV mass showed LVH in 28 patients often concentric characters.

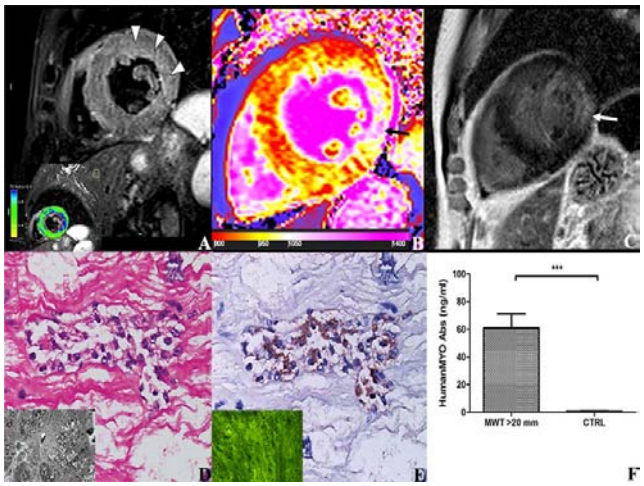
Discussion: We found a similar LVEF during and after the crisis , elevated pulse pressure was observed in the majority of patients during the crisis Transient diastolic

heart failure related to the sudden rise of the post load is almost constant. because transient systolic heart failure and / or mitral regurgitation were rare in these patients.
Conclusion:: The occurrence of hypertensive acute pulmonary edema may be life-threatening. The Doppler echocardiography is systematic and , as in any acute heart failure, if possible within 48 hours, so as not to miss a transient systolic dysfunction or ischemic mitral regurgitation.

P1076
Immune-mediated myocarditis in fabry disease cardiomyopathy

AF Frustaci[1]; RV Verardo[2]; CG Grande[2]; NG Galea[1]; IC Carbone[1]; MA Alfarano[1]; MAR Russo[3]; CC Chimenti[1]
[1]Sapienza University, Department of Cardiovascular, Respiratory, Nefrologic and Geriatric Sciences, Rome, Italy; *[2]INMI-IRCCS "Lazzaro Spallanzani", Laboratory of Cellular and Molecular Cardiology, Rome, Italy*; *[3]San Raffaele Pisana Hospital IRCCS, MEBIC CONSORTIUM, Rome, Italy*

Background: Glycosphingolipid accumulation in Fabry cells generates a pro-inflammatory response that may influence disease evolution and responsiveness to enzyme replacement therapy (ERT).
Purpose: Evaluate incidence, mechanism and impact of myocarditis in Fabry disease cardiomyopathy (FDCM).
Methods: Myocarditis, defined as CD3+T-lymphocytes > 7/mm2 associated with necrosis of glycolipid-laden myocardiocytes, was retrospectively evaluated in endomyocardial biopsies of 78 patients with FDCM: 13 with maximal wall thickness (MWT) < 11 mm (Group 1), 17 with 11-15 mm (Group 2), 30 with 16-20 mm (Group 3), 18 with MWT > 20mm (Group 4). Myocarditis was investigated by polymerase chain reaction (PCR) for cardiotropic viruses, serum anti-heart, anti-myosin, antinuclear antibodies and cardiac magnetic resonance (CMR).
Results: Myocarditis was recognized at histology in 48 of 78 patients with FDCM: 38% of Group 1, 41% of Group 2, 66% of Group 3 and 72 % of Group 4. Myocarditis was characterized by positive anti-heart, anti-myosin and anti-nuclear autoantibodies and negative PCR for viral genomes. CD3+ cells/mm2 correlated with myocyte necrosis, anti-myosin autoantibodies' titer and MWT ($p < 0.001$; r=0.7912, $p < 0.001$; r=0.8476, $p < 0.001$ r= 0.6133 respectively). CMR showed myocardial edema in 24 out of 78 patients (31%): 0% of Group 1, 23% of Group 2, 37% of Group 3 and 50% of Group 4.
Conclusions: Myocarditis is detectable at histology in up to 56% of patients with FDCM. It is immune-mediated and correlates with disease severity. It can be disclosed by anti-heart/anti-myosin auto-antibodies and in advanced phase by CMR. It may contribute to FDCM progression and ERT resistance.



Figure

P1077
T2 mapping by cardiovasular magnetic resonance in acute and recovered myocarditis: potential role in clinical surveillance

A Lota[1]; R Wassall[1]; A Scott[2]; R Wage[1]; G Smith[1]; A Tsao[2]; B Halliday[1]; JS Ware[2]; P Gatehouse[1]; D Firmin[1]; SA Cook[2]; JG Cleland[2]; DJ Pennell[1]; SK Prasad[1]
[1]Biomedical Research Unit of Royal Brompton London, London, United Kingdom; *[2]Imperial College London, London, United Kingdom*

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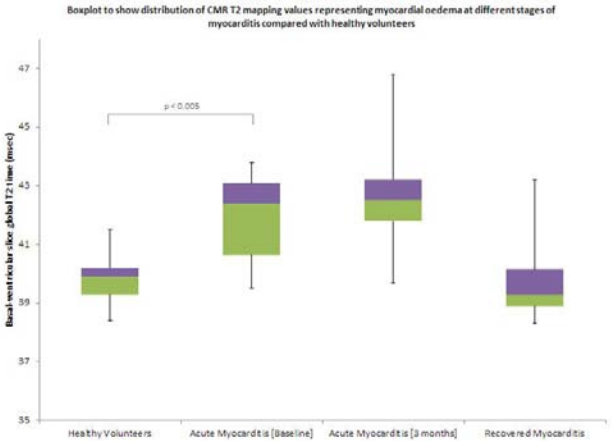
Background: Cardiovascular magnetic resonance (CMR) is a versatile imaging modality that allows assessment of myocardial oedema suggestive of active inflammation. Ongoing inflammation due to viral myocarditis is implicated in the progression to inflammatory dilated cardiomyopathy in one third of cases. Conventional CMR imaging relies upon qualitative visual analysis of T2-weighted images, but recent advances in T2 mapping have improved sensitivity and allow quantitative analysis on a pixel-wise level. In this study, we aimed to evaluate the role of T2 mapping to detect low-levels of ongoing cardiac inflammation at different stages of disease.
Method: Patients were recruited prospectively with confirmed acute myocarditis (chest pain, troponin elevation, unobstructed coronary arteries and CMR evidence of myocardial oedema; 11 inpatients, mean age 34±10 years, all male), and retrospectively with a past history of confirmed acute myocarditis (12 patients, mean age 35±13 years, all male, time from acute presentation 5.7±3.9 years). All patients underwent CMR on a 3T system (MAGNETOM Skyra, Siemens), and troponin-I and BNP were measured on the same day. Prospective patients were additionally re-assessed at 3-months. T2 mapping was performed using T2-prepared balanced steady-state free-single shot-images with 4 T2-prep times (0–75ms). TE/TR=1.1/2.5ms, flip-angle=35o, GRAPPA x2, 6/8ths partial Fourier, 1.9x2.2x8mm resolution, 360x285mm field of view. A global region of interest was manually drawn by a single blinded observer in the basal ventricular slice. Results were compared with 9 healthy volunteers (mean age 27±6 years, 56% male).
Results: In patients with acute myocarditis, mean global T2 was 42±1.4msec compared to 40±1.3msec in healthy volunteers ($p < 0.005$). No difference was found between T2 values at presentation and 3-month follow-up ($p = 0.1$) despite normalisation of troponin in all patients at 3 months. In the retrospective group, mean T2 had normalised to 40±1.5msec with preserved ventricular function, comparable to healthy volunteers. Unlike troponin, BNP remained mildly elevated in 3 patients (mean 23ng/mL) at 3 months, but none in the retrospective group.
Conclusion: Our findings suggest that T2 values remain persistently elevated at 3-months following acute presentation despite normalisation of cardiac troponin levels. Persistent inflammation is known to increase risk of relapse. Further investigation is required to assess whether T2 mapping provides a useful biomarker in this small but important subset of patients.



P1078
The effectiveness of immunosuppressive therapy in the virus-negative and virus-positive patients with lymphocytic myocarditis

OV Blagova[1]; AV Nedostup[1]; EA Kogan[1]; VA Sulimov[1]
[1]I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation

Purpose: to study short-term results and outcomes of antiviral and immunosuppressive therapy (IST) in patients with severe virus-positive and virus-negative myocarditis.

Methods: in 127 patients (81 male, 46.7 ± 12.7 years) with echocardiographic signs of dilated cardiomyopathy (mean left ventricle, LV, end-diastolic diameter, EDD, 6.3 [5.9; 7.0] cm, end-diastolic volume, EDV, 189.7 ± 73.9 ml, end-systolic volume, ESV, 135.8 ± 63.9 ml, LV ejection fraction, EF, 29.3 ± 10.7%, systolic pulmonary artery pressure, SPAP, 43.6 ± 16.4 mm Hg) myocarditis was verified by morphological and/or clinical study. For this purpose were performed morphological study of myocardium (35 endomyocardial biopsies, 12 intraoperative biopsies, 4 examination of explanted heart and 10 autopsies); anti-heart antibodies measurement as well as virus detection in the blood and myocardium (real-time PCR), Echo-CG, scintigraphy (n = 46), cardiac CT (n = 93), MRI (n = 29), coronary angiography (n = 53). We have identified two groups: patients with viral genome (parvovirus B19 and / or herpetic viruses) in the blood / myocardium (n = 52) and patients without virus genome (n = 75). They differ in LV EDD (6.7 ± 0.8 v 6.4 ± 0.7 cm), LV EF (25.9 ± 11.2 v 31.5 ± 9.8%) and SPAP (47.5 ± 16.3 v 40.7 ± 15.9 mm Hg), p < 0,01. The diagnosis of myocarditis was morphologically verified in 73.1% of virus-positive patients and in 30.7% of virus-negative patients.
Results: Pure viral myocarditis was diagnosed only in 7% of patients, immune - in 59%, mixed - in 34%. The anti-heart antibody level was equally high and did not differ significantly from the virus and the virus-negative-positive patients. Antiviral therapy (acyclovir, gancyclovir, IV immunoglobulin) allowed to achieve virus elimination from the blood in 81% of patients. IST was administered in 95 patients (34 virus-positive and 61 virus-negative): steroids (n = 63, 30 [22; 40] and 24 [16; 32] mg/day), hydroxychloroquine (n = 45, 200 mg/day), azathioprine (n = 8, 100 [75; 150] mg/day). At baseline IST and non-IST patients were differed by NYHA class (3 [2; 3] v 3 [3; 4]) and LV EF (30.3 ± 10.6 v 25.3 ± 9.2%), p < 0,05. The mean follow-up was 12 [6; 20] month. Significant (p < 0.05) decrease of LV EDD (6.5 ± 0.7 to 6.2 ± 0.7), SPAP (41.5 ± 16.2 to 34.4 ± 12.2), increase of LV EF (30.3 ± 10.6 to 39.2 ± 11.9), and significantly lower mortality (16.8% and 56.3%, p < 0.001; RR of all-cause mortality 0.55 (95%CI 0.38-0.80)) were found only in IST group. Significant changes of LV size and LVEF due to IST were achieved both in virus-negative and virus-positive patients. Virus-positive patients had significantly higher mortality (42.3 v 16.0%, p < 0.01, RR of all-cause mortality 2.64 (95% CI 1.44-4.86)) and the need for surgical treatment (67.7% and 37.3%, p < 0.01).
Conclusions: IST in patients with myocarditis is effective both with positive and negative viral genome in blood/myocardium; the presence of virus reduced effectiveness of therapy and was unfavorable prognostic factor.

P1079

Regulation of serum sRAGE shedding proteases ADAM-10 and MMP-9 in myocarditis and dilated cardiomyopathy

F Dahlem[1]; SR Simina-Ramona Selejan[1]; O Zamyatkin[1]; K Klingel[2]; R Kandolf[2]; M Boehm[1]; I Kindermann[1]
[1]Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany; *[2]University Hospital of Tübingen, Molecular Pathology, Tübingen, Germany*

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Purpose: Myocarditis can result in dilated cardiomyopathy and heart failure. RAGE (receptor for advanced glycation end products) plays a central role in multiple inflammatory and autoimmune diseases generating oxidative stress and inflammatory responses. Soluble RAGE (sRAGE) comprising only the RAGE ectodomain mainly derives from proteolytic RAGE cleavage by the peptidase ADAM-10 (A Desintegrin and Metalloprotease-10) and MMP-9 (Matrix Metalloproteinase-9), which both can be inhibited by TIMP-1 (Tissue Inhibitor of Matrix Metalloproteases-1). sRAGE is regarded as an anti-inflammatory decoy receptor neutralizing RAGE ligands. Inhibiting RAGE activation via sRAGE has been shown to attenuate experimental autoimmune myocarditis. The aim of this study was to evaluate the serum levels of active ADAM-10 and MMP-9, their inhibitor TIMP-1 and sRAGE levels in patients with myocarditis and post-inflammatory dilated cardiomyopathy.
Methods: Serum samples from patients with endomyocardial biopsy proven acute or chronic myocarditis (n = 20) and patients with post-inflammatory dilated cardiomyopathy (n = 20) were analyzed for sRAGE, active ADAM-10, active MMP-9 and TIMP-1 by Western blot. Healthy volunteers served as controls (n = 20; age-matched). Endomyocardial biopsies were investigated by histopathological analysis and immunohistochemistry; viral genomes were detected by PCR and in situ hybridization.
Results: sRAGE serum levels were significantly decreased in patients with myocarditis as compared to healthy controls (46% decrease). Active ADAM-10 and active MMP-9 were also significantly decreased in myocarditis (-55% and -34% decrease versus healthy controls). TIMP-1 showed an opposite regulation with significatly increased serum levels in patients with myocarditis (50% increase versus healthy controls). In post-inflammatory DCM ADAM-10 and MMP-9-activity was restored, TIMP-1 levels decreased to levels similar to controls and sRAGE levels were significantly improved.
Conclusion: Myocarditis is associated with decreased levels of anti-inflammatory serum sRAGE, with decreased levels of sRAGE-producing active proteases ADAM-10 and MMP-9 and increased levels of their inhibitor TIMP-1 as a possible mechanism affecting sRAGE serum levels in this pathological setting. These new observations might help develop new diagnostic and therapeutic strategies in preventing autoimmune myocarditis.

P1080

Changes in left ventricular ejection fraction in the first year after the diagnosis of inflammatory cardiomyopathy and its prognostic significance

J Krejci[1]; P Hude[1]; E Ozabalova[1]; D Mlejnek[1]; H Poloczkova[1]; V Zampachova[1]; I Svobodova[1]; K Benesova[2]; J Jarkovsky[2]; L Spinarova[1]
[1]St. Anne´s University Hospital, Masaryk University, Brno, Czech Republic; *[2]Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic*

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Introduction: An improvement in left ventricular (LV) systolic function is seen in approximately 60% of patients with biopsy-proven inflammatory cardiomyopathy (ICM). The improvement in LV function should be associated with a better prognosis.
Objective: To evaluate changes in LV ejection fraction (LVEF) during the first year after the diagnosis of ICM and to assess the prognostic significance of early LVEF changes.
Patients and methods: 86 patients with biopsy proven ICM (77% men, 23% women), LVEF at diagnosis 24.3 ± 7.2%; mean age 44.5 ± 12.6 years, NYHA 2.5 ± 0.6, time from onset of symptoms to diagnosis was 2.3 ± 2.2 months. ICM was defined as the presence 14 LCA + cells/mm2 and / or >7 CD3 + cells/mm2 of the biopsy sample. Echocardiographic controls were carried out at the time of diagnosis (V0) and then in third (V3), sixth (V6) and twelfth (V12) months after diagnostic endomyocardial biopsy.
Results: LVEF improved in the 3rd month to 35.8 ± 9.5%, at 6 months to 39.3 ± 12.1% and in the 12 months to 42.2 ± 12.1% (all p < 0.001 versus baseline). Improvement in LVEF between the controls V0 and V3 were 11.4 ± 9.7% (p < 0.001) and created 63% of the overall improvement in the first year. LVEF increased by 3.8 ± 7.3% (p < 0.001) between controls V3 and V6, and by 1.8 ± 7.7% (p = 0.070) between the V6 and V12 visits. LVEF value at control V3 was a significant prognostic factor for occurrence of the combined endpoint (HR: 0.43; 95% CI: 0.28 to 0.66) based on the 10% increase in LVEF. Similarly, LVEF improvement by 10% between controls V3 and V0 has emerged as the significant prognostic factor (HR 0.51; 95% CI: 0.34 to 0.76).
Conclusion: LVEF improvement occurs dominantly in the first 3 months after the diagnosis which makes almost 2/3 of the entire improvement in one year follow-up. Absolute value of LVEF at 3-month control and the change of LVEF in first three months were proved as the predictors of long-term prognosis.

P1081

Immunomodulatory treatment reduces intramycardial inflammation in patients with virus-negative inflammatory cardiomyopathy resulting in an improvement of LVEF in long-term follow-up: A 10 years observ

F Felicitas Escher[1]; U Kuehl[1]; D Lassner[2]; W Poller[3]; C Tschope[1]; B Pieske[1]; H-P Schultheiss[2]
[1]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; *[2]Institute of Cardiac Diagnostics and Therapy (IKDT), Berlin, Germany*; *[3]University Heart Center Hamburg, Hamburg, Germany*

Aim: To analyse the long-term outcome after immunosuppressive treatment of patients with virus-negative chronic myocarditis or inflammatory cardiomyopathy (CMi).
Methods: and Results: We investigated 114 patients with endomyocardial biopsy (EMB)-proven virus-negative chronic myocarditis or 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 (median 10.5 month [95% Confidence Interval (CI) 11.69 – 59.16]). At follow-up, the patients showed a significant improvement of left ventricular ejection fraction (LVEF) compared to baseline after 6 month period (LVEF rising from 44.6 ± 17.3% to 51.8 ± 15.5%, p = 0.006) and in the long-term follow-up (LVEF 52.1 ± 15.6%, p = 0.006). Simultaneously, EMB-analysis revealed significant reduction of quantified inflammatory infiltrates (CD3 + cells 16.03 ± 29.09 to 8.2 ± 9.0/mm^2, p = 0.002; CD2 + cells 12.62 ± 20.01/mm^2 to 6.61 ± 8.47/mm^2, p = 0.001; perforin + cells 3.94 ± 4.65/mm^2 to 1.03 ± 1.47, p = 0.0001), and cell-adhesion molecule HLA-1 (9.91 ± 5.55/Area Fraction (AF) to 6.65 ± 2.81/AF, p = 0.0001). In a subgroup analysis, Patients with initial LVEF ≤45% (n = 53) significantly increased with LVEF at follow-up (29.3 ± 8.8% to 41.7 ± 13.2% to 42.1 ± 13.1%, p < 0.0001, Group I), defined as CMi. Patients with initial LVEF >45%-60% (n = 25) significantly improved further or recovered completely,

regarding LVEF (53.0 ± 3.6% to 59.0 ± 9.4% to 59.8 ± 10.0%, p = 0.03, Group II). Patients with initial LVEF >60% (n = 36) remained stable and did not deteriorate over long-term follow-up (68.8 ± 6.7% to 67.5 ± 10.9% to 68.8 ± 10.7%, p = 0.5, Group III). Group II and III were defined as chronic myocarditis.
Conclusions: In patients with virus-negative chronic myocarditis or CMi we could show the effectiveness and beneficial effects of immunosuppressive treatment. Based on the normalization of the inflammatory process LVEF improvement is lasting for a long-term period of time.

P1082
Predictors for adverse events during hospitalization in patients with clinically suspected acute myocarditis: right ventricular systolic function and T wave inversion

D-G Dae-Gyun Park[1]; M-S Park[1]; W-W Seo[1]; S-E Kim[1]; J-H Lee[1]; K-R Han[1]; D-J Oh[1]
[1]Hallym University Kangdong Sacred Heart Hospital, Seoul, Korea Republic of

Background: Previous studies on biopsy-proven myocarditis referred to tertiary center could not reflect clinical course of acute myocarditis in real world due to selection bias. Purpose: we sought to determine predictors of serious adverse events, using serial check of electrocardiography, echocardiography and biomarkers during hospitalization in patients with clinically suspected acute myocarditis or myopericarditis.
Methods: We enrolled 20 patients admitted with clinical suspicion of acute myocarditis or acute myopericarditis. Coronary angiogram was performed to rule out acute coronary syndromes. We performed serially electrocardiography and echocardiography during hospitalization. Right ventricular systolic dysfunction (RVSD) was defined as decrease of tricuspid annular plane systolic excursion (TAPSE < 15 mm) or RV dilation. Cardiac enzymes, B-type nariuretic peptide (BNP), and inflammatory markers were measured. We defined serious events as death or percutaneous cardiopulmonary support (PCPS) use during admission. Results: Mean age was 42 years (male, 70%). Fuliminant myocarditis occurred in 5 patients (25%), of whom 3 patients survived. (PCPS) was applied to 3 patients, of whom one patient died. In total, six patients (30%) died within 3 months. Therefore, serious adverse events such as PCPS use and death occurred in 8 patients (40%). In all patients, mean value of initial left ventricular ejection fraction (LVEF), and septal wall thickness and posterior wall thickness were 41 ± 13%, 12.5 ± 3.0 mm, 12.5 ± 2.4 mm, respectively. We confirmed elevation of mean value of LV wall thickness and LV mass index at initial examination and subsequently significant decrease of mean value of LV wall thickness during follow-up examinations in all patients.. Especially, group without serious adverse event revealed significant decrease of LV wall thickness between initial and follow-up examinations, but group with serious adverse events did not. Those findings indicated recovery from initial edema in no adverse event group. RVSD at follow-up (serious adverse event group, 57% vs. no serious adverse event group, 0%; p = 0.009), absence of T wave inversion on serial electrocardiogram (25% vs. 83%; p = 0.019), peak creatine kinase-MB (132 ± 123 vs. 31 ± 32 ng/ml; p = 0.014), were significantly higher in group with serious adverse events than group without ones, but initial incidence of RVSD (62% vs. 17%; p = 0.052), initial LVEF, LVEF at follow-up (36.8 ± 20.3% vs 53.5 ± 14.7; p = 0.054), LV wall thickness, and BNP were not different statistically. Conclusions: During hospitalization in patients with suspected acute myocarditis, persistent RVSD might be a strongest predictor for serious adverse events such as death and PCPS use, whereas appearance of T wave inversion is suggestive of good prognosis.

P1083
Prospective study with acute myocarditis patients evaluated with cardiac magnetic resonance: meaning of temporal evolution of the imagiological findings

A Ana Marques[1]; I Cruz[1]; AR Almeida[1]; L Lopes[1]; S Alegria[1]; AC Gomes[1]; G Morgado[1]; I Joao[1]; M Ramalho[2]; H Pereira[2]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal; *[2]Hospital Garcia de Orta, Radiology, Almada, Portugal*

Introduction: The natural history of myocarditis remains variable and the predictors of unfavorable outcomes are unknown. The current european guidelines recommend the monitoring of these patients (pts) with both electrocardiogram (EKG) and echocardiogram. Cardiac magnetic resonance imaging (MRI) demonstrated an additional value in the diagnosis of acute myocarditis, however it´s prognostic value is not so well established, namely the presence and extension of late enhancement (LE).
Purpose: To evaluate the clinical evolution and the MRI findings of pts with myocarditis and to identify predictors of adverse events.
Methods: Prospective study with pts admitted in our center with the diagnosis of acute myocarditis according to symptoms, troponin elevation and MRI criteria (Lake Louise), since 1/2013. Selection of those who underwent clinical evaluation and MRI in two moments: acute episode and at least 6 months later (FUP).
Results: Of the 37 pts admitted with acute myocarditis, were included 20 that fulfill our criteria: 14 males (70%), mean age 26 ± 13 years, 3 pts (15%) with previous episode of myocarditis. At presentation 19 pts (95%) had chest pain; 17 (85%) mentioned prodromal symptoms. Only 1 patient evolved with atrial fibrillation and acute heart failure (HF). All pts were in sinus rhythm in the initial EKG, with ST segment elevation present in 16 pts (80%). The mean maximal troponin T was of 983 ± 136 ng/L (Reference value: < 13 ng/L). Coronary angiography was performed at 7 pts (35%), which excluded significant coronary lesions. In the initial MRI, all the pts had LE: 19 (95%) with subepicardial location, 2(10%) with intramyocardial location. FUP MRI was performed at 8.5 ± 6 months. There wasn't significant differences between the means of the left ventricular (LV) ejection fraction (55 ± 6% vs 56 ± 5%, p = 0.53), LV mass (57vs 54 g/m2, p = 0,35), LV end-diastolic volume (84 vs 82 mL/m2, p = 0.57), LV end-systolic (38 vs 36 ml/m2, p = 0.34) or LV systolic volume (47 vs 46 ml/m2; p = 0.76). 17 pts (85%) maintained areas of LE; as expected, there was a reduction in the number of segments with LE in 11 pts (55%) and this number was significantly lower in FUP MRI (4 ± 2.4 vs 2.6 ± 2.3; p = 0.011). In a mean follow-up of 594 ± 245 days, we registered 3 adverse events: 2 pts had very frequent symptomatic premature ventricular complexes and 1 patient evolved with new HF (NYHA class II symptoms). There wasn´t significant association between the occurrence of adverse events with the troponin value, presence of ST segment elevation or the MRI parameters analyzed, namely the presence, extension or location of the LE.
Conclusion: In this population, the rate of adverse events in the medium follow-up was very low and no independent predictors of adverse events were identified. It should be noted that, in most cases, the FUP cardiac resonance showed persistence of areas of enhancement which may constitute a pathophysiological mechanism for future adverse events.

P1084
Cardiopsychiatriy: the new cardioncology?

G George Joy[1]; M Bolstridge[2]; A Porras-Segovia[3]; E Whiskey[2]; S Shergill[1]; C Plymen[4]
[1]King's College Hospital, London, United Kingdom; *[2]South London and Maudsley NHS Foundation Trust, London, United Kingdom*; *[3]University of Granada, Granada, Spain*; *[4]Imperial College Healthcare NHS Trust, London, United Kingdom*

Introduction: Clozapine is the most effective drug for treatment-resistant schizophrenia, decreasing morbidity & mortality. Clozapine-associated tachycardia is a very frequent side-effect however, & a common reason for discontinuation of the drug. Studies have suggested that such tachycardia can indicate the development of myocarditis. We sought to look at our practice to determine how/what decisions were made by the reviewing cardiologists in those referred solely for tachycardia.
Method: Retrospective study of 16 referrals to a tertiary cardiology unit of patients whom had developed a tachycardia on starting clozapine: None had LV systolic dysfunction or evidence of myocarditis.
Results: Average heart rate (HR) on review was 105 ± 14bpm. All patients were in sinus rhythm. Median LVEF was 55%. There was no significant difference in HR in those with (109 ± 7bpm;31%) & without palpitation (107 ± 12bpml p = 0.43). 17 cardiologists were involved in decisions relating to patient management (mean visits 3.75). Rate control was used in 44%: Four different agents were used (Table 1). There was no significant difference in HR in those treated (102 ± 12bpm) vs untreated (112 ± 8bpm; p = 0.56.Fig 1). 40% of symptomatic patients were treated 45% of asymptomatic patients were treated. No patient died of cardiac causes during 6 years of follow-up.
Discussion: There are no guidelines to dictate management of clozapine tachycardia. Our study illustrates vastly varied treatment approaches to this complication. Decisions to treat appears to be clinician-dependant & not based on HR or symptomatology. When the decision to rate control was made, agent of choice also appears to be clinician dependent. Clozapine was often discontinued despite rate-control. Absence of clozapine use leads to a well-described higher mortality in treatment resistant schizophrenia, however the benefits of rate control in clozapine tachycardia is unknown. We propose a multidisciplinary approach to the management of those clozapine, similar to Cardioncology; the emerging field with proven positive patient outcomes. This would facilitate evidence based guidelines for all forms of clozapine cardiotoxicity and timely managment, taking into account the implications of stopping life saving psychiatric therapy.

Table 1

Rate control used	% (number) of clozapine tachycardia patients treated, total 9 (56%)	Treating HR (mean)
Bisoprolol	19% (3)	109
Ivabradine	13% (2)	102
Atenolol	6% (1)	115
Propranalol	6% (1)	100

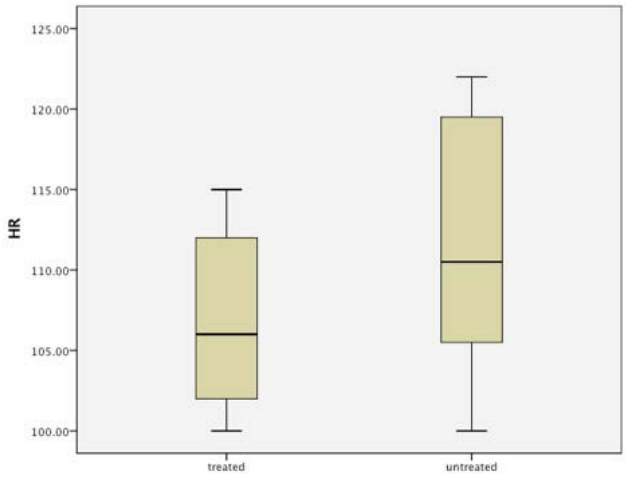


Figure 1

COMORBODITIES

P1085

Assessment of trastuzumab effect on both ventricles by 2D speckle tracking analysis

K Keramida[1]; J Bingcang[2]; R Wensel[3]; P Nihoyannopoulos[4]
[1]Hammersmith Hospital, London, United Kingdom; *[2]Barts Health NHS Trust, Cardiology Department, London, United Kingdom*; *[3]West Hertfordshire Hospitals, NHS Trust, Watford General Hospital, Cardiology, London, United Kingdom*; *[4]Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, United Kingdom*

Cardiac dysfunction as a complication of Trastuzumab therapy in patients with erb2-positive breast cancer is currently assessed by measurement of systolic function predominantly of the left ventricle (LV). Effects on right ventricular (RV) function are less well established. Thirty seven consecutive breast cancer patients with erb-2 overexpression (mean age 55 ± 13years) who received treatment with Trastuzumab were enrolled in this study. Echocardiographic examinations including 2-D, M-mode and tissue Doppler measurements, as well as 2D speckle tracking analysis performed at baseline and repeated after 2 months. In 22 of these patients (59,45%) Trastuzumab resulted in a significant reduction of LV Global Longitudinal Strain (LVGLS) from -21.66 ± 3.38 to -15.41 ± 7.78 (p = 0.001), as well as of RV Global Longitudinal Strain (RVGLS) from -20.53 ± 4.98 to -17.55 ± 4.58, (p = 0.008) and of RV free wall longitudinal strain (RVFWLS) from -24.82 ± 4.61 to -17.47 ± 5.31 (p = 0.045). However, common echocardiographic indices, such as LV ejection fraction (LVEF), Tricuspid Annular Plane Systolic Excursion (TAPSE) and S' wave of the tricuspid valve, as well as the dimensions of the RV were not significantly changed in these patients (Table 1). Furthermore, no significant correlation was found between ΔLVGLS (change) and ΔLVEF and similarly between ΔRVGLS and/or ΔRVFWLS and ΔTAPSE, ΔS' wave or ΔRV dimensions. In the 15 remaining patients (40,55%) LV and RV deformation mechanics and classical indices of systolic performance were not significantly changed after the first dose of transtuzumab (Table 2). Trastuzumab affects deformation mechanics of the RV simultaneously and in a similar way as the LV. Speckle tracking appears to be more sensitive than traditional echo indices in detecting this form of cardiotoxicity.

P1086

Carcinoid heart disease: the path to surgery

P Philippe Mortelmans[1]; MC Herregods[1]; F Rega[2]; E Van Cutsem[3]; P Timmermans[1]
[1]University Hospitals (UZ) Leuven, Cardiology, Leuven, Belgium; *[2]University Hospitals (UZ) Leuven, Cardiac Surgery, Leuven, Belgium*; *[3]University Hospitals (UZ) Leuven, Digestive Oncology, Leuven, Belgium*

Background: Neuroendocrine tumors can cause the rare carcinoid syndrome (0.5 -2.0 cases / million / year), characterised by diarrhea and flushing. Development of carcinoid heart disease with valve destruction is the major negative prognostic factor in these patients. The only effective cardiac treatment is valve replacement. However, the selection of candidates and determination of optimal timing remain unclear. Presymptomatic valve operation has not been associated with late survival benefit. Prospective trials are not available for this rare entity.
Purpose: We wanted to document the diagnostic process of carcinoid heart disease patients who underwent valve surgery, as well as their outcome and follow-up, in order to define gaps in current practice.
Methods: We retrospectively analysed the medical records of all carcinoid heart disease patients who underwent valve replacement in the largest tertiary cardiology and oncology center in Belgium between 2000 en 2016.
Results: All patients (n = 15), mean age 64, underwent tricuspid valve surgery. In 14 of them (93%) an additional valve was replaced, most often the pulmonary valve (n = 12). Two patients underwent quadruple valve replacement, one of them for proven left sided carcinoid involvement. Thirteen patients had liver metastases, and symptoms of heart failure were present in 87% (13/15) at the time of cardiac diagnosis. In hospital mortality was 27% (4/15). The survival after 3 and 12 months was 80% and 53% respectively. From those who left the hospital, 70% experienced an improvement of the functional status to NYHA I-II at time of the first follow-up. In patients who did not improve, mortality was 100% six months after surgery. Perioperative mortality was mainly due to infectious complications associated with prolonged critical illness. Thereafter, 3 cases were considered cardiac deaths. Mean preoperative right ventricular (RV) function (TAPSE) was better in the patients who survived more than 12 months (21mm) than in those who died between 3 to 12 months after surgery (16mm). The former group had a shorter mean interval from diagnosis of the carcinoid syndrome to cardiac diagnosis than the latter (13 versus 105 months). A lower mean preoperative chromogranin level was associated with a lower chance of perioperative death and a longer postoperative survival.
Conclusion: Mortality after valve surgery for carcinoid heart disease remains high. A possible cause is late cardiac referral of these oncology patients, whose generally poor condition makes differentiation between general fatigue and heart failure symptoms very challenging without echocardiography. We propose a systematic and multidisciplinary approach to all carcinoid syndrome patients. Our aim for the future is to identify an 'intermediate' group suitable for surgery. Patients with mild heart failure symptoms in combination with severe tricuspid regurgitation but without RV dilatation or dysfunction may be the target population.

Table P1085

Group 1(N=22)	Baseline	2 months after trastuzumab	p value	Group 2(N=15)	Baseline	2 monthsaftertrastuzumab	p value
LVGLS (%)	-21.66±3.38	-15.41±7.78	p = 0.001	LVGLS (%)	-18.59±3.92	-17.31±8.92	0.615
RVGLS (%)	-20.53±4.98	-17.55±4.58	p = 0.008	RVGLS (%)	-17.18±4.37	-17.96±1.94	0.494
RVFWLS (%)	-24.82±4.61	-17.47±5.31	p = 0.045	RVFWLS (%)	-21.44±5.24	-22.87±3.77	0.164
LVEF (%)	61.94±3.2	61.29±4.43	0.592	LVEF (%)	62.17±2.52	60.50±3.12	0.118
TAPSE (mm)	23.16±3.40	24.31±3.30	0.249	TAPSE (mm)	21±2.71	22.3±2.83	0.253
TV S' (cm/sec)	13.50±2.31	13.87±2.36	0.620	TV S' (cm/sec)	12±1.41	13.2±2.09	0.181
RVID basal (mm)	33.37±2.73	33.44±3.36	0.923	RVID basal (mm)	34.6±3.44	34.2±3.67	0.693
RVID mid (mm)	26.44±2.22	26.94±3.27	0.552	RVID mid (mm)	27.9±2.51	29±3.39	0.129
RVID height (mm)	72.62±4.98	71.81±4.70	0.515	RVID height (mm)	68.9±3.9	70.9±5.60	0.115

P1087

Comparison between the two score systems of surveillance, epidemiology and end results (SEER) and national surgical adjuvant breast and bowel project (NSABP) in predicting the risk of trastuzumab-rela

SY Se Yong Jang[1]; JH Sohn[2]; JH Roh[1]; MH Bae[1]; JH Lee[1]; DH Yang[1]; HS Park[1]; Enter your textY Cho[1]; SC Chae[1]
[1]Kyungpook National University Hospital, Daegu, Korea Republic of; [2]Kyungpook National University Medical Center, Cardiology center, Daegu, Korea Republic of

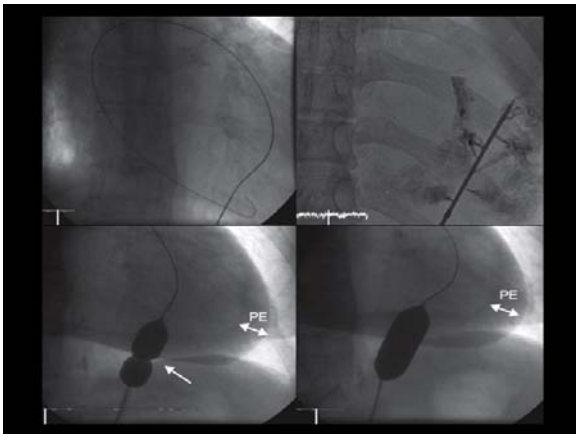
Background: Trastuzumab in an important treatment in patient with breast cancer and overexpress epidermal growth factor-2. Incidence of cardiac toxicity in patients treated with trastuzumab varies according to the patients factors. We aimed to compare two score systems of Surveillance, Epidemiology and End Results (SEER) and National Surgical Adjuvant Breast and Bowel Project (NSABP) in predicting the risk of trastuzumab induced cardiomyopathy in patients with breast cancer.
Methods: Among 458 consecutive patients who treated with trastuzumab between Mar 2011 and Apr 2015, 315 patients (314 female, mean age 51.1 ± 9.7) with breast cancer were available for calculating both score and included in present study. Cardiotoxicity defined as >15% absolute decrease in left ventricular ejection fraction (LVEF) from baseline and ≥10% decrease with LVEF below normal.
Results: During mean follow-up of 846 ± 471 days, 16 (6.0 %) patients experienced trastuzumab-related cardiotoxicity. Incidence of comorbid conditions which can be related to heart failure is low (e.g. 15.9% of hypertension, 5.7% of diabetes, 0.3% of coronary artery disease, 1.0% of heart failure, 0.6% of atrial fibrillation). Mean score of NSABP and SEER was 60.8 ± 14.2 and 2.2 ± 0.7. In univariate Cox proportional analysis model demonstrated only NSABP score is a significant predictor for cardiotoxicity. Receiver operating curve analysis showed area under curve of 0.715 and 0.501 for NSABP and SEER score in predicting trastuzumab-related cardiotoxicity. NSABP score showed better performance in predicting cardiotoxicity compared with SEER (p = 0.004).
Results: NSABP score predicts trastuzumab-related cardiotoxicity better than SEER score in patients with breast cancer and low-comorbidity, probably because SEER score is more largely based on comorbidity factors than NSABP score.

P1088

Minimally invasive treatment for malignant pericardial effusions with poor prognosis

FJ Francisco Javier Irazusta Cordoba[1]; S Jimenez-Valero[1]; D Gemma[1]; P Meras Colunga[1]; V Rial Baston[1]; O Gonzalez Fernandez[1]; AM Iniesta Manjavacas[1]; G Galeote Garcia[1]; A Sanchez-Recalde[1]; R Moreno Gomez[1]; JL Lopez-Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain

Introduction and purpose: It is becoming more prevalent in our hospitals to attend patients with right-sided heart failure symptoms due to malignant pericardial effusions. They also have a high recurrence rate after traditional treatment with pericardiocentesis. We sought to confirm the efficacy and feasibility of percutaneous balloon pericardiotomy (PBP) as the initial treatment of choice for these effusions.
Methods: Retrospective analysis of the clinical, echocardiographic, and follow-up characteristics of a consecutive series of PBP carried out in a single center in patients with advanced cancer and right-sided heart failure symptoms.
Results: Forty PBP were performed in 35 patients with a mean age of 61.8 years (55% females). Thirty-four patients had pathologically confirmed metastatic neoplastic disease (26 patients with tumoral cells in the pericardial liquid), seven of them have previously required pericardiocentesis, and in the remaining patients PBP was the first treatment for the effusion. All patients had a severe circumferential effusion (29mm by mean on transthoracic echocardiography [TTE]), and most presented evidence of hemodynamic compromise on TTE. In all cases, the procedure was successful, there were no acute complications, and it was well tolerated at the first attempt. There were no infectious complications during follow-up. One patient developed a large pleural effusion and in another one a pseudoaneurysm was observed in the right ventricle, even though none of them required further treatment. Eight patients needed a new pericardial procedure: 3 had elective pericardial window surgeries and 5 had a second PBP. Eighty per cent of patients died during follow-up (55,7 days by mean from the PBP) regarding their oncological disease
Conclusion: PBP is a simple and safe technique that can be effective in the prevention of recurrence in many patients with severe malignant pericardial effusion. The characteristics of this procedure make it particularly useful in this group of patients to avoid more aggressive, poorly tolerated approaches, since they have a very poor prognosis regarding to their oncological disease.



PBP

P1089

Acute kidney injury among patients hospitalized with acute decompensated heart failure: is it a frequent worsening factor of prognosis?

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

Introduction: Major registries (ADHERE, ESC-HF Pilot) had showed that the presence of cardiorenal syndrome type 1 worsens prognosis of patients with acute decompensated heart failure (ADHF).
Purpose: To study the prevalence of acute kidney injury (AKI) among patients with ADHF and evaluate the prognosis of hospitalized patients
Methods: Between July/2014 and July/2015, we studied a total of 308 hospital cases with ADHF. Changed creatinine level (Cr) in 7 days (1.5 fold) or changed Cr for 26.5 μmol/L in 48 hours were diagnosis criteria of AKI.
Results: AKI was found in 23.1% of cases. Patients hospitalized with AKI had an intact hemodynamic: high blood pressure and preserved EF. In Multi variable analyze, AKI was negatively correlated with SBP level at admission (OR = 0.97; 95% CI 0.961-0.993; p = 0.005). Risk of hospital mortality among patients with AKI had a negative correlation with DBP at admission (OR=0.41; 95% CI 0.924-0.958 p < 0.001) and a positive correlation with maximal Cr level at admission (OR = 1.009; 95% CI 1.003-1.014 p = 0.002)
Conclusion: About one of four patients hospitalized with ADHF can develop AKI. Most important predictor of AKI was SBP at admission. Hospital mortality increases in 7.4 folds among patients with AKI (95% CI 2.8-19.3 p < 0.001). The predictors of hospital mortality among patients with ADHF and AKI are DBP and Cr level at admission.

variable	With AKI(n = 71)	Without AKI(n = 207)	P value
Males,%	53.5	43.5	0.14
Mean age, years	72.9±10.5	72.0±10.2	0.52
Cr. at hospitalization	137.0(105.5-182.0)	114.4(96.3-138.7)	< 0.001
Maximal Cr. at hospitalization	191.8(142.0-241.1)	125.3(105.0-149.7)	< 0.001
Minimal Cr. at hospitalization	108.0(86.5-152.0)	105.2(92.0-125.5)	0.61
Mean SBP at admission, mmHg	141.6±28.9	140.0±30.2	0.86
Mean DBP at admission, mmHg	83.5±13.2	83.3±14.1	0.89
Mean EF, %	50.2±13.7	50.0±13.1	0.94
Patients with SBP < 125 mmHg, %	29.6	32.5	0.64
Hospital mortality, %	18.3	3.0	< 0.001

SBP-systolic blood pressure; DBP-diastolic blood pressure; EF-Ejection Fraction; Cr.-Creatinine level;AKI-acute kidney injury

P1090

Importance of renal dysfunction in a heart failure clinic

D Daniel Seabra[1]; H Guedes[1]; P Silva[1]; L Marques[1]; A Andrade[1]; J Azevedo[1]; P Pinto[1]
[1]*Hospital Centre do Tamega e Sousa, Cardiology Department, Penafiel, Portugal*

Background/Introduction: Cardiovascular homeostasis is guaranteed by the multifactorial relationship between the heart and the kidney, namely by haemodynamic, neurohormonal and inflammatory pathways. Heart failure (HF) and chronic kidney disease (CKD) can co-exist and interaction between them may be critical for treatment approach and patient prognosis.
Purpose: To assess the clinical impact of CKD in patients (pts) with HF with reduced ejection fraction (EF).
Methods: We conducted a retrospective study based on a cohort of pts from a HF clinic of a single hospital center. Included pts with reduced EF and previous diagnosis for, at least, six months. Divided in two groups: with CKD (GA) (defined as glomerular filtration rate ≤ 60mL/min/1.73m2) and without CKD (GB).
Appraised clinical characteristics and major cardiac events – hospitalization from HF (hospHF) or acute coronary syndrome (hospACS) and death from cardiovascular (CVm) and non-cardiovascular (nCVm) cause. Evaluated the relationship with anatomical and function aspects of left ventricle, namely size (indexed left ventricle end-diastolic diameter [LVEDDi]) and left ventricle EF (LVEF) in follow-up (FU).
Results: Included 290 pts, with a mean age of 60.56 ± 13.25 years and male predominance (75.2%). Noted a prevalence of 41% of ischemic etiology. The mean initial EF was 29.2 ± 10.8%. The FU was 39.9 ± 18.5 months with a mean EF during FU of 34.9 ± 12.5%.
GA formed by 92 pts and 198 in GB. GA was associated with female pts (43.1 vs 28%; p 0.017), higher age (67.7 vs 57.2 years, p < 0.001), lower height (164 vs 166 cm, p 0.032) and weight (73.6 vs 77.8 Kg, p 0.016).
CKD was significantly linked with arterial hypertension (p < 0.001) and diabetes mellitus (p < 0.001). There were no significant differences regarding the etiology of HF. The presence of atrial fibrillation (AF) correlated positively with the CKD (65 vs 21 pts; p 0.023). During the FU, GA had higher LVEDDi (34.46 vs 32.66 mm/m2, p 0.008) and significantly inferior LVEF (30.9 vs 36.8%, p < 0,001). Noted a superior number of major clinical events in pts with CKD - hospIC (p < 0.001), CVm (p 0.003) and nCVm (p < 0.001). The presence of CKD limited treatment with angiotensin-converting-enzyme inhibitor and mineralocorticoid receptor antagonists (p < 0.001) but was closely related with greater use of diuretic therapy (p < 0.001). The presence of CKD was associated with worse functional class (p < 0.001).
Conclusion(s): In this population, CKD is associated with cardiovascular risk factors such as hypertension and diabetes, as expected; however, it is noteworthy the relation with female gender and less height or weight. AF is associate with CKD and ventricle size and function appears to be important in cardiorenal link. Coexistence of HF and kidney disease hinders treatment and affects prognosis.

P1091

Treatment of anemic patients with chronic heart failure and chronic kidney disease: criteria of effectiveness

G Ganna Tytova[1]; O Liepieieva[2]; N Ryndina[1]; M B Teclebrhan[1]
[1]*Kharkiv National Medical University, Kharkiv, Ukraine*; [2]*City clinical hospital #27, CCU, Kharkov, Ukraine*

Anemia and renal dysfunction are common comorbid conditions associated with poor prognosis in patients with chronic heart failure (CHF).
Purpose: To analyze the predictive value of clinicoanamnestic indicators due to therapy effectiveness of anemia with CHF and CKD using an oral form of Fe(III)hydroxide complex polymaltose for optimization and providing an individual approach to every patient.
Materials and methods: 68 pts with CHF II-IV FC due to IHD and CKD II-III st. were exemined. Among the causes of CKD were: chronic pyelonephritis in 50 pts, diabetic nephropathy in 18 pts. All pts with CHF and CKD had anemia. Hb level was within 78-91g/l. Diagnosis of anemia was determined by criteria of the Medical Committee of Standards of Hematology (ICST,1989). CHF FC was established by NYHA. Availability and stage of CKD was determined according to the National Kidney Foundation USA (NKF) K/DOQ classification. Pts with CHF and CKD were treated according to the standards. Pts with anemic syndrome received Fe(III)hydroxide polymaltose complex 100 mg orally 1-2 times a day. Hb target level was within 110-120 g/l. The observation period was 3 months. Evaluation of prognostic properties was performed using non-uniform procedures Wald-Genkina. All signs were distributed by gradient with subsequent calculation of prognostic factors (PF) and the general informative features (I).
Results: To assess the prognostic value of clinicoanamnestic parameters, pts (n = 68) that received Fe(III) hydroxide polymaltose complex, at the end of treatment were divided into 2 groups: a) with good antianemic effect (n = 50)-achieved the target level of Hb;b) a satisfactory effect (n = 18)-Hb levels approach to the target one. Very high informational content (I≥6,0) is given to the duration of CHF(I = 9.55),CHF FC (I = 8.03),cardiac cachexia syndrome (I = 7.16). High predictive value (6,0>I≥1,0) to the severity of anemia (I = 5.88),lower extremities edema and dyspnea (I = 5.60), acute myocardial infarction (I = 1,94),post-infarction left ventricular aneurysm (I = 2.82),patient age (I = 2.50),severity of CKD (I = 3.28) and the presence of type 2 diabetes mellitus (I = 1.16). Moderate predictor properties (1,0>I≥0,50) identified in relation to BMI (I = 0.82),history of stroke (I = 0.76) and the presence of permanent atrial fibrillation (I = 0.50).
Conclusion: Clinicoanamnestic indicators revealed a high predictive informational content about the effectiveness of therapeutic correction of anemia with CHF and CKD using an oral form of Fe(III)hydroxide polymaltose complex that allows to include them into predictive algorithms. Most informative criteria: the duration and severity of CHF, cardiac cachexia formation on a background of biventricular cardiac decompensation, progression of renal dysfunction, severity of anemia, which leads to the desirability and feasibility of application of these criteria at all levels of preventive and curative care with the aim of stratification effectiveness of treatment strategies.

P1092

Renal filtration function in patients with chronic heart failure and permanent atrial fibrillation depending on left ventricle ejection fraction.

N Natalia Koziolova[1]; E Polyanskaya[1]; S Berestneva[1]; M Surovtceva[1]
[1]*Medical Academy, Perm, Russian Federation*

Aim: to evaluate renal filtration function in patients with chronic heart failure (CHF) and permanent atrial fibrillation (AF) depending on left ventricle ejection fraction (LV EF).
Methods and materials: 60 patients with CHF and permanent AF were examined. Renal filtration function was evaluated using serum creatinine, estimated glomerular filtration rate (eGFR) by CKD-EPI, and serum cystatin C level. Patients were divided into 3 groups depending on LV EF. The first group consisted of patients who had reduced LV EF < 40% (HFrEF, the average mean 37,2 ± 4,0%); the second one was of patients with mid-range LV EF from 40 to 49% (HFmrEF, the average mean 46,7 ± 5,2%); and the third group included patients with preserved LV EF ≥ 50% (HFpEF, the average mean 57,1 ± 3,8%).
Results: in the group of HFrEF the average serum creatinine was 96,5 ± 14,3 umole/L, eGFR 53,6 ± 7,9 mL/min/1.73m2; cystatin C level 2211,2 ± 128,8 mg/mL. In the second group with patients who had HFmrEF, the average serum creatinine was 91,3 ± 10,7 umole/L, eGFR 59,1 ± 6,4 mL/min/1.73m2; cystatin C level 1873,4 ± 220,6 mg/mL. In the group of HFpEF the average serum creatinine was 77,4 ± 9,9 umole/L, eGFR 63,0 ± 8,5 mL/min/1.73m2; cystatin C level 1405,2 ± 374,5 mg/mL. Statistics analysis with comparison of three groups showed reliable difference in cystatin C level (pmg = 0,004). There were no reliable differences between groups in serum creatinine and eGFR (pmg = 0,611 icy; pmg = 0,098, respectively).
Conclusion: In patients with CHF and permanent AF, worsening of renal function injury (evaluated using cystatin C) revealed along with decrease of LV EF. Levels of both creatinine and eGFR (CKD-EPI) did not have any correlation to LV EF in these patients.

P1093

Risk factors of cardiorenal syndrome at the patients with a chronic heart failure and preserved ejection fraction (HFpEF)

D Dina Shorikova[1]; E Shorikov[1]
[1]*Bucovinian State Medical University, Chernivtsy, Ukraine*

Purpose: to study probability of cardiorenal syndrome development due to the nontraditional risk factors at the patients with a chronic heart failure and preserved ejection fraction (HFpEF) in the Bukovina region (Ukraine).
Methods: 594 patients, all the inhibitants of Bukovina region of Ukraine, with HFpEF, the same anamnesis and severity were included in cohort study. During the 5-year period of investigation (2008-2012) the episodes of glomerular filtration reduction (less than 60 mg/ml/min*1,73m2) were fixed in protocol. It was used a case-control method, tables 2×2, χ^2 criterion, analisys of relative risk (RR) and odds ratio (OR).
Results: At the patients with weight index more than 25,0 kg/m2 RR of kardiorenal syndrome was 1,76 [1,18-2,61], OR - 1,95 [1,22-3,11]. Among nontraditional risk factors estimated the significance of fibrinogen level more than 3,0 g/l (RR - 1,50 [1,02-2,19], OR - 1,75 [1,15-2,66]), prothrombin index (RR - 2,66 [1,11-6,41], OR 2,84 [1,13-7,13]) and increase systolic pressure at the pulmonary artery (RR -2,84 [1,94-4,14], OR - 6,64 [3,51-12,5]). It was, also, set the reliable negative correlation between glomerular filtration and glycated hemoglobin level r = -0,56 (p < 0,05).
Conclusions: Cohort study of patients with HFpEF was shown the reliable risk of low glomerular filtration rate depending of the body mass index, fibrinogen level, prothrombin index, pulmonary artery pressure and glycated hemoglobin.

P1094

Effect of contrast-induced acute kidney injury on long-term outcomes of percutaneous coronary intervention

E Elena Vershinina[1]; AN Repin[1]
[1]*State Research Institute of Cardiology of Tomsk, department of rehabilitation, Tomsk, Russian Federation*

Purpose of the study: determine the impact of contrast-induced acute kidney injury (CI-AKI) on overall survival, survival without fatal cardiovascular events and rate of development large adverse cardiovascular events (MACE: cardiovascular death, acute coronary syndrome, stroke).
Materials and methods: retrospective study including 148 patients who were directed for elective percutaneous coronary intervention from 2009 to 2011. CI-AKI was diagnosed and classified according to RIFLE-AKIN criteria. The risk of CI-AKI was evaluated on a scale R. Mechran. Prevention of contrast-induced nephropathy (CIN) was carried according to the recommendations for the prevention of contrast-induced nephropathy ESC 2010. Long-term outcomes were evaluated in 5-7 years after these interventions.
Results: CI-AKI was found in 23 patients (15.5%), which had an increase in serum creatinine at the 37.8 ± 19.7 umol/l (42.5%). In the analysis of long-term outcomes found that after seven years of follow-up after interventions overall survival in the group of patients without CI-AKI was 87.6%, in patients with CI-AKI - 70%, the rate of survival without fatal cardiovascular events in the group of patients without CI-AKI was 89.4%, in patients with CI-AKI - 80%, the frequency of large cardiovascular events (MACE) in the group of patients without CI-AKI was 39.8%, in patients with CI-AKI - 45%. According to the analysis of Kaplan-Meier curves long-term overall survival and survival without fatal cardiovascular events after endovascular coronary intervention in patients without the development of periprocedural CI-AKI was significantly higher than in the group of patients with CI-AKI ($p \leq 0.05$). Conversely, frequency of large cardiovascular events (MACE) was significantly higher in the group of patients with CI-AKI compared the group without the periprocedural CI-AKI ($p \leq 0.05$).
Conclusion: development of periprocedural CI-AKI associated with adverse long-term outcomes after percutaneous coronary intervention.

P1095

Renal function injury in patients with chronic heart failure and permanent atrial fibrillation depending on brain natriuretic peptide.

N Koziolova[1]; E Polyanskaya[1]; S Berestneva[1]
[1]*Medical Academy, Perm, Russian Federation*

Aim: to study interconnection between renal function injury and NT-proBNP in patients with chronic heart failure (CHF) and permanent atrial fibrillation (AF).
Methods: and materials: 60 patients with CHF and permanent AF were examined. Renal filtration function was evaluated using serum creatinine, estimated glomerular filtration rate (eGFR) by CKD-EPI, and serum cystatin C level. Patients were divided into 3 groups depending on NT-proBNP level. The first group consisted of patients who had NT-proBNP < 125 ng/mL (18.3% of all); the second one was of patients with NT-proBNP from 125 to 800 ng/mL (46.7% of all); and the third group included patients with NT-proBNP >800 ng/mL (35.0% of all).
Results: in the group of NT-proBNP of normal range the average serum creatinine was 83,72 ± 10,05 umole/L, eGFR 68,82 ± 13,18 mL/min/1.73m2; cystatin C level 1063,41 ± 350,11 mg/mL. In the second group with patients who had NT-proBNP 125-800 ng/mL, the average serum creatinine was 86,79 ± 13,15 umole/L, eGFR 61,10 ± 14,83 mL/min/1.73m2; cystatin C level 1568,75 ± 231,64 mg/mL. In the group of NT-proBNP >800 ng/mL the average serum creatinine was 91,90 ± 11,51 umole/L, eGFR 52,22 ± 20,17 mL/min/1.73m2; cystatin C level 1911,76 ± 414,33 mg/mL. Statistics analysis with comparison of three groups showed reliable difference in cystatin C level (pmg < 0,001). There were no reliable differences between groups in serum creatinine and eGFR (pmg = 0,330 icy; pmg = 0,150, respectively). Correlation analysis showed moderate indirect interconnection between NT-proBNP and eGFR (r=-0,51, p = 0,003); and moderate direct interconnection between NT-proBNP and cystatin C (r=0,60, p < 0,001).
Conclusion: In patients with CHF and permanent AF, the progressive worsening of renal function injury (evaluated using cystatin C) revealed along with myocardial stress increase according to NT-proBNP.

P1096

Characteristics, treatments and outcomes of hospitalized and ambulatory heart failure patients with chronic obstructive pulmonary disease in the ESC heart failure long-term registry

M Canepa[1]; PL Temporelli[2]; A Rossi[3]; C Laroche[4]; S Anker[5]; MF Piepoli[6]; AJ Coats[7]; L Tavazzi[8]; A P Aldo Pietro Maggioni[9]
[1]*University of Genoa, Cardiology Unit, Department of Internal Medicine, Genoa, Italy*; [2]*IRCCS Fondazione Salvatore Maugeri, Cardiology Division, Veruno, Italy*; [3]*University of Verona, Department of Medicine, Verona, Italy*; [4]*European Society of Cardiology, EURObservational Research Programme, Sophia-Antipolis, France*; [5]*University Medical Center Göttingen (UMG), Innovative Clinical Trials, Department of Cardiology & Pneumology, Göttingen, Germany*; [6]*Polichirurgico Hospital G. da Saliceto, Department of Cardiology, Piacenza, Italy*; [7]*Australia and University of Warwick, Monash University, Coventry, United Kingdom*; [8]*Maria Cecilia Hospital, GVM Care&Research – ES Health Science Foundation, Cotignola, Italy*; [9]*ANMCO Research Center, Florence, Italy*

On behalf of: ESC-HFA LT HF Registry Investigators

Background. Chronic obstructive pulmonary disease (COPD) is a common comorbidity that worsens the clinical course of heart failure (HF), both in the acute and chronic phases of the syndrome.
Purposes: To describe characteristics, treatments and 1-year outcomes of hospitalized HF (HHF) and chronic HF (CHF) patients with and without COPD enrolled in the ESC HF Long-Term registry.
Methods: This observational registry enrolled HHF and CHF patients presenting to participating European centers from May 2011 to April 2013. Diagnosis of COPD was based on medical history and/or spirometry. Characteristics, treatments and outcomes of HHF and CHF patients with and without COPD were compared using Student's t-test or chi-square test as appropriate, and the independent association of COPD with clinical outcomes was assessed with multivariate Cox analysis.
Results: The registry included 6920 HHF and 9409 CHF patients, with a prevalence of COPD of 19% and 14%, respectively. In both groups, patients with COPD were older, more frequently men, with a worse clinical status and a higher prevalence of comorbidities, including atrial fibrillation, diabetes and renal dysfunction ($p < 0.001$ for all). Left ventricular EF was greater than 45% in about 25% of patients, more frequently in COPD than non-COPD HHF patients (38 vs. 32%, $p < 0.001$) but similarly in CHF patients (23 vs. 23%). At baseline both HHF and CHF with COPD were taking more diuretics, aldosterone antagonists and digitalis than non-COPD. In HHF, the increase at discharge in the use of disease-modifying drugs was greater in non-COPD than in COPD for ACE inhibitors (+14% vs. +7%), beta-blockers (+21% vs. +12%) and aldosterone antagonists (+21% vs. +17%). In CHF patients, beta-blockers were used more frequently in non-COPD patients (90% vs. 82%), balanced by a less frequent use of ivabradine (8% vs. 12%) ($p < 0.001$ for both). At 1-year follow-up, hospitalizations were more frequent in COPD than non-COPD, both in HHF (all-cause: 50% vs. 43%, for HF: 32% vs. 25%, $p < 0.001$) and CHF patients (all-cause: 36% vs. 27%, for HF-cause: 17% vs. 12%, $p < 0.001$). Multivariate analysis confirmed COPD as independently associated with hospitalizations both in HHF (all-cause: 1.16 [1.04-1.29], for HF: 1.22 [1.05-1.42]) and CHF patients (all-cause: 1.26 [1.13-1.41], for HF: 1.37 [1.17-1.60]). All-cause but not CV mortality was higher both in HHF (35% vs. 26%) and CHF patients (11% vs. 8%, $p < 0.001$ for both) with COPD, but this association was not confirmed in both groups after adjustment (p 0.11).
Conclusions: In both HHF and CHF, COPD was associated with a worse clinical profile. There was a gap in disease-modifying treatments between patients with and without COPD, which widened in HHF after hospitalization. COPD was independently associated with an increased risk of both all-cause and HF hospitalizations, but neither in HHF nor in CHF an independent association with all-cause mortality was observed at 1-year follow-up.

P1097

Endothelial function in patients with tobacco and biomass smoke-related chronic obstructive pulmonary disease

G K Perez Cortes[1]; A Orea-Tejeda[2]; DG Gonzalez-Islas[2]; AG Jimenez-Cepeda[2]; L Verdeja-Vendrell[2]; AG Navarrete-Penaloza[2]; RN Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; B Robles-Uribe[2]; FA Figueroa-Herrera[2]; SC Torres-Montiel[2]
[1]*Universidad Autonoma Benito Juarez de Oaxaca, Faculty of Medicine and Surgery, Oaxaca de Juarez, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas, Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico*

Background: Endothelial dysfunction (ED) is characterized by impaired bioavailability of vasoactive substances, favoring inflammation, vasoconstriction, increased vascular permeability, platelet aggregation, thrombosis and atherosclerosis. It is also an independent predictor of cardiovascular events. ED is highly prevalent in patients with COPD caused by tobacco (TS) and biomass (BS) smoke. These are the leading etiologies of COPD in Mexico. However, it is unknown whether there is a difference in ED between both etiologies of COPD.
Purpose: To assess the differences in endothelial function among COPD patients from tobacco and biomass.
Methods: A cross-sectional study was conducted in ambulatory patients (age 18 or older) with a diagnosis of COPD GOLD I-III. Subjects with mixed COPD etiology were excluded. Patients were divided into COPD by TS or BS, and underwent medical history and physical examination. ED was assessed using photoplethysmography. Endothelial dysfunction was considered with a pulse wave time of maximum amplitude / total time (TMA/TT) index ≥0.30. Multiple linear regression was performed to

determine the effect of the type of COPD on endothelial function.
Results: 97 patients were evaluated (age: 72.16± 9.95 years), of whom, 53.6% were women. In the BS group, women predominated (90.7% vs 24.1%, p < 0.001), they were older (76.1± 9.1 vs 69.0± 9.5, p < 0.001), had a higher prevalence of hepato-jugular reflux (50 % vs. 20.7%, p=0.022), and history of heart failure (30.2% vs. 16.7%, p=0.113), compared to those in the TS group. The overall prevalence of ED was 78.9%. Prevalence rate was higher in those with BS compared to TS (83.7% vs 75 %, p=0.299), although according to multiple linear regression, patients with BS had 0.04 more TAM/TT index than TS subjects (β: 2.5, CI 95 %; 1.2-3.7, p <0.001).
Conclusions: ED is higher in patients with COPD from biomass smoke than in patients from tobacco smoke. Although, the prevalence between the two groups was not statistically different, the patients in the BS group had a higher prevalence of heart failure, especially right heart failure.

P1098
Relationship between endothelial dysfunction and forced expiratory volume in first second (FEV1) in chronic obstructive pulmonary disease patients

RNSS Rocio Nayeli Sanchez Santillan[1]; GID Gonzalez Islas Dulce[1]; AOT Orea Tejeda Arturo[1]; VVL Verdeja Vendrell[1]; NPA Navarrete Penalosa[1]; PHV Pelaez Hernandez Viri[1]; RUB Roble Uribe B[1]; FHA Figueroa Herrera A[1]; TMS Torres Montiel S[1]; PCE Perez Cabanas E[1]; HCR Hernandez Zenteno R[1]; FTF Flores Trujillo F[1]; IVO Infante Vazquez O[1]; MMR Martinez Memije R[1]
[1]National Institute of Respiratory Disease "Ismael Cosio Villeagas", Heart Failure and Respiratory Clinic , mexico cityt, Mexico

BACKGROUND: The characteristic of Chronic Obstructive Pulmonary Disease (COPD) is the chronic inflammation in the small airways and alveoli, this takes to a limitation of the flux that is not reversible. Cardiovascular disease especially heart failure (HF) represents a high mortality and morbidity, being the cause of a worst prognostic in these patients. Has recently been found that an injury of the endothelium can contribute to emphysema and COPD and indirectly relates that the damaged in the pulmonary vasculature can developed such emphysema and COPD.
Purpose: To evaluate the relationship between endothelial dysfunction and respiratory function in patients with COPD and HF.
Methods: Cross sectional study, with 117 patients. The endothelial function was determined by Photopletysmography evaluating the amplitude, maximum amplitude time (MAT), total time of wave (TT), and the relation between both MAT/TT index, >30 was considerate as endothelial dysfunction.
Results: We evaluated 117 patients (mean age 71.4 + 11.09), the 60.7% of them had endothelial dysfunction (ED), and 56.8% were female. Those patients with ED have higher prevalence of cardiovascular disease (47.9% vs 9%, p=0.005), Pulmonary Arterial Hypertension (PAH) 21.6% vs 3% comparing it with those without ED. No significance difference were found in sex, age, weight, high, arterial hypertension, diabetes, obesity. A linear regression determined that these patients with ED has 11 % less of FEV1 comparing with those without ED. (β-11.251 p=0.05)
Conclusion: The patients with ED had a lower FEV1 compared with those without ED. In patients with EPOC those with ED will have a worst degree of EPOC and in which turn to the hypothesis that the ED is not only local but instead is at capillary, alveoli and systemic.

P1099
Association between heart failure and nonalcoholic fatty liver disease

KV Pivtorak[1]; VY Maslovskyi[1]
[1]National Pirogov Memorial Medical University, Vinnitsia, Ukraine

In the last decade the role of alcoholic fatty liver disease discuss as a disease, which determines not only the severity of injury, but associated with the progression of cardiovascular disease (CVD) and the development of type 2 diabetes mellitus (DM) and other system injuries [1,2].
Purpose: to determine the relationship between NAFLD and heart failure
Methods: The study involved 112 NAFLD patients with normal, overweight and obese without of type 2 diabetes mellitus and 64 patients with normal, overweight and obese with type 2 diabetes mellitus. Conducted anthropometric survey measured levels of AST, ALT, GGT, the degree of liver fibrosis using elastography (FibroScan), ECG and echocardiography. The stratification of CVrisk was carried by traditional SCORE scale version for countries with high risk. We determined the level of inflammatory mediators (TNF-α, IL-1, IL-6), markers (CRP, fibrinogen), endothelin -1, the activity of the Willebrand factor (vWF), the thickness of the intima-media complex, presence atherosclerotic plaque and stenosis of the carotid arteries, insulin resistance index HOMA-IR for all examined patients.
Results: In both groups was revealed left ventricular diastolic dysfunction and QT prolongation in patients with NAFLD and type 2 diabetes that was associated with the severity of the disease. Most patients with NAFLD by obesity showed a reduction in endothelium-dependent vasodilation, indicating the presence of endothelial dysfunction. The concentration of pro-inflammatory cytokines such as TNF-α and IL-6 in patients with NAFLD was 3-7 times higher than the similar parameters of patients with a similar degree of obesity, but without evidence NAFLD. The concentration of ET-1 in the blood plasma of patients with NAFLD has a strong direct correlation with the degree of cardiovascular risk of surveyed patients. It is found that many inflammatory mediators (TNF-α, IL-1, IL-6) and markers (C-reactive protein, fibrinogen) highly correlate with the degree of obesity, the concentration of ET-1, vWF and markers of insulin resistance, a predictor for cardiovascular risk.
Conclusions: Presents of diastolic dysfunction of left ventricular and heart failure, disturbances of endothelium-dependent vasodilation, the concentration of ET-1, mediators of systemic inflammation, increase the values of intima-media thickness, an increase the frequency of cardiac arrhythmias is highly correlated with the degree of cardiovascular risk. Presence of NAFLD dictates mandatory screening for cardiovascular disease in these patients.

P1100
Liver stiffness assessed by transient elastography is associated with congestion in patients with decompensated heart failure

A Soloveva[1]; M Bayarsaikhan[1]; I Garmash[2]; S Villevalde[1]; Z Kobalava[1]
[1]RUDN University, Department of Internal Disease Propaedeutics, Moscow, Russian Federation; *[2]RUDN University, Moscow, Russian Federation*

Objective: Heart failure (HF) has a negative impact on liver leading to hepatic fibrosis or even cirrhosis. Studies dealing with assessment of liver stiffness (LS) in decompensated heart failure (DHF) are relatively few and have contradictory results. The aim of the study was to assess LS by the transient elastography (TE) on admission and its associations in patients with DHF.
Methods: LS was measured using TE (FibroScan Echosens, France) in 94 patients with DHF on admission (60 male, 72 ± 10 years (M ± SD), arterial hypertension 96%, myocardial infarction 55%, atrial fibrillation (AF) 63%, diabetes mellitus 45%, known chronic kidney disease 29%, chronic anaemia 30%, left ventricular ejection fraction (EF) 40 ± 14%, EF < 40% 28%, NYHA IV 41%). Ten valid measurements were required with success rate of >60%. LS≤5.8 was considered normal and LS ≥5.9, 7.2, 9.5 and 12.5 kPa are considered fibrosis (F1-F3 METAVIR score) and cirrhosis (F4) according to thresholds in studies with chronic liver disease. Mann-Whitney test was performed. p < 0.05 was considered statistically significant.
Results: The median value of LS was 13.1 (interquartile range 7.4;26) kPa. Normal LS was observed in 15.9% of patients. Abnormal LS ≥5.9, 7.2, 9.5 and 12.5 kPa occurred in 8.5, 13.8, 10.6 and 51.1% of patients respectively.
Patient with vs without LS ≥12.5 kPa had higher incidence of ischemic HF (79 vs 65%, p < 0.05), chronic anaemia (42 vs 19%, p < 0.01), glomerular filtration rate <60 ml/min/1.73 m2 (71 vs 55%, p < 0.05), chronic AF (54 vs 36%, p < 0.01), NYHA IV (52 vs 35%, p < 0.05).
LS ≥12.5 kPa was associated with high incidence of signs of congestion: peripheral oedema (98 vs 87%, p < 0.05), rales (94 vs 74%, p < 0.001), jugular venous distension (44 vs 32%, p < 0.05), hepatomegaly (69 vs 35%, p < 0.01), ascites (33 vs 10%, p < 0.001), severe mitral and tricuspid regurgitation (38 vs 19% and 58 vs 10%, p < 0.001 for both) and higher diameters of inferior vena cava (25 ± 6 vs 21 ± 7 mm, p < 0.05), right and left atriums (64 ± 13 vs 59 ± 15 mm, p < 0.05 and 51 ± 11 vs 47 ± 11 mm, p < 0.001), right ventricular end diastolic diameter (33 ± 5 vs 30 ± 5 mm, p < 0.001), pulmonary artery pressure (56 ± 18 vs 45 ± 13 mmHg, p < 0.001), higher levels of NT-proBNP (4655 (3120;7009) vs 4319 (2500;4961) pg/ml, p < 0.001), serum urea (10.1 (7.3;13.5) vs 7.4 (5.9;9.8) mmol/l, p < 0.05) and creatinine (109 (100;129) vs 105 (88;125) μmol/l, p < 0,05).
Patient with LS ≥12.5 kPa had higher rate of vasopressor therapy (10.4 vs 0%, p < 0.01) and longer length of stay (9 (8;15) vs 9 (6;12) days, p < 0.05).
Conclusions: Abnormal LS was occurred in 84.1% of patients with DHF. LS ≥12.5 kPa was associated with signs of congestion and right-sided HF, higher rate of vasopressor therapy and longer length of stay.

P1101
Central venous pressure is the main hemodynamic determinant of liver function in advanced heart failure.

J K Vishram-Nielsen[1]; T Deis[1]; B Balling[1]; S Boesgaard[1]; K Rossing[1]; F Gustafsson[1]
[1]Rigshospitalet - Copenhagen University Hospital, Department of Cardiology, the Heart Centre, Copenhagen, Denmark

Background: The relationship between liver function (LF) abnormalities and hemodynamics in heart failure (HF) is still incompletely understood as previous studies mainly included patients without contemporary HF medications and did not investigate liver synthetic function.
Methods: We assessed the relationship between LF tests and hemodynamics in 309 consecutive patients with a left ventricular ejection fraction < 45 % treated with contemporary medical HF therapy, and undergoing right heart catheterization using Swann-Ganz catheters. Cardiac output was measured using thermodilution.
Results: Mean age was 50 + 13 years, and 239 (77%) were men. Only 22 (7%)

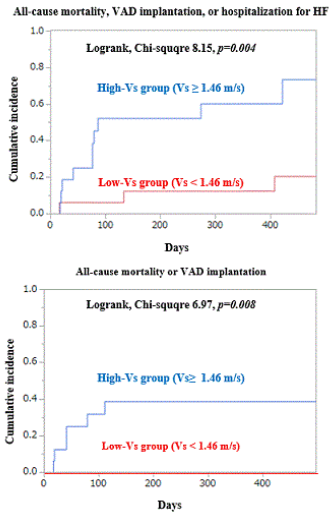
were treated with inotropes and none were receiving mechanical circulatory support. Median (IQR) alanine transaminase (ALT) was 32 (22-53) U/L, alkaline phosphatase (ALP) 82 (63-122) U/L and the International Normalized Ratio (INR) 1.1 (1.0-1.3). In univariate analysis, ALT related to pulmonary capillary wedge pressure (PCWP; β=0.016, $p<0.05$), but not to central venous pressure (CVP), cardiac index (CI), or mean arterial pressure (MAP). For ALP, there was only a significant relation to CVP (β=0.019, P=0.0004). In a sub-group analysis excluding those receiving warfarin (n=86), INR related to all four hemodynamic parameters: PCWP (β=0.011, $p<0.0001$), CVP (β=0.019, $p<0.0001$), CI (β= -0.073, P=0.0008), and MAP (β= -0.0003, P=0.031). In multivariate analyses including the four hemodynamic parameters, only the associations with CVP remained significant: ALP and CVP (β=0.031, P=0.0002), and INR and CVP (β=0.013, P=0.002).
Conclusion: In advanced HF patients treated with contemporary medical HF therapy, CVP was associated with both markers of biliary excretion and liver synthesis function. Decongestion may be most important to improve liver function in advanced HF.

P1102

Increased liver stiffness by virtual touch quantification method can predict poor clinical outcomes in patients with heart failure

K Kazunori Omote[1]; N Asakawa[1]; T Yoshitani[1]; K Noguchi[1]; Y Tokuda[1]; K Kamiya[1]
[1]Hokkaido University, Sapporo, Japan

Background: Heart failure (HF) is often associated with liver congestion, which has been proposed to increase liver stiffness. Tissue elastgraphy using virtual touch quantification method (VTQ) is a new noninvasive method to measure liver stiffness in HF patients.
Purpose: This study sought to determine the prognostic impact of liver stiffness assessed by VTQ method in HF patients with reduced ejection fraction (HFrEF).
Methods: Thirty two HFrEF patients [54.5± 18.9 years, 23male, left ventricular ejection fraction 34.0± 16.6%, plasma brain-type natriuretic peptide 1090± 1051 pg/ml] due to ischemic (n=5) or non-ischemic (n=27) cardiomyopathy were studied. Liver stiffness was measured from shear-wave velocity (Vs [m/s]) by VTQ. Studied patients were divided into 2 groups according to the median value of Vs; low (<1.46 m/s; n=16) and high (≥1.46 m/s; n=16) Vs groups, and the composite adverse cardiac events of all-cause mortality, ventricular assist device (VAD) implantation, and hospitalization for worsening HF were compared.
Results: During a median follow-up of 547 days, 13 (40%) adverse cardiac events including 4 VAD, 10 hospitalization, and 3 deaths occurred. High Vs group had more a composite adverse cardiac events compared with low Vs group (62.5% vs. 18.8%, p=0.004), and also all-cause mortality and/or VAD implantation (38.0% vs. 0%, p=0.008) (Figure). Univariate Cox regression analysis demonstrated that high Vs [hazard ratio (HR) 5.57; 95% confidence interval (CI) 1.66-25.3; p=0.005], low systolic blood pressure (sBP) (HR 0.97; 95%CI 0.93-0.99; p=0.031), and high serum creatinine (sCr) levels (HR 3.49; 95%CI 1.00-12.1; p=0.049) were significantly correlated with adverse cardiac events. Multivariable Cox regression analysis adjusted by Vs groups, sBP, and sCr levels demonstrated that high Vs was independently correlated with adverse cardiac events (HR 3.75; 95%CI 1.01-18.1; p=0.048).
Conclusion: Increased liver stiffness measured by VTQ can predict poor outcome in HF patients.



Figure

P1103

Left ventricular contractility and cardiac sympathetic derangement in patients with systolic heart failure and sleep disorder breathing

C Carmen D'amore[1]; F Marsico[1]; F De Martino[1]; F Renga[1]; S Paolillo[1]; V Parisi[2]; R Formisano[2]; B Trimarco[1]; P Perrone Filardi[1]
[1]Federico II University Hospital, Department of Advanced Biomedical Sciences, Naples, Italy; [2]Federico II University of Naples, Department of TranslationalMedical Science,, Naples, Italy

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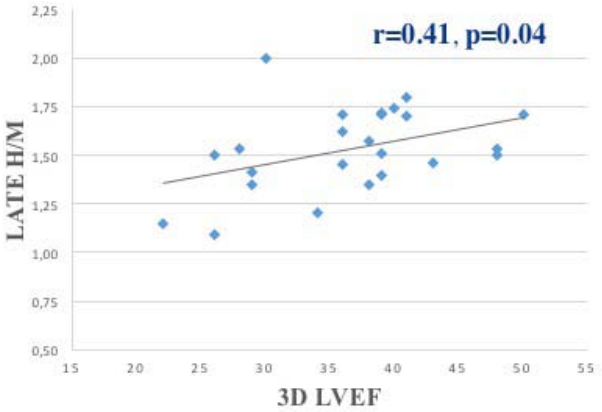
Background: Sleep-breathing disorders (SBD), either obstructive sleep apnoea (OSA) and central sleep apnoea (CSA), short sleep time and low sleep quality are highly prevalent in heart failure (HF) patients and adversely impact on the disease progression and prognosis. The effects of SBD in HF are mainly mediated through increased sympathetic nervous activity, contributing to the impairment of myocardial contractile function. Three-dimensional speckle tracking echocardiography (3D-STE) has been demonstrated to be more sensitive than 2D echocardiography in identifying impairment of left ventricular (LV) function. Yet, only few studies have investigated the correlation between cardiac sympathetic innervation and LV function abnormalities assessed by 3D-STE.
Purpose: Aim of the present study was to assess the relationship between cardiac adrenergic innervation and LV function measured by 3D-STE in HF patients with and without SBD.
Methods: Patients with HF and reduced systolic function were prospectively enrolled in the study. During the first day patients underwent 2D and 3D transthoracic echocardiography to evaluate LV ejection fraction (LVEF) and nocturnal cardiorespiratory monitoring to assess SBD presence and severity by apnoea/hypopnoea index (AHI). During the second day, cardiac adrenergic innervation was assessed by 123I-MIBG scintigraphy using early and late hart-to-mediastinum (H/M) ratio measurement and washout rate (WR).
Results: Thirty-five patients (33 men; 64±8 years) with systolic HF were included in the study. Of 35 patients, 24 (68%) showed a SDB (17 subjects with prevalent CSA and 7 subjects with prevalent OSA). Using AHI patients were divided into those with absent or mild SBD (AHI ≤15; n=20) and those with moderate to severe SBD (AHI>15; n=15). Patients with moderate-severe SDB had a greater reduction of 3D LVEF (33.2±5.9 vs 41.7±7.2; p=0.001) than patients with mild or absent SDB, whereas 2D LVEF did not reveal significant differences between the two groups (29.6±4.3 vs 32.0±7.2; p=0.261). 3D LVEF (31.3±6.7 vs 38.6±6.6; p=0.023) and 3D strain area (-9.4±2.9 vs -14.7±4.1; p=0.005) were significantly more reduced in patients with OSA compared to patients with CSA. 3D LVEF directly correlated with late H/M ratio in patients with SDB (r=0.41, p=0.04), but not in patients without SDB.
Conclusions: Patients with moderate-severe SDB and systolic HF show significantly more impaired left ventricle contractile function assessed by 3D-STE, compared to patients without SDB, that correlates with the impairment of cardiac adrenergic innervation and is not identified by conventional 2D echo.



CORRELATION BETWEEN 3D LVEF AND LATE H/M

P1104

A comparison between patients with central and obstructive sleep apnea in patients with heart failure: SICA-HF

T Bekfani[1]; CH Schoebel[2]; CH Pietrock[3]; M Valentova[4]; A Sandek[4]; N Ebner[4]; S Elsner[3]; W Doehner[3]; M Noutsias[1]; PC Schulze[1]; SD Anker[4]; S Von Haehling[4]
[1]University Hospital of Jena, Department of Cardiology, Jena, Germany; *[2]Charite - Campus Mitte (CCM), Cardiology, Berlin, Germany*; *[3]Charite - Campus Virchow-Klinikum, Department of Cardiology, Division of Applied Cachexia Research, Berlin, Germany*; *[4]University Medical Center Göttingen, Department of Cardiology, Göttingen, Germany*

On behalf of: SICA-HF

Background: Sleep-disordered Breathing (SDB) is a very common comorbidity in patients with heart failure (HF).
Purpose: The aim of this study was to demonstrate the characteristic differences between central (CSA) and obstructive (OSA) sleep apnea and to evaluate the mortality rate in patients with CSA.
Methods: We prospectively enrolled 111 outpatients (age: 67.6 ± 10.2years, sex: 81 men [73%], body mass index: 27.9 ± 4.4kg/m2, New York Heart Association class: 2.3 ± 0.7) with stable HF as part of SICA-HF study from 03/2010 till 09/2013. Echocardiography, spiroergometry, DEXA-scan and polygraphy (portable monitoring) assessments using the Embletta and Nox-Devices were done in all patients. We re-analyzed the tests of the polygraphy visually (manually) in cooperation with the department of sleep medicine at our hospital. SDB was defined as apnea/hypopnea index (AHI) >5 episodes/hour of sleep. CSA was defined as central AHI> 50% of the total AHI. The same was applied for OSA.
Results: We found that 74 patients have SDB (66.7%). 16 (55.2%) patients with HFpEF (LVEF>50%) and 55 patients (67.1%) with HFrEF showed SDB. Overall, 24 patients had CSA (21.6%), 47 patients showed OSA (42.3%) and 3 patients had mixed sleep apnea (2.7%). Compared to OSA, patients with CSA showed more advanced systolic heart failure as determined by reduced left ventricular ejection fraction (LVEF, 42 ± 15% vs. 28 ± 9%, p = 0.0001), dilated left ventricle [(left ventricle end-diastolic diameter (LVIDd): 64 ± 11 vs. 60 ± 9 mm, p = 0.006)] and thin walls of the left ventricle [interventricular septum diameter in diastole (IVSd) 11.9 ± 2.5 vs. 10.7 ± 2.3mm, p = 0.04; posterior wall diastolic diameter (PWD): 10.9 ± 2.1 vs. 9.6 ± 2.0mm, p = 0.02)]. Furthermore, CSA had worse renal function (GFR 60.1 ± 13.8 vs. 52.8 ± 15.8ml/min, p = 0.045) and reduced fat mass in the arms and legs (arms: 31.1 ± 10.9 vs. 26.7 ± 7.9%, p = 0.085, legs: 32.6 ± 11 vs. 27.6 ± 7, p = 0.047). CSA tended to be more common among patients with a coronary artery disease (p = 0.095). On polygraphy, CSA patients showed higher severity of SDB than those with OSA (higher AHI: 16.2 ± 12.0 vs. 31.5 ± 11.4 episode/h, p = 0.0001, and a higher oxygen desaturation index (ODI): 14.7 ± 11.7 vs. 28.0 ± 11.9 episode/h, p = 0.0001). Compared with those without SDB, patients with CSA showed elevated VE/VCO2 in the spiroergometry: 34.1 ± 7.8 vs. 39.9 ± 8.1, p = 0.047). Defining CSA as AHI>10/h we found a significant increase in the mortality among patients with CSA compared to those with no SDB (p = 0.03).
Conclusions: SDB is a very common comorbidity in patients with HF. CSA is associated with a higher mortality rate, more advanced stage of systolic heart failure and with more severe SDB.

P1105

Sleep apnea and long-term prognosis of acute myocardial infarction

O Ludka[1]; R Stepanova[1]; T Kara[2]; J Spinar[3]
[1]University Hospital Brno, Masaryk University, International Clinical Research Center, Department of Internal Medicine and Cardiology, Brno, Czech Republic; *[2]Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic and Foundation, Minnesota, United States of America*; *[3]Department of Internal Medicine and Cardiology, University Hospital Brno, Brno, Czech Republic*

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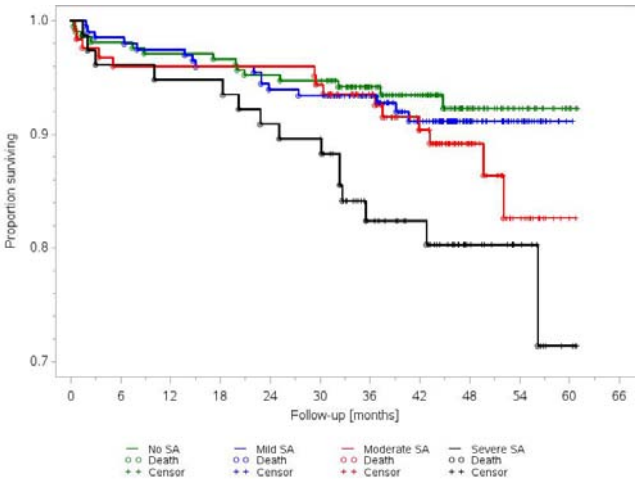
Purpose: Sleep apnea (SA) has a high prevalence in patients after myocardial infarction (MI). While SA might be a modifiable risk factor, recent data suggest that SA is severely underdiagnosed in patients after MI. There is also limited evidence about long-term prognosis of patients after MI according to SA categories. Therefore we sought to determine the relationship between SA and long-term prognosis among patients presenting with MI.
Methods: We prospectively studied 782 consecutive patients admitted to the hospital with the diagnosis of acute MI. The study was conducted in two tertiary care institutions, where primary percutaneous coronary intervention (PCI) is the standard of care in the treatment of acute MI. All subjects underwent sleep evaluations using a portable diagnostic device after at least 48 hours post-admission, provided they were in stable condition. Patients were followed for median follow-up of 43.3 months. Results: Almost all patients (98%) underwent urgent coronary angiography and 91% of patients underwent primary PCI. 175 (22.4%) patients had technically inadequate limited sleep studies (less than 4 h recording time or inability to score study due to excessive artifact). We therefore analyzed the data from 607 patients who had good quality sleep study records. Using a threshold of AHI > 5 events/hour, SA was present in 65.7% of patients after acute myocardial infarction. Mild SA was present in 32.6%, moderate in 20.4% and severe in 12.7%. There was a relation between the severity of SA and long-term prognosis. Patients after MI with increasing severity of SA had higher total mortality (p = 0.014, log-rank test). The Kaplan-Meier survival curves are presented. There was also a higher total mortality in reduced (REF) than in preserved left ventricular ejection fraction (PEF) patients after MI (21.7% vs 10.6%) in the group of moderate to severe SA (p = 0.033). Conclusion: Mortality of patients after MI significantly increased with increasing severity of SA. Whether treatment of SA after MI will significantly improve outcomes in these patients remains to be determined.



Kaplan-Meier survival curves

P1106

The CHA2DS2VASc score predicts cardiogenic shock in patients presenting with ST-segment elevation myocardial infarction

RC Serban[1]; A Scridon[1]; L Hadadi[1]; I Sus[1]; EK Lakatos[1]; Z Demjen[2]; D Dobreanu[1]
[1]University of Medicine and Pharmacy of Tirgu Mures, Tirgu Mures, Romania; *[2]Institute of Cardiovascular Diseases, Targu Mures, Romania*

Funding Acknowledgements: This work was supported by the University of Medicine and Pharmacy of Tirgu Mures Research Grant number 17800/1/22.12.2015.

Background: All factors included in the CHA2DS2VASc score have been associated with increased risk of ST-segment elevation myocardial infarction (STEMI), but their potential to predict hemodynamic status at presentation with STEMI has not been evaluated to date.
Purpose: We aimed to investigate the ability of the CHA2DS2VASc score to predict the presence of cardiogenic shock (CS) on admission for STEMI.
Methods: We evaluated data from 428 consecutive patients admitted for STEMI. For each patient, all factors included in the CHA2DS2VASc score were assessed, and the CHA2DS2VASc score was calculated. Association of these factors with the presence of CS on admission was assessed.
Results: 4.90% of STEMI patients presented CS at admission. Due to selection criteria, all patients presented vascular disease. Age, female sex, history of hypertension, diabetes mellitus, and stroke were not significantly different between patients with and without CS (all p>0.05). However, patients with CS had more frequently a history of heart failure (p < 0.01) and higher CHA2DS2VASc scores (4(2-6) vs. 3(2-4), p = 0.03). In multiple regression analysis, the CHA2DS2VASc score remained an independent predictor of CS (r=0.14, p = 0.004).
Conclusions: With the exception of a history of heart failure, none of the other factors included in the CHA2DS2VASc score correlated with the presence of CS on admission for STEMI. Meanwhile, the CHA2DS2VASc score was a strong, independent predictor of CS. The sum of cardiovascular risk factors, rather than each factor alone, may be a better predictor of hemodynamic impairment in STEMI patients.

P1107

Comparison of prevalence of contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention depending on definitions

A Anna Gaskina[1]; S Villevalde[1]; Z Kobalava[1]
[1]*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. The prevalence of CI-AKI are not well defined. The aim of the study was to evaluate the prevalence of CI-AKI in patients undergoing PCI using different definitions
Methods: 502 patients (346 male, 64 ± 12 years (M ± SD), arterial hypertension 92%, previous myocardial infarction 38%, diabetes mellitus (DM) 22%, known chronic kidney disease 19%, anemia 16%, heart failure 62%, left ventricular ejection fraction 40 ± 16%) who underwent PCI (stable angina pectoris (SAP), n=50; unstable AP/non-ST-segment elevation myocardial infarction (UAP/NSTEMI), n=236; STEMI, n=216) were examined. CI-AKI was assessed according KDIGO 2012 Guidelines and previously the most frequently used definition (25% increase of serum creatinine (SCr) from baseline or 0.5 mg/dl increase in absolute value within 48-72 hours of contrast administration. Mann-Whitney test was performed. $P < 0.05$ was considered statistically significant.
Results: According KDIGO 2012 definition incidence of CI-AKI was 18 %, in SAP patients 12%; UAP/NSTEMI, 15%; STEMI, 20%, $p < 0.01$. According previously used definition incidence of CI-AKI was: total population 20%, SAP, 16%; UAP/NSTEMI, 16%; STEMI, 18%, $p < 0.01$. Conclusions: The highest prevalence of CI-AKI both on the 2012 KDIGO Guidelines and earlier version was highest among the STEMI patients with primary PCI.

P1108

Non-cardiac comorbidities in HFrEF, HFmrEF and HFpEF - findings from BIOSTAT-CHF

K W Streng[1]; JF Nauta[1]; JL Hillege[1]; SD Anker[2]; JG Cleland[3]; CC Lang[4]; M Metra[5]; L Ng[6]; P Ponikowski[7]; DJ Van Veldhuisen[1]; A Zwinderman[8]; F Zannad[9]; K Damman[1]; P Van Der Meer[1]; AA Voors[1]
[1]*University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; [2]*University Medical Center Gottingen (UMG), Innovative Clinical Trials, Department of Cardiology and Pneumology, Gottingen, Germany*; [3]*Imperial College London, National Heart & Lung Institute, Royal Brompton and Harefield Hospitals, London, United Kingdom*; [4]*University of Dundee, School of Medicine Centre for Cardiovascular and Lung Biology, Dundee, United Kingdom*; [5]*University of Brescia, Institute of Cardiology, Department of Medical and Surgical Specialties, Brescia, Italy*; [6]*University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom*; [7]*Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; [8]*Academic Medical Center of Amsterdam, Department of Epidemiology, Biostatistics and Bioinformatics, Amsterdam, Netherlands*; [9]*University of Lorraine, Nancy, France*

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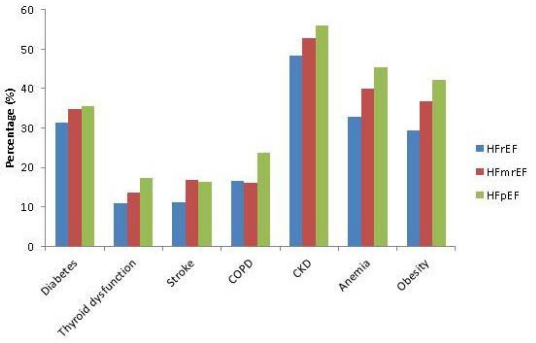
Background: Comorbidities play a major role in heart failure. Whether prevalence and prognostic importance of comorbidities differ between heart failure with preserved ejection fraction (HFpEF), mid-range (HFmrEF) or reduced ejection fraction (HFrEF) is unknown.
Methods: Patients from the index (n = 2516) and validation cohort (n = 1738) of The BIOlogy Study to Tailored Treatment in Chronic Heart Failure (BIOSTAT-CHF) were pooled for the present analysis. Seven non-cardiac comorbidities were assessed; diabetes mellitus, thyroid dysfunction, obesity, anaemia, chronic kidney disease (CKD), COPD and stroke. Patients were classified into 6 groups based on ejection fraction; HFrEF(< 40%), HFmrEF (40-50%) and HFpEF (≥50%), and having less or more than 3 comorbidities. Impact of each comorbidity on all-cause mortality was evaluated by population attributable risk (PAR).
Results: Patients with known LVEF and complete comorbidity data were included (n = 3499). Most prevalent comorbidity was CKD, with a prevalence of 50%. All comorbidities had a higher prevalence in HFpEF, except for stroke. Patients with 3 or more comorbidities had higher all-cause mortality rates in HFrEF (hazard ratio (HR) 1.57, $P < 0.001$) and HFmrEF (HR 1.39, $P < 0.001$), but not in HFpEF (HR 1.02, P=0.902). Highest PARs were seen for CKD in all HF groups, whereas obesity has an inverse PAR in HFpEF. Diabetes and stroke contributed significantly in HFrEF (11% and 6%) but were not significant in HFpEF (-1% and 0%).
Conclusions: Overall, comorbidities are more prevalent in patients with HFpEF, but having more comorbidities is associated with an increased all-cause mortality in HFrEF and HFmrEF, but not in HFpEF. CKD has the highest impact on mortality in all groups. History of stroke and diabetes have a significant impact on all-cause mortality in HFrEF, in contrast to HFmrEF and HFpEF.



Prevalence of comorbidities

P1109

Differences in comorbidities between men and women with heart failure exist.

M Marlies Heiligenberg[1]; JM Maaskant[1]; CHM Latour[1]
[1]*Amsterdam University of Applied Sciences, ACHIEVE — Centre of Applied Research, Faculty of Health, Amsterdam, Netherlands*

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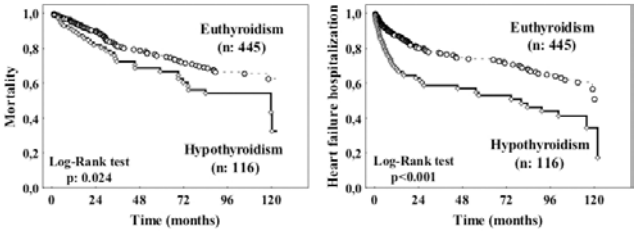
Background: Comorbidities in patients with heart failure (HF) increase morbidity, mortality and healthcare usage. Depression in HF patients is common and associated with negative outcomes. The prevalence of depression is higher in women with HF than in men. However, knowledge about the differences in comorbidities between men and women with HF, and between men and women with depression, is limited.
Purpose: The purpose of our study was to establish (1) differences in comorbidities between men and women with HF, and (2) differences in comorbidities between patients with HF with and without depression. We hypothesized that there are differences in comorbidities between men and women with HF (with and without depression).
Methods: The prevalence of 16 comorbidities was obtained by studying a database with 38.807 participants from 41 research projects in the Netherlands, executed between 2010-2013 (the Older Persons and Informal Caregivers Survey Minimal data set). Out of the 38.807 participants, only those patients who reported HF were included in this study. Mann-Whitney, Kruskal Wallis and Chi-square tests were used to analyze differences between groups.
Results: We included 7010 patients, who had reported HF. The median age was 80 (range 52-102 years), and 56.4% was female. Fifteen percent of the participants came from research projects in the general population, nursing home or retiring community, 25% from projects in a hospital setting and 60% from projects in a primary care setting. The following comorbidities were significant more prevalent in women compared to men: incontinence, osteoarthritis or rheumatoid arthritis, osteoporosis, hip and other fractures, dizziness with falling, vision disorders, and anxiety/panic disorder. Cancer and hearing disorders were more common in men. In addition, depression was registered more often in women than men: 13.0% vs. 9.5%. We compared patients with and without depression on the prevalence of comorbidities. Our results show that for both men and women, patients with depression had a higher prevalence of most comorbidities, than patients without depression. The prevalence of most comorbidities was highest in women with depression. Women with depression had 2 additional comorbidities and men 1 additional comorbidity compared to women and men respectively, without depression.
Conclusion: Women with HF report comorbidities (including depression) more often than men, and women with HF and depression have a higher number of additional comorbidities than men and the highest prevalence of most comorbidities. Patients with HF and depression have a higher prevalence of comorbidities than patients with HF without depression. This information is important for researchers, and warrants additional studies to investigate the effect of depression on combinations of comorbidities in men and women with HF, and whether depression is associated with increased health care usage in men and women with HF.

P1110

Hypothyroidism and heart failure outcome: a study with a long-term follow-up

C Caterina Rizzo[1]; D Grande[1]; P Terlizzese[1]; MS Lattarulo[1]; T Leopizzi[1]; MI Gioia[1]; B Licchelli[2]; E Guastamacchia[2]; V Triggiani[2]; M Iacoviello[3]
[1]*University of Bari, School of cardiology, Bari, Italy*; [2]*University of Bari, School of Endocrinology, Bari, Italy*; [3]*Polyclinic Hospital of Bari, Cardiology Unit, Cardiothoracic department, Bari, Italy*

Background: Abnormalities of thyroid function has been demonstrated to be associated to heart failure (HF) progression in patients affected by chronic heart failure (CHF). It's not clear the impact of a reduced thyroid function on long term outcome of this group of patients.
Aim of the study: To evaluate the impact of hypothyroidism (HT-H) on the progression of HF during a long-term follow-up.
Methods: From 2006 to 2015,we evaluated 675 consecutive CHF outpatients (523 males,64 ± 13years) in stable clinical conditions(>1mounth) and in conventional therapy. They have been carefully documented the presence of thyroid diseases. During follow-up, thyroid function has been evaluated every 4 months, more frequently (every 6 weeks) in patients receiving Levothyroxine or with high TSH levels, to optimize the TSH values in the normal range. The onset of HT-H during follow-up was defined as detection of TSH values above the upper limit. When HT-H was detected, thyroid replacement therapy was started according to guidelines. During follow-up were also evaluated hospitalizations related to exacerbation of HF and death.
Results: 455 patients(67.7%) were euthyroid at the enrollment and for the entire duration of follow-up,in 80 patients (11.8%) there was previous diagnosis of HT-H and in 40 patients (5.9%) the HT-H was detected at the time of the enrolment. During follow-up,52 patients (7.7%) developed HT-H. The remaining were affected by hyperthyroidism or low T3 syndrome. To avoid confounding effects due to the other thyroid abnormalities, we compared patients in euthyroid status at the enrolment and during follow-up and those with HT-H at the ernollment. Among these,during follow-up (median value of 47 months,maximum 123 months),133 patients died and 186 experienced at least one hospedalization due to acute decompensated HF. At Univariate Cox regression analysis,a significant association between HT-H and the events,i.e. mortality for all causes (HR:1.60;95%CI:1.08-2.38;p:0.019) and hospitalization for HF worsening (HR:2.13;95%CI:1.54-2.96;p: < 0.001) was found. At multivariate Cox regression analyses, HT-H remained associated only with HF hospitalization (HR:1.58;95%CI:1.09-2.29;p:0.015) but not with mortality (HR: 1.05;95%CI:0,67-1,65;p:0.819), after correction to LVEF < 35%, GFR < 60ml/min/m2 NTproBNP>1000pg/ml,NYHAIII,PA < 95mmHg. Figure shows Kaplan-Meier curves for events of patients in euthyroid status at the enrolment and during follow-up and of patients with HT-H at the ernollment.
Conclusion: In a long term follow-up, HT-H is independently associated with hospitalization due to HF worsening but not with mortality. We hypothesized that HT-H is able to induce hemodynamic instability leading to hospitalization, but its correction with thyroid hormone therapy could in part blunt its impact on patients'survival.



Kaplan-Meier curves

P1111

Epicardial obesity as a factor of structural and functional heart remodeling

T YU Kuznetsova[1]; M A Druzhilov[1]
[1]*Petrozavodsk State University, Petrozavodsk, Russian Federation*

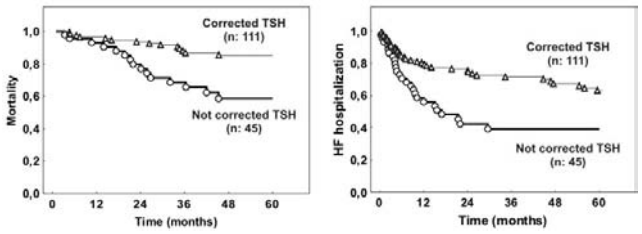
Background: Epicardial fat is considered as an independent risk factor, regardless of the severity of obesity in general. Several studies have demonstrated the possibility of myocardial lesion in epicardial obesity (EO) as a result of mitochondrial dysfunction and oxidative stress, apoptosis of cardiomyocytes, inflammation and fibrosis, disorders of adipokines and cytokines secretion.
Purpose: The aim is evaluate the association of EO with the presence of structural and functional heart remodeling.
Methods: 108 normotensive men without cardiovascular diseases were examined (age 48,7 ± 2,0, body mass index 31,6 ± 3,3 kg/m2, waist circumference 106,1 ± 5,7 cm). The diagnostic tests included the lipid and glucose profiles evaluation, echocardiography, bifunctional daily blood pressure monitoring with evaluation of arterial stiffness indicators (average daily aortic pulse wave velocity, augmentation index). Epicardial fat was visualized behind right ventricular free wall in B-mode at the parasternal position along left ventricular long axis at the end of systole. EO was diagnosed when epicardial fat thickness (EFT) was equal to or exceeded 75 percentile value (5,8 mm).
Results: Average EFT was 5,0 ± 1,2 mm. In patients with EO (n = 27) higher values of left ventricular mass index (119,4 ± 8,9 g/m2 vs 100,4 ± 15,9 g/m2, p < 0,001), left atrial volume indexed to body surface area (22,3 ± 3,4 ml/m2 vs 20,1 ± 2,2 ml/m2, p < 0,01), average daily aortic pulse wave velocity (8,4 ± 0,4 m/s vs 7,6 ± 0,4 m/s, p < 0,001), augmentation index (-39,4 ± 12,2 % vs -46,3 ± 10,6 %, p < 0,01). Compared groups did not differ in the systolic and diastolic blood pressure levels (118,4 ± 7,4/74,3 ± 4,8 mm Hg vs 117,5 ± 4,3/73,4 ± 4,2 mm Hg). In the EO group left ventricular hypertrophy and left ventricular diastolic dysfunction were detected more frequently: 25,9 % vs 6,2 % (p < 0,01) and 66,7 % vs 11,1 % (p < 0,01) respectively.
Conclusions: EO is associated with the parameters characterized the structural and functional heart remodeling. Higher values of left ventricular mass and left atrial volume indexes, higher frequency of left ventricular hypertrophy and left ventricular diastolic dysfunction were found in patients with EO diagnosed by measuring EFT.

P1112

The correction of TSH with thyroid replacement therapy is associated with a better outcome in chronic heart failure patients

D Dario Grande[1]; C Rizzo[1]; P Terlizzese[1]; MS Lattarulo[1]; T Leopizzi[1]; MI Gioia[1]; B Licchelli[2]; E Guastamacchia[2]; V Triggiani[2]; M Iacoviello[3]
[1]*University of Bari, School of Cardiology, Bari, Italy*; [2]*Polyclinic Hospital of Bari, Endocrinology and Metabolic Diseases Unit, Interdisciplinar Medicine Department, Bari, Italy*; [3]*Polyclinic Hospital of Bari, Cardiology Unit, Cardiothoracic Department, Bari, Italy*

Background: It has been previously demonstrated that thyroid hormone deficiency is associated with a worse outcome in patients affected by chronic heart failure (CHF). However, few data are available about the effects of thyroid replacement therapy on the prognosis of patients.
Aim of the study: The aim of the study was to evaluate the relationship among thyroid replacement therapy, correction of thyroid stimulating hormone (TSH) serum levels and outcome of a series of CHF outpatients.
Methods: We screened CHF outpatients in stable clinical conditions (>1 month) and in conventional therapy. All patients underwent a baseline clinical evaluation, a 12-lead ECG, an echocardiogram and routine blood tests. Thyroid hormones were assessed at the enrolment and routinely during follow-up (every 3-4 months or every 6-8 weeks if TSH level was altered at the previous control). All patients with history or newly diagnosed hypothyroidism were managed by endocrinologists. We considered hypothyroidism corrected when TSH serum levels were normalized by thyroid replacement therapy (levothyroxine).
Results: Out of 712 patients, in 180 patients (121 males, 67 ± 12 years, left ventricular ejection fraction, LVEF, 33 ± 10%, NYHA class 2.5 ± 0.5, NTproBNP 2125 ± 2975 pg/ml, GFR-EPI 64 ± 22 ml/min*1.73m2) hypothyroidism was diagnosed. Twenty-four patients were excluded because they were lost at follow-up or died within the first 3 months or because endocrinologists did not prescribe levothyroxine for TSH values not high enough. Among the remaining 156 patients in which levothyroxine was prescribed, in 111 patients a normal TSH value was obtained. During a mean follow-up of 38 months, 29 patients died (25 for cardiovascular causes) and 62 experienced at least one admission for acute decompensated heart failure. The failure in TSH correction was associated with an increased risk of all cause of death (HR: 3.31; 95%CI: 1.59-6.86; p: 0.001) and of heart failure hospitalization (HR: 2.27; 95%CI: 1.36-3.79; p: 0.002). At Cox multivariate analysis the failure in TSH correction remained associated with all cause mortality (HR: 2.57; 95%CI: 1.20-5.51; p: 0.002) and with heart failure hospitalization (HR: 1.78; 95%CI: 1.05-3.01; p: 0.03) after correction for NYHA class 3, LVEF < 35%, NTproBNP>1000, systolic blood pressure < 100 mmHg and GFR-EPI < 60. In the figure Kaplan Meier curves of patients with and without TSH correction are shown.
Conclusion: Our results support the possibility that hypothyroidism correction could improve the prognosis of CHF patients, although randomized controlled trials should be designed in order to demonstrate this hypothesis.

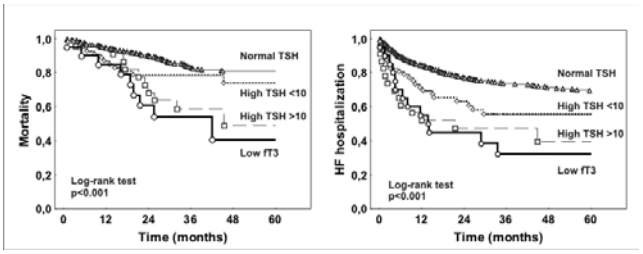


P1113

Thyroid hormones deficiencies and poor outcome in chronic heart failure outpatients

P Paola Terlizzese[1]; D Grande[1]; C Rizzo[1]; T Leopizzi[1]; MS Lattarulo[1]; MI Gioia[1]; B Licchelli[2]; E Guastamacchia[2]; V Triggiani[2]; M Iacoviello[3]
[1]*University of Bari, School of Cardiology, Bari, Italy*; [2]*Polyclinic Hospital of Bari, Endocrinology and Metabolic Diseases Unit, Bari, Italy*; [3]*Polyclinic Hospital of Bari, Cardiology Unit, Cardiothoracic Department, Bari, Italy*

Background: Impairment of thyroid function is by far the second most common endocrine comorbidity in patients suffering from chronic heart failure (CHF). However, the cut-off of TSH serum levels associated with worse outcome is still debated as well as the different impact of hypothyroidism and low T3 syndrome (LT3).
Aim of the study: to evaluate in a large sample of CHF patients the association between thyroid hormone deficiencies and poor outcome.
Methods: and results: From 2006 to 2015, we screened 712 consecutive CHF outpatients (551 males, 64 ± 14 years, left ventricular ejection fraction (LVEF) 33 ± 10%, NYHA class 2.3 ± 0.6, NTproBNP 2153 ± 4696 pg/ml, GFR-EPI 71 ± 25 ml/min*1.73m2) in stable clinical conditions (> 1 month) and in conventional therapy. All patients underwent assessment of thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxin (fT4). While 34 patients were excluded for hyperthyroidism, among the remaining 678, 58 (9%) showed a TSH level above the upper normal limit, but below 10 microU/ml, 23 (3%) a TSH value above 10 microU/mL, and 20 patients (3%) low fT3 (LT3) levels without changes in TSH levels. During a mean follow-up of 38 months, 122 patients died (101 for cardiovascular causes) and 202 experienced at least one admission for acute decompensated heart failure. TSH >10 microU/mL (HR:2.96; 95%CI: 1.54-5.68; p: 0.001) and LT3 (HR: 3.79; 95%CI: 1.91-7.54; p < 0.001), but not high TSH < 10 microU/mL (HR: 1.59; 95%CI: 0.871-2.91; p:0.13), were associated with an increased risk of death at univariate analysis. At multivariate Cox regression analysis, after correction for the presence of NYHA class 3, LVEF < 35%, NTproBNP >1000, systolic arterial pressure < 100 mm Hg and GFR-EPI < 60 mL/min, only LT3 remained significantly associated with events (HR: 2.75; 95%CI:1.38-5.49; p: 0.004). When the occurrence of heart failure hospitalization was considered, high TSH levels with a value < 10 microU/mL (HR 1.82; 95% CI: 1.18-2.83; p < 0.01), TSH>10 microU/mL (HR 2.84; 95%CI:1.61-5.01; p < 0.001) and LT3 (HR: 3.33; 95%CI: 1.89-5.88; p < 0.0001) were all associated with events at univariate regression analysis. At multivariate regression analysis TSH>10 microU/mL (HR: 1.91; 95%CI:1.06-3.46; p:0.03) and LT3 (HR: 2.39; 95%CI: 1.36-4.24; p:0.002), but not high TSH with value < 10 microU/mL, remained associated with HF hospitalization. Figure 1 shows Kaplan-Meier curves reporting the relationship between thyroid hormones levels and both outcomes.
Conclusion: in this observational study performed on a large cohort of CHF outpatients, we found that impaired thyroid function, particularly when very high levels of TSH (>10 microUI/mL) and low T3 levels are considered, has an independent adverse impact on CHF events. These results, if confirmed by future RCTs, could suggest a new therapeutic approach when dealing with TSH correction in CHF patients.



P1114

Influence of chronic comorbidities on the mortality of patients admitted for heart failure in a general hospital.

JJ Juan Jose Martinez Diaz[1]; ML Fernandez Gasso[1]
[1]*Hospital General Universitario de Santa Lucia, Cardiology, Cartagena, Spain*

BACKGROUND: The influence of comorbidities on the prognosis of patients admitted due to heart failure is unclear.
PURPOSE: To study the influence of chronic comorbidities in in-hospital and long-term mortality of patients admitted with a diagnosis of heart failure.
Methods: 256 patient with main diagnosis of heart failure were recruited. Demographic data, cardiovascular risk factors, prior cardiovascular disease, chronic comorbidities (COPD, renal failure or neoplasic disease) and mortality rates were analyzed.
RESULTS: The baseline characteristics of the sample are shown in Table 1. 23 patientes died during their hospital stay, 52 of them died during the following year. Those variables that showed a relationship with in-hospital mortality in a Chi-square analysis were included in a binary logistic regression model: COPD (OR 2.68, p = 0.045) showed to be a risk factor for in-hospital mortality. In a proportional hazards model of Cox, COPD (HR 2.3, p = 0.02) and renal failure (HR 2.65, p = 0.003) showed to be risk factors for mortality during the first year. A long-term survival analysis was performed (Kaplan Meier method) with similar results (Figure 1).
CONCLUSION: In patients admitted with main diagnosis of heart failure, COPD has been shown to be a risk factor for both in-hospital and one-year mortality as well as renal failure is a risk factor for mortality at one year.

Table 1

	Frequency	Percentage
Age 78,2 ± 9.8		
Men	127	49,6
Women	129	50,4
Arterial hypertension	238	93
Diabetes	97	37,9
Dyslipidemia	106	41,4
Smoking	13	5,1
Obesity	45	17,6
Prior cardiovascular desease -AMI -Stroke -Acute pulmonary edema	61 29 32 5	23,8 11,3 12,5 2
Functional class III-IV	34	13,3
Active infection	46	18
COPD	68	26,6
Renal failure	48	18,8
Neoplastic disease	14	5,5
Atrial fibrillation	109	42,6

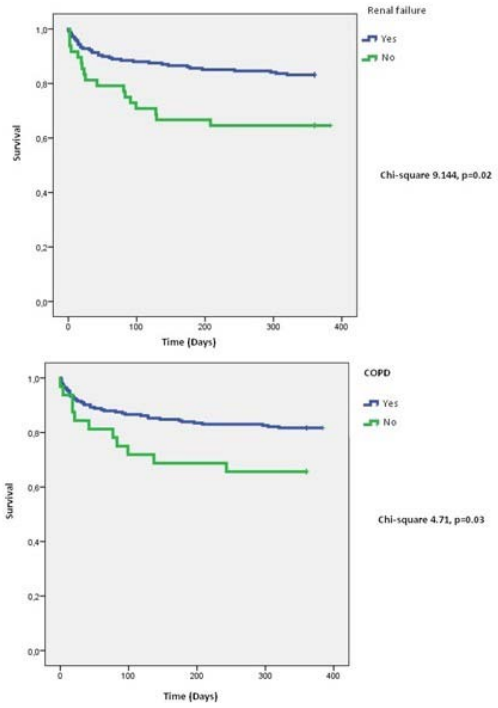


Figure 1

P1115

Different types of heart failure, different treatments?

S Sara Blasco[1]; FJ Camacho[1]; I Lobo[1]; C Collado[1]; P Gonzalez[1]; JA Sanchez-Brotons[1]; I Perez[1]; E Martinez De Morentin[1]; M Iravedra[1]; M Maestre[1]; J Lozano[1]; P Martinez Romero[1]; FJ Morales[1]
[1]*Puerto Real Hospital, Cardiology, Puerto Real, Spain*

Introduction: The latest Heart Failure and Cardiovascular Prevention ESC Guidelines have shown the benefits of empagliflozin in preventing and slowing down the progression of Heart Failure (HF) and reducing cardiovascular mortality. Our goal is to analyze whether the ESC Guidelines recommendations are being followed and if there are any differences according to the ejection fraction (HFrEF, HFmrEF, HFpEF).
Material and methods: Prospective and descriptive study of type 2 diabetic patients hospitalized in the Cardiology Service from June 15th to December 31st, 2016, comparing patients with HFrEF, HFmrEF and HFpEF..
Results: From June 15th to December 31st, out of a total of 121 diabetic patients hospitalized, 58 either had chronic heart failure or de novo HF. Average FEVI was 50% ± 14%, and according to the latest classification 29% had HFrEF,18% HFmrEF, and 51% HFpEF. There were significant differences in regards to gender (77% males in HFrEF, 70% HFmrEF, 50% HFpEF), HTA (77% of patients with HFrEF vs. 90% in patients withHFmrEF and 86% in patients with HFpEF), and creatinine clearance (ClCr < 60ml/min in 33% of patients with HFrEF vs. 60% in HFmrEF and 53% HFpEF), while there were none in age (67 ± 10 in HFrEF, 72 ± 12 in HFmrEF and 72 ± 10 in HFpEF), nor other cardiovascular risk factors such as dyslipidemia, smoking or obesity. All patients were being properly treated with Beta blockers, ACE inhibitor, and MRA drugs. Still, nearly a 50% of the hospitalizations in all DM 2 patients were due to Heart Failure. Regarding previous antidiabetic drugs, none of the patients were being treated with an SGLT2 inhibitor. 72% of HFrEF patients were under Metformin (22% on its own), 22% sulfonylureas, 11% DPP4 inhibitor and 44% under insulin. As for HFmrEF, 80% were under Metformin (20% as single-drug treatment), 20% sulfonylureas, 10% DPP4 inhibitor drugs and 40% under insulin. And finally, 50% of HFpEF patients were under Metformin (13% on its own), 13% under sulfonylureas, 16% under DPP4 inhibitor drugs and 43% under insulin. Nevertheless, 55% of HFrEF patients, 40% of HFmrEF patients and 23% of HFpEF had HbA1c levels out of the target range. At discharge, anti-diabetic treatment was modified in 19% of the patients, adding an SGLT2 inhibitor drug to 12% of the patients. We did not detect any complications, nor had to interrupt the treatment at the moment of publication.
Conclusions: We've detected that ESC guidelines aren't being followed in the use of anti-diabetic drugs in patients with cardiovascular diseases, unlike other cardiovascular risk factors that have well-established treatment protocols. Most of our patients could benefit from the use of the SGLT2 inhibitor. In this regard, there were no differences found after treatment modifications, but longer tracking period and bigger sample size are needed to validate these findings.

CYTOKINES AND INFLAMMATION

P1116

Inflammation and intestinal bacterial overgrowth in heart failure

A Anna Mollar Fernandez[1]; MP Villanueva[2]; G Minana[1]; A Villaescusa[1]; D Escribano[1]; P Palau[1]; E Santas[1]; A Bayes-Genis[3]; E Nunez[1]; F Mora[4]; M Minguez[4]; J Sanchis[1]; J Nunez[1]
[1]*University Hospital Clinic of Valencia, Cardiology, Valencia, Spain*; [2]*University Hospital Clinic of Valencia, clinical biochemistry, Valencia, Spain*; [3]*University Hospital Trias i Pujol, Cardiology, Barcelona, Spain*; [4]*University Hospital Clinic of Valencia, Gastroenterology, Valencia, Spain*

Background: Intestinal bacterial overgrowth has been related with poor prognosis in heart failure (HF); however, the pathophysiology of this association remains unclear. Along this line, some authors have postulated bacterial overgrowth might be implicated in the systemic inflammatory activation seen in HF. In this work, we aimed to determine whether inflammatory biomarkers were related with exhaled hydrogen (H2) and methane (CH4) after lactulose breath test as surrogates of intestinal bacterial overgrowth.
Methods: We enrolled 102 patients with advanced HF (stage C-D as per the ACC/AHA classification), NYHA II-IV and no signs of active infection. We analyzed plasma interleukin-1b (IL-1b), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor alpha (TNF-α), C-reactive protein (RCP) , procalcitonin (PCT), leukocytes and lymphocytes together with the assessment of exhaled H2 and CH4 after lactulose administration. Multivariable linear regression analysis was assessed to determine the risk factors that predicted the logarithm of the area under the receiving operator curve of H2 and CH4 (logAUC-H2 and logAUC-CH4, respectively).
Results: LogAUC-H2 was modest and significantly correlated with: IL-1b ($r = 0.21$, $p = 0.032$), TNF-alfa ($r = -0.23$, $p = 0.018$) and IL-10 ($r = 0.22$, $p = 0.029$). LogAUC-CH4 correlated with IL-1b ($r = 0.24$, $p = 0.018$). Non-significant correlation were found for IL-6, RCP, PCT, leukocytes and lymphocytes. In a multivariable setting, logAUC-H2 and logAUC-CH4 were both significant and positively associated with IL-1b ($\beta = 0.032$; IC= 0.0001-0.0025; $p = 0.002$) and ($\beta = 0.042$; IC= 0.016-0.068; $p = 0.002$).
Conclusions: In patients with HF, exhaled H2 and CH4 after a lactulose breath test were independently associated with surrogate markers of inflammation.

P1117

Predictive value of leukocyte count for in-hospital mortality in patients hospitalized for acute heart failure

M Monica Chivulescu[1]; L Antohi[1]; C Radulescu[1]; I Cosei[1]; A Covaliov[1]; R Radu[1]; AP Ambrosy[2]; C Macarie[1]; O Chioncel[1]; M Gheorghiade[3]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; [2]*Duke University Medical Center, Durham, United States of America*; [3]*Northwestern University, Chicago, United States of America*

Background: A large randomized clinical trial showed that low lymphocyte count during hospitalisation for acute HF (AHF) is an independent predictor of poor outcomes in the early post discharge period, but the data regarding the relationship between total leukocyte count and prognosis in this setting is limited.
Aims: The aim of this study was to characterize the relationship between leukocyte count and in-hospital mortality in patients hospitalized for AHF.
Methods: RO-AHFS registry prospectively enrolled 3224 consecutive patients with primary diagnosis of AHF. This is a post-hoc analysis of 2984 patients who had leukocyte count available at admission. Patients were stratified by quartiles of leukocyte count measured at admission (Table 1). In hospital mortality was determined in each quartile and compared by regression analysis.
Results: In univariate analysis, no liniar relationship has been found between leukocyte count and in hospital all cause mortality (HR=1.18 95% CI (0.93 -1.28) P=0.43). When mortality was analysed by each quartile, patients in the highest quartile experienced the highest rate of adverse hospital events and the worst outcome as compared to the patients from the lowest quartiles. (Q2 vs Q1 HR=0.98 CI 95% (0.83-1.08) P=0.71; Q3 vs Q2 HR=1.07 CI 95% (0.96-1.16) P=0.60; Q4 vs Q3 HR=1.09 CI 95% (1.04-1.11) P=0.048).
Conclusion: In addition to other known predictors, stratification by leukocyte count may help to identify patients at risk for in-hospital mortality. Future research, including prospective studies, may refine determinants of this relationship.

Table 1.

	Q1=4130-5180/ mmc	Q2=5205-6970/ mmc	Q3=7001-7728/ mmc	Q4=7955-9122 / mmc	P
	n=746	n=746	n=746	n=746	
Age (years)	68.4±10.6	69.5±11.8	69.1±14.2	70.8±11.3	0.008
Gender (female %)	43	41	44	39	0.08
LVEF < 45% (%)	65.2	64.3	68.9	70.1	< 0.001
Diabetus mellitus (%)	31.4	33.5	32	33.1	0.1
Ischemic etiology (%)	60.1	61.4	61.9	60.8	0.09
De novo HF (%)	29	28	23	20	< 0.001
SBP (mmHg)	139±27	136±29	140±31	135±22	0.06
BMI (kg/m^2)	27.9	29.2	27.1	26.1	0.03
serum creatinine (mg/dl)	1.4±0.9	1.4±0.8	1.3±1	1.4±0.9	0.6

Baseline characteristics of sub groups of patients divided by quartiles of leukocyte count. LVEF left ventricular ejection fraction. HF heart failure. SBP systolic blood pressure. BMI body mass index

P1118

Monocyte-to-lymphocyte ratio is strongly related to heart failure characteristics and hospitalizations in a coronary angiography cohort

CM Gijsberts[1]; GHJM Jelte Ellenbroek[1]; MJ Ten Berg[2]; A Huisman[2]; WW Van Solinge[2]; CS Lam[3]; FW Asselbergs[4]; HM Den Ruijter[1]; G Pasterkamp[2]; IE Hoefer[1]; DPV De Kleijn[1]
[1]*University Medical Center Utrecht, Experimental cardiology, Utrecht, Netherlands*; [2]*University Medical Center Utrecht, Clinical Chemistry and Hematology, Utrecht, Netherlands*; [3]*National Heart Centre Singapore, Singapore, Singapore*; [4]*University Medical Center Utrecht, Cardiology, Utrecht, Netherlands*

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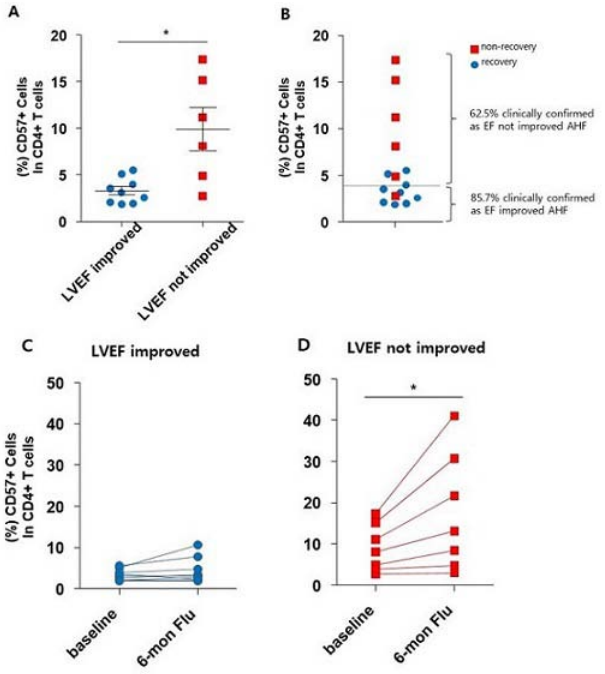
Background: Inflammation is a shared mechanism in coronary artery disease (CAD) and subsequent heart failure (HF) and circulating monocyte and lymphocyte counts predict CAD severity and outcomes.
Purpose: The aim of this study was to investigate whether the monocyte-to-lymphocyte ratio (MLR) correlates with biomarkers of HF and extent of CAD, as well as future HF hospitalizations in patients undergoing coronary angiography.
Methods: We studied 1754 patients undergoing coronary angiography for stable CAD, unstable angina or myocardial infarction. MLR was determined at blood draw prior to angiography and related cross-sectionally to HF biomarkers (ejection fraction [EF], N-terminal pro-B-type natriuretic peptide [NTproBNP] levels) and CAD severity, as well as longitudinally with risk of HF hospitalizations during follow-up.
Results: In the entire cohort, median (interquartile range) MLR was 0.32 (0.24-0.43). High MLR was defined as the upper quartile and significantly associated with non-stable CAD (unstable angina [Odds ratio=1.13; 95% confidence interval 1.06-1.21] or myocardial infarction [OR=1.10; 1.04-1.16]), more severe CAD (OR=1.39; 1.15-1.68), poorer EF (OR=1.63; 1.29-2.05) and higher NTproBNP levels (β=0.78; 0.59-0.96), all $p < 0.001$. The associations with non-stable CAD and NTproBNP remained highly significant after covariate adjustment. Over a mean follow-up of 1.3 years, 46 HF hospitalizations occurred. A high MLR was significantly and independently predictive of HF hospitalizations during follow-up (HR 2.1 [1.1-4.1], $p = 0.039$) after adjustment for covariates.
Conclusions: MLR is strongly related to HF markers and predicts HF hospitalizations during follow-up in coronary angiography patients. This supports a key role of monocyte and lymphocyte-mediated inflammation in the progression towards HF in patients with CAD.



P1119

CD4 + CD57 + T cells are increased and associated with clinical outcome in patients with acute heart failure

JC Youn[1]; MK Jung[2]; SW Choi[1]; SW Han[1]; KH Ryu[1]; SM Kang[3]; EC Shin[2]
[1]*Dongtan Sacred Heart Hospital, Hallym University, Division of Cardiology, Hwaseong, Korea Republic of*; [2]*Korea Advanced Institute of Science and Technology, Laboratory of Immunology and Infectious Diseases, GSMSE, Daejeon, Korea Republic of*; [3]*Yonsei University College of Medicine, Division of Cardiology, Severance Cardiovascular Hospital, Seoul, Korea Republic of*

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Background: The pathogenic role of T cells in heart failure (HF) has been well documented in recent animal studies. However, it is unclear which subpopulation of T cells contributes to pathogenesis in patients with HF. Therefore, we studied immunologic characterization of various subsets of T cells from consecutively enrolled acute HF patients.
Methods: We analyzed the frequency of senescent T cells in 37 acute HF patients (21 male, mean age 66 ± 16 years) and 37 healthy control subjects (21 male, mean age 61 ± 14 years) by multicolor flow cytometry. The immunological characteristics of T cells were evaluated by surface immunophenotyping and intracellular cytokine staining.
Results: The frequency of CD4 + CD57 + T cells was significantly increased in patients with acute HF compared to healthy control (CD4 + CD57 + T cell fraction: 4.97 ± 3.80% vs. 3.84 ± 3.28%, $p = 0.03$), while other senescent T cell fraction showed no significant difference. Functional reactivity of CD4 + CD57 + T cells from acute HF revealed that the frequency of IFN-γ or TNF-α secreting cells in the CD4 + CD57 + T cell population was significantly greater than that in the CD4 + CD57- T cell population. Moreover, both the baseline and 6 month follow-up CD4 + CD57 + T cell fraction and polyfunctional T cell signature were significantly related with the left ventricular ejection fraction recovery in patients with acute HF.
Conclusion: CD4 + CD57 + T cells are increased and associated with clinical outcome in patients with acute HF, suggesting a role for T cell driven inflammation in HF. A more detailed characterization of senescent CD4 + T cells may offer new opportunities for the prevention and treatment of HF.

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

P1120

Left ventricular mechanics in mitral valve prolapse

M Maxime Poilane[1]; C Cueff[1]; N Piriou[1]; P Jaafar[1]; D Guijarro[1]; JC Roussel[1]; JN Trochu[1]; T Le Tourneau[1]
[1]*University Hospital of Nantes Nord Laennec, Cardiology, Nantes, France*

Objective: Valve apparatus alterations may influence left ventricular (LV) mechanics in mitral valve prolapse (MVP). To assess LV mechanics and ventriculo-valvular interaction in MVP.
Methods: Patients with MVP (leaflet displacement > 2 mm above the annulus) and no significant MR (NoMR-MVP, regurgitant volume < 10 ml) and controls without MVP were prospectively enrolled. Patients with hypertension, diabetes, obesity (BMI ≥ 30), or known ischemic or non ischemic myocardial disease were not included. A comprehensive echocardiography was carried out with 2D speckle tracking myocardial longitudinal strain assessment, 2D mitral valve apparatus analysis, and ventriculo-atrial disjunction. Global and regional longitudinal strain were compared between the two groups and the determinants of myocardial deformation alteration were sought.
Results: 80 adult patients with NoMR-MVP and 96 controls were included. Patients did not differ with regard of age, sex, body surface area, heart beats or blood pressure. Posterior (PML) and/or anterior (AML) mitral leaflet prolapse were present in 71 (89%) and 32 (40%) patients, respectively. PML and AML positions averaged -4.9 ± 2.7 mm and -1.6 ± 2.8 mm, respectively. Ventriculo-atrial disjunction was found in 33 (41%) patients and averaged 5.0 ± 1.1 mm. Left ventricular end diastolic diameter indexed to body surface area (bsa) was slightly increased in noMR-MVP (28.7 ± 3.3 mm/m^2 vs 27.6 ± 2.8 mm/m^2 in Controls, $p = 0.014$). Posterior wall thickening tended to increase in NoMR-MVP with frank wall bulging in 30 patients (38%). Despite the third left chamber (between mitral annulus and prolapsed leaflets) forward stroke volume was preserved and even increased in NoMR-MVP (42 ± 8 ml/m^2 vs 39 ± 6 ml/m^2 in Controls, $p = 0.003$). Global Longitudinal Strain (GLS) was clearly better in NoMR-MVP (-21.4 ± 2.9 vs -19.8 ± 1.8%, $p < 0.0001$) compared with Controls, and LS was better in the basal as well as mid-ventricular or apical regions compared with controls (all $p < 0.0001$). Differences were greater in infero-lateral and lateral walls. In univariate analysis, GLS (in absolute value) was associated with male gender (β=0.18, P=0.019), anterior mitral leaflet length/bsa (β=0.19, P=0.011), the magnitude of PML prolapse (β=0.33, $p < 0.0001$) or AML prolapse (β=0.29, $p < 0.0001$), and the magnitude of atrio-ventricular disjunction ($\beta = 0.39$, $p < 0.0001$). In multivariate analysis, male gender (β=0.16, P=0.057), and the magnitude of

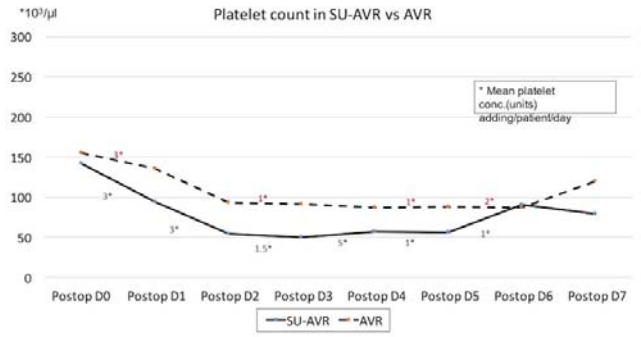
atrio-ventricular disjunction ($\beta = 0.38$, $p < 0.0001$) were determinants of GLS.
Conclusion: In No-MR MVP with no other myocardial disease, MVP and associated abnormalities have a significant impact on LV structure and mechanics. The chronic increase in GLS may be the witness of myocardial wall function and structure remodelling in MVP independently of the presence of MR.

P1121
Outcomes of sutureless aortic valve replacement (SU-AVR) in moderate-to-high risk patients with unexplained postoperative thrombocytopenia

P Puwadon Thitivaraporn[1]; S Chiramongkol[1]; C Kittayarak[1]; N Pornpatrtanarak[1]; J Namchaisiri[1]; S Singhatanadgige[1]; P Ongcharit[1]; V Benjacholamas[1]
[1]*King Chulalongkorn Memorial Hospital, Cardiovascular thoracic surgery department, Bangkok, Thailand*

On behalf of: Chula Cardiac Center

OBJECTIVES: The aim of this study was to compare perioperative and postoperative outcomes of first series SU-AVR and AVR in developing country.
Methods: We conducted a retrospective study of SU-AVR in moderate-to-high risk patients (pts). Data of those underwent AVR or SU-AVR from January 2013 to May 2016 were obtained. A 1:1 propensity matching with sex, age and Society of Thoracic Surgeons (STS) score in same period study of AVR group. Preoperative, intraoperative and post-operative echocardiograms (day 3-7) were obtained. Primary outcome was 30-day mortality. Secondary outcomes were perioperative, intraoperative outcomes and complications. After matching, demographics, comorbidities and outcomes of interest were compared using x2 (Fischer's exact) and student t-tests for categorical and continuous variables, respectively.
Results: 277 pts in both AVR and SU-AVR groups. Until now, there are 10 patients (5 were male, median age of 81.5 years) undergone SU-AVR with propensity compared to AVR in the same period of study. Sutureless valve were successfully implanted in 9/10 pts. The subjects were 50% male and 50% female with mean age at 81.5 years old. The median STS score in SU-AVR group was 5.77 (2.1-79) vs 5.81 (2.5-34.8) in AVR group. The most common presenting symptom was progressive dyspnea at mean functional class 3. The median Cardiopulmonary bypass (CPB) time was 120 min (48-276) in SU-AVR vs 148 min (103-261) in AVR, $p = 0.61$. The median cross-clamp duration was 93.5 min (37-157) in SU-AVR vs 124 min (73-168) in AVR, $p = 0.14$.
Postoperative: echocardiogram demonstrated impressive outcomes in SU-AVR group, defined as reduced mean pressure gradient from 53.1 to 12 mmHg without left ventricular impairment (from 57% pre-operatively to 61% post-operatively vs $p = 0.41$). 30-day mortality was 20% in both SU-AVR and matched AVR group ($p = 1.00$). All patient in SU-AVR developed postoperative thrombocytopenia. Platelets level decreased from 225 *103/µl preoperatively to 94.5, 54.5, 50.1 at postoperative day (POD) 1, 2 and 3, respectively compared with 135.5, 93.4, 91.8 in AVR group ($p = 0.04$, 0.16 and 0.20, respectively). The maximal drop of platelets was found on POD 3. The requirement of platelets transfusion was higher in SU-AVR group compared to AVR (Leucocyte-poor platelet concentration 14.5units vs 4units) ($p = 0.04$).
Conclusion: There was no difference in 30-day mortality among moderate-to-high risk SU-AVR vs AVR. Despite SU-AVR was associated with favorable CPB and clamp time, SU-AVR found related to postoperative thrombocytopenia in all patients.

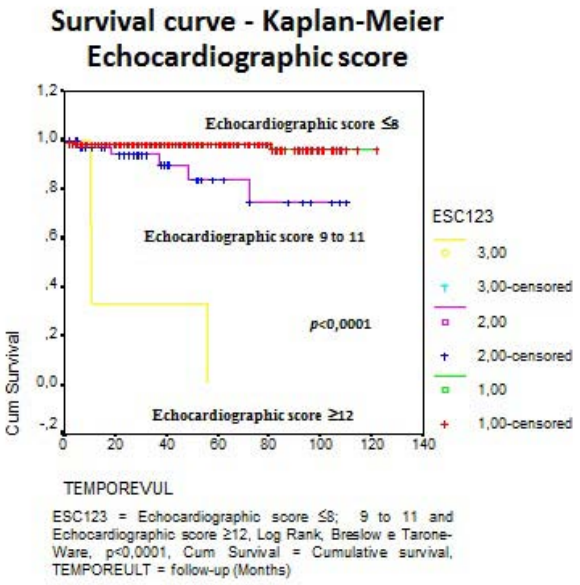


SUAVR vs AVR platelet level

P1122
Percutaneous mitral balloon valvotomy. echocardiographic score, risk factors for death and major events in long-term follow-up.

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[1]; AAB Aragao[1]; LLB Bandeira[2]; ILPB Anjos[2]; VF Marcolla[1]
[1]*Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil*; [2]*Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

Percutaneous mitral balloon valvotomy (PMBV) has emerged as an alternative to surgical treatment of mitral stenosis.
Objective: To dentify the independents 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 317 patientes were followed-up 156 ± 144(1987 e 2013) 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 were 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 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 m2.
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. Independents predictors of survival were pre procedure echo score ≤ 8 and the absence of severe mitral valve regurgitation during the procedure.



P1123
Long-term evaluation of the Ross procedure: clinical and echocardiographic follow-up at 20 years

S Sara Guerreiro[1]; R Ribeiras[1]; J Queiroz E Melo[1]; M Canada[1]; E Horta[1]; C Reis[1]; M Castro[1]; J Carmo[1]; J Mesquita[1]; N Vale[1]; D Matos[1]; C Strong[1]; JP Neves[1]; M Mendes[1]
[1]*Hospital de Santa Cruz, Lisbon, Portugal*

Background: Ross surgery is a technically complex procedure used in children and young adults requiring replacement of the aortic valve (AV), in which the native pulmonary valve is switched to the aortic position - autograft (Ag) - and a cryopreserved homograft (Hg) is implanted in a pulmonary position. This procedure offers

some advantages compared to mechanical prostheses: absence of anticoagulation, low risk of endocarditis and thrombogenicity and equivalent survival. However, the durability and incidence of re-operation remains a major concern. The aim was to evaluate the long-term clinical and echocardiographic results of Ross procedure.
Methods: Single-centre retrospective study that included a cohort of 52 adult patients: mean age at surgery of 44 ± 12 years old, 58% men, 33% rheumatic disease and 29% congenital aortic disease. Clinical endpoints included global mortality and the need for valve reoperation due to failure of one graft. Echocardiographic follow-up included the presence of the aortic Ag or pulmonary Hg deterioration by at least moderate regurgitation or stenosis with a mean gradient≥20mmHg. The median clinical follow-up was 20 ± 3 years (1040 patients/year) and the echocardiographic follow-up was 19 ± 4 years.
Results: The indication for surgery was in 40% the predominance of AV stenosis, in 21% prevalence of regurgitation and 31% mixed aortic disease. The subcoronary technique was the most used in 85% of the cases. The median time of cardiopulmonary bypass was 151 ± 34 min and the median time of hospitalization was 8 ± 3 days. Concomitant mitral surgery was performed in 21% of patients. During the follow-up, the overall survival was 81% and the free survival of graft re-operation was 83% - Figure 1. Of the patients who were not re-operated and were alive at the end of follow-up, 11 patients (31%) had moderate AV regurgitation; 6 (15%) moderate pulmonary regurgitation and only 1 patient with moderate pulmonary stenosis - Figure 1.
Conclusion: In the long-term follow-up of the Ross procedure, the subcoronary approach proved to have excellent clinical and hemodynamic results with low rates of reoperation. Moderate aortic regurgitation was a frequent and concordant finding amongst other studies with no clinically significant impact on the mean follow-up and at the 20 years follow up mark.

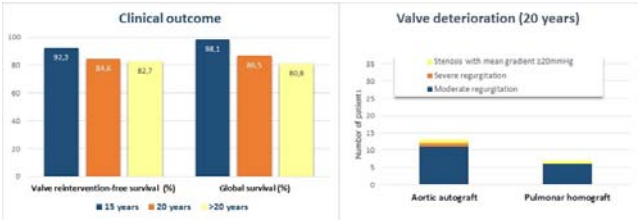


Figure 1

P1124

Indexed device landing zone calcium volume predicts moderate/severe aortic regurgitation after tavi with 1st and 2nd generation self-expandable prosthesis

S Sara Moura Ferreira[1]; J Almeida[2]; P Fonseca[2]; T Dias[2]; C Guerreiro[2]; R Barbosa[2]; P Teixeira[2]; N Pelicano[1]; N Ferreira[2]; R Faria[2]; P Braga[2]; V Gama[2]
[1]Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal; [2]Hospital Center of Vila Nova de Gaia/Espinho, Cardiology, Vila Nova de Gaia, Portugal

Introduction: Calcification of the device landing zone (DLZ) is linked to residual aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI). The mechanisms remain incompletely understood and the performance of next-generation transcatheter heart valves (THV) has not been thoroughly investigated.
Aim: We aimed to (i) clarify the influence of calcification patterns on the incidence of moderate/severe AR (ii) assess the performance of different first- and next-generation systems self-expandable prosthesis regarding calcium at the DLZ and residual AR.
Methods: Retrospective, observational study including all patients with severe aortic stenosis submitted to TAVI with self-expandable prosthesis between August 2007 and October 2016. Calcification of the DLZ was quantified for all available contrast scans, using a dedicated software (3mensioValvesTM), with a threshold for calcium detection set at 850 Hounsfield Units. All patients underwent transthoracic echocardiography within 1–3 days following the procedure. We used a Mann Whitney U test to compare DLZ calcium volume between patients with moderate/severe AR and patients with milder degrees of AR after being submitted to TAVI. A receiver operating characteristics (ROC) curve was used to obtain the best cut-off value of DLZ calcium volume to predict ≥moderate AR after TAVI with Self-Expandable Prosthesis. Then DLZ calcium volume was transformed into a categorical variable with 2 groups and a binary logistic regression analysis was conducted to test the strength of prediction of the projected value of DLZ calcium volume to assess development of AR ≥moderate after TAVI.
Results: TAVI with self-expandable prosthesis was performed in 180 patients in our centre (47,8% male, mean age 79.7 ± 7.8 years old). Most of the devices implanted were 1st Generation Self-Expandable Prosthesis (n = 112, 62.2%). The incidence of moderate/severe AR after TAVI was 15.8%. Body surface area (BSA) indexed DLZ calcium volume was significantly different between patients with moderate/severe (231.7 ± 53.9) and those with milder degrees of AR (138.4 ± 11.2), (p = 0.01). Area under the curve (AUC) for BSA indexed DLZ calcium volume was 0.64 (95% CI 0.53–0.75 p < 0,05). We considered the best cut off point for BSA indexed DLZ calcium volume to be 107.1 (sensitivity 73.1%, specificity 52.6%). In a binary logistic regression model, an BSA indexed DLZ calcium volume equal or above 107.1 was associated with 3 times increase in the probability of moderate/severe AR after TAVI with self-expandable prosthesis. Importantly, there were no significate differences in the incidence of moderate/severe AR after TAVI with self-expandable prosthesis, regarding device generation (X2 (1)=0.1, p = 0.83).
Conclusion: Calcification of the DLZ predicts moderate/severe AR after TAVI with Self-Expandable Prosthesis; the incidence of moderate/severe AR did not differ significantly between 1st and 2nd generation devices.

P1125

The improvement of right ventricular function in heart failure patients following percutaneous mitral valve repair using MitraClip system

O M Galuszka[1]; S Rutschow[1]; M Gross[1]; D Steffens[1]; U Rauch-Krohnert[1]; U Landmesser[1]; M Kasner[1]
[1]Charite - Campus Benjamin Franklin, Department of Cardiology, Berlin, Germany

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: 48 patients (52% women, 76 ± 6 years) with moderate-to-severe mitral regurgitation (MR 2+) undergoing PMVR using the MitraClip system underwent transthoracic echocardiography at baseline and at and six-months 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) > 60mmHg.
Results: MitraClip© implantation resulted in significant improvement of RV systolic strain (-15.7 ± 2.3% vs. -19.1 ± 2.9%, p < 0.001), improved New York Heart Association (NYHA) class (3.0 ± 0.5 vs. 2.3 ± 0.7, p < 0.05), diminished RA volumes (46 ± 10ml vs. 38 ± 10 ml, p < 0.001) as well as reduced estimated pulmonary pressure (sPAP; 52.5 ± 11.5 mmHg vs. 42.5 ± 14.1 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 ± 2.1% vs. -16.1 ± 2.7%, p < 0.001), accompanied by reduced sPAP (68.1 ± 7.5 mmHg vs. 55.7 ± 7.2 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, is beneficial for heart failure patients by improving 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, and thus RV failure, exhibit little clinical benefit from the procedure.

P1126

Prior surgical mitral commissurotomy and echocardiographic score influence in mitral balloon valvuloplasty

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[1]; AAB Aragao[1]; VF Marcolla[1]; SA Simoes[2]; LLB Bandeira[3]; ILPB Anjos[3]; M Nascimento[1]
[1]Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil; [2]Rio de Janeiro State Government, Military Undersecretary from Rio de Janeiro State Government, Rio de Janeiro, Brazil; [3]Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil

Background: Percutaneous mitral balloon valvuloplasty is effective in mitral stenosis
Objective: to evaluate prior mitral surgical commissurotomy (PMC) and echocardiographic score (ES) in the results and complications of mitral balloon valvuloplasty (MBV).

Methods: From 1987 to 2013, 526 procedures with Inoue balloon, double or single Balt balloon technique; 480 without PMC named primary MBV group (PMBVG) and 46 that have been submitted to PMC, the PMC group. The PMCG was older than PMBVG (42.7 ± 12.4 vs 36.9 ± 12.5 years, p = 0.0030). Gender, atrial fibrilation and NYHA functional class were similar. In PMBVG and PMCG, respectively, ES were 7.2 ± 1,4 and 7.7 ± 1.5 points (p = 0.0158) and mitral valve area (MVA) 0.94 ± 0.21 and 1.00 ± 0.22 cm2 (p = 0.0699).
Results: - Pre-MBV: mean pulmonary artery pressures (MPAP) were 37.8 ± 14.2 and 37.6 ± 14.4 mmHg, p = 0.9515; mean gradient (MG) 19.6 ± 6.9 and 18.3 ± 6.9 mmHg, p = 0.2342; MVA 0.90 ± 0.21 and 0.93 ± 0.19 cm2, p = 0.4092, respectively, whem compare PMBVG and PMCG. Post-MBV: MPAP were 26.8 ± 10.2 and 26.6 ± 10.9 mmHg, p = 0.9062; MG 5.4 ± 3.5 and 6.3 ± 4.2 mmHg, p = 0.1492; MVA 2.04 ± 0.42 and 1.92 ± 0.41 cm2, p = 0.0801, respectively. Mitral regurgitation (MR) were similar pre and post-MBV. Severe MR post-MBV in 10 patients: 8 in PMBVG and 2 in PMCG, p = 0.2048. As there were not found significant diferences, the total group were divided in ES ≤ 8 and >8 groups: Pre-MBV: MPAP 37.5 ± 13.9 and 39.3 ± 16.6 mmHg, p = 0.4041; MG 19.7 ± 6.8 and 18.3 ± 7.3 mmHg, p = 0.1753; MVA 0.90 ± 0.21 and 0.94 ± 0.20 cm2, p = 0.0090 respectively. Post-MBV: MPAP 26.7 ± 10.1 and 28.0 ± 10.6 mmHg, p = 0.3730, MG 5.5 ± 3.6 and 5.5 ± 3.3 mmHg, MVA 2.06 ± 0.42 and 1.90 ± 0.40 cm2, p = 0.0090.
Conclusions: The groups with and without prior mitral commissurotomy in MBV were compare and no differences were found in pre- and post-procedure, as mean pulmonary artery pressure, mean mitral gradient, mitral valve area, and mitral regurgitation. Although PMCG was older, with higher ES, its hemodynamics datas were similar. Whem the entire group was divided based on echo scores, those with echo scores >8 had highse MV (p = 0.0090). and smaler mitral valve areas post-valvuloplasty. The valve anatomy were more important than prior commissurotomy

P1127

Emergent balloon mitral valvotomy in pregnant women presenting with refractory pulmonary edema

M Majed Hassine[1]; M Boussada[1]; M Ben Messoud[1]; M Mahjoub[1]; Z Dridi[1]; F Betbout[1]; H Gamra[1]
[1]Cardiology A Department – Fattouma Bourguiba University Hospital, monastir, Tunisia

Background: Mitral stenosis is the most common valvular heart lesion found in pregnancy. When severe, it leads to significant risk of mortality for both mother and fetus, since the hemodynamic adaptations to pregnancy are badly tolerated. Many pregnant women with mitral stenosis present in a critically ill condition. The role of balloon mitral valvotomy (BMV) in such patients is ill-defined.
Objectives: We sought to evaluate the feasibility, efficacy and safety of emergent BMV in pregnant patients with refractory pulmonary edema and to determine maternal and fetal outcome.
Methods: Of 88 patients undergoing BMV during pregnancy from January 1990 to December 2011 in Cardiology A Department of Monastir Hospital, 28 women were in New York Heart Association functional class IV and underwent emergent BMV. During the procedure, radiation exposure was minimized by means of total abdominal and pelvic shielding.
Results: The mothers's mean age at the time of BMV was 28.86 ± 5.7 (range 19–43) years, and the gestation period was 30 ± 5.1 (range 20 –39) weeks. Ten patients were primiparas. Mitral valve (MV) was assessed using the Wilkins score which averaged 7.4 ± 1.8 (range 4 to 14). Fluoroscopy time was 7.8 +/-1.9 minutes. The BMV procedure was successful in 25 (89.3 %) patients with a dramatic improvement in patient symptoms. The mitral valve area increased from 0.8 ± 0.2 cm2 to 2.2 ± 0.42 cm^2 (p < 0.0001). The mitral valve pressure gradient decreased from 22.2 ± 9.3 to 5.7 ± 4 mm Hg (p < 0.0001). The left atrial pressure decreased from 29.4 ± 9.3 to 15.4 ± 7.3 mm Hg (p < 0.0001). The pulmonary artery pressure decreased from 58.8 ± 21.1 to 37.2 ± 14.3 mm Hg (p < 0.0001). One patient developed severe mitral regurgitation and required urgent mitral valve replacement. There was no maternal mortality or significant foetal morbidity. Pregnancy was uneventful in all patients, all babies were born at full term by spontaneous vaginal delivery in 24 cases (85.7 %) and by cesarian section for obstetrical reasons in 4 (14.3%), with no obvious malformations (4 of them were twin babies). None of the babies needed intensive care monitoring. The average Apgar scores at 1 min were 8.6 ± 1. The mean birth weight was 3.1 Kilograms ranged from 1.9 to 3.8 kg.
Conclusion: During pregnancy, emergent BMV is safe and feasible in patients with symptomatic mitral stenosis and severe pulmonary edema. There is marked symptomatic relief, along with excellent maternal and fetal outcomes.

P1128

Impact of permanent pacemaker implantation on clinical outcome among patients undergoing transcatheter aortic valve replacement

E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; A Ruiz-Salas[2]; JM Garcia-Pinilla[2]; L Morcillo-Hidalgo[2]; MF Jimenez-Navarro[2]; JH Alonso-Briales[2]; JM Hernandez-Garcia[2]; J Alzueta-Rodriguez[2]; E De Teresa-Galvan[1]
[1]Department of Cardiology , Malaga, Spain; [2]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

Very few data exist on the clinical impact of permanent pacemaker implantation (PPI) after Transcatheter Aortic Valve Replacement (TAVR). The aim of this study was to assess the impact of PPI after TAVR on late outcomes in a large cohort of patients.
Methods: and Results — A total of 531 consecutive patients without prior PPI undergoing transcatheter aortic valve replacement were included. Of them, 125 patients (23.5%) required a PPI within the first 30 days after TAVR, median time 3 days (2.82-5.53 days) and 15 patients required a PPI in the follow-up, median 274 days (225-958 days). At a mean follow-up of 37 ± 25 months, there was a tend more mortality in patients with PPI (40% vs. 32.5% p = 0.067), but no association was observed between the need for PPI and all-cause mortality (hazard ratio, 1.15; 95% confidence interval, 0.839–1.576; P=0.381), cardiovascular mortality (hazard ratio, 0.992; 95% confidence interval, 0.539–1.824; P=0.979), and it was associated with more rehospitalisation for heart failure (hazard ratio, 1.942; 95% confidence interval, 1.023–3.686; P=0.042). 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 59.4 ± 14 % to 62.6 ± 9% after TAVI and decreased to 60.9 ± 10% at 1 years and 59 ± 6 at 4 years (p for post-TAVI trend 0.034).
Conclusions: The need for PPI was a frequent complication of TAVR and it was associated with increased admission for heart failure, and rehospitalization for heart failure after. A new PPI did have a negative effect on left ventricular function over time. However, but not associated with any increase in overall or cardiovascular death, a mean follow-up of 2.84 years.

P1129

Long-term outcomes after TAVR in patients with severe aortic stenosis and a reduced left ventricular ejection fraction

E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; F Carrasco-Chinchilla[2]; AJ Dominguez-Franco[2]; JM Garcia-Pinilla[2]; I Rodriguez-Bailon[2]; MF Jimenez-Navarro[2]; JH Alonso-Briales[2]; JM Hernandez-Garcia[2]; E De Teresa-Galvan[2]
[1]Department of Cardiology , Malaga, Spain; [2]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

Left ventricular systolic dysfunction is associated with increased peri-operative risk in patients undergoing surgical aortic valve replacement. Recently, Transcatheter Aortic valve Replacement (TAVR) has emerged as an alternative to surgical aortic valve replacement for patients considered at high or prohibitive operative risk. We aim to analyze impact of a low ejection fraction in patients undergoing TAVR.
Methods: Between April 2008 and December 2016, 582 patients with symptomatic aortic valve stenosis who were considered high risk or non-surgical candidates underwent implantation with the auto-expandable prosthesis. Echocardiographic data were collected before and after the procedure. Impaired LV function was defined by a left ventricular ejection fraction (LVEF ≤ 40%). In 104 patients (17.9%) had reduced left ventricular ejection function
Results: The patients with reduced LVEF had more comorbidities compared with normal function: Charlson index 4 ± 1.8 vs. 3.2 ± 1.7, p = 0.001; Karnosfky index 49.8 ± 18 vs. 63.7 ± 17, P = 0.001), Frailty 30.8% vs. 19.2%, p = 0.009, worse Logistic EuroSCORE 27.1 ± 17 vs. 15.4 ± 9., p < 0.001, were more often males (60.6% vs. 36.4%, p = 0.001, more symptomatic (NYHA class IV 55.8% vs. 24.3%, p < 0.001, were younger (76.6 ± 9 vs. 80 ± 5, P = 0.001) and had a higher prevalence of prior coronary artery disease (63.5% vs. 40%, p = 0.001). Patients with reduced LVEF showed a good evolution of left ventricular ejection fraction over time (pre, post-procedure and 1 years): 33.8 ± 5 vs. 44.3 ± 11 vs. 51.6 ± 12%, respectively p = 0.001 No difference was observed between the 2 groups in mortality at 30-days (5.8% vs. 2.9%, p = 0.150). At a mean follow-up of 37 ± 25 months, there were non-significant differences with late mortality (29.6% vs. 34.1%, p = 0.395).
Conclusions: In patients with severe aortic stenosis and a low ejection fraction, TAVI is associated with better LVEF recovery and the immediate and long-term outcome after TAVR not seem to differ between patients with an impaired and preserved LVEF

DEVICES / CRT/ ICD / SURGERY

P1130

Interventricular lead distance and the response to cardiac resynchronization therapy

T Chumarnaya[1]; M Trifanova[2]; T Lyubimtseva[3]; V Lebedeva[3]; M Trukshina[3]; I Poroshin[4]; D Lebedev[3]; O Solovoyva[4]
[1]Institute of Immunology and Physiology of Russian Academy of Sciences, Ekaterinburg, Russian Federation; *[2]Urals State Medical University, Ekaterinburg, Russian Federation*; *[3]Almazov Federal Heart Centre, Saint Petersburg, Russian Federation*; *[4]Ural Federal University, Yekaterinburg, Russian Federation*

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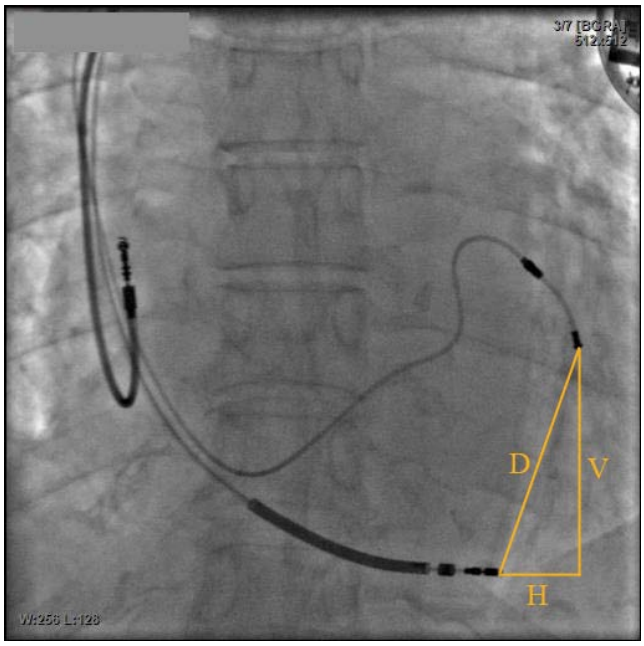
Cardiac resynchronization therapy (CRT) is one of recent advancements in heart failure (HF) treatment. However, the clinical improvement has proved to be highly variable and insufficiently predictable. Despite application of established selection criteria, 20–40% of the patients do not respond to CRT. The our aim was to test a hypothesis on the influence of lead positioning in the ventricular walls on CRT response. We examined 53 first-time CRT recipients with NYHA class III-IV HF, with sinus rhythm, left bundle branch block, QRS duration>120 ms, left ventricular ejection fraction (LV EF) <35%. Response to CRT was defined in 6 months after operation as: a decrease in the LV end-systolic volume≥15%, a relative increase in the LV EF, a decrease in the functional class of chronic HF. All patients were classified as responders (n=28) or non-responders (n=25). The anatomic inter-lead distance, the horizontal and vertical components (Fig. 1) were determined with using patient chest radiographs recorded in the antero-posterior (AP), 30° left anterior oblique (LAO) and 30°right anterior oblique (RAO) positions. All individual measurements for a patient were normalized by the end-diastolic LV linear dimension (LVLD) to take into account differences in the heart size between patients. A comparison between groups was made with using SPSS 22.0 software packages. The data are presented as Mean±SD. The area under the ROC-curves (AUC) was used to assess diagnostic significance of the parameters. No correlation between the interventricular lead distance and response to CRT was found (Table1). We could speculate that not only the leads position in the ventricles are essential for CRT success, but functional characteristics of myocardium and patho-physiological factors have to be accounted to predict CRT responders. These hypotheses will be further tested by our group.

Inter-ventricular lead distance

Position	Inter-lead distance (normalized by the LVLD)	Responders	Non-responders	p (t-test)	AUC
AP	Anatomic	0.81 ± 0.4	0.75 ± 0.3	0.606	0.53
	Horizontal component	0.54 ± 0.4	0.54 ± 0.3	0.997	0.53
	Vertical component	0.48 ± 0.4	0.42 ± 0.3	0.564	0.58
LAO	Anatomic	1.08 ± 0.4	1.26 ± 0.4	0.184	0.56
	Horizontal component	0.95 ± 0.5	1.11 ± 0.4	0.290	0.52
	Vertical component	0.37 ± 0.3	0.46 ± 0.3	0.439	0.58
RAO	Anatomic	0.82 ± 0.4	0.69 ± 0.2	0.216	0.59
	Horizontal component	0.53 ± 0.4	0.43 ± 0.3	0.294	0.62
	Vertical component	0.53 ± 0.4	0.42 ± 0.3	0.384	0.51



Inter-lead distance

P1131

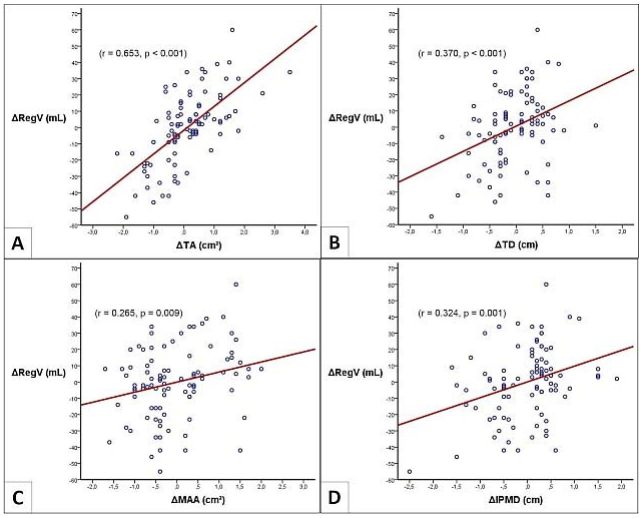
The effect of CRT on mitral valve geometry: Incidence and predictors of reversed mitral remodeling

O Karaca[1]; B Cakal[1]; O Omaygenc[1]; HM Gunes[1]; SD Cakal[1]; F Kizilirmak[1]; E Ibisoglu[1]; U Savur[1]; F Celebi[1]; DD Naki[1]; F Kilicaslan[1]
[1]Medipol University Faculty of Medicine, Cardiology Clinic, Istanbul, Turkey

Background: Improved valvular geometry by CRT possibly impacts on mitral regurgitation (MR) response. We aimed to establish the precise definition, incidence, and predictors of reversed mitral remodeling (RMR), as well as the association with MR response and short-term CRT outcome.
Methods: Ninety-five CRT recipients were analyzed for the end-point of MR response defined as the absolute reduction in regurgitant volume (RegV) at 6 months. To identify RMR, changes in mitral deformation indices were tested for correlation with MR response and further analyzed for functional and echocardiographic CRT outcomes.
Results: Overall, MR response was observed in 50 patients (53%). Among the echocardiographic indices, the change in tenting area (TA) had the highest correlation with the change in RegV ($r=0.653$, $p<0.001$). The mean TA significantly decreased in MR responders (4.15 ± 1.05 cm^2 to 3.67 ± 1.01 cm^2 at 6 months, $p<0.001$) and increased in non-responders (3.68 ± 1.04 cm^2 to 3.98 ± 0.97 cm^2, $p=0.014$). The absolute TA reduction was used to identify patients with RMR (47%) which was found to be associated with higher rates of functional improvement ($p=0.03$) and volumetric CRT response ($p=0.036$) compared to those without RMR. Non-ischemic etiology and the presence of LBBB independently predicted RMR at multivariate analysis.
Conclusion: Reduction in TA is a reliable index of RMR, which relates to MR response, and functional and echocardiographic improvement with CRT. Both LBBB and non-ischemic etiology predict RMR.

	Univariate Analysis		
Variable	Odds Ratio	95% CI	p value
Non-ischemic etiology	4.083	1.709 - 9.759	0.012
Baseline QRS duration	0.998	0.987 - 1.010	0.197
Atrial fibrillation	1.216	0.481 - 3.075	0.042
LVEF	0.980	0.966 - 0.994	0.332
LBBB morphology	2.545	1.052 - 6.160	0.023
	Multivariate Analysis		
	Odds Ratio	95% CI	p value
Non-ischemic etiology	3.130	1.169 - 8.380	0.021
Atrial fibrillation	1.040	1.023 - 1.057	0.114
LBBB morphology	2.491	1.086 - 5.714	0.032

Predictors of reversed mitral remodeling (RMR) after CRT.



Geometric indices and MR response

P1132

Heart failure diagnostic sensor measurements during clinically stable epochs in ambulatory heart failure patients

RS Gardner[1]; DG Nair[2]; Z Eldadah[3]; B Stancak[4]; P Thakur[5]; R Wariar[5]; Y Zhang[5]; Q An[5]; V Averina[5]; R Sweeney[5]; JP Boehmer[6]
[1]Golden Jubilee National Hospital, Clydebank, United Kingdom; *[2]Cardiology Associates of North East Arkansas, Arkansas, United States of America*; *[3]Washington Hospital Center, Washington, United States of America*; *[4]East-Slovak Institute of Cardiovascular Diseases, Kosice, Slovak Republic*; *[5]Boston Scientific, Research, Arden Hills, United States of America*; *[6]Penn State Milton S Hershey Medical Center, Hershey, United States of America*

On behalf of: MultiSENSE Study Investigators

Background: A multi-sensor algorithm based on implanted device based sensor data has been shown to detect impending worsening Heart Failure (HF) events. The objective of this analysis was to characterize the "normal" range of these sensor values when patients were estimated to be clinically stable, and compare it to pre-HF event periods.
Methods: The MultiSENSE trial enrolled 900 patients implanted with a COGNIS CRT-D and followed them up to 1 year. Device software was modified to permit collection of chronic diagnostic sensor data including heart sounds, respiration, thoracic impedance, heart rate and activity. HF status was assessed by in-office physical assessment at routine follow-up visits scheduled either every three months if the patients had remote monitoring, or 6-8 weeks if not. Patients were deemed to be clinically stable between successive follow-up visits if their NYHA classification was unchanged, weight change was within 5 lbs (2.27kg) and no adverse events were reported between the visits. Sensor data from clinically stable epochs were compared with 7 day average sensor data prior to independently adjudicated worsening HF events defined as HF admissions or unscheduled visits with intravenous HF treatment using 2 sampled t-test.
Results: Of 900 patients, 676 patients yielded 1667 clinically stable epochs of duration 60 ± 22 days, while 88 patients had 146 HF events. Table summarizes sensor data during clinically stable epochs and prior to worsening HF as mean (μ) ± standard deviation (σ).
Conclusions: All individual HF diagnostic sensors used in the multi-sensor algorithm are different when patients are clinically stable versus when they are experiencing worsening HF events. Additional studies are needed to investigate if interventions in response to early recognition of these changes will reduce HF events.

Daily Trend	Clinically Stable epochs	Prior to worsening HF	p values		
μ ± σ	N	μ ± σ	N		
S1 (mG)	2.58 ± 0.95	674	1.99 ± 0.72	87	< 0.0001
S3 (mG)	0.93 ± 0.31	674	1.32 ± 0.42	85	< 0.0001
Thoracic Impedance (Ohm)	50.0 ± 8.6	674	43.2 ± 9.53	88	< 0.0001
Respiratory Rate (median, br/min)	17.8 ± 2.39	674	19.8 ± 3.3	87	< 0.0001
Day-time RSBI (br/min/Ohm)	8.18 ± 2.56	674	10.9 ± 3.85	88	< 0.0001
Night Heart Rate (bpm)	69.8 ± 8.2	673	76.3 ± 10.5	88	< 0.0001
Activity (hours)	2.49± 2.2	673	1.10± 1.36	88	< 0.0001

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

HF sensor values during clinically stable epochs and pre-HF events:

P1133

Cardiac resynchronization therapy with versus without a defibrillator: insights from device interrogation and mode of death analysis.

P Pieter Martens[1]; FH Verbrugge[1]; P Nijst[1]; M Dupont[1]; D Nuyens[1]; H Van Herendael[1]; M Rivero-Ayerza[1]; WH Tang[2]; W Mullens[1]
[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium; *[2]Cleveland Clinic Foundation, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland, United States of America*

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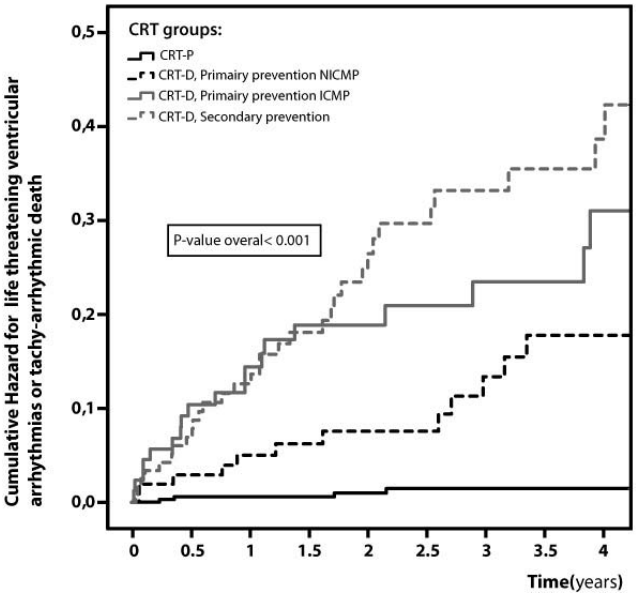
BACKGROUND: Both Cardiac resynchronization therapy (CRT) and implantable cardio-defibrillators (ICD) reduce mortality. However, the incremental value to one-other remains a topic of debate.
Methods: Baseline characteristics, mode of death and device interrogations were retrospectively evaluated in consecutive CRT-Pacemaker (CRT-P) and CRT-Defibrillator (CRT-D) patients implanted between October, 2008, and August, 2015. Preference for implant of CRT-P was given in older patients with multiple comorbidities or pacing induced non-ischemic cardiomyopathies. For patients with a primary prevention indication of the CRT-D, independent predictors associated with a clinical context of reduced benefit of the ICD-component were determined, defined as absence of non- lethal (detected on device interrogation) and lethal ventricular tachy-arrhythmias (mode of death analysis) during follow-up.
Results: A total of 687 patients were followed for 38 ± 22 months. CRT-P was implanted in 361 (52.5%) and CRT-D in 326 (47.5%). CRT-P recipients were older (75.7 ± 9.1 versus 71.8 ± 9.3; < 0.001) and had a higher comorbidity burden (p < 0.001). During remote tele-monitoring follow-up, 4 CRT-P patients were detected with episodes of sustained ventricular tachycardia for which semi-elective upgrade to CRT-D occurred. All-cause mortality was higher in CRT-P versus CRT-D patients (p = 0.003). However, mode of death analysis revealed a predominant non-cardiac mode of death in CRT-P recipients (70% versus 38% in CRT-D, p = 0.002) with only one patient dying from tachy-arrithmic death in the CRT-P group. Figure 1 illustrates the hazard for ventricular arrhythmias (combined from all device interrogations) or tachy-arrithmic death in CRT-P vs. CRT-D. Indicating a

lower burden in CRT-P vs CRT-D patients, with additional differences in the latter group between primary prevention indication (non-ischemic or ischemic etiology of heart failure) or secondary prevention indication for the ICD-component. Regression analyses revealed that the presence of advanced age, NYHA class IV, intolerance to beta-blockers and underlying non-ischemic cardiomyopathy independently associates with a reduced benefit of the primary prevention CRT-D on top of CRT-P.
Conclusions: The majority of contemporary heart failure patients as currently selected for CRT-P exhibit mainly non-cardiac driven mortality and low ventricular arrhythmia burden, suggesting little incremental value of the addition of a defibrillator.



Arrhythmia burden in CRT-P vs CRT-D

P1134

Risk reduction in cardiovascular deaths or hospitalizations in subgroups of CRT patients optimized using the SonR contractility sensor: RESPOND-CRT subgroups analyses

L Padeletti[1]; J Brachmann[2]; J Brugada[3]; R Villuendas[4]; JC Deharo[5]; S Asbach[6]; H Manyam[7]; M Zecchin[8]; D Debarshi[9]; J Singh[10]
[1]IRCCS Multimedica of Milan, Cardiology, Milan, Italy; *[2]Hospital Coburg, Coburg, Germany*; *[3]Hospital Clinic de Barcelona, Barcelona, Spain*; *[4]Germans Trias i Pujol University Hospital, Badalona, Spain*; *[5]Hospital La Timone of Marseille, Marseille, France*; *[6]Universitäts-Herzzentrum Freiburg, Freiburg, Germany*; *[7]University of Tennessee Erlanger Hospital , Chattanooga, United States of America*; *[8]Azienda Ospedaliero-Universitaria Ospedali Riuniti, Trieste, Italy*; *[9]LivaNova, Clamart, France*; *[10]Massachusetts General Hospital, Boston, United States of America*

On behalf of: RESPOND-CRT investigators
Funding Acknowledgements: The study was sponsored by LivaNova CRM

Purpose: RESPOND-CRT is a prospective, double-blinded, multi-center, non-inferiority trial designed to assess the safety and efficacy of the SonR system in heart failure (HF) patients (pts) eligible for cardiac resynchronization therapy (CRT). SonR is a contractility sensor-based system that automatically adjusts atrio-ventricular (AV) and inter-ventricular (VV) timings according to pts needs.
Methods: After implant, pts were randomized (2:1) to receive repetitive, automatic AV and VV optimization with SonR versus AV and VV Echo-guided optimization at discharge. We conducted a secondary analysis on time to first event of cardiovascular (CV) deaths or CV hospitalizations in subgroups of pts with renal failure (RF - Glomerular Filtration Rate GFR < 60), and history of atrial fibrillation (AF). An adjusted Cox regression analysis was performed on all adjudicated events up to 24 months. The type of CV events is presented.
Results: The study randomized 998 pts to either SonR (n = 670) or Echo (n = 328). For CV deaths or CV hospitalizations, in pts with history of AF (153 patients), SonR was associated with 56% risk reduction (HR=0.44, 95%CI: 0.26-0.76, p < 0.01) and in pts with RF (165 patients), 44% risk reduction (HR=0.56, 95%CI: 0.36-0.88, p = 0.01). HF and A/V rhythm disorders were the main reasons for CV hospitalization (table).

Conclusion: CRT optimization using the SonR contractility sensor was associated with additional benefits through significantly reduced risk of CV deaths or CV hospitalizations in pts with history of AF or RF.

Listings of CV deaths / hospitalizations

	AF history patients - N=153	RF patients - N=165		
Nb pts (%)	SonR - N=99	Echo - N=54	SonR - N=104	Echo - N=61
ALL CV hospitalizations	32 (32.3%)	28 (51.9%)	44 (42.3%)	36 (59.0%)
- Cardiovascular death excluding HF*	1 (3.1%)	0 (0.0%)	1 (2.3%)	0 (0.0.%)
- HF episode leading to death*	1 (3.1%)	0 (0.0%)	3 (6.8%)	2 (5.6%)
- HF hospitalization	16 (50.0%)	16 (57.1%)	22 (50.0%)	19 (52.8%)
- Atrial rhythm disorder	4 (12.5%)	5 (17.9%)	4 (9.1%)	4 (11.1%)
- Ventricular rhythm disorder	4 (12.5%)	3 (10.7%)	2 (4.5%)	3 (8.3%)
- CVA / Stroke	1 (3.1%)	0 (0.0%)	2 (4.5%)	0 (0.0%)
- Myocardial infarction	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)
- Heart transplant	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- Other cardiovascular event	4 (12.5%)	4 (14.3%)	9 (20.5%)	8 (22.2%)
CV deaths (without CV hospitalization)$	0	2	1	0

* Only deaths that happened during a CV hospitalization$ CV deaths that happened without any CV hospitalization

P1135

Impact of left ventricular scar and synchronization parameters on reverse lewft ventricular remodeling

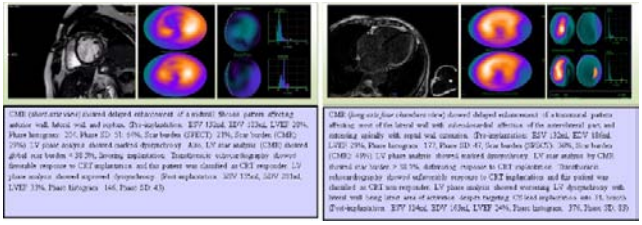
W Walid Ahmed[1]; W Samy[1]; O Tayeh[1]; N Behairy[2]; A Hassan[1]
[1]Cairo University Hospitals, Critical care department, Cairo, Egypt; *[2]Cairo University Hospitals, Radiology department, Cairo, Egypt*

BACKGROUND: Left ventricular dyssyunchrony and scar could predict response to cardiac resynchronization therapy (CRT)
PURPOSE: Explore role of LV dyssynchrony and scar impacts on reverse LV remodeling
Methods: Thirty patients received CRT. Assessment of left ventricular (LV) dyssynchrony by Gated SPECT LV phase analysis. Cardiac magnetic resonance with late gadolinium enhancement technique to examine LV scar burden.
Results: Thirty patients received CRT (mean age 58.7 ± 9.0, 24 males). Reverse LV remodeling (decline ≥15% from baseline LV end-systole) was documented in 19 patients. Temporal changes in LV dyssynchrony parameters were correlated to LV reverse remodeling. Non-responders showed higher scar burden by CMR (41.2 ± 7.8 vs 30.3 ± 11.1, P. 008). Left ventricular phase analysis parameters were correlated to summed rest score and CMR scar burden. Multivariate regression showed CMR scar burden (P < .001), delta change in histogram BW (P. 006) and delta change in histogram SD (P. 005) were independent predictors of reverse LV remodeling. Predicting CRT non-response showed a cutoff 36.5% of global LV scar burden had a sensitivity of 81.8% and specificity of 68.4%.
Conclusion: Reverse LV remodeling was associated with temporal improvements in LV dyssynchrony parameters. LV scar had an unfavorable impact. Improving dyssynchronous contractions resulted into better reverse LV remodeling.

ROC analysis for CRT non response status

	AUC*	P	Cut-off	Sensitivity	Specificity
Global scar burden CMR	78.0%	.012	36.5%	81.8%	68.4%
Delta change in histogram BW	90.0%	< .001	-28.8%	100.0%	73.7%
Delta change in histogram SD	91.6%	< .001	-27.1%	100.0%	73.7%

AUC area under curve



CRT responder and non-responder

P1136

Changes and predictive value of filtered qrs duration for mortality in non ischemic heart failure patients with cardiac resynchronization therapy

YM Minami[1]; A Suzuki[1]; T Shiga[1]; K Ejima[1]; M Shoda[1]; N Hagiwara[1]
[1]*Tokyo Women's Medical University, Department of cardiology, Tokyo, Japan*

Introduction: Cardiac resynchronization therapy (CRT) improves quality of life, and reduces the risks of hospitalization for heart failure (HF) or death in selected heart failure patients. The Aim of this study is to evaluate the association between changes of filtered QRS duration (fQRS) recorded by signal averaged electrocardiograph (SAECG) after Cardiac resynchronization therapy (CRT) and mortality.
Methods: This study included 103 consecutive non-ischemic HF patients who implanted CRT between 2004 to 2015. Patients were divided into narrowing fQRS and widening fQRS groups according to the changes of fQRS before and after CRT. The impact of narrowing fQRS on all-cause mortality was investigated.
Results: During a median follow-up time of 33 [18-50] months, 27 (26%) patients died from any cause. 50 (49%) patients with widening fQRS after CRT had more frequently ischemic heart disease and had shorter fQRS before CRT than patients with narrowing fQRS after CRT. There is a significantly higher rate of patients with reverse remodeling in patients with narrowing fQRS after CRT than patients with widening fQRS. Cox proportional hazards analysis found that widening fQRS was a significantly associated with reduced mortality (HR: 2.98, 95% CI 1.21-7.35, $P < 0.05$).
Conclusion: After CRT, HF patients with narrowing fQRS showed significantly higher responder rate than patients with widening fQRS. Narrowing fQRS is an independently associated with reduced mortality in HF patients receiving CRT.

P1137

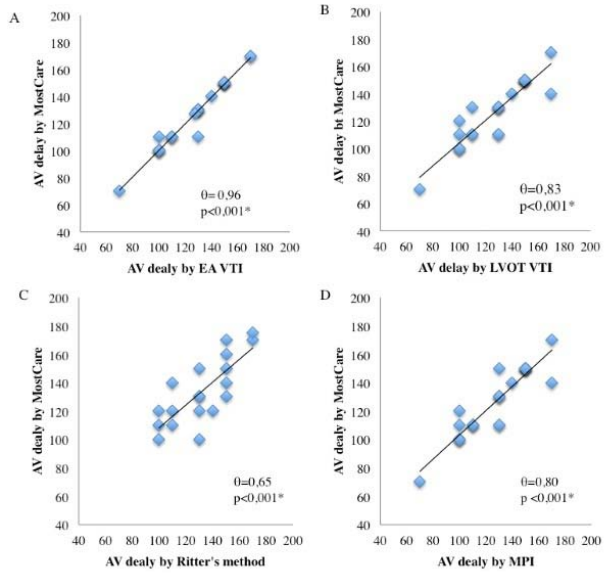
Cardiac resynchronization therapy optimization by pressure recording analytical method: feasibility, efficacy and correlation with electrocardiographic and echocardiographic methods

D Castagno[1]; M Bisi[1]; PG Golzio[1]; C Budano[1]; A Bissolino[1]; M Anselmino[1]; F Ferraris[1]; C Giustetto[1]; F Gaita[1]
[1]*Division of Cardiology, Department of Medical Sciences, University of Turin, Turin, Italy*

BACKGROUND: Nonresponse to cardiac resynchronization therapy (CRT) affects up to 40% of system recipients. Suboptimal device programming has been identified as one of the main determinant factors of poor CRT response.
PURPOSE: To investigate the efficacy of AV and VV optimization performed using haemodynamic parameters obtained with the pressure recording analytical method (PRAM), a new, minimally invasive technique allowing beat-by-beat stroke volume (SV) and cardiac output (CO) monitoring from the pressure signals recorded in femoral or radial arteries.
Methods: After implant, consecutive CRT recipients (patients with symptomatic heart failure despite optimal medical therapy, in sinus rhythm and with complete left bundle branch block) underwent PRAM-based device optimization aiming at the highest SV and CO. Correlation between PRAM-based, standard ECG (QRS axis, QRS duration and presence of R wave in lead V1) and echocardiographic (mitral and aortic velocity time integral [VTI], Ritter's method, myocardial performance index [MPI]) CRT optimization was also investigated.
Results: Twenty-five patients (mean age = 67 ± 11 years, female = 8, mean LVEF = 29% ± 5%, ischaemic aetiology = 8) had CRT implanted. Simultaneous biventricular pacing with standard programming (AV 110/130 ms, VV 0 ms) determined a significant improvement in cardiac performance which was further enhanced after PRAM-based AV and VV delays optimization (Table). Mitral and aortic VTI showed the best correlation with PRAM-based optimization which was only poorly correlated with MPI and Ritter's method (Figure).
Conclusions: PRAM-based optimization is effective in maximizing CRT hemodynamic response and may be useful in reducing nonresponse.

	Baseline	Standard AV/VV	PRAM-based AV optimization	PRAM-based VV optimization	P-value for trend
Stroke volume (ml)	63.4	66.6	71.4	75.5	< 0.001
Cardiac output (l/min)	4.0	4.3	4.6	4.8	< 0.001
Cardiac index (l/min/m^2)	2.3	2.5	2.6	2.7	< 0.001
dP/dt (mmHg/ms)	0.87	0.93	0.95	0.96	0.08
EA VTI (cm)	21.8	23.5	24	24.1	0.022
LVOT VTI (cm)	17.9	18.0	18.7	20.2	0.009

VTI = velocity time integral; LVOT = left ventricular outflow tract



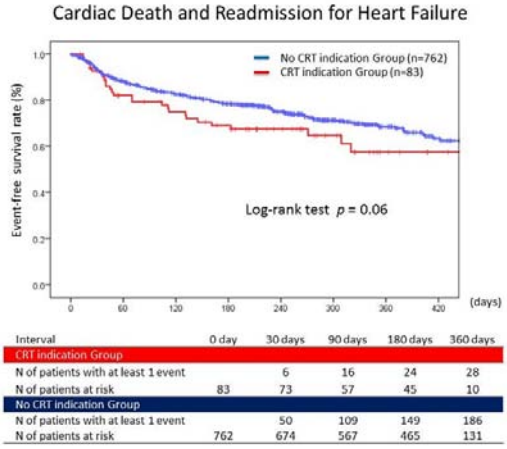
P1138

The prognosis of patients with acute decompensated heart failure indicated for cardiac resynchronization therapy

R Reo Hata[1]; Y Kawase[1]; H Tasaka[1]; T Tada[1]; K Kadota[1]
[1]*Kurashiki Central Hospital, Cardiology, Kurashiki, Japan*

Background: The prognosis of patients with acute decompensated heart failure (ADHF) with reduced ejection fraction and wide QRS indicated for cardiac resynchronization therapy (CRT) remains unclear.
Purpose: To determine the prognosis of ADHF patients indicated for CRT.
Methods: We retrospectively analyzed 864 consecutive patients hospitalized for ADHF between February 2015 and June 2016 and divided them into two groups based on having CRT indication or non-CRT indication, excluding 19 patients undergoing CRT: 83 patients with CRT indication as CRT group and 762 patients with non-CRT indication as non-CRT group. CRT indication was defined as left ventricular ejection fraction ≤35% and QRS width ≥120 msec, which was equivalent to classes I and IIa of the Japanese Circulation Society's CRT indication guidelines. We compared cardiac events (CE), defined as a composite of cardiac death and readmission for heart failure, between the two groups.
Results: The median follow-up period was 243 days. The 180-day cumulative CE-free survival rate tended to be lower in the CRT group than in the non-CRT group (68.0% versus 77.4%, p = 0.06). Subgroup analysis in CRT group was performed to further stratify cardiac events. CRT group was divided into two groups: CE group (n = 37) and CE-free group (n = 58). Between the CE group and CE-free group, significant differences were found in the rates of readmission for HF (61% vs. 36%, p = 0.04), prior ventricular tachycardia/fibrillation (38% vs. 12%, p < 0.01), the

level of hemoglobin < 11 g/dL (61% vs. 31%, p = 0.01), and estimated glomerular filtration rate (eGFR) < 45 ml/min/1.73m2 (79% vs. 40%, p < 0.01). Multivariate Cox proportional hazards model showed that prior ventricular tachycardia/fibrillation (hazard ratio, 3.04; 95% confidence interval [CI], 1.37 to 6.74; p = 0.01), and eGFR < 45 (hazard ratio, 4.11; 95% CI, 1.58 to 7.70; p < 0.01) were independent predictors of CE.
Conclusion: ADHF patients with CRT indication tended to have poorer prognosis than those with non-CRT indication. Prior ventricular tachycardia/fibrillation and decreased renal function were predictors of poor prognosis of ADHF patients indicated for CRT.



P1139
Atrial fibrillation at follow-up does not worsen the prognosis of cardiac resynchronization therapy

B Belen Alvarez[1]; FJ Garcia Seara[1]; D Iglesias Alvarez[1]; RA Abellas Sequeiros[1]; L Gonzalez Melchor[1]; M Rodriguez Manero[1]; XA Fernandez Lopez[1]; A Martinez Monzonis[1]; A Varela Roman[1]; JL Martinez Sande[1]; JR Gonzalez Juanatey[1]
[1]University Clinical Hospital of Santiago de Compostela, Department of Cardiology, Santiago de Compostela, Spain

OBJECTIVES: The aim of this study was to evaluate the impact of atrial fibrillation (AF) in the follow-up in patients with heart failure receiving cardic resynchronization therapy (CRT).
BACKGROUND: CRT has been demostrated good outcomes in sinus rhythm (SR). However, the prognosis of patients who develop AF at follow-up is unknown. Although it is believed that they have a worse prognosis
Methods: We investigated the long-term outcomes HF or mortality in 328 consecutive patients implanted with a CRT device in a single terciary center between 2001 and 2015. We categorize the patients into three groups: SR, basal AF and AF in the follow-up. Multivariable Cox proportional hazards models were used to determinate the effect on rhythm on the clinical outcomes.
Results: 138 (37.7%) patients were on SR, 123 (37.5%) were on basal AF and 67 (20.4%) were on AF at follow-up. Baseline characteristis were shown in Table 1. Basal AF was associated with an increased risk of HF/mortality in unadjusted analysis (HR 1.80, CI95% 1.28-2.54, p0.001) and adjusted analysis(HR 1.70, CI 95%1.21-2.65,p0.004) compared with SR. AF at follow-up was not associated with an increased risk of HF/mortality in unadjusted analysis (HR 1.39,CI95%0.94-2.08,p0.103) and adjusted analysis compared with SR (HR 1.45, CI95% 0.93-2.25, p0.103)
Conclusions: Patients with basal AF was associated with worse outcomes in HF/mortality events compared with SR. However, AF at follow-up was associated with similar risk of HF/mortality than SR

Table 1. Baseline Characteristics

	SINUS RHYTHM 138(42.1%)	BASAL AF 123(37.5%)	AF AT FOLLOW-UP 67(20.4%)	p-value
Age, years	69±10	71±9	70±9	0.269
Sex male, n(%)	103(74.6)	105(85.4)	45(67.2)	0.011
Ischemic cardiomyopathy, n(%)	52(37.7)	41(33.3)	26(38.8)	0.682
NYHA class, n(%) II III IV	45(32.6) 85(61.6) 8(5.8)	25(20.3)90(73.2) 8(6.5)	9(13.4) 55(82.1) 3(4.5)	0.023
CRT-D, n(%)	71(51.4)	65(52.8)	36(53.7)	0.948
DM, n(%)	37(26.8)	24(19.5)	16(23.9)	0.380
Sinus vein, n(%)	21(15.7)	36(29.3)	12(18.2)	0.085
Anterior Lateral Posterior	73(54.5) 40(29.9)	59(48.0) 28(22.8)	38(57.6) 16(24.2)	
Glomerular filtration rate	62±26	58±23	62±21	0.336
Hemoglobine	13±2	13±2	13±1	0.086
LVEF(%)	27±8	28±7	26±6	0.121
LVESV, ml	168±61	156±59	177±57	0.081

CRT-D: Defibrillator with Cardiac Resynchronization Therapy; DM: diabetes mellitus; LVEF: left ventricular eyection fraction; LVESV: left ventricular end systolic volumen; NYHA: New York Heart Association

P1141
Effects of tailored telemonitoring in patients with heart failure: an 8-year follow-up

A Arno Gingele[1]; HPB Brunner-La Rocca[1]; BR Ramaekers[1]; CK Knackstedt[1]; JB Boyne[1]
[1]Academic Hospital Maastricht, Department of Cardiology MUMC, Maastricht, Netherlands

On behalf of: TEHAF investigators
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Aims: There is evidence that telemonitoring decreases mortality and heart failure (HF) related hospital admission in patients with HF. Nevertheless, most studies follow their patients for only several months. Thus, little is known about the long-term effects of telemonitoring.
Methods: and Results: In 2007, the TEHAF study was initiated to compare tailored telemonitoring to usual care with respect to time until first HF-related hospital admission. Totally, 382 patients were included with a follow-up period of 1 year. No differences in time to first HF-related admission between intervention and control group could be found. In order to investigate long-term effects of telemonitoring, a retrospective analyses was performed. Primary endpoint was time to first hospital admission. Secondary endpoints were, amongst others, HF and all-cause mortality, hospital admission due to HF and days alive and out of hospital (DAOOH). Electronic files of all included patients were reviewed between October 2007 and September 2015. No difference in time to first HF-related hospital admission (log-rank test, p = 0.15), all-cause mortality (log-rank test, p = 0.43) or DAOOH (two-sample t-test, p = 0.87) could be found. Patients of the intervention group had significant less HF-related hospital admission (Incident rate ratio 0.54, 95%CI 0.31-0.88). However, HF related mortality was non-significantly higher in the intervention group (log-rank test, p = 0.058).
Conclusion: Telemonitoring did not significantly influence long-term outcome in our study, but there were some interesting, though controversial results on HF-related event. Therefore, sufficiently large studies with long-term follow-up period are needed to estimate the effect of telemonitoring on HF-related outcome.

P1143
Daily non-invasive hemodynamic-telemonitoring objectifies the efficacy of mitral clip-implantation in patients with advanced heart failure

E Herrmann[1]; B Luu[1]; A Ecke[1]; S Fichtlscherer[1]; AM Zeiher[1]; B Assmus[1]
[1]JW Goethe University, Cardiology, Frankfurt am Main, Germany

Patients with advanced systolic heart failure frequently suffer from concomittant progressive mitral regurgitation (MR), which increases the risk of hospitalization for cardiac decompensation. Treatment of severe MR with mitral clip-implantation

can considerably improve the clinical symptoms and possibly reduce the risk of rehospitalization. We report on our intial experience in patients with an implanted pulmonary artery pressure sensor (PAP), who developed severe MR requiring correction. Due to severe comorbidity, the heart team proposed an interventional approach using mitral clip-implantation. Here, we report on the possibility to directly measure the efficacy of the interventional mitral clip-procedure using ambulatory hemodynamic-telemonitoring.
Methods: Patients fitted with a PAP-sensor and severe, symptomatic MR received a mitral clip-implantation.
Results: 4 patients (mean age of 66 (±6) years) with advanced systolic heart failure (NYHA III, LVEF 21 ± 3%, cardiac index 1.8 ± 0.3) previously fitted with an implanted PAP-sensor received mitral clip-implantation for severe MR (VCmean 7 ± 1 mm). In comparison to the PAP values 4 weeks before the mitral clip-procedure, PAP was profoundly and significantly reduced in all 4 patients both after 30 days (delta PAPsys -16 ± 4, delta PAPmean -11 ± 5, delta PAPdiast -7 ± 3 mmHg, $p < 0.02$) as well as after 90 days (delta PAPsys -19 ± 4, delta PAPmean -13 ± 4, delta PAPdiast -9 ± 2 mmHg, $p < 0.02$). Reductions in PAP were accompanied by a significant clinical and echocardiographic improvement. No patient died and there was no hospitalization for cardiac decompensation.
Conclusion: In patients with advanced heart failure, the success of the interventional mitral clip-procedure on clinical symptoms can be confirmed by hemodynamic-telemonitoring demonstrating a profound and significant reduction of pulmonary artery pressure using an implanted PAP-sensor. Thus, daily non-invasive hemodynamic-telemonitoring allows for the first time a continuous investigation of the efficacy of interventional therapies in patients with chronic heart failure.

P1144
Axillary implantation of Impella CP allows early rehabilitation of patients in cardiogenic shock bridged to heart transplantation.

D Couto-Mallon[1]; F Estevez-Cid[2]; C Velasco-Garcia[2]; JM Herrera-Norena [2]; C Iglesias-Gil[2]; M Solla-Buceta[3]; L Seoane-Quiroga[3]; V Aller-Fernandez[3]; S Fojon-Polanco[3]; M Balsa-Canto[4]; E Barge-Caballero[1]; G Barge-Caballero[1]; MJ Paniagua-Martin[1]; MG Crespo-Leiro[1]; JJ Cuenca-Castillo[2]
[1]University Hospital Complex A Coruña, Cardiology, A Coruña, Spain; *[2]University Hospital Complex A Coruña, Cardiac Surgery, A Coruña, Spain*; *[3]University Hospital Complex A Coruña, Intensive Care, A Coruña, Spain*; *[4]University Hospital Complex A Coruña, Rehabilitation, A Coruña, Spain*

Introduction: Axillary implantation of Impella CP device (Abiomed, Inc) is a novel implantation method for patients in cardiogenic shock (CS), which facilitates a better placement of the device and allows mobilization of patients while on support.
Purpose: To describe our pilot experience using axillary implantation of Impella CP as a bridge to heart transplantation (HT) allowing better rehabilitation on support
Methods: Retrospective single-centre descriptive study of CS patients bridged to HT on support with Impella® CP through axillary artery between March and December of 2016. We collect data about survival, time of mechanical ventilation after HT, days in ICU, days to hospital discharge and major complications including bleeding or infection.
Results: 4 patients were bridged to HT with a transaxillary Impella® CP. Data of patients are in the table below. All Impella CP devices were surgically implanted using a Dacron graft. Patients 1, 2 and 3 had received an intraaortic balloon pump before Impella® CP. All patients were extubated immediately after Impella® CP implantation and started an early rehabilitation program consistent in kinesitherapy, respiratory physiotherapy and active movements. Median time on device support was 13.5 days (IQR 11.25 to 15.5). In one patient the device had to be repositioned because of displacement. Median time of ICU stay after HT was 7.5 days (IQR 5.5 to 9.75 days) and median time to hospital discharge after HT was 29.5 days (IQR 26 to 33.5 days). All patients were discharged alive. Major complications after HT were bleeding in one patient with cardiac tamponade and an ischemic stroke in other patient with significant bilateral carotid stenosis. Patient recovered without neurologic sequelae.
Conclusion: Axillary implantation of Impella® CP seems to be a valid strategy for bridging patients in INTERMACS 1 and 2 for HT allowing early initiation of rehabilitation therapy while on support.

P1145
Morphological and functional features of left ventricular remodeling after ventricular assist devices support

V Valeriya Krachak[1]; A Smalenski[2]; L Shestakova[1]; O Yudina[2]; D Krachak[1]
[1]Republican Scientific and Practical Centre of Cardiology, Extracorporeal circulation, Minsk, Belarus; *[2]City Clinical Pathologoanatatomic Bureau, Minsk, Belarus*

Introduction: 38 ventricular assist devices (VAD) implantations as a bridge to transplantation and a bridge to transplant candidacy were performed in our center between 2009-2016. Currently, 18 (47.4%) patients were transplanted, 14 (36.8%) died and 6 (15.8%) are on VAD support.
Purpose: The purpose of this study was to evaluate the left ventricular (LV) remodeling after VAD implantation, using echocardiography parameters and myocardial biopsies.
Methods: Morphological and functional parameters were studied in 18 VAD patients, the mean age of the patients was 47,1 ± 12,9 years, 99% of them were men, with ischemic cardiomyopathy (ICM) in 50%, dilated cardiomyopathy (DCM) in 43,75% and giant cell myocarditis (GM) in 6,25%. VADs were implanted for 213,5 (118.5: 370) days and then heart transplantation was performed. Echocardiographic parameters, such as left ventricular ejection fraction (LVEF), end-diastolic volume of the left ventricle (LV EDV), end-systolic volume of the left ventricle (LV ESV) before VAD implantation and after VAD explantation were analyzed in all patients as signs of cardiac remodeling. Myocardial biopsies were collected from the LV apex during VAD implantation and explantation in 8 of 18 patients. Diameters of cardiomyocytes, which were determined in transversally sectioned cells as indicators of myocardial hypertrophy degree were evaluated.
Results: Baseline echo parameters before VAD implantation were: LV EF - 17.5 (13: 18.75)%, LV EDV -281.5 (223: 402.5)ml, LV ESV- 230.5 (185.75: 353) ml. During mechanic support LV EF changed to 34 (18:40)% ($p < 0.02$) and LV EDV - to 165 (104.5: 231.5) ml ($p < 0.02$), LV ESV - to 108 (60: 191) ml ($p < 0.02$). Diameter of cardiomyocytes was 28,82 ± 7,25 mm before VAD implantation and after explantation it was 18,86 ± 4,31 mm ($p < 0.001$). Changes in diameter of cardiomyocytes were -5.13 (-11.09: 1.41) mm. There was a negative correlation between the duration of VAD use and the diameter of cardiomyocytes ($r = -0.86$, $p < 0.02$).
Conclusions: Prolonged VAD support was associated with LV myocardial remodeling such as an increased LVEF, reduced LV EDV and ESV, as well as decreased myocardial hypertrophy, as evidenced by a decline of cardiomyocyte diameter. In addition, there is a notable correlation between the prolonged VAD use and the diameter of cardiomyocytes.

P1146
mortality in patients with cardiogenic shock treated with the impella cp microaxial pump for left ventricular failure

JT Jan-Thorben Sieweke[1]; D Berliner[1]; J Tongers[1]; LC Napp[1]; U Flierl[1]; F Zauner[1]; J Bauersachs[1]; A Schaefer[1]
[1]Hannover Medical School, Cardiology and Angiology, Hannover, Germany

Background: Despite advanced therapies cardiogenic shock (CS) is still associated with high mortality. It is to be noted that out-of-hospital cardiac arrest and right ventricular (RV) failure in addition to left ventricular (LV) failure impair prognosis. Data indicating benefit of mechanical circulatory support in CS, but the choice of the device is still challenging. The Intra-aortic balloon pump had been frequently

P 144 Patients bridged to HT

Patient	Gender	Age	Heart condition	INTERMACS profile at implan tation	Time of support (days)	Intubation after HT (hours)	ICU stay after HT (days)	Days to discharge after HT	Complications
1	Male	65	Idiopathic dilated cardiomyopaty	2	20	11	6	30	Cardiac tamponade
2	Male	68	Ischemic cardiomyopathy	1	6	72	9	44	Ischemic stroke
3	Male	55	Idiopathic dilated cardiomyopathy	2	13	96	12	29	None
4	Male	56	Eosinophilic myocarditis	2	14	12	4	17	None

ICU: Intensive care unit; HT: Heart transplant.

used in CS, but was previously found to provide no mortality benefit. Many shock centres now prefer active LV support as provided by the Impella microaxial pump. A recent underpowered prospective trial, however, demonstrated no mortality benefit for Impella over balloon-pump in CS, but all patients in the Impella cohort (vs. 83% in the balloon-pump group) had been resuscitated before implantation.

Methods: and Results: We investigated consecutive patients (58 ± 13 years) with cardiogenic shock presenting at our institution, who received an ImpellaCP for isolated LV support (n = 62). 61% had been resuscitated before Impella insertion. In a hierarchical analysis we assessed all patients supported on ImpellaCP for CS irrespective of the necessity for resuscitation before implantation, as well as patient subgroups stratified by resuscitation before LV support. Overall survival was 48% at hospital discharge, 43% after 6 months and 38% after 12 months. 30-day mortality increased after out-of-hospital cardiac arrest (resuscitated: 65%: non-resuscitated: 21%), with concomitant RV failure (RV+: 100%; RV-: 33%), and when Impella implantation was performed after PCI in case of ischemic CS (pre-PCI: 40%; post-PCI 61%). Patients in our local registry, who fitted the inclusion/exclusion criteria of the SHOCK-II trial had a markedly lower mortality (24% at 30 days) compared to the published trial.

Conclusion: Active hemodynamic support with ImpellaCP in singular LV failure results in lower than previously reported mortality rates. RV failure or pre-implantation cardiac arrest critically influences observed mortality and should be taken into account when performing clinical trials aiming to address mortality in CS patients.

P1147

A proposed algorithm to assist first responders in resuscitation of patients with left ventricular assist devices (LVADs)

K Chu[1]; SA Schaffer[1]

[1]*St. Boniface General Hospital, University of Manitoba, Winnipeg, Canada*

Background: The prevalence of patients with left ventricular assist devices (LVAD) is increasing. If a LVAD patient collapses, emergency personnel must decide if immediate cardiopulmonary resuscitation (CPR) is safe, necessary, and effective. Even within implanting centers, expertise on LVAD emergencies is limited to the advanced heart failure and cardiovascular surgical units.

Purpose: To propose an addition to the Advanced Cardiac Life Support algorithm specifically for LVAD patients and determine its application in case examples.

Methods: We reviewed and summarized the literature to devise an addition to the current Advanced Cardiac Life Support algorithm specific to LVAD patients. We then applied it to three cases.

Results: Continuous flow LVAD patients inherently do not have a pulse. Its absence cannot be used as a marker of hypoperfusion and need for CPR. As long as the LVAD is operating, there should be blood flow into the LVAD and out of the heart. Uncertainty in how to manage this population may lead to delayed resuscitative measures reducing probability of favorable outcomes. In our proposed algorithm, priority is to determine if an unconscious patient has adequate perfusion and to restore it quickly prior to neurological injury if necessary. Unconsciousness may be related to low cardiac output from LVAD malfunction, but non-LVAD related causes remain on the differential. LVAD malfunction is associated with audible alarms and visible messages on patient controllers. If the patient controller indicates normal functioning (lights on, no alarms), absolute LVAD failure and low output is unlikely. If unconsciousness is due to low cardiac output resulting from LVAD malfunction or primary cardiac pathology (e.g. right ventricular arrhythmias, low LV pre-load) immediate efforts to restore perfusion is essential. CPR has a theoretical risk of cannula dislodgement and should be deferred if alternative therapies are immediately available. Published case series have not demonstrated this. The controller should be quickly identified and examined. Check all connections from patient to driveline to controller to batteries/power base. Given the complexity and risk of controller exchange and rarity of failure, routine exchange without confirmation of malfunction is discouraged. If connections are intact, LVAD lights are off or alarming and no LVAD hum is auscultated, start immediate compressions. If a dysrhythmia is suspected and defibrillator is quickly accessible, this can be delayed. We applied our algorithm to cases involving an unconscious, spontaneously breathing patient in an outpatient hospital lab, a cardiac arrest called to the emergency room, and paramedics arrival to a patient with the LVAD alarming.

Conclusion: CPR in LVAD patients is safe and sometimes necessary. Our proposed algorithm assists first responders to provide timely and life-saving medical care to this special group of patients.

Figure 1: Proposed addition to Advanced Cardiac Life Support algorithm for LVAD patients. LVAD: left ventricular assist device, EHS: Emergency Health Services, LOC: level of consciousness, ICH: intracranial hemorrhage, GIB: gastrointestinal bleeding, AED: Automated External Defibrillator

P1148

Acute kidney injury early after CF-LVAD implantation is associated with high mortality rates: a multicenter study.

R Rahat Muslem[1]; K Caliskan[1]; S Akin[1]; A Constantinescu[1]; GJ Whitman[2]; RJ Tedford[3]; DA Hesselink[4]; AJJ Bogers[5]; SD Russell[3]; OC Manintveld[1]

[1]*Erasmus Medical Center, Cardiology, Rotterdam, Netherlands*; [2]*Johns Hopkins University of Baltimore, Cardiothoracic Surgery, Baltimore, United States of America*; [3]*Johns Hopkins University of Baltimore, Cardiology, Baltimore, United States of America*; [4]*Erasmus Medical Center, Nephrology, Rotterdam, Netherlands*; [5]*Erasmus Medical Center, Cardiothoracic Surgery, Rotterdam, Netherlands*

Purpose: Data on the consequence of acute kidney injury (AKI) after continuous-flow left ventricle assist devices (LVAD) are scarce and inconsistent. In the current study, the incidence and predictors of AKI and its impact on mortality and renal function in the first year after LVAD implantation was evaluated.

Methods: A retrospective multicenter cohort study was conducted, including all patients (age ≥18) undergoing LVAD implantation (91% HeartMate II, 9% HVAD). The definition proposed by the Kidney Disease Improving Global Outcome criteria (KDIGO) was used to define AKI.

Results: Overall, 241 patients (mean age 52.4 std. 12.9 years, 76% male, 64% BTT) were included. AKI criteria was met in 169 (70%) LVAD patients, of who 109 (45%) had AKI stage I, 22 (9%) stage II and 38 (16%) stage III. The need for inotropic support and pre-existent severe kidney failure (eGFR <30 ml/min/1.73 m2) were independently associated with the development of AKI and subsequent higher AKI stages. One-year mortality rates in patients without AKI, AKI stages I, II and III were 18.7%, 26.4%, 23%, 51%, respectively (log-rank p = 0.001, Figure 1A). In multivariable analysis AKI stages ≥ II were independently associated mortality (HR 2.2 (95% CI 1.1-4.5), p = 0.027) and worse renal function (β -7.4 (95% CI -12.6 to -2.1), p < 0.01) at 1 year.

Conclusion: AKI is highly frequent after LVAD implantation. More severe AKI stages are associated with higher mortality rates and impaired renal function at one year after LVAD implantation.

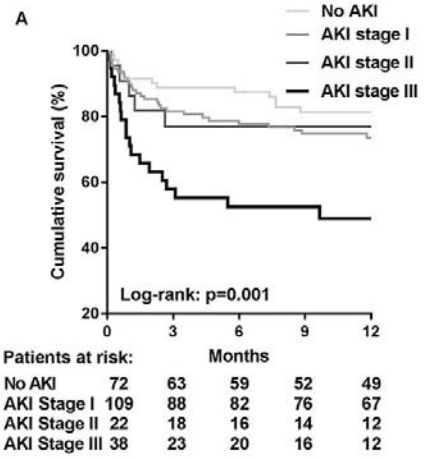


Figure 1 Kaplan-Meier curve for survival

P1149

Outcomes of patients with or without implantable cardioverter defibrillators on continuous-flow left ventricular assist device support

VJ Goh[1]; CP Lim[2]; D Sim[2]; KL Kerk[2]; TE Tan[2]; C Sivathasan[2]; JL Soon[2]; L Teo[2]
[1]*Duke-NUS Graduate Medical School Singapore, Singapore, Singapore*; [2]*National Heart Centre Singapore, Singapore, Singapore*

Background/Introduction: The role of Implantable Cardioverter Defibrillators (ICDs) in patients implanted with continuous-flow Left Ventricular Assist Devices (LVADs) remains controversial. Pre-LVAD ventricular arrhythmia (VA) was shown to be a major predictor of post-LVAD VA, suggesting that patients with pre-LVAD VA could benefit from ICD implantation. There is, thus far, little evidence for the routine implantation of ICDs for patients undergoing LVAD surgery.
Purpose: We aimed to study whether ICD implantation in patients with or without pre-LVAD VA affected the outcomes of patients on LVAD support.
Methods: We performed a retrospective analysis of 72 consecutive patients receiving LVADs between May 2009 and April 2016 in a single tertiary hospital in Singapore. Data analysed included demographic variables, ICD reports, and other clinical attributes. Group A was defined as patients who received ICD implantation pre-LVAD surgery, while group B did not have ICDs implanted going into LVAD surgery. Outcomes assessed included all-cause mortality, all-cause hospitalisation and clinically significant VA (defined as any post-LVAD VA resulting in hospitalisation, cardioversion, ICD implantation, or ICD therapy occurring ≥30 days post-LVAD implantation).
Results: Our cohort comprised of majority (81%) male, 49% with ischaemic cardiomyopathy, 43% INTERMACS profile 1 or 2 at LVAD implantation with a median of 22 months (IQR 12, 39) on LVAD support. Half of the patients had ICD implanted prior to LVAD surgery. Group A (n = 36) was older (53 ± 12 vs. 47 ± 13, p = 0.04), had higher incidence of pre-LVAD VA (47% vs. 22%, p = 0.05), and larger pre-LVAD end-diastolic left ventricular internal diameter (LVIDd) (7.1 ± 1.0 vs. 6.5 ± 1.3, p = 0.02). There was no significant difference between the two groups in terms of all-cause mortality and hospitalisation (Group A vs. Group B: 22% vs. 8%, P=0.2 and 86% vs. 86%, P=1.0, respectively). However, there was a higher rate of clinically significant post-LVAD VA in Group A than Group B (44% vs. 11%, p = 0.003). Compared to patients without pre-LVAD VA, a higher proportion of patients who had pre-LVAD VA tended to experience clinically significant VA post-LVAD in Group A (71% vs. 21%, p = 0.006) but not Group B (13% vs. 11%, P=1.0). However, pre-LVAD VA did not result in a difference in mortality in either group (Pre-LVAD VA vs. none: Group A 18% vs. 26%, P=0.7; Group B 0% vs. 11%, P=1.0) (Figure 1). The presence of ICD did not confer a mortality benefit in patients with pre-LVAD VA (Group A 18% vs. Group B 0%, p = 0.5).
Conclusion(s): ICD implantation pre-LVAD surgery did not confer a mortality benefit regardless of presence of pre-LVAD VA. Our findings do not support the practice of routine ICD implantation prior to LVAD surgery.

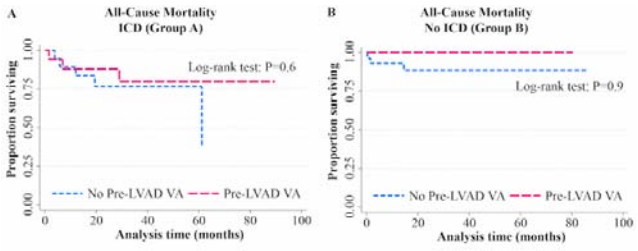


Figure 1

P1150

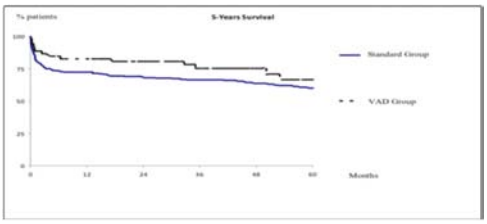
Bridge to transplantation versus standard heart transplantation: heart transplantation performed after ventricular assistance device is associated with improved survival.

T Petroni[1]; C D'alessandro[2]; A Combes[3]; JL Golmard[4]; N Brechot[3]; E Barreda[2]; M Laali[2]; P Farahmand[2]; S Varnous[2]; P Weber[2]; A Pavie[2]; P Leprince[2]
[1]*Clinique du Pont de Chaume, Department of Cardiology, Montauban, France*; [2]*Hospital Pitie-Salpetriere, Department of Thoracic and Cardiovascular Surgery, Cardiology Institute, UPMC, APHP, Paris, France*; [3]*Hospital Pitie-Salpetriere, Intensive Care Unit, Cardiology Institute, UPMC, APHP, Paris, France*; [4]*Hospital Pitie-Salpetriere, Department of Biostatistics and Medical Information, UPMC, APHP, Paris, France*

Aim: Mechanical circulatory support is an alternative strategy as a bridge-to-transplantation for critical situations such as circulatory shock or graft shortage. The purpose of this study was to evaluate long-term results and outcome after heart transplantation performed in patients with ventricular assistance device (VAD) versus no mechanical circulatory support.
Methods and Results: All the patients who underwent heart transplantation between 2005 and 2012 were included in this monocentric retrospective study. We compared 52 VAD patients who underwent heart transplantation to 289 patients transplanted without VAD. Mean age was 46 ± 11 years in the VAD group vs 51 ± 13 years in the standard group (p = 0.01) and 17% of the VAD patients were women vs 25% (p = 0.21). Ischemic time was longer in the VAD group (207 ± 54 vs 169 ± 60 min, p < 0.01). There was no difference of primary graft failure (33% vs 25%, p = 0.22) and 1-year mortality (17% vs 28 %, p = 0.12). Independent risk factors for 1-year mortality were preoperative VAD (OR 0.40 [0.17-0.97], p = 0.04), recipient age>60 years (OR 0.2.35 [1.34-4.14], p < 0.01), recipient creatinine (OR 1.005 [1.001-1.010], p = 0.02), BSA mismatch (OR 4.85 [1.34-17.54], p = 0.02) and ischemic time (OR 1.005 [1.001-1.010], p = 0.02). Five-year survival was 66% in VAD group vs 60% in standard group (p = 0.72). Independent risk factors for 5-years survival were recipient age>60 years (HR 1.570 [1.05-2.34], p = 0.02), recipient creatinin (HR 1.005 [1.002-1.008], p = 0.02) and ischemic time (HR 1.004 [1.001-1.007], p = 0.01).
Conclusion: Bridge-to-transplantation by VAD reduced one-year mortality and improved mid-term survival rate after heart transplantation.

Risk Factor	OR (95% CI)	p
Group VAD	0.399 (0.165-0.967)	0.02
Recipient Age > 60 years	2.353 (1.339-4.135)	< 0.01
Recipient Creatinin	1.005 (1.001-1.010)	0.02
BSA Mismatch > 0.15	4.847 (1.340-17.536)	0.02
Ischemic Time	1.005 (1.001-1.010)	0.02

Risk-Adjusted Multivariable Analysis for Death Risk at 1 year.



Kaplan-Meier curve of survival after HTx

P1151

Cangrelor use in the treatment of left ventricular assist device pump thrombosis

CM Christopher Bianco[1]; BP Dhakal[1]; M Zacharias[1]; SG Al-Kindi[1]; R Barcelona[1]; L Meece[1]; C Elamm[1]; MR Robinson[1]; R Benatti[1]; M Ginwalla[1]; BP Sareyyupoglu[1]; BP Medalion[1]; SG Park[1]; G Oliveira[1]
[1]*University Hospitals Case Medical Center, Cleveland, United States of America*

Background: Left ventricular assist device (LVAD) pump thrombosis (PT) treated with conventional pharmacologic therapy is associated with a 6 month mortality rate of nearly 50%. Pump exchange or transplantation is the definitive therapy, however many patients are suboptimal candidates and an attempt at medical therapy is appealing. Several strategies involving escalating anticoagulants, antiplatelets, or thrombolytics have been utilized; however none has emerged superior. Our group has shown the P2Y12 inhibitor ticagrelor, in conjunction with heparin and aspirin, was beneficial in resolving PT and avoiding pump exchange. However, a relatively long half-life limits its use in expectant medical management with the potential for urgent pump exchange. Cangrelor, a potent, reversible P2Y12 inhibitor that allows rapid restoration of normal platelet function within 1 hour of cessation may facilitate a more effective, safer strategy.
Purpose: LVAD PT is common, however suboptimally treated with conventional medications. A novel treatment strategy utilizing cangrelor may prove effective and safe in cases of suspected PT.
Methods: We performed a case review of patients with suspected PT (evident by sustained power elevations >10W or >2W from baseline with peak elevated LDH >3x ULN) who were treated with cangrelor at a large academic center between

8/2015 and 1/2017. Successful pharmacologic treatment was defined as freedom from death, pump exchange, or transplantation during index hospitalization.
Results: Cangrelor was utilized in 4 patients with 5 episodes of suspected PT. All 4 patients had Heartmate II devices implanted as destination therapy between 8/2014 and 6/2015. Cangrelor treatment was successful in 3/5, while 2/5 required pump exchange. All patients treated with cangrelor remain alive to date. One patient originally treated successfully with cangrelor developed another episode of suspected PT 14 months later, he was treated with cangrelor again, but eventually required pump exchange. There were no major bleeding events during cangrelor infusion, 1 patient who underwent pump exchange had to return to OR for continued post-op mediastinal bleeding. Two patients, both safely and successfully treated, were deemed at elevated risk for major bleeding events, one by history of intracranial bleed and the other with recurrent GIB. A mean of 3.6 antiplatelet or anticoagulant agents were attempted prior to cangrelor initiation. Mean duration of cangrelor infusion was 6 days. Mean decrease of serum LDH from cangrelor initiation to hospital discharge or pump exchange was 45%.
Conclusions: Cangrelor use for treatment of suspected PT is associated with a reasonable success rate and excellent safety profile in this small series. To our knowledge, this is the first reported case series of cangrelor use in PT. Further study of cangrelor use in the management of PT is warranted.

P1152

Heart transplantation: to bridge or not to bridge

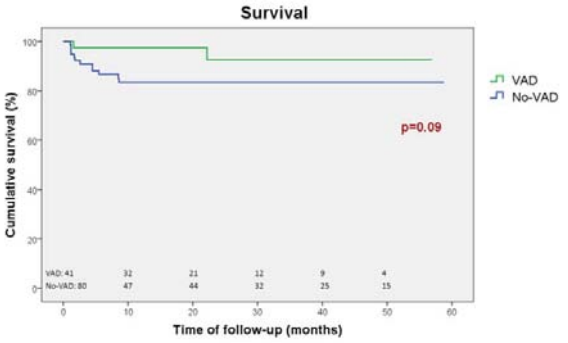
M Massimiliano Carrozzini[1]; T Bottio[1]; F Toto[1]; M Comisso[1]; E Manzan[1]; V Tarzia[1]; J Bejko[1]; G Gerosa[1]
[1]*University Hospital of Padova, Cardiac Surgery Unit, Padua, Italy*

Background/Introduction: It is unclear if the use of left-ventricular-assist-device (LVAD) as bridge-to-transplantation can improve post-transplant outcomes.
Purpose: We aimed to compare results of heart transplantation with or without previous bridging with an implantable continuous-flow LVAD.
Methods: All consecutive patients who underwent heart transplantation at our institution between January-2012 and December-2016 were included. LVAD used were Jarvik2000 and HeartWare. Patients were dived in VAD and No-VAD groups according to previous implantation of an LVAD or not.
Results: : Included are 128 patients: 44 VAD and 84 No-VAD. Emergent transplantation ($p = 0.03$), previous staying in ICU ($p = 0.01$) and para-corporeal mechanical support ($p < 0.01$) were more frequent in No-VAD. VAD vs No-VAD had similar 30-day-mortality (7% vs 5%, $p = 0.69$), whereas ICU-stay (6 ± 4 days vs 12 ± 15, $p < 0.01$) and hospital-stay (37 ± 16 vs 45 ± 28, $p = 0,03$) were longer in No-VAD. Postoperative complications were comparable among groups, except for pleural/pericardial-effusion ($p = 0.01$) and tracheostomy ($p < 0.01$), more frequent in No-VAD. After a mean follow-up of 25 ± 19 months mortality was higher in NO-VAD group (5% vs 15%, $p = 0,14$) though not significantly. Rate of cellular-mediated-rejection ($p = 0.17$) and antibody-mediate-rejection ($p = 0.97$) were similar.
Conclusion(s): LVAD as bridge-to-transplantation showed a trend toward better post-transplant outcomes. A larger patient population is needed to confirm our results.

Post-transplant outcomes

	VAD (N=44) N (%) Mean ± SD	No-VAD (N=84) N (%) Mean ± SD	P value
Postoperative ECMO	7 (16)	16 (20)	0,66
Postoperative CRRT	11 (25)	28 (33)	0,33
Postoperative revisionfor bleeding	3 (7)	12 (14)	0,26
Postoperative cerebral event	5 (11)	10 (12)	0,93
Postoperative pleural/pericardial effusion requiring procedure	4 (9)	24 (28)	0,01
Postoperativetracheostomy	0 (0)	12 (14)	< 0,01
30-day-mortality	3 (7)	4 (5)	0,69
ICU-stay (days)	6 ± 4	12 ± 15	< 0,01
Hospital-stay (days)	37 ± 16	45 ± 28	0,03
Follow-up-mortality	2 (5)	12 (15)	0,14
Cellular-mediated rejection	25 (57)	37 (44)	0,17
Antibody- mediated rejection	1 (2)	2 (2)	0,97

VAD-ventricular assist device; ECMO-extracorporeal membrane oxigenator; CRRT-continuous renal replacement therapy



P1153

Clinical outcomes at 5-years following transcatheter aortic valve replacement in patients with aortic stenosis

E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; AJ Dominguez-Franco[2]; JM Garcia-Pinilla[2]; L Morcillo-Hidalgo[2]; MF Jimenez-Navarro[2]; JH Alonso-Briales[2]; JJ Gomez-Doblas[2]; JM Hernandez-Garcia[2]; E De Teresa-Galvan[2]
[1]*Department of Cardiology , Malaga, Spain*; [2]*University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

The durability of transcatheter heart valves and long-term clinical outcomes are unknown. The aim of this study was to evaluate clinical and hemodynamic outcomes 5-years after Transcatheter Aortic Valve Replacement (TAVR).
Methods: Between April 2008 and December 2011, 224 patients underwent TAVR for the treatment of severe symptomatic aortic stenosis with the auto-expandable prosthesis
Results: the mean age and EuroSCORE were $79.2 \pm$ 6.4 years and 19.8 ± 13% respectively. Mean aortic valve gradient decreased from 50 ± 15 mm Hg to 8.6 ± 3.8 mmHg after TAVI, to $11.1 \pm$ 9 mm Hg at 4 years and $22.7 \pm$ 12 mmHg at 5 years (p for post-TAVI trend 0.03). Mean aortic valve area increased from 0.6 ± 0.16 cm2 to $1.59 \pm$ 0.3cm2 after TAVI to $1.48 \pm$ 0.2 at 4 years and $0.97 \pm$ 0.3 cm2 (p for post-TAVI trend 0.01). Mean left ventricular ejection fraction increased from 61.1 ± 15 % to 65.5 ± 11% after TAVI, to 58.2 ± 17% at 4 years and $60.7 \pm$ 8% at 5 years (p for post-TAVI trend 0.001) Late mortality after a mean of $52.29 \pm$ 28 months was 58.3% and in only 37 patients was cardiovascular mortality. Survival rates at 1 to 6 years were at 86.1%, 77.8%, 70.4%, 64.8%, 53 % and 44.3% respectively. At 5 years, 3 patients had severe prosthetic valve dysfunction (severe stenosis and moderate transvalvular regurgitation). Median survival time after TAVI was 3.91 years (95% confidence interval [CI]: 3.6 to 4.21), and the risk of death was significantly increased in patients with frailty (adjusted hazard ratio [HR]: 3.25; 95% CI: 1.76 to 6.01),$p = 0.001$, Charlson index [HR= 1.24 (95% CI 1.11-1.37), $p < 0.001$], Acute kidney injury after TAVR [HR= 1.942 (95% CI 1.10-3.42) $p = 0.022$] and lef ventricular ejection fraction [HR= - 0.352;(95% CI 0.166-0.745)$p = 0.006$].
Conclusions: Our study demonstrated favorable long-term outcomes after TAVR. Signs of prosthetic valve failure were observed in 1.33% of patients

P1154

Alternative solution for central hemodynamics parameters assessment with a new tacho-oscillometric device

S Padaryan[1]; E Elena Shavarova[2]; Y Kotovskaya[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*; [2]*Russian Peoples Friendship University, Moscow, Russian Federation*

Background and aim: to evaluate blood pressure (BP) parameters, measured with a new tacho-oscillographic device using volume-compressive oscillometry (VCO), compared with Korotkoff auscultation method and parameters of central BP measured with applanation tonometry. The main advantages of VCO comparing to other oscillometry technic of BP registration is formation and recording the curve automatically in synchronism with the cuff inflation and recording the artery response by changing the cuff volume throughout the all period of cuff compression. It could prevents appearing of extra-vibrations and sound phenomenon due to "water hammer". Strong association between hemodynamic parameters measured by VCO and by invasive method of BP registration was found previously: for systolic (SBP) ($r=0.96$, $p < 0.0001$), for diastolic (DBP) ($r=0.92$, $p < 0.0001$) BP.

Methods: 68 subjects were included in the study: 28 young (< 35 yrs) healthy volonteers and 40 elderly hypertensive pts (>60 yrs). BP were measured by a trained health care provider using a mercury sphygmomanometer and the Korotkoff sound technique. Central SBP, DBP were evaluated in supine position with SphygmoCor device. BP measurement was also performed using new tacho-oscillometric cuff-based device EDTV-Hemodin. This device analyses recorded tachooscillogram and evaluates diastolic, mean, lateral (true systolic) and end-systolic pressure.
Results: 65% of subjects were male and mean BMI was 24.9 ± 4.1 kg/m2. Mean SBP, measured using Korotkoff method was 125.97 ± 9.88 mm Hg, DBP - 70.17 ± 9.14 mm Hg. Mean central SBP measured with SphygmoCor 109.9 ± 10.2 mm Hg; mean central DBP - 72.25 ± .63 mm Hg. Mean SBP and DBP measured with EDTV-Hemodin were 111.7 ± 11.83 and 51.37 ± 10.56 mm Hg respectively. We found correlations using Spearman's rank between mean central SBP measured with SphygmoCor and SBP measured with EDTV-Hemodin ($r=0.41$, $p < 0.05$). Correlation, using Bland-Altman's plot was found between SBP measured by SphygmoCor and EDTV-Hemodin (bias -1.87 mm Hg [-5.43; 1.76]). There were no associations between assessment BP using EDTV-Hemodin and auscultation method. Positive correlation in both groups between measurement of central SBP with SphygmoCor (103.67 ± 6.31 mm Hg and 115.94 ± 9.19 mm Hg respectively) and SBP evaluated with EDTV-Hemodin (108,05 ± 11,56 mm Hg and 115.00 ± 11.05 mm Hg respectively) - for the first group bias was - 4.38 [-9.89;1.13] mm Hg; for the second - bias was 0.94 [-4.56; 6.45] mm Hg. Conclusion: SBP and DBP by VCO were significantly lower, than comparing to Korotkoff method. There is association between central SBP measured by SphygmoCor and SBP by VCO. VCO diagram could considered as indicator of aortic stiffness. Further study is required to validation and evaluation of the clinical significance of new tachooscillometric device.

P1155

Cardiac device implantation rate in heart failure patients:A study based on a tertiary cardiology service in Ireland.

D Ranganathan[1]; S Fall[1]; M Carey[1]; B Khan[1]; D Moore[1]
[1]*Adelaide & Meath Hospital, Cardiology Department, Dublin, Ireland*

Background: HFrEF is defined as left ventricular ejection fraction (LVEF) of ≤40%. Goals of therapy in HFrEF are to reduce mortality and morbidity as well as to improve functional status and reduce hospital admissions secondary to decompensation. The European CRT survey showed that patients who received CRT device had symptomatic improvement and overall survival rate >90%, replicating the outcomes shown in randomised control trials.
Purpose: This study aimed to evaluate if patients referred to our Heart Failure Clinic (HFC) were appropriately considered for an implantable device after optimal medical therapy (OMT) as per ESC 2013 guidelines.
Methods: Patient referrals from January 2015 to December 2015 were analysed through an online portal – Cellma. Out of 179 patients referred, 90 patients (50.0%) had HFrEF. Further information (such as NYHA class of symptoms, ECG – looking for evidence of LBBB/QRS interval, medical therapy) was collected through Cellma. 23 patients had incomplete information (missing echocardiography, ECGs) were omitted from the study.
Results: Of 67 patients, 19 patients were female and 48 were male. The mean age was 67.29 years with the oldest patient at 93 and youngest at 33. 53 out of 67 patients had an LVEF ≤ 35% post OMT. 61 patients were on ACEi/ARB, 62 patients on beta-blocker, 4 patients on nitrates and 63 were on diuretics (55 on loop, 50 on potassium sparing diuretic and 41 on a combination of the two). Of these, 19 patients had NYHA class 2-3 symptoms and 12 patients (18% in sinus rhythm) qualified for device therapy. Of these 12 patients, 1 patient passed away prior to treatment, 5 had appropriate device in-situ, 3 patients could have benefitted more from a different device (i.e. resynchronization therapy) and 3 patients despite meeting criteria had no device in-situ (at time of study).
Discussion: In our study, 90% of patients were on appropriate combination of medication for HFrEF. 25% of patients, despite meeting criteria for device therapy, did not have a device in-situ. Furthermore, 25% of patients who had device in-situ could have probably benefitted from resynchronization therapy. Given these patients were followed up regularly in a specialist HF clinic in a tertiary referral university teaching hospital, there is selection biasness and underestimation of the general heart failure population. The low rate of device implantation is not a unique issue highlighted in our study. The Swedish pacemaker and implantable cardioverter-defibrillator registry concluded there is marked variation in the rate of device implantation across Europe and within each country. Italy, which has one of the highest CRT-D implantation rates in Europe, noted reasons including creation of dedicated referral pathway and high number of implanting centers. A more exclusive study exploring the reasons for non-adherence to device implantation guidelines and ways to bridge the gap should be conducted to target this issue.

P1156

Acute effects of spinal cord stimulation on cardiac autonomic control and function in patients with heart failure

J Jan Naar[1]; D Jaye[2]; C Linde[3]; P Neuzil[1]; P Doskar[1]; F Malek[1]; F Braunschweig[3]; L H Lund[3]; L Mortensen[3]; B Linderoth[4]; G Lind[4]; F Kueffer[2]; J Koehler[2]; M Stahlberg[3]
[1]*Na Homolce Hospital, Department of Cardiology, Prague, Czech Republic*; [2]*Medtronic Plc, Cardiac Rhythm and Heart Failure, Minneapolis, United States of America*; [3]*Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden*; [4]*Karolinska Institute, Department of Clinical Neuroscience, Stockholm, Sweden*

Background/Introduction: Heart failure with reduced ejection fraction (HF) is characterized by sympathetic over-activity and baroreceptor desensitization. Spinal cord stimulation (SCS) can reduce sympathetic nerve activity in animal models of HF but data in patients with HF is limited.
Purpose: We aimed at testing the hypothesis that SCS acutely improves heart rate variability (HRV) and baroreceptor sensitivity (BRS) in patients with chronic HF.
Methods: HF patients with a SCS device implanted (Th1-Th4 spinal cord level) were included in this study. SCS was delivered (stimulation amplitude: 90% of maximally tolerated, all eight electrodes active) for 15 minutes. ECG and beat-to-beat non-invasive hemodynamics (finger plethysmography) were recorded continuously during SCS-90% and compared to a 5 min baseline period immediately before SCS (SCS-OFF). This was repeated using different SCS stimulation settings: Output 60% of maximally tolerated (SCS-60%), cranial electrode configuration (SCS-CRAN) and caudal electrode configuration (SCS-CAU).
Results: Fifteen patients (73% males, mean age 65 ± 8 years, mean left ventricular EF 43 ± 14%) were included to this study. SCS-90% did not influence HRV, BRS or hemodynamics (table). Similarly, SCS-60%, SCS-CRAN and SCS-CAU did not change HRV, BRS or hemodynamics compared to SCS-OFF.
Conclusion: SCS delivered acutely at ≤90 % of maximally tolerated output does not appear to improve autonomic balance or baroreceptor sensitivity in patients with heart failure.

Variable	SCS-OFF	SCS-90%	p-value
Heart rate variability (n=11, median [IQR])			
Heart rate (bpm)	65.6 [55.7-70.9]	64.6 [53.6-69.8]	0.06
SDNN (ms)	55.7 [25.5-87.4]	50.9 [35.8-73.9]	0.82
LF power (ms^2)	511 [154-1557]	300 [154-1081]	0.89
HF power (ms^2)	290 [66-821]	322 [97-579]	0.69
LF/HF (ratio)	1.8 [1.1-3.6]	1.7 [0.8-3.7]	0.82
Baroreceptor sensitivity (n=10, median [IQR])			
BRS (ms/mmHg)	10.4 [4.7-12.8]	6.3 [3.0-10.5]	0.35
Hemodynamics (n=15, mean±SD)			
Stroke volume (ml)	74±20	74±19	0.82
Mean blood	82±10	83±8	0.53

Table

P1157

Long term performance and effects of single pass VDD pacing leads in cardiac resynchronization therapy

R Sosdean[1]; C Tutuianu[1]; RI Macarie[2]; B Enache[1]; C Mornos[1]; A Ionac[1]; S Pescariu[1]
[1]*Victor Babes University of Medicine and Pharmacy, Clinic of Cardiology, Timisoara, Romania*; [2]*Profilaxis Medical Center, Cardiology, Timisoara, Romania*

Background: The use of single pass VDD leads for cardiac resynchronization therapy (CRT) is suggested in several reports to be beneficial in terms of costs, complication rate, intervention and fluoroscopy time, but data in the literature about the long-term performance and effects is scarce. The problem consists in the possible failure of the floating atrial dipole to properly detect atrial activity, especially in patients with dilated cardiomyopathy (DCM). Also, the lack of atrial pacing capability may result in VVI biventricular pacing in case of severe bradycardia.
Purpose: In this study we aimed to analyze the long term performance of the VDD pacing leads, replacing the right atrium and right ventricle leads, for CRT, in terms of pacing parameters and effects on patients' evolution.
Methods: A number of 20 consecutive patients implanted with VDD CRT pacing systems between 2000 and 2014, with available data at baseline and after at least 2 years of CRT, while in sinus rhythm, were retrospectively analyzed. The analysis concerned the intervention details, pacing parameters, and NYHA class and left ventricular ejection fraction (LVEF) (Simpson method) evolution. We used paired t-test and Fisher exact test to compare numerical and nominal variables, respectively, and Pearson test for correlations ($p < 0,05$ as statistically significant).

Results: All 20 patients with VDD CRT pacing systems, aged 60,8 ± 7,2 years, 18 (90%) with nonischemic DCM, had a normal left atrial function, with a left atrium <5cm (4,66 ± 0,48cm), a normal-sized right atrium, without a documented history of atrial fibrillation. The average acute atrial sensing was 3,12 ± 0,43mV, but the chronic atrial sensing was significantly lower- 1,42 ± 0,58 (p = 0,006). We detected a 98,47 ± 2,24% of CRT pacing (>98% CRT pacing in 16 patients- 80%). Ventricular detection (atrial undersensing and/or ventricular arrhythmias) was found in only 3 patients (15%) and it was responsible for <5% loss of CRT pacing. VVI pacing was detected in 11 patients (55%) (between 1-4,9% in 8 patients- 40%, and between 5-10% in 3 patients- 15%). The LVEF improved significantly by 10,7 ± 7,5% (p < 0,001), with <5% improvement in only 3 patients (15%). 13 patients (65%) clinically improved by 1 NYHA class and 3 (15%) by 2 NYHA classes (p < 0,001). NYHA class failed to improve in only 4 patients (20%). There was no significant negative correlation between the small percent of VVI pacing and the echocardiographic/clinical response (Pearson r= -0.22, p = 0,34 and r= -0,29, p = 0,2, respectively).
Conclusions: In spite of the high variability of the atrial sensing, the VDD pacing lead seems capable of maintaining CRT in a reasonable percent of time, with a significantly favorable clinical and echocardiographic evolution of the patients. VVI pacing intervened in a very low percent without interference with patients' evolution. These results may be a good starting point for future prospective randomized studies.

P1158

Caval flow regulator catheter balloon in acute heart failure: echocardiographic data.

J E Jose E Herrera[1]; J A Herrera[1]; I Palacios[2]; M Semigran[2]; R Levine[2]
[1]Unidad de Ecocardiografia ab, Porlamar, Venezuela; *[2]Massachusetts General Hospital, Interventional Cardiology, Boston, United States of America*

Background: We reported the hemodynamic changes of the first 6 CHF case in humans, using Percutaneous Transluminal Caval flow Restriction (PTCR). This innovative method reduced preload in CHF. We are reporting the echocardiographic data results of the 6 consecutive patients with CHF, treated with intermittent preload reduction of flow with Caval restriction with Balloon.
Materials and Methods: 6 patients with CHF who met protocol criteria were evaluated. 4 were ischemic, and 2 non ischemic. We performed baseline echocardiogram, coronary angiogram and right heart catheterization. Caval flow restriction was started, catheter balloon was introduced in the femoral vein and echo guided, placed before hepatic vein drainage. The balloon was inflated to cover Inferior Vena Cava (IVC) remaining area completing 100% occlusion, and 70% (sub-occlusion) during expiration resulting in intermittent flow restriction. The balloon was kept inflated for 30 minutes, right catheterization and echocardiogram were repeated during inflated balloon.
Results: Table 1.
Conclusion: We are reporting our echocardiography datan in 6 patients with CHF treated with intermittent reduction of preload with Caval restriction with Balloon, Hemodynamic and echocardiographic changes obtained in these patients, suggest, that this innovative approach can play a role in the treatment of CHF patients.

Echo Data bed & during balloon inflation

ECHO VARIABLES	BEFORE BALLOON	DURING BALLOON	% OF CHANGE	P VALUE	
1	LVEDD (cm)	6.44	5.74	-11	0.009
2	LVESD (cm)	5.20	4.76	-9	0.010
3	EF (% Simpson)	32.83	39.93	+21	0.011
4	EA ratio	1.43	1.14	-21	0.049
5	E/E' Lateral	23.42	15.76	+33	0.142
6	Mitral TVI (cm)	20.35	14.99	-27	0.011
7	Aortic TVI (cm)	18.67	14.77	-21	0.104
8	Cardiac Output (L/min)	4.09	4.5	+9	0.175
9	LA Volumen (ml)	84	73.45	-13	0.034
10	Stroke Volume	54.83	51	-7	0.401

Table 1. Echo Data significance was defined as p < 0.05

P1159

Safety of aspirin therapy in patients for elective coronary artery bypass grafting

K Krivoshapova[1]
[1]Research Institute for Complex Problems of Cardiovascular Diseases, Kemerovo, Russian Federation

Objective: To evaluate safety of coronary artery surgeries with preoperative aspirin management.
Materials and Methods: 168 patients, treated with aspirin in the preoperative period, were included in the current study (Group I). The comparison group (Group II) included 218 patients, who did not receive aspirin preoperatively. Intra- and postoperative blood loss, the rate of redo procedures, caused by bleedings, the rate of blood transfusions as well as blood product volumes were evaluated. The data were analyzed sis using the SPSS 13.0 software package for Windows.
Results: The intraoperative blood loss was similar in both groups (495.2 ± 66.8 ml in Group I vs. 490.5 ± 68.6 ml in Group II, p = 0,67), whereas postoperative blood loss within 6 h and 12 h was significantly higher in Group I (within 6 h of surgery - 160.3 ± 92.9 ml, p = 0.0001; within 12 h of surgery – 245.3 ± 150.3 ml, p = 0.0001) compared to Group II (within 6 h – 116.4 ± 55.2 ml, p = 0.0001; within 12 h – 161.0 ± 127.9 ml, p = 0.0001). However, there were no significant differences in the total blood loss within 24 h (314.7 ± 250.8 ml in Group I vs. 250.8 ± 127.4 ml in Group II, p = 0.08; mean difference 63.9 ml, CI 95% from 0.7 to 128.5 ml, p = 0,13). The rates of blood transfusions were significantly higher in Group I (91.9%) compared to Group II (16.2%, p = 0.001); thus, resulting in increased rate of red cell concentrate transfusions (29.8% vs. 7.5% respectively, p = 0.0001) and platelet concentrates transfusions (78.0% vs. 7.5%, respectively, p = 0.0001). However, the rates of fresh frozen plasma transfusion were similar in both groups (29.8% vs. 7.5%, respectively, p = 0.023). It should be noted that the average volume of blood product transfusions for each patient did not significantly differ in both groups. Moreover, the rates of redo procedures, caused by bleedings, were similar in both groups (3.6% in Group I vs. 1.9% in Group II, p = 0.35).
Conclusions: Patients, receiving aspirin before elective CABG, reported a significant increase in postoperative blood loss within 6 h and 12 h as well as increased need in blood product transfusions. Nevertheless, the total blood loss within 24 h as well as the redo rates, caused by bleedings, did not differ significantly.

P1160

Challenges of pregnancy after aortic coarctation repair

H Helena Nascimento[1]; M Braga[1]; V Ribeiro[1]; C Cruz[1]; MJ Maciel[1]
[1]Sao Joao Hospital, Porto, Portugal

Introduction: Major advances in cardiology and cardiac surgery determined an increment of women with corrected heart conditions that are reaching childbearing age. The incidence of foetal and maternal complications during this period is widely variable among female with congenital heart diseases.
Material and methods: A retrospective analysis of pregnant women with the diagnosis of repaired aortic coarctation (CoA), being followed-up in a Grown-up Congenital Heart Disease (GUCH) Centre. Epidemiological and clinical data were collected and inserted in a registry database.
Results: From 46 female patients (pts) (mean current age 39 ± 10 years-old), 25 have been pregnant (54%). Among these patients, 16 pts (64%) presented a concomitant congenital heart defect, being bicuspid aortic valve the most commonly observed (n = 6 pts, 24%), followed by associated ventricular septal defect (VSD) (n = 5, 20%) and ductus arteriosus (n = 5, 20%). Surgical repair of CoA was the intervention of choice for most women (n = 20, 80%). Hypertension was diagnosed in 11 pts (44%). There were a total of 28 pregnancies (2 ongoing). All patients were submitted to foetal echocardiography and in 3 cases foetal cardiac defects were diagnosed in utero (11%). A complex cardiomyopathy associated with major malformations was identified in 2 pregnancies, leading to medically supervised abortions. During childbearing or the peripartum period, there were no cases of eclampsia or pre-eclampsia, vascular complications or dead. There were no contraindications to vaginal delivery because of the congenital heart disease. However, caesarean sections were performed in 48% of the cases. The live-birth-rate was 81% (3 spontaneous abortions). At birth, mean gestational age was 38 ± 2 weeks and mean weight was 2991 ± 3grams.
Conclusion: Our study supports that successful pregnancy is possible for most women with CoA, as long as adequate care during pregnancy, delivery, and postpartum period is provided. This underscores the importance of pregnancy follow-up with a specialized multidisciplinary team in a GUCH centre.

P1161

Elevated postoperative right atrial pressure predicts post-heart transplant 1-year mortality

V Kittipibul[1]; S Puwanant[1]
[1]*Chulalongkorn University, Department of Medicine, Faculty of Medicine, Bangkok, Thailand*

Background: Mean right atrial pressure (mRAP) is a practical hemodynamic parameter to reflect preload and right ventricular function. Clinical significance of postoperative mRAP in heart transplant has not been well studied.
Objectives: 1) To study the association between postoperative mRAP and post-heart transplant outcomes. 2) To study the trend and natural behaviour of mRAP after heart transplant.
Methods and Results: Fifty-one consecutive de novo adult heart transplant patients (42 ± 13 years, female 35%, cold ischaemic time 236 ± 67 minutes, donor age 27 ± 9 years) at our institution from January 2008 - September 2016 were analyzed. Mean RAP was measured by pulmonary artery catheter after heart transplant. Of 51 patients, 98% (50 patients) had elevated postoperative mRAP ≥ 15 mmHg. Mean RAP continuously increased postoperatively with the highest measured mRAP at 56 (2-396) hours [or 2.3 days] post-heart transplant. The median of highest measured mRAP was 26 (12-39) mmHg. Highest measured mRAP post-heart transplant was not significantly associated with recipient age, cold ischaemic time, preoperative mean pulmonary pressure, preoperative pulmonary vascular resistance, or donor age. The highest measured mRAP was a predictor of 1-year mortality with the area under the ROC curve of 0.65 and the optimal mRAP cut-off of 24.5 mmHg. Patients with highest measured mRAP ≥ 24.5 mmHg had higher 1-year mortality than patients with highest measured mRAP < 24.5 mmHg (35% vs 5%, p = 0.02) (Figure 1). Highest measured mRAP ≥ 24.5 mmHg was associated with 1-year mortality (Hazard ratio was 7.8 [95%CI = 1.01 - 60.5, p = 0.049]). There was no significant difference in intensive care unit length of stay (LOS) (14 ± 10 days vs. 11 ± 5 days, p = 0.2), post-heart transplant hospital LOS (45 ± 30 days vs. 36 ± 18 days, p = 0.2) or acute cellular rejection (ACR) grade ≥ 2R at 1 year post-heart transplant (16% vs 29%, p = 0.4) between patients with highest measured mRAP ≥ 24.5 mmHg and < 24.5 mmHg respectively.
Conclusions: (1) Elevated mean right atrial pressure, mRAP ≥ 15 mmHg, in post-operative de novo heart transplant was common (98%). Mean RAP continuously increased postoperatively with the highest measured mRAP at 2.3 days post-heart transplant. (2) Among post-heart transplant outcomes, highest measured postoperative mRAP ≥ 24.5 mmHg was associated with 1-year mortality. Whether therapies aiming at mRAP reduction improve post-heart transplant survival needs to be further studied.

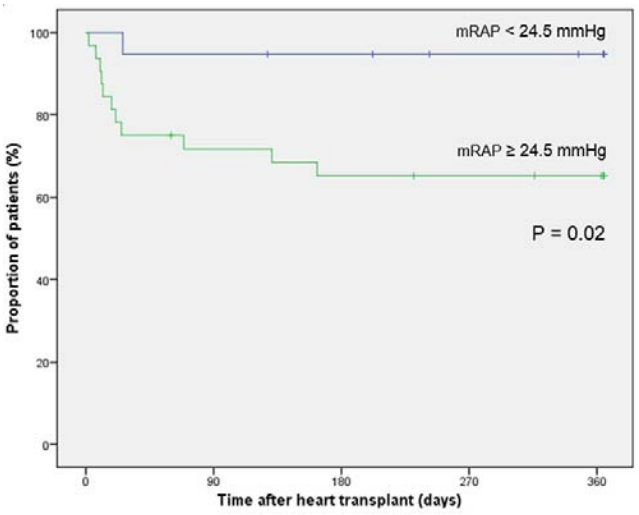


Figure 1:survival after heart transplant

P1162

Long term outcome in adults with repaired coarctation of the aorta

H Helena Nascimento[1]; M Braga[1]; V Ribeiro[1]; C Cruz[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Introduction: Coarctation of the aorta (CoA) accounts for 5 to 8% of all congenital heart defects and is frequently associated with other heart lesions. Even after an initial successful repair or intervention, residua, sequelae and complications may occur.
Material and methods: We performed a retrospective analysis of patients (pts) (>18 years-old) with the diagnosis of repaired CoA, being followed-up in a Grown-up Congenital Heart Disease Centre. Epidemiological and clinical data were collected and inserted in a registry database.
Results: From a total of 117 adult pts, 39.3% were female and the mean age was 34.9 ± 9.2 years old. Concomitant congenital heart disease was present in 89 pts (76%), being bicuspid aortic valve the most commonly observed (52 cases, 44.4%), followed by associated ventricular septal defect (22 cases, 18.8%) and ductus arteriosus (10 cases, 8.5%). Concerning genetic disorders: 4 pts had the diagnosis of Turner syndrome, 1 had Down syndrome and 1 presented Noonan syndrome. Arterial hypertension was highly prevalent in the CoA pts (65 cases, 57.0%) and a combination of 2 or more antihypertensive agents was used in 26 pts (22.2%).CoA correction was surgical in 105 pts (89.7%) and percutaneous in 12 pts (10.3%), with a stent implantation in 75% of the cases. After 25.2 ± 8.1 years of follow-up, the most frequently observed complication was recurring CoA, detected in 18 pts (15.4%). Surgery was the intervention of choice in 10 of the re-CoA pts (55.5%) and percutaneous angioplasty (with stent implantation) was done in the 8 remaining pts (44.5%). In 13 pts a heart re-intervention was conducted, within an average of 17.0 ± 8.6 years, to correct another heart-related condition. Regarding cerebrovascular events, there was only one case of intracranial bleeding from a ruptured vascular aneurysm, repaired with a vascular clip. Other complications: aortic aneurysm (2), pseudo aneurysm (1), aortic dissection (1), stent migration (2) and laryngeal nerve palsy (1). Only two non-cardiovascular related deaths occurred.
Conclusion: The population of pts with a repaired CoA is growing. Our study highlights that despite a good long-term outcome, complications may occur, even many years after the initial repair. Therefore, a close and specialized surveillance of these pts is mandatory in order to allow an early diagnosis and guide an appropriate management.

BETA BLOCKERS

P1163

Increase of beta-blocker dose and QT interval in heart failure - do we really know it all by heart? Results from CIBIS ELD study.

S Apostolovic[1]; D Dragana Stanojevic[1]; S Salinger-Martinovic[1]; R Jankovic-Tomasevic[1]; D Djordjevic-Radojkovic[1]; T Kostic[1]; V Mitic[1]; V Atanaskovic[1]; S Dakic[1]; HD Dungen[2]; E Tahirovic[2]
[1]*Clinic for Cardiovascular Diseases, Nis, Serbia*; [2]*Charite - Campus Virchow-Klinikum, Department of Internal Medicine-Cardiology, Berlin, Germany*

On behalf of: CIBIS ELD

Backgroud. At high heart rates patients on beta-blockers (BB) have a shorter QT-interval than those not using them. QT-interval shortens faster with increasing heart rate in patients on BB. These observations could explain the beneficial effect of beta-blockers on exercise-induced ventricular arrhythmias and sudden death in heart failure (HF) patients.
Purpose: We wanted to investigate what are the effects of increasing BB dosage, during 12 weeks, on QT interval. The second aim was to determine is there a difference between cardioselective (bisoprolol) and non-cardioselective (carvedilol) BB influence on QT interval. Also, we wanted to investigate is there a difference in influence of BB on QT interval in patients with reduced and preserved ejection fraction (HFrEF, HFpEF).
Methods: In CIBIS ELD study 876 patients with HF were enrolled. Prior to randomization participants had to be clinically stable and to be beta blocker (BB) naive or on ≤25% of the guideline-recommended target or equivalent dose. We up-titrated BB (bisoprolol or carvedilol) up to maximum tolerated dose, over three months. 297 patients had HFpEF, average age 73.42 ± 5.9 years and 34.4% were male. 579 patients had HFrEF, average age 72.66 ± 5.6 years, 73.3% were male. ECG was done after 10 minutes of rest in supine position, uncorrected QT interval was measured.
Results: Uncorrected QT interval was 392.41 ± 51.34 ms for the whole study group, 392.10 ± 53.54 ms for males and 392.94 ± 94 ms for females at the beginning of the study. After 12 weeks of BB up-titration QT intervals were 406.11 ± 51.34 ms for the whole group (significantly increased, p < 0.001), 404.90 for males and 408.23 ms for females. Accordingly, heart rate significantly decreased after 12 weeks from 73.79 ± 14.57 to 67.65 ± 12.41 beats per minute (p < 0.001). There were no significant differences between QT intervals at the end of the study in patients treated with different beta blockers (bisoprolol: 408.86 ± 51.80 ms vs. carvedilol: 403.40 ± 50.80 ms) and in those with HFrEF or with HFpEF (401.78 ± 55.61 ms vs. 417.17 ± 36.76 ms). We found no correlation between left ventricle ejection fraction and QT intervals in patients with HFrEF and with HFpEF.
Conclusions: The QT interval is an index of ventricular repolarisation that is directly

influenced by myocardial health and autonomic nervous system activity. In HF, stimulation of central sympathetic drive, a decrease in heart rate variability and baroreceptor function, among other mechanisms, ameliorate QT prolongation (during heart rate increase) which is a risk factor for sudden death. In our HF patients with reduced and preserved ejection fraction, both cardioselective and non-cardioselective BB, had similar effects on QT interval (slight increase at rest, paradoxically) and on heart rate (decrease at rest). It seems that BB exert their beneficial effect on QT prolongation during heart rate increase.

P1164

Beneficial effects of beta-blockers and ivabradine combination in patients hospitalized due to worsening of heart failure: findings from

Y Lopatin[1]; A Grebennikova[1]; H Sisakian[2]; H Hayrapetyan[3]; Z Pagava[4]; T Abdullaev[5]; L Voronkov[6]; V Tseluyko[7]; A Chesnikova[8]; M Glezer[9]; N Koziolova[10]; G Dadashova[11]; S Berkinbaev[12]; A Rakisheva[12]; A Kurliandskaya[13]
[1]Volgograd State Medical University, Volgograd Regional Cardiology Centre, Volgograd, Russian Federation; *[2]University State Hospital 2, Yerevan, Armenia*; *[3]Erebouni Medical Center, Yerevan, Armenia*; *[4]Centre of Vascular and Heart Diseases , Tbilisi, Georgia Republic of*; *[5]Specialized Cardiology Center of the Republic of Uzbekistan, Tashkent, Uzbekistan*; *[6]NSC Institute of Cardiology M.D. Strazhesko, Kiev, Ukraine*; *[7]Kharkiv National Academy of Postgraduate Education, Kharkiv, Ukraine*; *[8]State Medical University of Rostov-on-Don, Rostov-on-Don, Russian Federation*; *[9]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*; *[10]Perm State Medical Academy, Perm, Russian Federation*; *[11]Scientific Research Institute of Cardiology, Baku, Azerbaijan*; *[12]Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*; *[13]Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background. Hospitalization is an opportunity to optimize heart failure (HF) therapy and to improve the quality of further patient care, and in particular to reduce the readmission rate. The aim of the study was to analyze the effects of the beta-blockers (BBs) and ivabradine combination versus BBs alone in patients with sinus rhythm hospitalized due to worsening HF.
Methods: The international Optimize Heart Failure Care program was designed to improve the outcomes of HF hospitalization through patient education and engagement, and post-discharge planning. This analysis included data collected over 12 months from 414 patients (mean age 61.8 ± 0.9 years, 74.6% male) with sinus rhythm hospitalized due to worsening HF, NYHA II-IV (mean 2.73 ± 0.03), left ventricular ejection fraction (LVEF) < 40% (mean 28.7 ± 0.5%), mean systolic/diastolic blood pressure 124.1 ± 1.5/79.1 ± 0.8 mm Hg and mean heart rate (HR) 83.7 ± 1.1 bpm. Physicians participating in the Optimize Heart Failure Care program were free to choose the strategy of simultaneous use of BBs and ivabradine (Group 1) or BBs alone (Group 2).
Results: In total, 37.2% of hospitalized patients with HF received the combination of BBs and ivabradine (Group 1), and 62.8% were on BBs therapy alone (Group 2). There were no differences in terms of age, sex, NYHA functional class, LVEF between the two groups of patients, however, the baseline HR in Group 1 was significantly higher than in the patients who did not receive ivabradine (88.9 ± 1.3 bpm vs. 78.6 ± 0.9 bpm, $p < 0.05$). After 12 months of follow-up, 76.1% of patients in Group 1 received at least half of the target dose of BBs (compared with 65.5% in Group 2, $p < 0.05$). HR control was more effective in Group 1 than in Group 2 (-17.9% vs. -11.8%, $p < 0.05$). Moreover, after 12 months of follow-up the rate of repeat hospitalizations due to worsening HF was significantly lower in the patients receiving the combination of BBs and ivabradine compared with BBs therapy alone (9.1% vs. 30.4%, $p < 0.01$).
Conclusions: The co-administration of beta-blockers and ivabradine in hospitalized patients with heart failure produces a meaningful reduction of the rate of readmissions for worsening heart failure and may be considered as a promising strategy for this category of patients.

P1165

Are beta-blockers effective in children with congestive heart failure? - A Cochrane review

S Samer Alabed[1]; S Al Dakhoul[2]; A Sabouni[3]; Y Bdaiwi[4]; A Frobel-Mercier[5]
[1]University of Sheffield, Academic Unit of Radiology, Sheffield, United Kingdom; *[2]Leeds Teaching Hospitals NHS Trust, Paediatrics, Leeds, United Kingdom*; *[3]Cairo University, Medicine, Cairo, Egypt*; *[4]Damascus Univeristy, Faculty of Medicine, Damascus, Syrian Arab Republic*; *[5]AstraZeneca, Quantitative Clinical Pharmacology, Mölndal, Sweden*

On behalf of: Cochrane Heart
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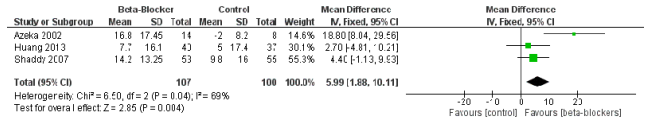
Introduction: Beta-adrenergic blockers are considered a cornerstone in the management of heart failure in adults. Beta-blockers reduce the heart rate and contractility consequently lowering the workload of the heart and improving its performance. This effect is estimated to be parallel in children and beta-blockers are used clinically despite lack of proven evidence to support such guidelines. Nevertheless, due to the variances in aetiology, pharmacokinetics and comorbidities between adults and children with congestive heart failure, it is fundamental to determine the safety and effectiveness of beta-blockers in children in a systematic review.
Purpose: A Cochrane systematic review of all randomised controlled trials (RCT) to assess the effect of beta–blockers in children with congestive heart failure.
Methods: The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and LILACS were search up to November 2015 for relevant RCTs. Two review authors independently screened the search results, extracted and assessed data from the included trials.
Results: The systematic review includes seven RCTs with a total of 420 participants. Four small studies with 20 to 30 children each, and two larger studies of 80 children each, showed an improvement of congestive heart failure with beta-blocker therapy. A larger study with 161 participants showed no evidence of benefit over placebo in a composite measure of heart failure outcomes. The included studies showed no significant difference in mortality or heart transplantation rates between the beta-blocker and control groups. No significant adverse events were reported with beta-blockers, apart from one episode of complete heart block. A meta-analysis of left ventricular ejection fraction (LVEF) and fractional shortening (LVFS) data showed a very small improvement with beta-blockers. However, the primary outcomes could not be pooled in meta-analyses. There were vast differences in the age, age range, and health of the participants (aetiology and severity of heart failure; heterogeneity of diagnoses and co-morbidities); there was a range of treatments across studies (choice of beta-blocker, dosing, duration of treatment); and a lack of standardised methods and outcome measures.
Conclusion: The available data suggests a trend that beta-blockers might be beneficial in the treatment of paediatric congestive heart failure. However, there is no sufficient evidence to recommend or discourage the use of beta-blockers in children with congestive heart failure or to propose a dosage scheme.



Meta-analysis of LVEF

P1166

Quality of life is similar in patients with chronic stable heart failure on vasodilating and non-vasodilating beta blockers.

R B Pharithi[1]; EEE Egom[1]; T Mannion[1]; L Devaney[1]; S Fall[1]; M Carey[1]; A Jago[1]; S Fay[1]; A Maher[1]; V Maher[1]
[1]The Adelaide and Meath Hospital, Tallaght, Heart Efficiency Unit, Cardiology Department, Dublin, Ireland

Beta-blockers with additional nitric oxide-mediated vasodilating properties are beneficial in patients with heart failure but its unknown if they are better than non-vasodilating Beta blockers.
Aim: To compare quality of life in patients with chronic heart failure stabilised on vasodilating and non-vasodilating beta-blockers.
Methods and Results: 163 patients having chronic stable heart failure for at least 6 months were evaluated according to their treatment with vasodilating or non-vasodilating betablockers. Modified Kansa city cardiomyopathy score was used to assess quality of life. See Table 1
Conclusion: There was no difference in the quality of life of patients on vasodilating and non-vasodilating beta-blockers. While vasodilation should improve quality of life, the lack of difference in our study may reflect that patients may already have maximal vasodilation due to their other therapeutic agents such as ACE or ARBs. This indicates that beta blocker choice is not essential in otherwise optimally treated patients.

Patients characteristics			
GroupsN=163	Non-vasodilating Beta-blockers (n = 132)	Vasodilating Beta-blockers (n = 31)	P value
Age (yrs)	66.7±12.2	67.0±13.2	ns
Left ventricle EF (%)	39.9±12.2	39.7±11.3	ns
LVIDd(cm)	6.4±1.0	6.2±1.1	ns
Anti-proBnp	1243±1812	1692±2253	ns
Heart rate	71.0±14.7	69.8±15.27	ns
ACE inhibitors	122(92.4)	31(100)	ns
Calcium blockers	17 (12.9)	2 (6.5)	ns
MR antagonists	91 (68.9)	24 (77.3)	ns
Kansas City Cardiomyopathy Questionaire			
Physical limitation	69.7±22.2	67.6±32.1	ns
Symptom stability	54.3±17.4	54.8±18.6	ns
Symptom frequency	75.5±17.4	74.6±24.6	ns
Symptom Burden	77.5±23.2	77.1±25.4	ns
Symptom Total score	76.9±23.2	74.6±26.5	ns
Self-efficacy	78.2±23.8	75.9±30.0	ns
Quality of life	66.8±27.0	64.7±26.7	ns
Social limitation	66.7±29.6	66.6± 29.7	ns
Overall summary	70.222.6	68.425.7	ns
Clinical summary	73.4±23.1	72.2±22.6	ns

P1167

The impact of 12 month beta-blocker therapy on left and right ventricular volumes and ejection fraction and functional status of heart failure patients with midrange ejection fraction

MG Poltavskaya[1]; IYU Giverts[1]; EE Yakubovskaya[1]; AL Syrkin[1]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Objectives: Recently heart failure patients with "grey area" left ventricular ejection fraction (LVEF) in the range of 40-49% were classified as having HF with mid-range EF (HFmrEF). The beneficial effects of beta-blockers on cardiac remodeling and prognosis are well established in HF with reduced but not preserved EF. The aim of the study was to evaluate the impact of beta-blockers (BB) on left (LV) and right ventricular (RV) systolic function and the distance of 6 minute walk test (6mwt) in patients with HFmrEF.
Methods: we performed the retrospective analysis of 38 patients (32 male, 6 female, mean age 58,9 ± 10,0 years) with HFmrEF NYHA class I-III mainly of ischemic origin who were followed up 12 months after the initiation of metoprolol succitate SRXL or carvedilol. Beta-blockers were added to otherwise optimal therapy unchanged for 3 months or more and up-titrated to target or maximal tolerated doses. Standard clinical evaluation, echocardiography (EchoCG), redionuclide ventriculography (RVG) and 6mwt were performed 3, 6 and 12 months after the start of BB therapy.
Results: After 12 months of BB therapy marked improvement of LVEF measured both by echoCG (from 43,5 ± 2,2% to 48,4 ± 6,1%; = + 4,8%; p = 0,003) and RVG (from 41,6 ± 1,4% to 56,4 ± 7,4%; = + 15,4%; p = 0,05) and end-systolic volume by echoCG (from 100,4 ± 40,7% to 80,9 ± 33,8%; =-19,4%; p = 0,018) was observed. The parameters of RV hadn't changed significantly. 6mwt distance increased from 428,6 ± 97,2 to 541,4 ± 79,0m (= + 112,9 m; p = 0,001). Significant improvement of LV parameters and exercise tolerance was found after 3 months of BB therapy and further improved to 12 months.
Conclusions: In patients with heart failure with mid-range EF 12-month beta-blocker therapy is associated with beneficial effect on LV systolic function and exercise capacity similar to that observed in HF with reduced EF.

P1168

Bisoprolol compared with carvedilol and metoprolol succinate in the treatment of patients with chronic heart failure

H Hanna Froehlich[1]; L Torres[1]; T Taeger[1]; D Schellberg[1]; A Corletto[1]; S Kazmi[2]; K Goode[2]; M Grundtvig[3]; T Hole[4]; HA Katus[1]; JGF Cleland[5]; D Atar[6]; AL Clark[2]; S Agewall[6]; L Frankenstein[1]
[1]*University Hospital of Heidelberg, Heidelberg, Germany*; [2]*Castle Hill Hospital, Hull, United Kingdom*; [3]*Innlandet Hospital, Lillehammer, Norway*; [4]*Norwegian University of Science and Technology, Medical Faculty, Trondheim, Norway*; [5]*Imperial College London, London, United Kingdom*; [6]*Oslo University Hospital, Oslo, Norway*

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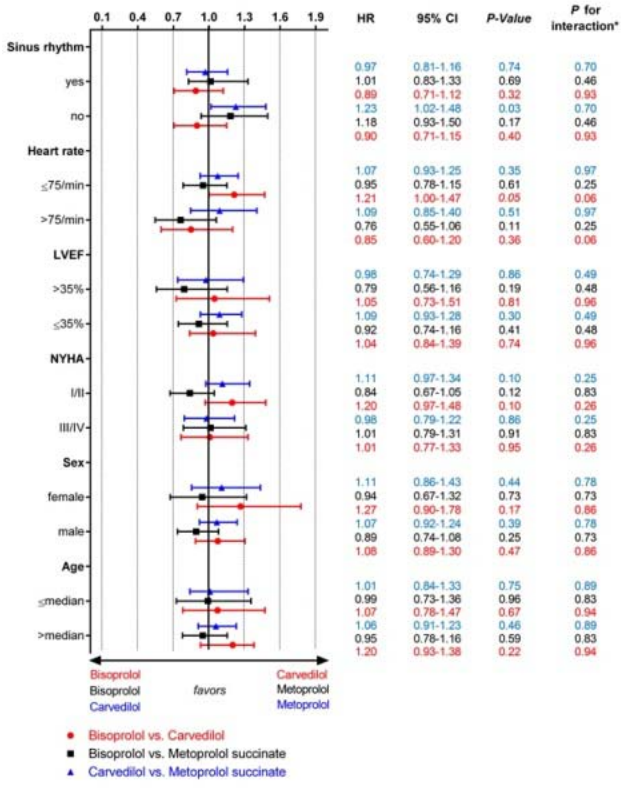
Aims: Beta-blockers are recommended for the treatment of chronic heart failure (CHF). However, it is disputed whether beta-blockers exert a class effect or whether there are differences in efficacy between agents.
Methods: and results: 6,010 out-patients with stable CHF and a reduced left ventricular ejection fraction prescribed either bisoprolol, carvedilol or metoprolol succinate were identified from three registries in Norway, England, and Germany. In three separate matching procedures, patients were individually matched with respect to both dose equivalents and the respective propensity scores for beta-blocker treatment. During a follow-up of 26,963 patient-years, 302 (29.5%), 637 (37.0%), and 1,232 (37.7%) patients died amongst those prescribed bisoprolol, carvedilol, and metoprolol, respectively. In univariable analysis of the general sample, bisoprolol and carvedilol were both associated with lower mortality as compared with metoprolol succinate (HR 0.80, 95% CI 0.71-0.91, p < 0.01, and HR 0.86, 95% CI 0.78-0.94, p < 0.01, respectively). Patients prescribed bisoprolol or carvedilol had similar mortality (HR 0.94, 95% CI 0.82-1.08, p = 0.37). However, there was no significant association between beta-blocker choice and all-cause mortality in any of the matched samples (HR 0.90; 95% CI 0.76-1.06; p = 0.20; HR 1.10, 95% CI 0.93-1.31, p = 0.24; and HR 1.08, 95%CI 0.95-1.22, p = 0.26 for bisoprolol vs. carvedilol, bisoprolol vs. metoprolol succinate, and carvedilol vs. metoprolol succinate, respectively). Results were confirmed in a number of important subgroups.
Conclusion: Our results suggest that the three beta-blockers investigated have similar effects on mortality amongst patients with CHF.



Subgroup analyses

HORMONES - NEUROHUMORAL REGULATION

P1169
Gender differences in neurohumoral activation in heart failure

L G Sahakyan[1]; RA Mayrapetyan[1]; LUSG Sahakyan[1]; HS Sisakyan[1]
[1]*Yerevan State Medical University after M. Heratsi, Yerevan, Armenia*

Background: Heart failure (HF) is a clinical syndrome that affects both men and women. The differences in neurohumoral activation between men and women are incompletely understood.
Purpose: The aim of this study was to evaluate gender differences in plasma levels of several humoral markers and perform comparative analysis between men and women.
Methods: We examined 80 patients with compensated heart failure II to IV class by NYHA classification (mean age 67 ± 10 years; 33% women) who underwent routine echocardiography and measurement of plasma procollagen type 1 N-terminal propeptide (P1NP), endothelin 1 (ET-1), nitric oxide (NO), tumor necrosis factor-alpha (TNF-A) levels.
Results: Significant differences were observed in plasma levels of ET-1 (p = 0,047) and P1NP (p = 0,010) between men and women. No significant sex-related differences were found in TNF-A (p = 0,317) and NO (p = 0,077) levels.
Conclusions: We found biomarker-related differences between male and female heart failure patients. Plasma levels of ET-1 and P1NP were significantly higher in women compared with men.

Biomarker levels in men and women

-	Male	Female	p-value
ET-1 (pg/ml)	20,7±8,5	24,7±8,5	0,047
TNF-A (pg/ml)	114,1±37,4	105,8±33,1	0,317
P1NP (ng/ml)	36,4±14,7	48,1±25,3	0,010
NO (mmol/l)	16,5±9,9	20,7±10,5	0,077

P1170
Assessment of intact fibroblast growth factor 23 in patients with heart failure with reduced ejection fraction

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

Background: Biomarkers can contribute to the prognostication of patients with heart failure (HF) and to implementation of more tailored based approach. Fibroblast growth factor 23 (FGF-23) is the most potent phosphaturic hormone and also regulates bone and mineral metabolism. FGF-23 is a strong and independent factor of adverse cardiovascular events and death in HF patients. However, most of the studies were based on the measurement of C-terminal FGF23 and only few have investigated the concentrations of intact FGF-23 (iFGF-23) in HF.
Purpose: We determined the circulating levels of iFGF-23 in patients with HF with reduced ejection fraction (HFrEF) as well as its relation with cardiac biomarkers and adverse cardiovascular events.
Methods: One hundred thirty three chronic HF patients (females n=31; males n=102; NYHA II-IV; mean age: 67 years; etiology: ischemic n=92, dilated cardiomyopathy n=41; mean EF: 23 %) were enrolled in the study. The primary outcome was CV death. Levels of iFGF-23 were measured at baseline with a recently released fully automated and sensitive immunoassay. The 95th percentile of the reference interval of this assay is 81 pg/mL. Levels of 25-hydroxyvitamin D (25OHD), 1,25-dihydroxyvitamin D (1,25(OH)2D), PTH(1-84), B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP), soluble ST2 (sST2) and Galectin-3 (Gal-3) were also determined.
Results: The median plasma level of iFGF-23 was 73 pg/mL and 56 patients (42%) had values higher than the 95th of the reference interval. HF patients NYHA III-IV have significantly higher iFGF23 (81 pg/mL) than NYHA II (57 pg/mL). Concentrations of iFGF23 were not significantly different between dilated and ischemic cardiomyopathies (67 vs. 77 pg/mL). Intact FGF23 correlated with left ventricular ejection fraction (r = -0.18; P = .04), estimated glomerular filtration rate (eGFR; r = -0.43; P < . 001), PTH(1-84) (r = 0.41; P < . 001), (1,25(OH)2D) (r = -0.46; P < . 001), Gal-3 (r = -0.39; P < . 001) but not with age, (25OHD), BNP, NT-proBNP or sST2. After 8 years of follow-up, 106 patients reached the primary endpoint. Concentration of iFGF23 was significantly higher in HF patients who died in comparison to survivors (87 vs 57 pg/mL). In patients with eGFR >60 mL/min levels of iFGF23 remain associated to adverse cardiovascular events.
Conclusions: Intact FGF23 is a strong and independent predictor of cardiovascular mortality in chronic HF.

P1171
Testosterone replacement in patients with advanced heart failure and hormone deficiency

M Marina Navarro Penalver[1]; M Gomez Bueno[2]; P Garcia Pavia[2]; J Lupon Roses[3]; J Comin Colet[4]; E Roig Minguell[5]; D Saura Espin[1]; DA Pascual Figal[1]
[1]*Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain*; [2]*University Hospital Puerta de Hierro, Cardiology, Madrid, Spain*; [3]*Hospital Universitario Germans Trias i Pujol, Barcelona, Spain*; [4]*Hospital del Mar, Barcelona, Spain*; [5]*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*

Background: Chronic heart failure (CHF) is characterized by progressive anabolic impairment with a decline in testosterone levels, which has been associated with a poor prognosis. We aim to determine wether testosterone therapy improves clinical outcomes in these patients.
Methods: We designed a multicenter randomized double-blind trial including patients with CHF, systolic dysfunction (LVEF < 40%) and both total testosterone (TT) and free testosterone (FT) deficiency (TT < 2.7 ng/ml and FT >59 pg/ml).Patients were assigned to receive 1000 mg of testosterone undecaonate or placebo injected intramuscularly at inclusion,3,6 and 9 months. We evaluated the occurrence of adverse side effects, the imporvement in cardiac function (assesed by echocardiography and NT-proBNP determinations),functional capacity (6 minutes walk test, 6MWT) and quality of life (Minnesota Living with Heart Failure test, MLHF) (clinicaltrials.gov Id:NCT01813201).
Results: 29 ambulatory male patients (age 65 ± 8,62% ischemic etiology,30 ± 6 %LVEF, NYHA II-III) were prospectively recruited. Testosterone deficiency was confirmed in all subjects with a mean TT (2.41 ± 0.9 ng/ml) and median FT (4.35 pg/ml [Q1-Q3 2.9-6.2]). After a 12 month follow-up we found and increase in TT levels (+3.1 vs +0.5, p = 0.002) but not in FT levels (+3.35 vs. +1.45, p = 0.1) in the therapy group. There were any adverse side effects of testosterone administration. During follow-up one patient died and other was admitted to the hospital because of heart failure in placebo group and none in therapy group.4 patients of each group required intravenous diuretics. These differences were not statistically significant. We did not find any differents between groups in NT-proBNP levels, functional capacity or quality of life (table). Only LVEF was slightly higher in placebo group.
Conclusion: Testosterone therapy in CHF patients with hormone deficiency was neither associated with adverse side effects nor improvement of cardiac function, functional capacity or quality of life. Small sample size and improvement in TT levels but not in FT levels might limit study results.

P1172
Initial experience using LCZ696 in real life: tolerability and clinical evolution in a short term.

R Rafael Bravo Marques[1]; F Torres Calvo[1]; S Lopez Tejero[1]; A Valle Alberca[1]; C Corona Barrio[1]; PA Chinchurreta Capote[1]; JR Siles Rubio[1]; FE Mesa Prado[1]; AC Milan Pinilla[1]; AI Perez Cabeza[1]; D Moreno Sanjuan[2]; R Mesa Rico[1]; G Rosas Cervantes[1]; F Ruiz Mateas[1]
[1]*Hospital Costa del Sol, Cardiology, Marbella, Spain*; [2]*University of Malaga, Malaga, Spain*

Introduction: The prevalence of chronic heart failure (HF) has been increased, due to the improvement in the management and treatment of most of heart diseases and the longer life expectancy of the population, becoming an important public health problem. The optimal treatment recommended for patients with HF and ventricular dysfunction, with ACE inhibitors, ARBs, beta-blockers and mineralocorticoid inhibitors, has been shown to reduce the morbidity and mortality of these patients, but it is still necessary to design further treatments that improve prognosis. Recently, clinical practice guidelines of HF have aproved using LCZ 696 in patients with HF with reduced eyection fraction (HfrEF) and functional class (FC) ≥II.
Material and methods: We conducted a prospective observational study of patients with HfrEF assessed in our outpatient clinic, who started treatment with LCZ696 between October-November 2016. We analyzed their baseline characteristics and the one-month evolution in functional class, analytical parameters and drug tolerance.
Results: We analyzed 22 patients, with a mean age of 65.4 ± 10.4 years, being 81.8% male. Fifty percent were hypertensive, 22.7% diabetic and 31.8% dyslipemic. Chronic kidney disease was present in 31.8%, with a mean FG of 81ml/min (Cockcroft-Gault). The cause of heart failure was dilated cardiomyopathy in 72,7% and in ischemic heart disease in 27.3% fh them. The mean telediastolic diameter of left ventricle was 62.4 ± 7.2mm, with an average LV ejection fraction of 34.7 ± 9.9%. Atrial fibrillation was present in 31.8%. defibrillator was carried among 18,1% and cardiac resynchronization therapy at the same proportion. At the beginning, the

majority were in FC II (59.1%) and the rest in FC III. Mean baseline systolic blood pressure was 126.2 ± 20.7mmHg and diastolic 76.9 ± 13.7mmHg and mean heart rate was 66.6 ± 12.5bpm. Pretreatment was optimal in all cases (maximum tolerated doses of ACEI, ARB II, BB, mineralcorticoids). ARNI was started (after stopping ACE inhibitors in 59.1% and the rest ARI II), at low doses in 54.5%, at medium doses 31.8% and the rest at high doses. After one month of follow-up, the goal was improvement in FC, 18.2% of patients were FC I and 63.6% FC II. Concerning analytical parameters, we observed a reduction of NT-ProBNP (from 5575.3 to 3538.6μg/L) and uric acid (from 7.6 to 6.6mg/dL). We found a non-significant decrease in blood pressure (119 ± 17.8/71.0 ± 12.6mmHg), which allowed us to optimize the treatment with LCZ696, being at medium dose 50%, at high dose 36,4% and the rest at low doses. Only one patient stopped taking medication due to economic issues.
Conclusions: The treatment with LCZ696 in a group of patients in real-life was well tolerated in all cases, without a significant decrease in blood pressure, being able to optimize the dose of LCZ696. It was related to improvement in the functional class and in analytical parameters, even with a short follow-up.

METABOLISM - DIABETES MELLITUS - OBESITY

P1173
Neck circumference as a predictor of arterial hypertension

AG Abril Guadalupe Jimenez Cepeda[1]; A Orea-Tejeda[2]; D Gonzalez- Islas[2]; G Perez-Cortes[2]; L Verdeja- Vendrell[2]; A Navarrete-Penaloza[2]; R Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; A Figueroa-Herrera[2]; B Robles Uribe[2]; SC Torres-Montiel[2]
[1]*Universidad Autonoma del Noreste, Nutricion Clinica , Saltillo, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clínic , Mexico, Mexico*

Background: Neck circumference (NC) is a simple, reliable non invasive and low cost anthropometric method. It has been related to overweight, obesity and metabolic risk factors since it is an etopic fat deposit responsable for large release of systemic free fatty acids. It has been found relation of the NC with the systemic arterial hypertension. However, it is unknown if the NC is realated wich blood pressure (BP) increase Objectives: To determine if there is an increase in BP due to an increase in NC.
Methods: A cross- sectional studio, >18 years old apparently healthy subjects were included. Subjects with diabetes and hypertension were excluded. Weight, height, body mass index, NC and BP were evaluated.
Results: Fifty-four patients were recruited, age 49 ± 13.3 years. 55.5% were women and 44.4% were men. Men had higher weight (83.58 ± 10.6 vs 74.2 ± 14.1 p = 0.01), height (1.7 ± 0.4 vs 1.5 ± 0.06, p < 0.001), NC (40.7 ± 2.2 vs 35.4 ± 2.3, < 0.001), systolic blood pressure (SBP) (132 ± 14.4 vs 119.5 ± 19.1, p = 0.011) and diastolic blood pressure (DBP) (80.1 ± 7.9 vs 72.2 ± 11.6, p = 0.006), than women. According to the linear regression it was observed that for each centimeter in NC increases 2.5 mmHg in SBP, (β: 2.5, CI 95%, 1.2 to 3.7, p < 0.001) and 1.6 the DBP, (β: 1.6, 95% CI, 0.9 to 2.3, p < 0.001). In addition, for each kilogram of weight, the SBP increased by 0.5 mmHg (β: 0.5, CI 95%, 0.2 to 0.8, p = 0.002) and 0.4 mmHg in the DBP, (β: 0.4, CI 95%, 0.2 to 0.6, P < 0.001).
Conclusions: For each centimeter in NC increases 2.5 mmHg the SBP and 1.6 mmHg the DBP.

P1174
Lipid control across very high cardiovascular risk profiles

PM Paulo Maia Araujo[1]; A Nunes[1]; SM Leite[1]; JD Rodrigues[1]; S Amorim[1]; E Martins[1]; M Campelo[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Cardiology, Porto, Portugal*

Introduction: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide. In the last decades, a significant proportion of the reduction in CVD burden is attributed to cardiovascular (CV) prevention, including a more effective control of CV risk factors, namely dyslipidaemias. With the publication of the "2011 ESC Guidelines for the management of dyslipidaemias" (2011 ESC-G), there were introduced specific LDL targets for each level of CV risk. For patients (pts) at very high CV risk (VHCVR), a goal of LDL < 70mg/dL was defined. The objective of this study was to analyze lipid control in this population, between different groups of pts.
Methods: The study population corresponded to pts at VHCVR, as defined by the 2011 ESC-G. We performed a retrospective evaluation of pts in this category admitted in our department in 3 different time periods: pts admitted in the year prior to the guideline publication (2011: A), in the next year (2012: B) and 5 years after (November/2015-November/2016: C). Data from clinical variables and from lipid control were collected and those 3 groups were compared.
Results: A total of 1143 pts were included in the analysis (315 from A, 342 from B and 486 from C), of whom 821 (71.8%) were male, with a mean age of 67.5 ± 11.7 years. There were no significant differences in gender proportion or mean age between groups. Of the total population, 44% of pts had a prior Acute Coronary Syndrome (ACS), 13% had a prior Stroke, 15% had Peripheral Artery Disease (PAD), 54% were diabetic and 18% had moderate/severe Chronic Kidney Disease (CKD). Only 24.7% (n = 282) had achieved the goal LDL value < 70mg/dL, with no significant differences between the 3 time periods (p = 0.25). In pts with a prior ACS, over time, there was a progressive increase of the achievement of target LDL between the 3 groups: 24% (A) vs 34% (B) vs 39% (C), p = 0.02. However, there were no significant differences between the 3 time periods in pts: with a prior Stroke - 30% (A) vs 36% (B) vs 40% (C), p = 0.54; with PAD - 26% (A) vs 43% (B) vs 32% (C), p = 0.21; diabetics – 23% (A) vs 25% (B) vs 31% (C), p = 0.13; with CKD – 34% (A) vs 30% (B) vs 32% (C), p = 0.88.
Conclusions: Despite what would be expected, 5 years after the publication of the 2011 ESC-G, adequate lipid control is still far from desirable. Only pts with a prior ACS had a significant difference in the achievement of target LDL values over time and were more likely to have adequate lipid control. Particular attention to lipid control should be paid to other pts at VHCVR as well.

P1175
Clinical features of obese and heart failure with reduction ejection fraction (hfref) in mexican patients: a cohort

EJJ Chuquiure[1]; J Oscar Fiscal-Lopez[1]; L Ana Marin-Mejia[1]; R Nayeli Isidro-Hernandez[1]; N Frida Rodriguez-Quiroz[1]; M Maria Jose Chuquiure Gil[2]; M Mendez Gabriela[3]
[1]*Instituto Nacional de Cardiologia "Ignacio chavez", Mexico City, Mexico*; [2]*Instituto Tecnologico de Estudios Superiores de Monterrey, Escuela de Medicina, Monterrey, Mexico*; [3]*Universidad del estado de México, Medicina, ciudad neza, Mexico*

Purpose: Mexican population has a high obesity rate in childhood as adults. The main purpose of this work is to describe Clinical Characteristics of the impact of Obesity in patients with Heart Failure with Reduction Fraction (HFrEF) in the confirmation of a comparative cohort.
Material and Method: We analyzed consecutively a group of patients from the Instituto Nacional de Cardiologia Heart Failure Clinic. All over 18 years old, both genders with clinical, laboratory and Imaging Diagnosis according 2016 European and AHA-ACC clinical Guidelines. In our Investigation Obesity was defined as BMI greater than 25 Kg/m2. According Age, LVEF and NYHA Class were matched in two groups for a suitable comparison. We describe clinical history, PTCA or CABG records, laboratory findings, echocardiographic diameters, hospitalization feature. The principal point at follow-up was hospitalization for Heart failure impairment. For statistical difference we declare p value equal or less than 0.05.
Results: A total of 257 patients were evaluate, according our matching criteria two group were formed: Obese: 191 (74.31%) and Non-obese: 66 (25.68%). Both groups were homogeneous in: Age 56.79 + 4.87 vs56.79 + 4.23, LVEF: 29.50 + 1.2 vs. 28.19 + 1.1 y NYHA I-II: 91.62% vs. 92.42 (p = ns for all). Gender male were also similar (68.87% both). Expected statistical significance differences in BMI were seen: 29.83 + 3.95 vs 22.53 + 2.10 (p < 0.005). Metabolic Syndrome Clinical Components were evidently more seen in obese group: Diabetes History (19.89% vs. 9.09%, p < 0.05), Hypertension (21.46% vs10.60%, p < 0.05) and Dyslipidemia (17.80% vs. 10.15%, p < 0.05). No statistical differences in Echocardiographic diameters were observed. All non-obese patients were maintained in sinus rhythm compared to 12.5% Atrial Fibrillation in obese (p < 0.05).
Conclusions: The present Cohort is the first report on patients with HFrEF in the Obese Mexican population. High rates of hospitalization in Emergency Room due Heart Failure exacerbation in the obese group were observed, possibly associated with Metabolic Syndrome components.

BMI (25 Kg/m^2)	25- 29.99	30-34.99	35- 39.99	>40.00
REHOSPITALIZATION RATE (%)	14.41	16.66	15.38	28.57

Greater quarterly increases in readmissions at emergency room due to Heart Failure deterioration according BMI

P1176

Prevalence and factors predictive of preclinical diastolic dysfunction (stage B heart failure) in a predominantly Hispanic cohort with type 2 diabetes

S-H Siu-Hin Wan[1]; AS Pumerantz[2]; F Dong[2]; P Vila[2]; C Ochoa[2]; HH Chen[1]
[1]Mayo Clinic, Rochester, United States of America; *[2]Western University of Health Sciences, Pomona, United States of America*

Background: People with type 2 diabetes mellitus (DM2) are predisposed to developing cardiac structural changes, diastolic dysfunction (DD), and heart failure (HF). Prior research has shown that preclinical DD (Stage B HF) is common among people with DM2. However, the characteristics and risk factors of DD development in people with DM2 remain incompletely defined.
Objective: To define the clinical and echocardiographic characteristics of a cohort of adult patients with DM2, and to identify risk factors for development of DD.
Methods: A retrospective analysis of consecutive adults with DM2 in California, USA. Patients without signs or symptoms of heart failure (HF) underwent 2D and Doppler echocardiography screening, and grouped into two cohorts: normal diastolic function and DD. Obesity was defined as a BMI ≥30 kg/m2 and overweight BMI between 25-30 kg/m2. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate (eGFR, by CKD-EPI equation) <60 mL/min/1.73m2 (i.e., Stages 3A-5). DD was defined as those with medial E/e' ≥15 or left atrial volume index ≥ 34 mL/m2. Multivariate logistic analysis was performed to identify factors associated with the presence of DD.
Results: Among 387 study patients, the mean age was 54.4 ± 12.9 years and 299 (77%) were Hispanic. 37.5% had DD and 62.5% had normal diastolic function. There was no difference in percentage of Hispanics with DD and normal diastolic function (78 vs. 76%, $p = 0.4$). Mean hemoglobin A1c was 8.1% for the DD group and 8.6% for the normal diastolic function group ($p = 0.02$). When compared to those with normal diastolic function, the DD group had more females (66 vs 53%, $p = 0.015$), was older in age (mean 59 vs 51 years, $p < 0.01$), and had longer duration of diagnosed DM2 (12 vs 10 years, $p = 0.01$). Furthermore, those with DD had more cardiovascular comorbidities, including coronary artery disease (14 vs 4%, $p < 0.01$) and hypertension (86 vs 68%, $p < 0.01$). There was also greater proportion of CKD (25 vs 6%, $p < 0.01$) and obese and overweight (70 vs 65% and 25 vs 23%, respectively; $p = 0.04$) among the group with DD. LVMI in the DD group was also greater (118 vs 96 g/m2, $p < 0.01$).
Using multivariate logistic analysis, several significant predictors of DD in adults with DM2 were identified: older age (adjusted OR (AOR) 1.31 [1.18, 1.46]); female gender (AOR 1.72 [1.06, 2.81]); overweight (AOR 3 [1.04, 8.64]) and obesity (AOR 3.86 [1.42, 10.48]); and the presence of at least Stage 3A CKD (AOR 4.9 [2.38, 10.1]).
Conclusions: Preclinical DD (stage B HF) was common (37.5%) among our predominantly Hispanic cohort with DM2. Those with DD were more likely to be female, older in age, obese or overweight, and have at least moderate (Stage 3A) CKD. These findings suggest that populations with similar ethnic and racial demographics, asymptomatic, obese or overweight, middle-aged to elderly women with at least Stage 3A CKD should be screened for preclinical DD (stage B HF).

P1177

Prescription of anti-diabetic-glucose-lowering agents and clinical outcomes in asian patients with heart failure and type 2 diabetes mellitus

Y Yvonne Chia[1]; THK Teng[2]; WT Tay[2]; J Tromp[3]; AM Richards[4]; LH Ling[4]; W Shimizu Sw Park[5]; CL Hung T Ngarmukos[6]; HB Liew S Zhang[7]; C Narasimhan B Siswanto[8]; EB Reyes Cm Yu[9]; I Anand[10]; J Yap[2]; M Macdonald[11]; CSP Lam[2]
[1]Duke-NUS Graduate Medical School Singapore, Singapore, Singapore; *[2]National Heart Centre Singapore, Singapore, Singapore*; *[3]University of Groningen, Groningen, Netherlands*; *[4]National University Heart Centre, Singapore, Singapore*; *[5]Nippon Medical School, Tokyo, Japan; Sejong General Hospital, Bucheon, Korea Republic of*; *[6]Mackay Memorial Hospital, Taipei, Taiwan; Ramathibodi Hospital, Bangkok, Thailand*; *[7]Queen Elizabeth Hospital, Malaysia; Fuwai Hospital, Beijing, China People's Republic of*; *[8]CARE Hospital, Hyderabad, India; National Cardiovascular Center Universitas, Jakarta, Indonesia*; *[9]Manila Doctors Hospital, Manila, Philippines; Prince of Wales Hospital, Hong Kong, Hong Kong SAR People's Republic of China*; *[10]University of Minnesota, Minneapolis, United States of America*; *[11]Changi General Hospital, Singapore, Singapore*

Background: Diabetes mellitus (DM) is a common comorbidity among patients with heart failure (HF). Anti-diabetic agents are important for glycaemic control, but some may worsen HF, whereas newer agents have recently been reported to improve cardiovascular outcomes. The prescription patterns of anti-diabetic agents in Asia are unknown.
Purpose: To determine the prescription patterns of anti-diabetic agents, and their association with mortality and HF hospitalisation, among Asian patients with HF and DM.
Methods: We studied prescription of anti-diabetic and HF medications among 5276 patients with HF and reduced ejection fraction (< 40%) from Northeast Asia (South Korea, Japan, Taiwan, Hong Kong, and China), South Asia (India), and Southeast Asia (Thailand, Malaysia, Philippines, Indonesia, Singapore) in the prospective ASIAN-HF study. Patients were followed for the composite outcome of 1-year all-cause mortality or 1st HF hospitalisation.
Results:DM was present in 2177 (41%) patients (61 ± 11 years old, 21% women), of whom 1493 (69%) were prescribed anti-diabetic agents (761 [51%] monotherapy, 549 [37%] dual therapy). The most common anti-diabetic agents prescribed were metformin (54%), sulfonylureas (53%) and insulin (24%). Prescription varied by geography: metformin and sulfonylureas were more commonly prescribed in South and Southeast Asia (55-68%, compared to 33-34% in East Asia); whereas dipeptidyl peptidase-4 (DPP-4) inhibitors (38% vs 6% in Southeast Asia) and alpha-glucosidase inhibitors (25% vs 5% in Southeast Asia) were more commonly prescribed in East Asia. Patients with anti-diabetic therapy (vs without) were younger (60 ± 11 y vs 62 ± 11 y) and more likely to have hypertension (69% vs 64%) and to receive angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers (76% vs 68%) or beta-blockers (81% vs 74%)(all $p < 0.01$), but similarly likely to have chronic kidney disease and atrial fibrillation. One-year composite outcome occurred in 481 (22%) of 1983 patients with 1-year follow-up. Adjusting for age, sex, body size, blood pressure, EF, NYHA, ischemic aetiology, hypertension and atrial fibrillation, metformin therapy was associated with reduced risk of the primary endpoint (vs no metformin, adjusted HR=0.80, 95%CI 0.66-0.97) while there was no significant association with the usage of sulfonylureas (aHR=0.88, 95%CI 0.72-1.07), insulin (aHR=1.16, 95%CI 0.91-1.48) or DPP-4 inhibitors (aHR=0.77, 95%CI 0.56-1.06).
Conclusions: Wide geographical variation in prescribing patterns of anti-diabetic agents was observed among patients with HF across Asia. The lower hazard of a 1-year composite outcome with metformin support the ESC HF guidelines recommendation to consider metformin as first-line therapy unless contraindicated in these patients.

P1178

Polyunsatturated fatty acids supplementation impairs HDL function in heart failure

R Raphael Wurm[1]; L Schrutka[1]; D Moertl[2]; R Berger[3]; N Pavo[1]; M Huelsmann[1]; K Distelmaier[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Hospital St. Polten, Department of Cardiology, St. Polten, Austria*; *[3]KH Barmherzige Brueder, Department of Cardiology, Eisenstadt, Austria*

Aims: The aim of this study was to assess the effects of oral treatment with polyunsaturated fatty acids (PUFA) on the anti-oxidative capacity of HDL in patients with heart failure (HF) of non-ischemic origin.
Methods: Patients with advanced chronic HF who were on stable optimized therapy for ≥ 3 months were randomized in a 1:1:1 fashion to receive 1g/day or 4g/day of n3-PUFA, or placebo, respectively for 12 weeks.
HDL anti-oxidant capacity was measured using a 2',7'-DCF-based cell free fluorescent assay that determined the ability of apo-B depleted serum to inactivate or aggravate previously oxidized LDL
HDL inflammatory index (HII was calculated by subtracting the intensity signal of DCF alone from that of DCF incubated with apo-B depleted patient sera and log-transformed before analysis. A higher HII indicates a poorer anti-oxidative function.
Results: Forty-three patients with a median age of 60 years and a median HDL level of 41 mg/dl were included (Table 1). There was no difference in HII at baseline. After twelve weeks of treatment, we found a significant dose-dependent effect of PUFA treatment on the median change of HII (-0.11 (IQR -0.37 – 0.17) for placebo, 0.13 (-0.01 – 0.28) for 1g/day PUFA, 0.38 (0.08 – 0.51) for 4g/d, $p = 0.03$, Figure 1).
Discussion: Treatment with PUFA impairs HDL anti-oxidative function in a dose-dependent manner. This might provide one explanation for the rather small clinical benefit of this treatment.

Table 1 - Baseline characteristics

	Placebon=16	1g n3-PUFA n=14	4g n3-PUFA n=13	
Age	56 (46 - 63)	59 (52 - 65)	65 (57 - 68)	
Female	25%	21%	/	
Etiology	Hypertension Myocarditis- Valvular disease Alcohol Other	70%6%/ 13%13%	64%7%/ /29%	46%23%8% 8%15%
NYHA III	93%	85%	92%	
LVEF %	25 (18 - 30)	27 (22 - 35)	28 (19 - 30)	
BMI	27 (24 - 32)	26 (25 - 28)	28 (26 - 30)	
eGFR	70 (59 - 88)	61 (40 - 82)	77 (52 - 103)	
Triglycerides	130 (95 - 168)	151 (96 - 190)	102 (72 - 161)	
HDL	42 (32 - 57)	43 (32 - 51)	37 (32 - 58)	
CRP	0.46 (0.13 - 15)	0.49 (0.19 - 0.83)	0.60 (0.2.9 - 16)	

Numbers are percentages within group or median (interquartile range). PUFA – polyunsaturated fatty acids, NYHA – new york heart association class; LVEF – left ventricular ejection fraction, BMI – body mass index, eGFR – estimated glomerular filtration rate; LDL – low density lipoprotein, HDL – high density lipoprotein, CRP – c-reactive protein.

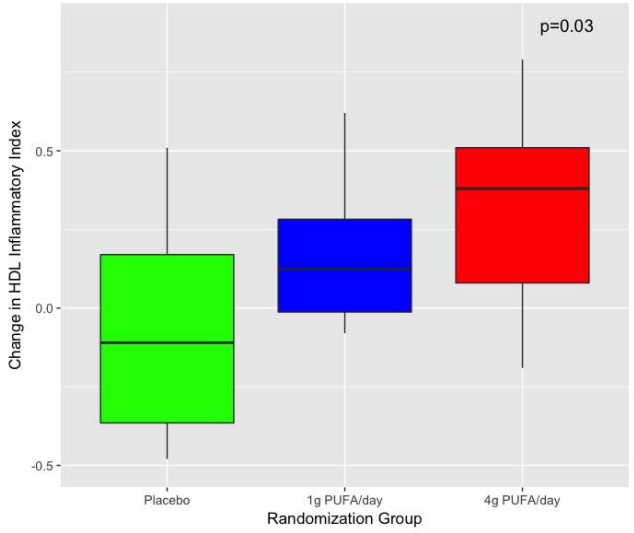


Figure 1

P1179

Lipid transfer to HDL in patients with heart failure was diminished and is correlated with IL-6 levels

A E Ana Elisa Marabini Martinelli[1]; RC Maranhao[1]; PO Carvalho[1]; MNC Curiati[1]; BM Oliveira[1]; FR Freitas[1]; AC Pereira-Barretto[1]
[1]Heart Institute of the University of Sao Paulo (InCor), Laboratory of lipid metabolism, Sao Paulo, Brazil

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Background: It is now consensual that the various protective functions of HDL should be explored beyond HDL-cholesterol.
Propose: We investigate plasma lipids, lipid transfers to HDL and BNP levels obtained from patients with HF with those from patients with CAD without HF (non-HF).
Methods: Forty-eight HF patients were studied, 25 with functional class NYHA I/II and 23 with NYHA III/IV, as well as 50 non-HF patients matched for gender and age. All HF had ejection fraction ≤40%. Levels of IL-6, BNP, CETP, LCAT, oxidized LDL (oxLDL) and paraoxonase 1 (PON-1) activity were determined. Transfers of radioactive unesterified and esterified cholesterol, triglycerides and phospholipids from a donor artificial emulsion to HDL was determined by an in vitro assay.
Results: Total, LDL and HDL cholesterol and triglycerides did not differ among the 3 groups, but apo A-I and apo B was lower in both HF groups compared to non-HF ($p = 0.01$, $p < 0.001$).Transfer of esterified and unesterified cholesterol, triglycerides and phospholipids (in %) was lower in HF-III/IV than in non-HF (HF-III/IV: 5.44 ± 1.76, 6.29 ± 2.05, 19.05 ± 2.5, $6,29 \pm 2,05$; non-HF: 6.24 ± 0.85, 7.33 ± 1.48, 20.21 ± 1.43, $7,40 \pm 1,47$; respectively, $p < 0.05$), but transfers were not different between HF-I/II and non-HF. Levels of oxLDL was lower in HF-III/IV than in non-HF ($p < 0.0001$). CETP mass was lower in HF-III/IV than in HF-I/II ($p = 0.0206$). LCAT activity was lower in patients with HF than non-HF subjects ($p = 0.0384$). Transfer of lipids to HDL, apo A-I, apo B, oxLDL and LCAT are inverse correlated with IL-6 and BNP levels. Conclusion: Alterations in the markers related with the plasma lipid metabolism seemed to be more pronounced in the most severe forms of HF. These alterations were correlated with IL-6 and BNP, importants biomarkers of HF, which could suggest that they could play a role in the evolution of the disease.

P1180

Arterial structure is associated with telomere length and glycemic variability in diabetic patients without heart failure

E N Dudinskaya[1]; NV Brailova[1]; ON Tkacheva[1]; ID Strazhesko[2]; SA Boytsov[2]; MV Shestakova[3]
[1]Pirogov Russian National Research Medical University , Moscow, Russian Federation; *[2]National Research Center for Preventive Medicine, Moscow, Russian Federation*; *[3]Endocrinology Research Center, Moscow, Russian Federation*

Background and aims: It is known that telomere length (TL) shortening is a biomarker of cellular aging and associated with vascular changes. Glycemic variability (GV) in type 2 diabetes mellitus (T2DM) patients may be involved in vascular aging, but pathogenic mechanisms of this effect are not well established. The aim of our study was to investigate the association between GV, vascular aging and TL in T2DM patients.
Materials and Methods: The study group included 50 T2DM patients without symptoms of heart failure (mean age 58.4 ± 7.9 years, median diabetes duration - 1.0 year and a HbA1c of 7.27 ± 0.69 %). NT-proBNP was < 100 ng/ml, ejection fraction was > 50%. All subjects were measured for TL by quantitative PCR; arterial stiffness evaluated by carotid-femoral pulse wave velocity (PWV); carotid intima-media thickness (IMT), plaque presence determined by ultrasonography in carotid arteries. The mean amplitude ofglycemicexcursion (MAGE), the standard deviation of blood glucose values (SD) and the continuous overlapping net glycemic action (CONGA) were calculated from continuous glucose monitoring system data for assessingGV. Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC, USA).
Results: The majority of patients with T2DM had subclinical atherosclerosis (78.1%) and shortened telomeres (< the median of TL 9.75) (71.4%). Correlation analysis showed significant association between IMT and TL (r=-0.39, p=0.006), IMT and GV parameters: MAGE (r=0.42, $p = 0.007$), SD (r=0.41, $p = 0.009$), CONGA (r=0.27, $p = 0.093$) and for MAGE this relationship remained significant in multiple linear regression analysis (β=0.040, $p = 0.020$, multiple $R2 = 0.290$). Multiple linear regression analysis also revealed significant independent association between plaque presence and CONGA (β=1.088, $p = 0.040$, multiple $R2 = 0.457$). It was not revealed relationship between vascular stiffness (PWV) and GV. TL was correlated only with CONGA (r=-0.31, $p = 0.054$), but very long telomeres (> the TL 10.00) were associated with all GV parameters: MAGE (r=-0.39, $p = 0.015$), SD (r=-0.43, $p = 0.007$), CONGA (r=-0.42, $p = 0.008$).
Conclusion: Glycemic variability is associated with subclinical atherosclerosis and TL shortening in T2DM patients. Thus, we can suppose that the glycemic variability plays a principal role in TL shortening and vascular aging in T2DM patients without heart failure.

HEART FAILURE IMAGING

P1181

Role of MR imaging in the diagnosis and the management of hypertrophic cardiomyopathy

M Attia[1]; I Ines Kasraoui[1]; H Neji[1]; I Kammoun[2]; S Hantous[1]; I Baccouche[1]; K Ben Miled[1]
[1]*ABDERRAHMEN MAMI HOSPITAL, RADIOLOGY, TUNIS, Tunisia*; [2]*ABDERRAHMEN MAMI HOSPITAL, CARDIOLOGY, Tunis, Tunisia*

Background: Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiomyopathy and the most common cause of sudden cardiac death among young people. Clinical manifestations and electrocardiographic findings of HCM are nonspecific and diverse. Traditionally, echocardiography has been the easiest and most reliable technique for establishing a diagnosis of HCM. However, cardiac magnetic resonance (MR) today enables a more accurate and reliable assessment of maximal wall thickness, increasing the diagnostic yield by identifying subtle forms of myocardial hypertrophy. Furthermore, MR may be helpful in risk stratification by identifying massive LV hypertrophy or extensive areas of myocardial fibrosis heralding disease, which further impacts prognosis and patient management.
Purpose: :The aim of this study is to present the MR imaging findings in HCM and to discuss the role of MR imaging in diagnosis, and risk profiling of HCM.
Methods: We reviewed all cardiac MRI studies carried out between May 2015 and January 2017 with a suspicion of HCM due to the results in echocardiography. A 1.5 tesla MRI is used to perform exams (Ingenia, Philips Healthcare). Cardiac MRI studies were performed using the following protocol : Cine imaging with bright blood prepared steady state free precession (SSFP) in the short axis, 2, 3 and 4 chamber plane, Black blood T2 in short axis, PSIR in short axis, 2 and 4 chamber plane ad IR-RT in short axis, 2 and 4 chamber plane.
Results: : The final study group consisted of 16 patients with a median age of 55 years (extremes 33 and 74 years). We found no sex prevalence with female to male ratio = 1. Most common symptoms were atypical thoracic pain, dyspnea and arrhythmia. One patient had a family history (his brother) of sudden death in young age (30 years). Asymmetric sigmoid HCM with septal hypertrophy was the most common phenotype (38%). Septal reverse curve HCM (6%), concentric hypertrophy (19%), mid ventricular hypertrophy (19%), apical hypertrophy (12%) and focal hypertrophy (6%) were less frequent. The mean of the maximal thickness of LV wall was 19.6mm ($\pm$ 3.5). Right ventricular was involved in 2 cases (12%). LV sub aortic outflow obstruction with systolic anterior motion of the mitral valve (SAM) and a high velocity jet (signal void) were found in 9 cases (56%). Involvement of the mitral valve apparatus with increased length of the mitral valve leaflets were seen in 3 cases (16%). One patient presented a "burned out" HCM with impaired systolic function (ejection fraction 28%). All the others patients had preserved systolic function. Delayed myocardial enhancement with gadolinium was found in 10 cases (62%).
Conclusion: : MRI should be considered in patients with HCM at their baseline assessment.

P1182

Association of right ventricular dysfunction in left ventricular dysfunction with chronic obstructive pulmonary disease patients

P Paul Jaime[1]; D Gonzalez-Islas[1]; J Schalch-Ponce De Leon[1]; JR Belmontes-Barraza[1]; A Orea-Tejada[1]; L Verdeja-Vendrell[1]; A Jimenez-Cepeda[1]; GK Perez-Cortes[1]; R Sanchez-Santillan[1]; V Pelaez-Hernandez[1]; B Robles-Uribe[1]; A Figueroa-Herrera[1]; S Torres-Montiel[1]
[1] *National Institute of Respiratory Diseases Ismael Cosio Villegas, Mexico city, Mexico*

Introduction: Right ventricular dysfunction is associated with Chronic Obstructive Pulmonary Disease (COPD) for their effects on cardiac functions, affecting the pulmonary vasculature besides these patients has a major risk to develop pulmonary hypertension.
Objective: To evaluate the association of left ventricular dysfunction in patients with right ventricular dysfunction
Materials and Methods: A cross sectional observational study was conducted on 20 patients older than 18 years old, with confirmed COPD diagnosis, included through history taking, clinical examination, echocardiogram and gated radioisotopic ventriculography or gated myocardial perfusion imaging with Single Photon Emission Tomography/Computed Tomography (SPECT-CT). Statistical analysis was done by linear regression adjusted for pulmonary hypertension.
Results: Right ventricular dysfunction was present in 6 patients, mean age 62.3 $\pm$ 17.28 years, There were not significative difference in comorbidities. Right ventricular dysfunction subjects had higher left ventricular end dyastolic volume ($\beta = 38$ milliliters 95 % IC 11.41 to 64.94, $p = 0.009$) than among the patients without right ventricular dysfunction.
Conclusion: This study shows that the patients with right ventricular failure have a higher left ventricular end diastolic volume than patients without right ventricular failure, then the risk of both, left and right ventricular failure is higher with COPD patients and could be investigated.

P1183

Takotsubo syndrome: cardiac magnetic resonance versus new HFA diagnostic criteria to confirm the diagnosis

MJ Miguel Jose Corbi Pascual[1]; C Urraca Espejel[1]; JJ Portero-Portaz[1]; S Calero-Nunez[1]; C Ramirez-Guijarro[1]; MI Barrionuevo-Sanchez[1]; G Gallego-Sanchez[1]; CM Olmeda-Brull[2]; J Navarro-Cuartero[1]; D Prieto-Mateos[1]; FM Salmeron-Martinez[1]; MA Simon-Garcia[1]; JG Cordoba-Soriano[1]; A Tercero-Martinez[1]; R Fuentes-Manso[1]
[1]*Albacete. University General Hospital, Albacete, Spain*; [2]*Villarrobledo. General Hospital., Villarrobledo, Spain*

Introduction: Takotsubo Syndrome (STK) is an acute reversible heart failure syndrome distinct from acute coronary syndrome (ACS), although the initial presentation has similar features. Many patients (P) are discharge from the hospital with uncertain diagnosis until, recovery of ventricular function in the follow-up, confirm the diagnosis. Given the new evidence, new diagnostic criteria have been proposed by the European Society of Cardiology Heart Failure Association (HFA).
Purpose/Methods: The objective was to compare the degree of accuracy of new HFA diagnostic criteria versus findings in Cardiac Magnetic Resonance (CMR) to confirm the diagnosis in P with suspected diagnosis of STK. We collect all P with suspected diagnosis of STK admitted to our hospital from January 2009 to April 2016.
Results: We included 70 P with suspected diagnosis of STK. The average age was 69 years, 86% women and 54% presented some stressful trigger (emotional most frequently). The 71% was HTA, 19% diabetics, 38% had dislipemy, 6,3% presented a history of ischemic heart disease. Killip class III or IV were observed in 21,4% of P, but only 13% needed administration of, vasoactive amines. 24% of these patients identified as STEMI underwent urgent PCI, 91% of them had normal coronary arteries. ECG showed ST segment elevation in 65% and 92% evolved to T wave inversion. 90% of P presented apical dyskinesia, 8% mid-ventricular and the remaining 2% presented basal dyskinesia. At discharge, 96% were prescribed beta blockers, ACE inhibitors/ARBs, statins or ASA. Regarding follow-up, STK diagnosis was confirmed by HFA criteria in 92% of P. However, it would be confirmed in 84% using the CMR (12% AMI and 4% myocarditis). Three P died (4.28%) of non-cardiac causes during follow-up, and other four had a CV event (ACS, an episode of IC and two STK recurrences).
Conclusions: In our series, STK diagnosis was confirmed by HFA criteria in more than 90% of P. Notwithstanding, CMR findings would reclassify up to 15% of P in other diagnoses. CMR would be of significant utility for the correct diagnosis of these P, because even with the new HFA criteria, some P with other pathologies would be included as STK. CMR should be considered as a new diagnostic criterion in future classifications.

Table 1 P1183

Dilated cardiomyopathy	before CRT	after CRT	P-value	Ischemic cardiomyopathy	before CRT	after CRT	P-value
LVEDV index(ml\m^2)	126.7±42.0	'108.7±35.5	0.14	LVEDV index(ml\m^2)	114.0±22.2	107.6±23.8	0.44
LVESV index (ml\m^2)	88.8±33.1	68.5±27.9	0.04	LVESV index (ml\m^2)	77.6±19.4	68.4±18.5	0.18
LVEF (%)	30.4±5.3	36.8±6.8	< 0.001	LVEF (%)	31.7±6.2	36.1±6.7	0.06
RV basal diameter (cm)	3.9±0.7	3.8±0.7	0.38	RV basal diameter (cm)	3.9±0.5	4.0±0.5	0.5
S' (cm/s)	12.0±3.2	12.1±2.8	0.9	S' (cm/s)	10.3±2.3	10.3±3.1	0.9
TAPSE (mm)	15.6±5	20.0±5	0.08	TAPSE (mm)	18±3	18.7±4	0.9
2D RV FAC (%)	36.1±9.6	37.4±6.8	0.7	2D RV FAC (%)	28.2±7.8	24.6±10.1	0.5
SPAP(mm Hg	50.5±13.5	36.4±10.6	< 0.001	SPAP (mm Hg)	45.8±14.6	44.8±14.4	0.9

LVEDV index, left ventricular end-diastolic volum index; LVESV index, left ventricular end-systolic volume index;LVEF, left ventricular ejection fraction; S', tissue Doppler–derived tricuspid lateral annular systolic velocity;TAPSE,Tricuspid annular plane systolic excursion;2D RV FAC,fractional area change of Right ventricle ;SPAP,systolic pulmonary artery pressure.

P1184

The analysis of parameters of echocardiography of patients with cardiomyopathy after cardiac resynchronization therapy

S M Svetlana Gerasimenko[1]; V I Gerasimenko[1]
[1]*Federal Center of Cardiovascular Surgery, Astrakhan, Russian Federation*

Background: There are areas of controversy exist regarding the imaging assessment of patients (pts) with CRT.The analysis of echocardiographic data about positive CRT responders is still collecting nowadays.
Purpose: The aim of this work is to find out the change of parameters of echocardiography of pts that have cardiomyopathy before and after one year CRT.
Methods: All pts were divided into two groups: group 1-pts with dilated cardiomyopathy(DCM) (24 men and 13 women; aged 54,5 ± 9,4) and group 2-pts with ischemic cardiomyopathy (22 men and 2 women; aged 56,4 ± 8,2) and chronic heart failure (CHF) were included in the study. In the first group, pts with CHF NYHA functional class III were 78%, in the second group 86.3%. The diagnosis is based on clinical researches, that also include coronarography.We compared the values of the EF, LVEDV index ,LVESV index, fractional area change of RV , S', RV basal diameter, the level of SPAP , TAPSE before and after CRT.
Results: (Table 1) The parameters of echocardiography of pts with cardiomyopathy before and after CRT.
Conclusions: We received in a year after CRT it was discovered, that positive dynamic of echocardiographic measures can be observed with DCM pts in comparison with pts with ischemic cardiomyopathy. The pts who have DCM turn out to be more perspective responders for CRT. The extensive research on the topic, and development of new imaging techniques, are likely to contribute to more accurate assessment of these pts, thus improving management.

P1185

Evaluation of left ventricular systolic function in Chron disease _ a study of strain analysis by 2D speckle_tracking

M Oliveira[1]; MR Lourenco[1]; O Azevedo[1]; T Curdia Goncalves[1]; MJ Moreira[1]; F Castro[1]; L Calvo[1]; B Faria[1]; P Von Hafe[1]; J Portugues[1]; J Cotter[1]; A Lourenco[1]
[1]*Hospital Guimaraes, Guimaraes, Portugal*

INTRODUCTION: Crohn's disease (CD) is a chronic inflammatory bowel disease that affects the gastrointestinal tract but has also extraintestinal manifestations. Cardiac involvement is considered rare and limited to sporadic cases of myocarditis, endocarditis and pericardial effusion. Myocardial deformation imaging is the most sensitive technique to evaluate left ventricular function. There is only one recent study in literature evaluating left ventricular function by myocardial deformation imaging in CD patients.
OBJECTIVE: The aim of this study was to evaluate left ventricular systolic function with two-dimensional speckle tracking echocardiography in patients with CD and correlate these findings with the activity and extension of disease.
Methods: Cross-sectional study including 40 patients with CD, followed in hospital consultation of Gastroenterology, and no other causes of left ventricular dysfunction. We collected clinical and demographic data. We performed 2D transthoracic echocardiogram including conventional echocardiography and tissue Doppler imaging (TDI). We performed 2D strain analysis by speckle-tracking and determined global longitudinal strain.
Results: Patients were predominantly female (57%), with mean age of 34,4 ± 10,33 years old and mean disease duration of 8,21 ± 6,43years. Harvey-Bradshaw activity index showed that 30 patients were in remission, 8 patients had mild disease activity and 2 patients had moderate disease activity. 32,5% patients had already been submitted to surgery because of CD complications. CD patients had significantly lower ejection fraction than controls (58,18 ± 0,66 vs. 65,58 ± 0,82 %, p < 0.001) but within normal range. TDI systolic velocity (average S') was normal and similar in CD patients and controls (10,75 ± 0,26 vs. 10,50 ± 0,40 cm/s, p = 0,591). CD patients had significantly worst values of global longitudinal strain than controls (-20,03 ± 0,33 vs. -21,81 ± 0,30 %, p < 0.001). In CD patients, global longitudinal strain was not correlated with disease activity (p = 0.390) or disease duration (p = 0.483) nor was associated with past complications (p = 0.592), previous surgery (p = 0.598) or medication (p = 0.484).
Conclusion: Our study showed that CD, like other systemic inflammatory diseases, leads to an impairment of left ventricular ejection fraction and global longitudinal strain. This is one of the first studies evaluating left ventricular systolic function in CD by myocardial deformation imaging.

P1186

Ventricular function according to severity stages of chagas disease: an echocardiographic viewpoint of the natural history

LE Luis Eduardo Echeverria[1]; ZM Roa[2]; LS Calvo[2]; MC Villamizar[2]; C Luengas[2]; AM Chavez[2]; J Rodriguez[1]; R Campo[2]; LZ Rojas[2]
[1]*Foundation Cardiovascular of Colombia, Heart failure and cardiac transplant, Floridablanca, Colombia*; [2]*Foundation Cardiovascular of Colombia, Santander, Floridablanca, Colombia*

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Background: There are few studies that assess myocardial deterioration in Chagas patients with different severity stages, especially through techniques such as Global Longitudinal Strain (GLS). Evaluating and understanding the natural history of the disease and the progression of cardiac alterations by means of echocardiographic vision may help early identification of asymptomatic individuals with incipient myocardial changes.
Purpose: Evaluate the echocardiographic characteristics and the myocardial deformity in patients with different severity stages of Chagas disease.
Methods: A cross-sectional study. Continuous variables are expressed as mean ± standard deviation or median (first and third quartile). Chi-square or Fisher test were applicable for categorical variables. An analysis of variance (ANOVA)/Kruskal-Wallis test and Scheffé test were used to identify differences between groups.
Results: A total 121 patients. Left ventricle volume and mass increase was evident throughout the groups, including patients with preserved systolic function with EKG changes typical of Chagas disease (stage B); although these changes were statistically significant when compared to stage D, they were non-significant for stages A and C. Statistically significant SLG alteration was found for all Chagas cardiac disease stages (p = 0.000). Late right ventricular function deterioration was another interesting find, as evidenced by abnormal TAPSE, only in the most advanced stage C and D (p = 0.000) (Table 1).
Conclusions: SLG was the only echocardiographic measure able to differentiate early stages (A vs B) of the disease, suggesting it is an indicator of incipient myocardial damage in this population. However, these findings will require confirmation through a study of larger and randomized sample.

Tsble P1186

Echocardiogram	A (n = 21)	B (n = 26)	C (n = 29)	D (n = 45)	p-value
LVEF (%)	61 ^{CD} (58 -64)	61^{CD}(59-65)	47^{D}(43-52)	25(20-31)	0.0001
LV ESV (ml)	28 ^{D}(22-32)	37 ^{D}(27-42)	53 ^{D}(39-70)	133(102-213)	0.0001
LV EDV (ml)	74^{D}(59-85)	97 ^{D}(78-112)	101 ^{D}(82-139)	182(146-281)	0.0001
LV mass index (g/m2)	65 ^{CD}(61-72)	89^{D}(78-100)	111^{D}(80-143)	154(122-186)	0.0001
LV GLS (%)	-23 ^{BCD}(-24; -21)	-21^{CD}(-21; -18)	-15^{D}(-17;-13)	-8(-9; -6)	0.0001
LA volume index (ml/m2)	24^{D}(23-29)	32^{D}(22-39)	41^{D}(31-55)	59(45-76)	0.0001
TAPSE	22^{CD} ± 3.1	22^{CD} ± 3.7	18^{D} ±4.1	14 ± 4.8	0.0000
LVDD	50 ^{CD}(45-52)	52 ^{CD} (47-55)	60 ^{D} (52-62)	67 (62-72)	0.0001
LVSD	30 ^{CD}(28-32)	32 ^{CD} (30-35)	44 ^{D} (37-49)	59 (53-64)	0.0001

Table 1.Echocardiographic findings according to severity stages of Chagas cardiomyopathy (n = 121).

P1187

Value of 3D echocardiography in assessment of super-response to cardiac resynchronisation therapy in patients with chronic heart failure

VA Kuznetsov[1]; DV Krinochkin[1]; AM Soldatova[1]; NN Melnikov[1]; GV Kolunin[1]; TN Enina[1]
[1]*Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Tyumen, Russian Federation*

Background: Cardiac resynchronisation therapy (CRT) is an effective treatment for patients with chronic heart failure (CHF). Selection of patients with the prognosis of favorable response to CRT is one of the important issues.
Purpose: To reveal clinical and functional features in patients with CHF and super-response to CRT.
Methods: The study included 59 subjects (88% men, mean age 52.9 ± 9.0 years): 33 patients with ischemic and 26 patients with nonischemic cardiomyopathy. The main criteria of patients selection: NYHA II-IV functional class; left ventricular (LV) ejection fraction (LVEF) < 35%; signs of mechanical dyssynchrony assessed by 3D echocardiography, duration of QRS complex. 39 subjects had sinus rhythm and 20 patients - permanent atrial fibrillation. Combined CRT/ICD devices were implanted in 40 patients. 3D echocardiography with assessment of systolic dyssynchrony index (SDI) was performed at baseline and 6 months after CRT. Patients were divided into groups: I (n = 18) - increase in LV end-systolic volume (ESV) >30% (super-responders); II group (n = 41) - increase in LV ESV < 30%.
Results: At baseline no significant differences in clinical and functional characteristics were observed between the groups. 6 months after implantation both groups demonstrated reduction in NYHA functional classes (in group I from 2.69 to 2.00, p = 0.001; in group II from 2.70 to 2.18, p = 0.007). In patient with super-response significant increase in 6-minute walk test was observed (from 327 ± 95 m to 407 ± 46 m; p = 0.013), in group II increase in mean distance was not significant (from 329 ± 106 m to 370 ± 127 m, p = 0.126). Significant increase in LVEF and decrease in end-diastolic volume and ESV were found in both groups during CRT. At baseline SDI was significantly higher in patients with super-response (9.8 ± 3.5% vs 7.4 ± 4.4%; p = 0.035).
Conclusion: In the group of patients with super-response to CRT clinical improvement and exercise tolerance were detected along with LV reverse remodeling. More significant LV mechanical dyssynchrony including 3D echocardiography in patients with CHF was associated with super-response to CRT.

P1188

Left atrial minimum volume is more strongly associated with left ventricular filling pressures than the left atrial maximum volume

I Hamdi[1]; K Houissa[1]; C Chourabi[1]; A Belouaer[1]; K Taamallah[1]; L Riahi[1]; A Haggui[1]; N Hajlaoui[1]; D Lahidheb[1]; W Fehri[1]; H Haouala[1]
[1]*Cardiology departement, Military Hospital of Tunis, Tunis, Tunisia*

Aim: Left atrial (LA) maximum volume (LAV max) is an indicator of left ventricular filling pressure. However, systolic function is a determinant of LAV max, whereas the LA minimum volume (LAV min) is directly exposed to left ventricular pressure. Our aim was to demonstrate that LAV min is better correlated to filling pressure than LAV max.
Methods: This prospective study enrolled 49 patients (mean age : 62.7 years, range 44-89, 85% male) with ischemic cardiomyopathy (mean left ventricular ejection fraction : 47.57 %). All patients underwent transthoracic echocardiography and N-terminal pro-B- type natriuretic peptide (NT-proBNP) measurement within 24 hours. All LA volumes measureents were indexed by body surface area, LAV min : LA end-diastolic volume at the first frame after mitral valve closure, LAV max : LA end-systolic volume right before mitral valve opening.
Results: In linear regressions, LAV min was better associated with E/E' (r=0.572, p < 0.0001) than LV max (r=0.434, p = 0.003). LAV min was also more correlated with NT-proBNP (r=0.636, p < 0.0001) than LAV max (r=0.418, p = 0.003). The area under the receiver-operating curve (AUC) to detect E/E' >15 was 0.848 (p < 0.001) for LAV min and 0.721 (p = 0.02) for LAV max. The optimal LAV min cut-off to predict E/E'>15 was 20 ml/m^2 (sensitivity of 85% and specificity of 73%). To detect an NT-proBNP level of 450 ng/L, LAV min yielded a significantly larger AUC 0.75 (p < 0.004) than LAV max (0.608, p = 0.21).
Conclusion: Our findings support that LAV min may be more closely related to left ventricular filling pressures than LAV max in patients with ischemic cardiomyopathy.

P1189

Early reverse remodeling and improvement of echo parameters after introduction of sacubitril/valsartan in 80 stable and well treated HFrEF patients

V Maurin[1]; A Canu[1]; A Bernard[2]; S Lafitte[1]; F Picard[1]
[1]*University Hospital of Bordeaux, Bordeaux, France*; [2]*University Hospital of Tours, Tours, France*

Background: Sacubitril/valsartan is recommended to optimize pharmacological therapy of HFrEF patients, who remain symptomatic despite optimal treatment. If the benefits on prognosis have already been demonstrated in the PARADIGM trial, the effects on cardiac function, chambers dimensions and load conditions are unknown.
Objectives: We report the results of our monocentric cohort of 129 consecutive systolic HF patients, treated with Entresto between October 2015 and July 2016, studied with serial echocardiographic examinations acquired before and after 3 months of treatment. All echo were blind analysed in an external ESC accredited core lab echo.
Results: 129 patients were initiated with Entresto, 5% patients were excluded because of confounding factors (supposed alcoholic or rhythmic cardiomyopathy, concomitant CRT or valvular surgery), 11% discontinued treatment for adverse events, 3.8% were transplanted, 0.5% died of cardiovascular cause and 8% had missing data during the follow up period. 80 patients had finally echocardiographic examination before and after 3 months of treatment. Mean age was 59 years old, 76 % of patients were men, 52% had ischemic HF, and median duration of HF was 9,6 years. All patients were in stable hemodynamic condition with an optimized medical treatment at baseline (97.5% were treated with ACE-I or ARB, 98% with BB and 87.5% with MRA), the mean level of BNP was 531 pg/ml. 5% of the patients were in NYHA class 1, 70% in class 2, and 25% in class 3. At 3 months, 86% of patients received the target dose (97/103 mg), 8% the half dose (49/51mg), and 2% the low dose (24/26mg) whereas the dose of furosemide decreased significantly (83 vs 153 mg, p < 0.0001). Patients exhibited a significant reduction in left ventricular dimensions and volume (LVED diameter: 64.8 ± 10.9 vs 67,2 ± 8.6, p = 0.003, LVED volume: 204.1 ± 79.3 vs 218.8 ± 79.1 mL, p < 0.001, LVES volume: 142.7 ± 70.1 mL vs 158.9 ± 68.0 mL, p < 0.001) while ejection fraction increased by 18% (31.9 ± 8.2 % vs 28.4 ± 7.7 %, p < 0.0011) and global longitudinal strain increased by 9% (8,8 ± 3 vs 7,4 ± 2,7, p = 0,002). Diastolic function improved significantly, left atrial volume was significantly smaller (left atrial volume index: 39,5 ± 13,9 vs 43,7 ± 15,2mL/m^2, p = 0,005) and systolic pulmonary pressures decreased significantly (from 42.5 ± 12.3 to 38.8 ± 12.0 mmHg, p = 0.012). However, no significant change was observed in mitral regurgitation grade (1,1 ± 0,9 vs 1,2 ± 1, p = 0,2), neither in right ventricular dimensions (Right ventricular diastolic area, cm^2: 20.0 ± 4.3 vs 19,5 +/- 4,9, p = 0,64) or function (S', cm/s: 10.0 ± 2.7 vs 9.7 ± 2.7, p = 0,125).
Conclusions: Sacubitril/valsartan induces early reverse remodeling and improves pressure conditions in stable and well treated HFrEF patients.

P1190

Sedation on transesophageal echocardiography: correlation of Midazolam and fentanyl with alcohol

T R Tania Regina Afonso[1]
[1]*Hospital Israelita Albert Einstein, cardiologia MDP, Sao Paulo, Brazil*

BACKGROUND: Transesophageal echocardiography is performed using conscious sedation. Excessive alcohol users are commonly cited as difficult to sedate. Few studies compared and analyzed doses of medication to achieve sedation in these groups. OBJECTIVES: Goal predict the need for a high dose of sedative in patients who use alcohol.
Methods: A prospective study was conducted comparing patients who reported being resistant to alcohol with those who reported not being resistant, the mean dose of fentanyl and Midazolan was analyzed in both groups. RESULTS: A total of 52 patients were analyzed. Comparing groups of patients reporting resistance and nonresistance. The Group that reported resistance to alcohol used the statistically higher sedation dosage to achieve conscious sedation Midazolan mean 8.20 ± 3.12 mg first group and mean 5.30 ± 2.70 in the second group, the dose of anxiolytic did not change Significant mean 53.33 ± 12.91 first group and mean 45.95 ± 19.11 in the second group. Conclusions: Identifying patients who are difficult to sedate before transesophageal echocardiography is important because adequate sedation is associated with a better analysis of the cardiac anatomy and its malformations and patient comfort. In patients using alcohol, it is important to predict the need for higher doses of medication to achieve adequate sedation.

P1191

Subclinical functional and structural cardiomyopathy among patients infected with human immunodeficiency virus in the era of highly active antiretroviral therapy

M Maria De Las Nieves Montoro Lopez[1]; CI Soto[2]; R Florez Gomez[1]; A Alonso Ladreda[1]; I Ponz De Antonio[1]; JI Bernardino[2]; E Refoyo Salicio[1]; JJ Rios Blanco[2]; M Moreno[1]; G Guzman Martinez[3]
[1]*University Hospital La Paz, Department of Cardiology, Madrid, Spain*; [2]*University Hospital La Paz, Internal Medicine, Madrid, Spain*; [3]*National Centre for Cardiovascular Research (CNIC), Madrid, Spain*

Background. The development of highly active antiretroviral therapy (HAART) has entailed a significant decrease in AIDS-related complications and mortality. However, cardiovascular disease has become the main cause of mortality in developed countries. This study was aimed to compare echocardiographic parameters among outpatient HIV+ patients on HAART and a control group.
Methods: We conducted an analytic, observational, cross-sectional study in a tertiary hospital in Madrid (Spain). We included HIV infected patients under routine follow-up in the specialized Internal Medicine clinic of our institution. A group of non-infected HIV patients was also included. All of them provided written informed consent and underwent a comprehensive transthoracic echocardiogram (TTE) at the Imaging Unit of the Cardiology department. Clinical data, including cardiovascular risk factors were recorded.
Results: A total of 100 HIV patients and 16 controls were included. Baseline characteristics were similar between both groups. HIV+ patients showed statistically significant higher left ventricle (LV) mass, wall thickness and LV volume values than non-HIV patients. Moreover, the right ventricle (RV) free wall was also thicker in the HIV group compared to control group. Although the mean ejection fraction was similar between both groups, the mean RV fractional area change was significantly lower in the HIV+ group than in the control group.
Conclusion: Outpatient HIV infected patients on HAART show higher values of LV and RV wall thickness, higher LV volumes and lower RV systolic function compared to non-infected patients. The prognostic value of these subclinical abnormalities should be assessed in future studies.

Ecocardiograpghic parameters

	HIV(n = 100)	Controls (n= 16)	p value
LV mass/BSA (g/m^2)	89 (73-105)	69 (61-84)	0.002
LVEDV/BSA (ml/m^2)	56 (50-67)	45 (37-53)	0.001
LVESV/BSA (ml/m^2)	21 (17-25)	16 (12-20)	0.002
LVEF (%)	62 (57-67)	65 (60-68)	0.13
RV free wall thickness (mm)	5.0 (5.0-6.0)	4.0 (3.7-4.7)	0.001
RV fractional area change (%)	40 (36-46)	49 (39-63)	0.01
Tricuspid regurgitation velocity (m/sec)	2.36 (2.04-2.58)	2.10 (1.85-2.50)	0.44

Comparison of conventional echocardiographic variables between the studied groups. LV: left ventricle, BSA: body surface area, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction, LA: left atrium, RV: right ventricle, TAPSE: tricuspid annulus plane systolic excursion

P1192

Left ventricular hypertrophy predictors after repaired aortic coarctation

H Helena Nascimento[1]; M Braga[1]; V Ribeiro[1]; C Cruz[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

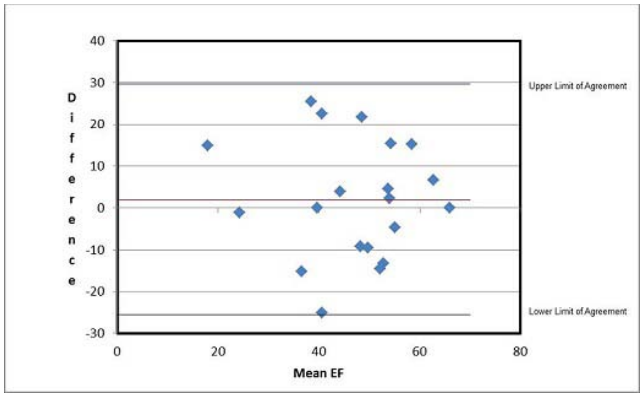
Background and purpose: Aortic Coarctation (CoA) is a narrowing of the aorta, most commonly located distal to the origin of the left subclavian artery. Despite successful correction of this vascular defect, left ventricular hypertrophy (LVH) may persist. The primary goal of this study was to determine the predictors of LVH in this group of patients (pts).
Material and methods: This study was based on a retrospective analysis of 117 pts (>18 years-old) with the diagnosis of repaired CoA, followed-up in a Grown-up Congenital Heart Disease Centre. Epidemiological, clinical and echocardiographic data were collected and inserted in a registry base.
Results: From a total of 117 adult pts, 39.3% were female and the current mean age was 34.9 ± 9.2 years old. Surgical repair was performed in 105 pts (89.7%): resection with subclavian artery flap aortoplasty (36); head-to-head anastomosis (21) and woven Dacron patch (18). Remaining 12 pts (10.3%) were submitted to percutaneous intervention. Mean age at CoA correction was 9.7 years old. All pts were in sinus rhythm and electrocardiogram (ECG) voltage criteria for LVH were present in 33 pts (28.2%). LVH voltage criteria on ECG correlated significantly with the presence of LVH on transthoracic echocardiogram (ECO) (OR 7.75, CI 3.04-19.71, p < 0.001). Regarding ECO data, LVH was observed in 29 (24.7%) of the pts, and only two pts had mild to moderate left ventricular systolic dysfunction. Associated ventricular septal defect (VSD) (OR 3.6, CI 1.35-9.82, p = 0.013) was a predictor of LVH on ECO. Likewise, these group of pts presented a superior left atrial diameter (LAD) (37.7 ± 4.9 vs. 34.5 ± 5.4 mm, p = 0.008) and a E/e' (9.6 ± 2.5 vs. 8.1 ± 1.9, p = 0.053). Pts with LVH have been more often submitted to re-intervention (OR 2.53, CI 1.03-6.20, p = 0.053). Other variables as sex, age of repair and type of intervention were not determinants of LVH on ECO. LVH pts had a currently well-controlled blood pressure with a mean systolic blood pressure of 128.7 ± 11.6 mmHg with an average of 1.2 ± 0.7 anti-hypertensive agents. Beta-blocker was the most frequent used drug (70.0%), followed by blockers of the renin-angiotensin system (40.4%).
Conclusion: Our study reinforced that ECG voltage criteria strongly correlated with LVH on ECO LVH. Moreover, LVH on ECO was associated with VSD, higher LAD and re-intervention. Also, despite optimal blood pressure control, patients with repaired CoA may present LVH long after correction, suggesting the need for lower blood pressure targets for these pts.

P1193

Ejection fraction can be accurately detrmined using a cloud based platform on mobile devices

A Salacata[1]; J Kapala[1]; S Panknin[1]
[1]*Mid Michigan Medical Center, Alpena, United States of America*

Despite its shortcomings, left ventricular ejection fraction (EF) remains the most widely used measure of systolic function. Echocardiography remains the most widely used modality for measuring EF given its widespread availability, portability, reliability and low cost. Given the digital nature of echocardiographic data, echocardiograms can potentially be viewed and analyzed using mobile devices. We therefore performed this preliminary study to compare echocardiographic EF derived on a widely available mobile device. METHOD We randomly selected 20 transthoracic echocardiograms (TTE) with regional wall motion abnormalities from which identifying information was removed. All studies were acquired using GE Vivid 7 system then converted from native to mp4 format with a compression ratio of 69:1 using a commercially available web/cloud based service for analysis, archiving and retrieval. They were then interpreted in random order by an echocardiographer with level 3 training on a standard computer display (STRD) with a minimum LCD display size and resolution of 20" x 24" and 1600 x 1200 pixels, and an iPad 2 (MBL) with a screen size and resolution of 5.82" x 7.76" and 1024 x 768 pixels. EF was determined using a previously derived method1 of that scored segmental wall motion in the 4 and 2 chamber views. RESULTS Of the 20 subjects (15 male, mean age 71.2 ± 3.74 years), 3 had suboptimal studies requiring contrast administration for LV opacification. There was no significant difference in the mean EF by STRD vs. MBL (47.9 ± 13.44, range 28.05-66, vs. 45.89 ± 14.25, 24.83-66, p = 0.53). There was good agreement between both methods by regression analysis (R=0.55, p = 0.01), and as demonstrated using a Bland-Altman plot (average difference between methods = 2.0, 95% CI ± 14.07). CONCLUSION TTE EF can be reliably evaluated on a mobile device with results comparable to EF obtained by STRD. This will potentially lead to faster and timelier availability of this important piece of information. Additional studies on a larger number of mobile platforms should also be carried out.



BIOMARKERS

P1194

The value of NT-proBNP in the diagnosis of cardiac disease in patients with alcoholic liver cirrhosis

V Romanova[1]; P Lazarev[1]; G Kiyakbaev[1]; V Moiseev[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Objective: to study the relationship between the level of NT-proBNP and the presence of structural and functional cardiac changes in patients with alcoholic liver cirrhosis (LC).
Methods: Our study included 80 alcoholic LC patients (mean age 53.1 ± 12 years) without any history of cardiovascular and respiratory disease. The number of patients with Child-Pugh classes A, B, and C was 12 (14.8%), 22 (27.2%), 46 (59.2%), respectively. We performed ECG with QTc measurement, echocardiography with assessment of left ventricular ejection fraction (LVEF), left ventricular diastolic function, left ventricular myocardial mass index (LVMI), systolic pulmonary artery pressure (SPAP) and cardiac output [CO = stroke volume (SV) x heart rate]. Plasma values of NT-proBNP were evaluated in 60 patients.
Results: The level of NT-proBNP plasma was elevated (> 125 pg/ml) in 46 (80%) patients, while there was a direct association between the level of NT-proBNP and severity of LC, estimated by MELD (R=0.39, $p < 0.05$) and Child-Pugh (R=0.35, $p < 0,05$) scores. The mean value of NT-proBNP in all patients amounted to 621.5 pg/ml (min 33 pg/ml, max 3849 pg/ml). No correlations between the level of NT-proBNP and parameters reflecting the presence of cardiac changes (size and area of the left and right atrial cavities, end-diastolic size, end-systolic size, thickness of interventricular septum and posterior wall of the left ventricle, LVMI, SV, EF, diastolic dysfunction, global longitudinal LV strain, QTc interval duration). We observed a positive correlation between the CO values and the level of NT-proBNP (R= 0.29, $p < 0.05$).
Conclusion: NT-proBNP increase was observed in majority of the patients with alcoholic LC and directly correlated with the severity of liver disease. The level of NT-proBNP is directly associated with CO and not with other echocardiographic parameters, which suggests that this marker could reflect the overload of sympathoadrenal system, and not heart failure, in this patient population.

P1195

Not changes in heart failure therapy but patient characteristics at admission predict unsuccessful guidance of therapy to a target of more than 30% NT-proBNP reduction

S Susan Stienen[1]; K Salah[1]; YM Pinto[1]; WE Kok[1]
[1]*Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands*

On behalf of: PRIMA II

BACKGROUND: NT-proBNP-guided therapy targeting a reduction of more than 30% from admission to discharge was not superior to conventional therapy for acute decompensated heart failure (ADHF) in the PRIMA II trial (presented at HFSA 2016, not yet published). In the subgroup of NT-proBNP-guided patients who received guidance of HF treatment , we studied which clinical variables predict unsuccessful guidance towards an NT-proBNP reduction of more than 30% at discharge.
Methods: In PRIMA II (NTR3279) 201 and 203 patients admitted for ADHF were randomized at the moment of clinical stability to NT-proBNP-guided versus conventional therapy respectively. Guided therapy (intensification of HF therapy) was performed actively in NT-proBNP-guided patients who failed to have a reduction of more than 30% from admission to randomization (N=68). Baseline characteristics of patients who were successfully guided (N=35) versus unsuccessfully guided (N=33) towards an NT-proBNP reduction of more than 30% were compared. A change in HF therapy was defined as initiation or increase in dosage of HF therapy, and HF therapy consisted of ACEi, beta blockers, MRA, CRT, electrical cardioversion and coronary angiography. Predictors of unsuccessful guidance (less than 30% reduction at both randomization and discharge) were determined using logistic regression analyses.
Results: Independent predictors of unsuccessful guidance were age over 80 years (OR 4.0, 95% CI 1.2-14, $p = 0.03$), rales at admission (OR 8.6, 95% CI 1.4-52, $p = 0.02$), atrial fibrillation at admission (OR 3.8, 95% CI 1.1-13, $p = 0.04$), and lower estimated glomerular filtration rate (per unit decrease: OR 1.05, 95% CI 1.01-1.08, $p = 0.01$). Changes in HF therapy did not predict unsuccessful guidance of therapy.
Conclusion: Non response of NT-proBNP-guided therapy in ADHF patients is dependent on patient characteristics at admission and not on intensification of HF therapy (pharmaceutical or interventional). Future studies should focus on NT-proBNP-guided therapy in patients in whom it is possible to successfully guide therapy.

P1196

Sacubitril/valsartan prevents the acute increase of n-terminal brain natriuretic peptide induced by exercise training in subjects with heart failure

G Giuseppe Caminiti[1]; V Cioffi[1]; G Cascelli[1]; N Punzo[1]; G Campolongo[1]; M Volterrani[1]
[1]*IRCCS San Raffaele Pisana Hospital, Rome, Italy*

Background: long-term administration of sacubitril/valsartan decreases levels of N-terminal brain natriuretic peptide (NT-proBNP). Its effects on changes of NT-ProBNP mediated by exercise training are not known. Aim: to evaluate if the administration of sacubitril/valsartan modulates the acute changes of NT-proBNP induced by exercise training in patients with heart failure and reduced ejection fraction (HFrEF).
Methods: The study enrolled 14 patients with HFrEF, males/females 11/3, NYHA functional class II/III who were elegible for treatment with sacubitril/valsartan. The experimental protocol was conducted in two sessions: the first before starting treatment with sacubitril/valsartan 97/103 bid; the second after a week of aimistration of the drug. At both exercise sessions, blood samples for NT-Pro BNP assessment were collected at rest, between 8:00 and 9:00 am, and 30 minutes after stopping training. The self-perceived dispnoea was evaluated by Borg scale. The exercise session lasted 1 hour during which patients performed endurance training at 60-75% of VO2 peak. Results: At T1 levels of NT-proBNP increased from 1835 ± 145 to 1973 ± 264 ($p = 0.0003$). The T1 Borg'score at the end of training was 4.6 ± 1.1. At T2 levels of NT-proBNP at rest were similar than after training (from 1216 ± 323 to 1288 ± 201; $p = 0.13$). Both NT-proBNP values at T2 were significantly reduced compared to correspondent values obtained at T1. The T2 Borg score was 2.8 ± 0.8. Conclusion: the administration of low doses of sacubitril/valsartan decreased NT- proBNP levels and prevented the acute increase of NT- proBNP and improved dispnoea early after endurance training in patients with HFrEF.

P1197

The diagnostic and economic implications of using a plasma nt-probnp of 300 or 400ng/litre as the threshold for ruling out the diagnosis of heart failure in a non selected british population

J Jessica Webb[1]; J Draper[1]; S Claridge[1]; T Jackson[1]; L Fovargue[2]; S Piper[3]; E Bolca[1]; S Rivolo[2]; R Rajani[1]; S Kapetanakis[1]; A Mcdiarmid[1]; T Mcdonagh[3]; R Razavi[2]; G Carr-White[1]
[1]*St Thomas' Hospital, Cardiology Department, London, United Kingdom*; [2]*King's College London, Division of Imaging Sciences and Biomedical Engineering, London, United Kingdom*; [3]*King's College Hospital, Cardiology Department, London, United Kingdom*

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Background: The 2014 National Institute of Clinical Excellence (NICE) guidelines on the management of acute heart failure recommend a plasma NT-proBNP threshold of 300pm/ml to assist in ruling out the diagnosis of heart failure (HF), updating previous guidelines recommending using a threshold of 400pg/ml.
Purpose: This study sought to determine the diagnostic and economic implications of using these thresholds in a large unselected UK population.
Methods: In our institution, all consecutive patients with suspected heart failure underwent NTProBNP testing from September 2014 to September 2015. The reason for all the patient's admission was recorded using hospital notes and imaging

results, including the patients with NTproBNP under 400pg/ml. Patient and clinical demographics were recorded as well as clinical outcomes (mean follow-up of 15.8 months (SD 8.7)).
Results: 697 were diagnosed with symptomatic HF following echocardiography and consultant review. From reviewing all the reasons for diagnosis, lowering the threshold from 300 to 400pg/ml would have involved screening an additional 61 patients and theoretically identified 6 patients with symptomatic HF. At 300pg/ml the sensitivity was 0.987 with a positive predictive value (PPV) of 0.396 and an accuracy of 0.467. Using a threshold of 400pg/ml, sensitivity was 0.973, PPV 0.407 and accuracy of 0.492. The economic implications of lowering the threshold would have involved additional costs of £58,116.07 (£952.72 per patient screened or £9686.01 per HF patient identified). The six patients identified with a NTproBNP between 300-399pg/ml were already known to the HF service.
Conclusion: The recent updated NICE guidelines to lower the plasma NT-proBNP threshold of 300ng/litre to rule out the diagnosis of heart failure had a significant impact on the heart failure team and costings, but would potentially improve heart failure detection (additional 6 patients identified).

Costing for different NTproBNP threshold		
Model screening patients with NTproBNP 300-399pg/ml	Number of Patients	Total Costs (£)
Cost of blood tests (£32.64/each)	61	1991.04
HF Team screening review (Nurse review £26.47/hour)	61	1614.67
Number of additional echocardiograms (£65.70/echo)	57	3744.90
Additional length of stay (£400/day x 2 days)	55	44,000
Change in stay for 6 patients correctly identified as having HF (increase by 1 day)	6	2400
Number of patients with HF readmitted within a month (and so no payment made according to BPT - £6179)	0.71	4365.46
OVERALL DIFFERENCE		58,116.07
Cost Implications of lowering the NTproBNP threshold to 300pg/ml		

P1198
Natriuretic peptides for detection of heart failure in patients with atrial fibrillation from the community
S Van Doorn[1]; GJ Geersing[1]; AW Hoes[1]; F H Frans Hendrik Rutten[1]
[1]University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands

Heart failure (HF) may develop in patients with atrial fibrillation (AF), and the other way around. Both share shortness of breath and reduced exercise tolerance as key symptoms, and elevated natriuretic peptide levels. We aimed to assess the diagnostic value of amino-terminal pro B-type natriuretic peptide (NTproBNP) for uncovering heart failure in patients with atrial fibrillation.
Methods: Individual patient data from four opportunistic HF screening studies in older high-risk persons from the open population (≥60 years and type 2 diabetes, ≥65 years and chronic obstructive pulmonary disease, ≥65 years and shortness of breath, and ≥65 years and multimorbidity). All participants underwent an extensive clinical assessment, blood testing, electrocardiography, and echocardiography. Presence or absence of HF was established by an expert panel following the criteria of the European Society of Cardiology on HF. We used a two-stage mixed effects regression meta-analysis to calculate discrimination; efficiency; the proportion of missed cases and sensitivity, specificity and predicted values.
Results: In 1,941 individuals with median age 72.3 (IQR 67.4-77.7) years and 49.7% male, 196 (10.1%) cases had atrial fibrillation. Heart failure was uncovered in 82 (42.5%) patients with AF. Median NTproBNP levels of AF patients with and without uncovered HF were 744 pg/mL and 211 pg/mL, respectively. Fourty-three (21.9%) AF patients had NTproBNP value below 125 pg/mL. At this cutpoint, the sensitivity was 93%, specificity 36%, and the positive value and negative predictive value 52% and 87%, respectively.
Conclusion: In older high-risk AF patients from the community the prevalence of unrecognized HF is very high (42.5%), and straightforward echocardiography should be considered.

P1199
Diagnostic accuracy of plasma ntprobnp in patients over 80 years of age in a non selected british population
J Draper[1]; J Jessica Webb[1]; E Bolca[1]; Y Yiu[1]; L Fovargue[2]; S Rivolo[2]; B Porter[2]; B Sieniewicz[1]; S Kapetanakis[1]; A Mcdiarmid[1]; S Piper[3]; R Rajani[1]; T Mcdonagh[3]; R Razavi[2]; G Carr-White[1]
[1]St Thomas' Hospital, Cardiology Department, London, United Kingdom; [2]King's College London, Division of Imaging Sciences and Biomedical Engineering, London, United Kingdom; [3]King's College Hospital, Cardiology Department, London, United Kingdom

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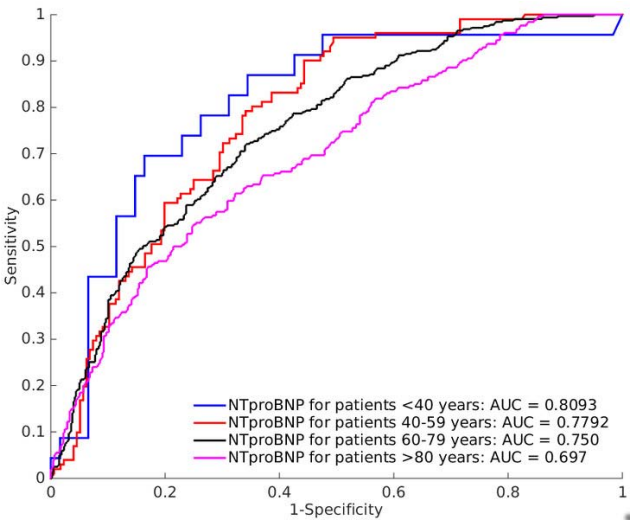
Background: The current NICE guidelines recommend 300pg/ml for the threshold of ruling out heart failure (HF). However, NTproBNP is known to increase with age although the performance of this biomaker is unclear in very elderly patients.
Purpose: This study sought to define the diagnostic accuracy of plasma NTproBNP in patients over 80 years of age in a large unselected population of HF patients admitted to a Tertiary Hospital in the United Kingdom.
Methods: All 2077 consecutive patients over a 12 month period were screened for HF through our NTproBNP led heart failure service and were followed up for a mean of 15.8 ± 8.7 months, Patients were categorised by age (< 40, 40-59, 60-79 and >80 years old), HF classification, gender, ethnicity (Afro Caribbean, Caucasian and Asian) and outcome (time to HF hospitalisation or all cause death).
Results: Of the 2077 patients screened, 697 patients had symptomatic HF (mean age 72.7 ± 14.5years; 57.8% male) and 36% were over 80 years of age. The AUC of NTproBNP for diagnosis of HF was 0.734 for all heart failure patients. The AUC was calculated for the 4 age categories and there was a reduction seen as age increased ($p = 0.02$ 60-79 v >80: $p = 0.01$ 40-59 v >80; $p = 0.04$ <40 v >80years), Figure 2. There was a 5.3% reduction in receiver operating characteristic curve (ROC) area for patients over 80 years compared to those under 60-79 years of age. All patients with NTproBNP requested were investigated and in patients over 80 years of age, the lowest NTproBNP recorded in a patient with HF was 450pg/ml. At a threshold of 400pg/ml in patients over 80 years of age, the negative predictive value (NPV) was 1, sensitivity 1 and accuracy of the test 0.42. In contrast the NPV was 0.93, 0.95, 0.95 sensitivity 0.97, 0.96, 0.91 and accuracy 0,54, 0.61, 0.67 for patients 60-79, 40-59 and under 40 years of age respectively. Increasing the NTproBNP threshold in patients over 80 years of age for ruling out HF to 500 and 600pg/ml, changed the NPV to 0.94, 0.90, the sensitivity to 0.98, 0.96 and the accuracy to 0.46, 0.48 respectively. Furthermore, increasing the NTproBNP threshold to 500pg/ml in elderly patients resulted in a NPV of 0.95, 0.92 and 1 in Caucasian, Afro Caribbean and Asian patients respectively. Moreover using a NTproBNP threshold of 600pg/ml resulted in NPV of 0.9, 0.87 and 1 for Caucasian, Afro Caribbean and Asian patients respectively.
Conclusions: Over a third of the patients with HF identified in a large unselected UK population were over 80 years of age. All patients were investigated and the lowest NTproBNP recorded in patients over 80 years of age with HF was 450pg/ml, with a difference observed between Caucasian, Afro Caribbean and Asian patients. This data would suggest that the NTproBNP threshold for ruling out HF in patients should be altered if patients are over 80 years of age and according to ethnicity.



AUC for Different Age groups

P1200

Semaphorin 4D levels in heart failure patients: do we have a novel biomarker of heart failure besides BNP?

NA Willner[1]; Y Goldberg[2]; E Schiff[1]; Z Vadasz[3]
[1]*Bnai Zion Medical Center, Internal Medicine Ward B, Haifa, Israel*; [2]*University of Haifa, The Department of Bio-Statistics, Haifa, Israel*; [3]*Bnai Zion Medical Center, The Division of Clinical Immunology, Haifa, Israel*

Background: Semaphorin 4D (Sema4D) is a transmembrane glycoprotein expressed on platelets and T-cells, mainly involved in inflammation processes, axonal guidance during embryonal development, angiogenesis and malignant cells proliferation. Heart failure (HF) is caused by diverse pathophysiological processes including inflammation and neuro-hormonal activation, thus potentially influence Sema4D levels.
Purpose: The study had several aims: 1. Comparing Sema4D serum levels in HF patients with control group, with post-hoc analysis of potential confounders like kidney function, medical comorbidities and ejection fraction. 2. Analysis of the correlation between NT-pro-BNP and Sema4D, in order to examine the possible role of Sema4D as a biomarker for HF. 3. Evaluation of Sema4D serum levels in HF patients- during the acute phase and following remission.
Methods: 60 patients hospitalized with complaints clinically suspected to be HF exacerbation were enrolled for the HF group. 45 patients were diagnosed with HF exacerbation by echocardiographic findings and positive NT-pro-BNP with normal CRP were included in the study. Controls were age matched healthy individuals declaring no chronic diseases or medications. First NT-pro-BNP and Sema4D samples were taken on admission to hospital, and a repeated measurement was done on patients' discharge. Both NT-pro-BNP and Sema4D serum levels were done using commercial kits according to the manufacturer instructions.
Results: In the HF group, mean age was 72.2 ($\pm$3.5) years old, 72.7% were women, and mean NT-pro-BNP levels was 3.5570 ($\pm$0.56) pg/ml, compare with mean age of 76.5 ($\pm$12.5) years old, 42.2% women and mean NT-pro-BNP levels of 1.8 ($\pm$0.26) pg/ml in controls (p value 0.05, 0.07 and $<$0.001, respectively). Sema4D levels were significantly higher in HF patients than healthy controls (2143.04 $\pm$ 1253 ng/ml vs. 762.18 $\pm$ 581.6 ng/ml, $p<0.001$, respectively. Higher creatinine levels were found to predict both higher levels of NT-pro-BNP and Sema4D ($p=0.05$ and $p<0.014$, respectively), while reduced ejection fraction was found to predict higher NT-pro-BNP only ($p<0.001$ and $p=0.87$, respectively). When comparing mean Sema4D levels on admission and discharge, a significant reduction was found (3534.94 $\pm$ 1650.55 and 2455.67 $\pm$ 1424, $p=0.03$); NT-pro-BNP levels did not change significantly (3.41 $\pm$ 0.75 and 3.38 $\pm$ 0.6, $p=0.79$).
Conclusions: Sema4D levels in HF patients' serum are significantly higher than in healthy controls, with the highest levels being in patients with chronic kidney disease. Unlike NT-pro-BNP, Sema4D is not elevated in HF patients with reduced ejection fraction compare with HF patients with preserved ejection fraction. Clinical improvement caused rapid reduction in Sema4D levels, which may be related to the inflammatory process in HF. Further research of Sema4D and HF is essential, but those preliminary findings might indicate a possible role for Sema4D as a biomarker of acute heart failure.

P1201

Copeptin and inflammatory markers in patients with different variants of acute coronary syndrome.

I Irina Sukmanova[1]; IA Sukmanova[1]; OS Tanana[1]
[1]*Altay region cardiologist hospilal, acute infarction, Barnaul, Russian Federation*

Purpose: of the study was to acsess the dynamics of the concentration of copeptin, biomarkers of inflammation and their relationship patients with MI and unstable angina.
Materials and methods: the study included 49 divided into 2 groups: with aim -26 people - the first group, the average age of 64.2 $\pm$ 1.6 unstable angina– 23-the second group, at the age of 62.1 $\pm$ 2.2 years. All patients were assessed on the first and sixth day of hospitalization was estimated the level of CPK MB, troponin I, copeptin, interleukin 1b, IL 6, TNF α, for admission was conducted by ECHO and coronary angiography.
Discussion: Patients of the first group the level of CPK MB and troponin I levels at baseline and after 12 hours was significantly higher than the second group. Peak concentrations of as MB CPK, and troponin I were determined after 12 hours in the first group, the second group in the growth of the concentration of these indicators was not. Concentration copeptin source exceeded the reference values in patients of the first group, the second source and the dynamics were within acceptable values. After 12 hours it was noted the increase in copeptin to 0.7 $\pm$ 0.1 a, which was significantly higher than the corresponding figure of the second group 0,4 $\pm$ 0,01, $p=0.04$. To 6 days, the concentration of copeptin in the first group were close to baseline, but was slightly above normal. There was a slight increase in the concentration of TNF a in patients of the first group (1,3 $\pm$ 0,1 and 1,4 $\pm$ 0,1, $p=$ of 0.219) from the first to the 6th day of hospitalization. In the second group and the source in the dynamics of the concentration of TNF a did not exceed reference values. Patients of the first group there was a significant increase of concentration of IL 1b (from 2.2 $\pm$ 0.1 to 4.8 $\pm$ 0,1,$p=0,032$) and decreased concentration of IL 6 (from 7.6 $\pm$ 1.6 in the first day to 5.7 $\pm$ 0,7, $p=0.026$) to the 6-th day of hospitalization. The level of IL 1b in both groups the source and in the dynamics exceeded the reference values, without significant differences between patients with MI and unstable angina. The level of IL 6 in the source and the dynamics were above reference values in patients of both groups, and in the first group the concentration of IL 6 was the original and 12 hours is slightly higher than in the second group, 6 days decreased the concentration of IL 6 in the first group and increased in the second. In patients and THEY identified a direct relationship to the concentration of copeptin with CRA (r=0.5, P=0.01), creatinine (r=0.46, $p=0.01$), CPK levels occur after 6 hours (r=0.45, $p=0.02$), troponin I (r=0.16, $p=0.04$) and TNF a (r=0.38, $p=0.04$).
Conclusions: the significant increase in the level of copeptin and proinflammatory markers in the dynamics was observed in patients with AMI, also revealed the direct correlation between copeptin with markers of inflammation and damage.

P1202

C-reactive protein decrease during hospitalization predicts medium and long term mortality only in heart failure patients with preserved ejection fraction

P Lourenco[1]; J Pereira[1]; A Ribeiro[1]; J Ferreira-Coimbra[1]; I Barroso[2]; JT Guimaraes[3]; P Bettencourt[3]
[1]*Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal*; [2]*Sao Joao Hospital, Department of Biochemistry, Porto, Portugal*; [3]*Faculty of Medicine University of Porto, Unidade de Investigação e Desenvolvimento Cardiovascular do Porto, Porto, Portugal*

Background: Inflammation has been associated with heart failure (HF) progression and worse prognosis. The prognostic role of high sensitivity C-reactive protein (hsCRP) in the acute HF setting is less well established and the impact of its variation widely unknown. We aimed to study the prognostic impact of hsCRP variation and if it differed in patients according to left ventricular function.
Methods: We analyzed patients prospectively included in an acute HF registry. All patients were drawn a venous blood sample at admission and discharge and an echocardiogram was performed during hospitalization. Both patients with HF with reduced ejection fraction (HFrEF) and those with HF with preserved ejection fraction (HFpEF) were eligible. Patients with acute coronary syndromes causing acute HF, patients with primary valvular disease, and those with missing data regarding admission or discharge hsCRP were excluded. Relative variation of hsCRP (ΔhsCRP) during hospitalization was calculated using the formula: [(admission hsCRP – discharge hsCRP)/ admission hsCRP]X100. Patients were followed up to 3 years and the endpoint under analysis was all cause-death. A multivariate Cox-regression model (variables in the model: age, gender, discharge BNP and hsCRP, NYHA class and infection occurrence) was used to assess the prognostic impact of ΔhsCRP (both as continuous and as a categorical variable: cut-off 40% decrease ¯ median value) and a stratified analysis according to left ventricular function (HFrEF and HFpEF) was performed.
Results: We studied 439 patients, mean age 75 years, 50.1% male and 69.2% had HFrEF. Median admission hsCRP was 20.0mg/L, and median discharge hsCRP was 12.4mg/L. HsCRP decreased during hospitalization in 294 (67.0%); median (IQR) ΔhsCRP was 38 (-22 to 73) %. During the 3-year follow-up 247 patients (56.3%) died, 73 (54.1%) in HFpEF patients and 174 (57.2%) in those with HFrEF. The multivariate-adjusted HR of 3-year mortality in HFpEF patients with hsCRP decrease$\geq$40% during hospitalization was 0.56 (95% CI: 0.32-0.99). A decrease$\geq$40% in hsCRP was not mortality-associated in HFrEF patients - HR=0.90; 95% CI: 0.64-1.26. There was interaction between ΔhsCRP and left ventricular dysfunction; p for interaction was of 0.02. Similar results were obtained when ΔhsCRP was analyzed as a continuous variable.
Conclusions: A decrease$\geq$40% in hsCRP in acute HF associated with a 44% decrease in the 3-year death risk in HFpEF patients. No association between ΔhsCRP and prognosis existed in HFrEF patients. The prognostic impact of hsCRP decrease was significantly different between HFpEF and HFrEF patients. Our results suggest that inflammation plays a different role according to left ventricular function.

P1203

Is there a c-reactive protein value beyond which one should consider infection as the cause of acute heart failure?

J Pereira[1]; A Ribeiro[1]; J Ferreira-Coimbra[1]; I Barroso[2]; JT Guimaraes[3]; P Bettencourt[3]; P Lourenco[1]
[1]*Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal*; [2]*Sao Joao Hospital, Department of Biochemistry, Porto, Portugal*; [3]*Faculty of Medicine University of Porto, Unidade de Investigação e Desenvolvimento Cardiovascular do Porto, Porto, Portugal*

BACKGROUND: Heart Failure (HF) is a condition that courses with low-grade inflammation.High sensitivity C-reactive protein (hsCRP) is an established inflammatory marker widely used in clinical practice. A cut-off value of hsCRP beyond which an infection should be sought has never been studied in HF. We aimed to determine the best CRP cut-off for infection prediction in acute HF.
Methods: We analyzed patients prospectively included in an acute HF registry. All patients were drawn a venous blood sample upon admission,hsCRP was measured. An infectious condition was considered according to the discharge diagnosis list as judge by the attending physician.A ROC curve was used to determine the best hsCRP cut-off for infection prediction. Variables associated with infection in acute HF were assessed using logistic regression analysis.RESULTS: We studied 615 acute HF patients. Mean age 76 years, 45.2% male,60.3% had systolic dysfunction. Median admission hsCRP was 20.3 (9.5-55.5)mg/L and in 41.6% an infection was the cause of decompensation. The area under the ROC curve for admission hsCRP in the prediction of infection was 0.79 (0.76-0.83). The best hsCRP cut-off for infection prediction was 25mg/L with a sensitivity of 72.7%, a specificity of 77.2%, a positive predictive value f 69.4% and a negative predictive value of 79.9%. Age and elevated hsCRP (continuous and categorical)were the only variables independently associated with concomitant infection(Table).
Conclusions: We suggest 25mg/L as a cut-off beyond which an infection should be sough as the cause of acute HF decompensation. Almost 80% of the patients with CRP < 25mg/L are not infected and 69.4% of those with higher CRP have a concomitant infection.

	OR (95% CI)	p-value
Age, per year	1.02 (1.00-1.04)	0.01
hsCRP≥25mg/L	8.96 (5.91-13.56)	< 0.001
Male sex	0.69 (0.44-1.08)	0.11
Diabetes mellitus	0.89 (0.72-1.09)	0.25
Coronary heart disease	0.69 (0.45-1.06)	0.09
Admission systolic blood pressure, per mmHg	1.00 (0.99-1.00)	0.24
Haemoglobin, per g/dL	0.94 (0.85-1.04)	0.26
BNP per 100 pg/mL	1.00 (1.00-1.02)	0.35
Creatinine per mg/dL	0.89 (0.68-1.17)	0.40
Left ventricular systolic dysfunction	0.78 (0.50-1.24)	0.30

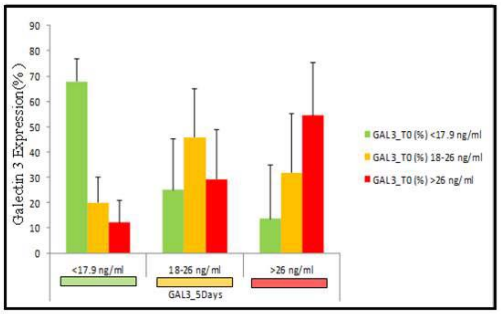
Predictors of an infectious condition underlying decompensated heart failure: multivariate model

P1204

Galectin-3 levels at presentation and left ventricular ejection fraction (LVEF) prediction in patients with STEMI/NSTEMI acute myocardial infarction. An observational study.

M Ciaccio[1]; B Lo Sasso[1]; BD Leoni[2]; C Scazzone[1]; L Agnello[1]; G Bivona[1]; D Butera[1]; S Favero[2]; C Bellia[1]
[1]*University of Palermo, Palermo, Italy*; [2]*Abbott Diagnostics , Rome, Italy*

Background and Aim: The role of circulating Galectin-3 (Gal-3), a fibrosis marker, as a predictor of Left Ventricular Ejection Fraction (LVEF) in patients with acute myocardial infarction (AMI) is poorly investigated. The aim is to investigate serum Gal-3 levels in patients presenting at the Emergency Department with AMI (STEMI and NSTEMI) in relationship with LVEF.
Patients and Methods: We enrolled 152 patients diagnosed with AMI and with either preserved (HFPEF, n=80) or reduced (HFREF; n= 72) ejection fraction, of whom 44 and 55 with STEMI and 36 and 17 with NSTEMI respectively. Serum Gal-3 levels were assessed by Architect i1000SR (ABBOTT Laboratories) at the baseline and after 5 days from presentation. A logistic multivariate curve regression model (MCRM) was developed for investigating Gal-3 and type of infarct contribution on early LVEF prediction. The diagnostic performance was assessed by ROC curve analysis.
Results: Independently from primary Percutaneous Coronary Intervention (pPCI) and AMI type, Gal-3 remained constant in nearly 60% of patients (< 17.8 ng/ml and >26 ng/ml). In NSTEMI patients log-transformed Gal-3 serum levels was higher in REF than PEF (P < 0.01). MCRM showed that Gal-3 (OR=0.974, 95% CI: 0.954-0.995 P=0.01) and infarct type NSTEMI/STEMI (OR=0.213, 95% CI: 0.125-0.471), P < 0.001), were independent influencing factors of the basal LVEF. ROC curve best cut point was at 22.8 ng/ml (AUC 0.658; 95% CI 0.513-0.803; Sensitivity= 0.88; Specificity= 0.47) in NSTEMI.
Conclusions: In NSTEMI patients serum Gal-3 basal values at presentation could be predictive of preserved or reduced LVEF with high sensitivity, but in STEMI this was not observed.



Gal-3 dynamics after 5 days

P1205

Predictors of adverse cardiac events in heart failure patients of different functional class

M G Kaliadka[1]; A K Alena Kurlianskaya[1]; T L Denisevich[1]; Y P Ostrovsky[1]
[1]*Research & Practical Centre "Cardiology", Minsk, Belarus*

Aim: To reveal predictors of adverse cardiac events in pts with different functional class (FC) of severity of heart failure (HF) by NYHA.
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

FCCHF	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%

P1206

Five years risk prediction in patients with heart failure: clinical data and biomarkers interaction

M Maria Coronel[1]; J Blanchet[1]; E Perna[1]; J Cimbaro Canella[1]; S Macin[1]; B Gonzalez Arjol[1]; F Medina[1]; M Brizuela[1]; L Borgo[1]
[1]*J.F. Cabral Cardiology Institute, Corrientes, Argentina*

Chronic heart failure (CHF) and acute heart failure (AHF) are associated with high short- and long-term morbidity and mortality. However, there are few data in our country about long term follow up of this condition.

Objectives: 1-To characterize long-term follow up of patients with heart failure. 2-To identify clinical variables and biomarkers related with long-term prognosis.
Methods: Between January and August 2011, 100 patients with CHF and 144 with AHF were prospectively included. At admission, high sensitivity Troponin T (HsTnT, ROCHE), BNP, CA 125 and urinary NGAL (ABBOTT) were measured. The end points were 5-years survival (SUR) and 5-years hospitalization free survival (HOSP-S).
Results: Mean age was 67 ± 13 years, male 68%, 41% had ischemic etiology, and 22% with ejection fraction ≥ 50%. The mean follow-up was 42 ± 23 months, median 54, interquartil range 16-62 months. The SUR at 66 months was 47 ± 3,5% and the HOSP-S was 28 ± 3%, without significant differences between CHF and AHF. The variables associated with SUR were COPD (p = 0.02), anemia (0.002), atrial fibrillation (0.002), hospitalization for AHF during last year (0.004), previous functional class (FC) 3-4 (0.001), age (< 0.001), creatinin (< 0.001), sodium (0.002), CA125 > 14 U/ml (0.02) and HsTnT > 23 ng/l (0.005): Independent predictors for mortality were COPD (p = 0.031; HR=1.6; 95%CI=1.05-2.5), FC 3-4 (< 0.001; 2.3; 1.5-3.4), age (0.001; 1.03; 1.01-1.04), creatinin (0.001; 3.6; 1.1-1.7), sodium (< 0.001; 0.94; 0.91-0.97) and HsTnT >23 ng/l (0.019; 1.69; 1.09-2.63). The variables associated with HOSP-S were COPD (p = 0.02), anemia (0.01), atrial fibrillation (< 0.001), hospitalization for AHF during last year (0.001), FC 3-4 (< 0.001), age (0.002), creatinin (< 0.001), sodium (0.04), BNP > 180 pg/ml (0.03) and HsTnT >23 ng/l (< 0.001). Independent predictors for HOSP-S were FC 3-4 (p < 0.001; HR=2.2; 95%CI=1.5-3.0), atrial fibrillation (0.001; 1.7; 1.2-2.4), age (0.029; 1.02; 1.01-1.03), creatinin (0.003; 1.2; 1.1-1.5), sodium (0.006; 0.96; 0.92-0.98) and BNP >180 pg/ml (0.003; 1.7; 1.2-2.4).
Conclusions: The five years follow up of patients with heart failure evidenced that only one out two survive, and one out three survive without hospitalization for AHF. Simple clinical variables could help to the early identification of poor outcome. A biomarker of myocardial damage appeared as mortality predictor whereas one of myocardial stress was associated with combined events

P1207

Abnormal potassium level predicts short-term readmissions in patients with acute dyspnea

R Zeimaite[1]; J Celutkiene[2]; D Aniulyte[3]; A Kavoliuniene[4]; A Mebazaa[5]; D Kablucko[2]; K Stasaitis[4]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; [2]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania; [3]Lithuanian University of Health Sciences, Faculty of Medicine, Kaunas, Lithuania; [4]Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania; [5]University Paris Diderot , U942 Inserm, Hospital Lariboisière, Paris, France

On behalf of: GREAT network
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Introduction: Potassium imbalance is included in some clinical risk scores to assess the prognosis of acute heart failure (AHF) patients. The importance of hypo-/hyperkalemia in prediction of short-term outcomes in a wide population of acute dyspnea patients is less clear.
Purpose: We aimed to evaluate the prognostic value of abnormal blood potassium levels in prediction of short-term mortality and readmissions in acute dyspnea patients.
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the emergency department with acute dyspnea due to AHF and other reasons. Blood potassium levels at the time of admission and number of deaths and rehospitalizations due to cardiovascular and other reasons in 1 and 3 months of follow up were collected. Data of 445 study patients (mean age 68 years) were included in the analysis. Hypokalemia and hyperkalemia were defined as blood potassium level <3.8 mmol/l and >5.2 mmol/l, respectively. Data were analyzed using SPSS v23 statistical package with binary logistic regression.
Results: Of 445 patients (185 female) 101 subjects (22.7%) were hypokalemic, 330 – normokalemic, 14 (3.1%) had hyperkalemia. AHF was diagnosed in 243 patients (54.6%); other diagnoses in 201 (45.2%) remaining participants included atrial fibrillation (7%), exacerbation of COPD/asthma (11.4%), pulmonary embolism (6%), pneumonia (16.4%), acute coronary syndromes (6.2%). Hypo- and hyperkalemia were found in 21.4% and 2.9% of AHF patients. Regardless of the presence of AHF diagnosis hypokalemia was associated with significantly increased risk of 3-month cardiovascular readmissions and 1-month non-cardiovascular readmissions, OR=1.024 (CI 0.998;1.050) and OR=2,189 (CI 1.023;4.686), respectively (p < 0.05). Hyperkalemia was a significant predictor of 3-month cardiovascular readmissions with OR=4.489 (CI 1.319;15.274). No significant association of abnormal potassium level with 1- or 3-month all-cause or cardiovascular mortality was found.
Conclusions: In prospective observational cohort one in four patients with acute dyspnea were found to have abnormal potassium level at admission. Both hypo- and hyperkalemia independently of final diagnosis are associated with higher rate of short-term readmissions due to cardiovascular as well as non-cardiovascular reasons.

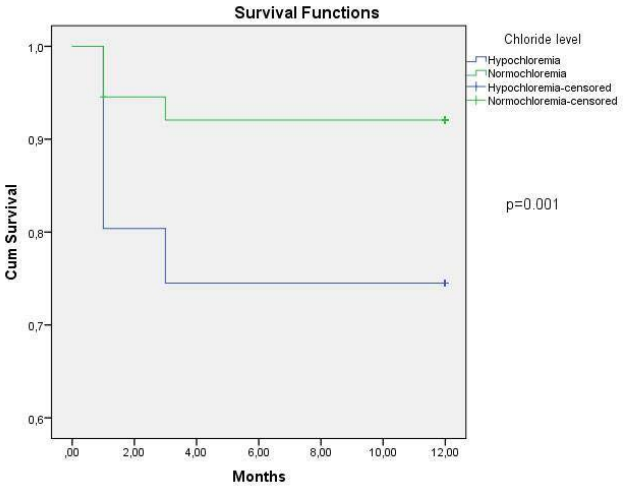
P1208

Prognostic value of hyponatremia and hypochloremia in patients with dyspnea

J Bugaite[1]; D Gabartaite[1]; V Juknevicius[2]; A Mebazaa[3]; J Celutkiene[2]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; [2]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania; [3]University Paris Diderot , U942 Inserm, Hospital Lariboisière, Paris, France

On behalf of: GREAT network
Funding Acknowledgements: The work was supported by the Research Council of Lithuania, grant Nr. MIP-049/2015 and approved by Lithuanian Bioethics Committee, Nr. L-15-01.

Introduction: Hyponatremia and hypochloremia have been reported as important predictors of mortality in acute heart failure (AHF). The prognostic significance of low sodium and chloride level in a wider population of patients with acute dyspnea is unknown.
Aim: To evaluate whether hyponatremia and hypochloremia had a significant value in predicting short-term rehospitalizations and mortality of patients with acute dyspnea admitted to the emergency department.
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the emergency department with acute dyspnea due to decompensated HF, exacerbation of chronic obstructive pulmonary disease (COPD), pneumonia, pulmonary embolism and other reasons. Electrolyte concentration on admission and rate of mortality and rehospitalizations at 1 and 3 months follow up were collected. Data of 307 study patients (mean age 68.4 ± 12.7 years) were included in the analysis. The study group consisted of 143 women (46.6%) and 164 men (53.4%). Data were analyzed using SPSS v23 statistical package using Cox proportional-hazards regression analysis. A p-value < 0.05 was considered statistically significant.
Results: On admission 8.8% of patients had hyponatremia (sodium concentration < 134 mmol/l) and 16.6% were hypochloremic (chloride concentration < 98 mmol/l). Patients with hyponatremia had greater chance to be rehospitalized due to all causes (hazard ratio [HR] = 2.6; 95% confidence interval [CI]: 1.48 to 4.55; p = 0.001) and due to cardiovascular causes during 3 months period (HR = 3.31; 95% CI: 1.45 to 7.58; p = 0.005). There was no statistically significant association between hyponatremia and patients' mortality in three months period. Admission serum chloride level during hospitalization for acute dyspnea was independently associated with 3-month mortality (HR = 3.36; 95% CI: 1.62 to 6.99; p = 0.001), but not with rehospitalizations. AHF was the main cause of admission to the hospital in hyponatremic and hypochloremic groups (respectively 81.48% and 78.43%), other causes were pulmonary embolism, COPD, hydrothorax, pneumonia, bronchitis, sepsis, pulmonary carcinoma and B cell lymphoma. In hyponatremia group patients with AHF were rehospitalized more often than non-AHF patients (p = 0.045). However, there was no statistically significant difference in deaths of AHF and non-AHF patients with hypochloremia. No statistically significant correlation between blood electrolytes concentration and diabetes mellitus or renal disease was found.
Conclusion: Sodium and chloride concentrations are significant predictors of outcomes in acute dyspnea patients admitted to the emergency department. Hypochloremia is more hazardous to patients' outcomes compared to hyponatremia.



Kaplan-Meier curve of survival

P1209

Predictive value of a novel 4- miRNAs diagnostic panel after acute myocardial infarction: Independent validation from the MITOCARE study

E Eric Schordan[1]; S Schordan[1]; TS Hall[2]; AI Larsen[3]; D Erlinge[4]; SE Jensen[5]; S Halvorsen[2]; D Atar[2]; H Firat[1]; Y Devaux[6]
[1]Firalis SAS, Molecular Diagnostics, Huningue, France; *[2]Ulleval University Hospital, Department of Cardiology B, Oslo, Norway*; *[3]Stavanger University Hospital, Department of Cardiology, Stavanger, Norway*; *[4]Lund University, Department of Cardiology, Lund, Sweden*; *[5]Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark*; *[6]CRP-Sante, Cardio Vascular Research Unit, Luxembourg, Luxembourg*

On behalf of: Cardiolinc network
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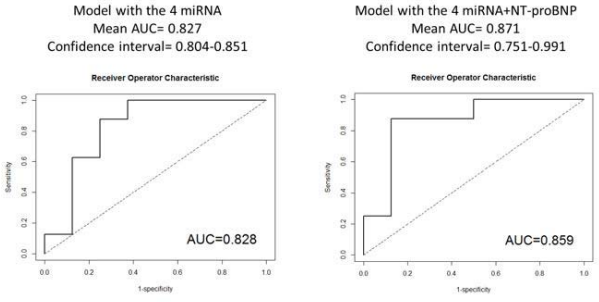
Following acute myocardial infarction (AMI), a significant proportion of patients develops heart failure (HF) due to left ventricular remodelling (LVR). The early identification of patients developing LVR is essential for evidence-based intervention and pharmacological therapy. Novel biomarkers might pave the way for improved prediction approaches. Since the discovery of their stability in the bloodstream, miRNAs, short oligonucleotides which down-regulate gene expression, have been extensively studied for their potential to diagnose AMI. We previously identified a panel of 4 circulating miRNAs (miR-16-5p/27a-3p/101-3p/150-5p) able to significantly improve the prediction of post-AMI LVR by a multivariable clinical model including N-terminal pro-brain natriuretic peptide (Nt-pro-BNP). In the present study, we aimed to confirm the predictive value of the 4-miRNA panel in an independent cohort obtained from the MITOCARE study, a prospective randomized clinical trial conducted from 2011 to 2013. We enrolled 90 patients with STEMI treated by primary PCI. The HTG EdgeSeq targeting sequencing platform was used to assess the levels of miRNAs in plasma samples collected 3 days after AMI. Cardiac function was assessed by echocardiography at discharge and after 1 month. Left ventricular ejection fraction (LVEF) at 1 month was used to classify patients into 3 categories: LVEF < =40 (n = 14), LVEF between 41 and 50 (n = 34) and LVEF>50 (n = 41). Random forest model was used for predictive modelling and individual AUC, and confidence intervals (CI) were calculated for each miRNA. miR-16-5p/27a-3p/101-3p/150-5p individual AUC were 0.81, 0.75, 0,84 and 0,61, respectively. The combination of the set of 4 miRNAs showed an average AUC of 0.83 (CI 0.80-0.85). Combining the 4 miRNAs with NT-pro-BNP resulted in an AUC of 0.87 (CI 0.75 and 0.99). In conclusion, we here confirm the independent predictive value of the 4 miRNAs (miR-16-5p/27a-3p/101-3p/150-5p) for the prediction of HF development after AMI. HTG EdgeSeq technology proves to be an efficient and clinically-applicable tool to measure circulating miRNAs. These results motivate the development of molecular diagnostic kits based on miRNAs to aid in outcome prediction after AMI.



ROC Curve

P1210

Identification of novel biomarkers for prediction of clinical outcome in acute myocardial infarction patients by Olink platform.

S Sandra Schordan[1]; T Nuhrenberg[2]; P Ruile[2]; E Schordan[1]; A Mostefai[1]; H Firat[1]; D Trenk[2]; FJ Neumann[2]
[1]FIRALIS SAS, Research and Developement, HUNINGUE, France; *[2]University Heart Center Freiburg-Bad Krozingen, Bad Krozingen, Germany*

On behalf of: CardioSAVE research consortium
Funding Acknowledgements: EuroTransBio

Introduction: Early diagnosis, Percutaneous Coronary Intervention (PCI) and biomarkers have contributed substantially to the treatment of Acute Myocardial Infarction (AMI) by reducing the size of the infarct and mortality due to cardiac ischemia. Despite advances in care, prognosis in term of Heart Failure (HF) remains poor. Once HF has developed, 30 to 40% of patients die within one year and 60 to 70% within 5 years of diagnosis. The earlier patients who are prone to develop HF are identified, the more efficiently a prophylactic treatment can be adapted.
Aim: The aim of this project is to identify new biomarkers for the prediction of HF and translate this into a diagnostic test for risk stratification, prognosis and monitoring of treatment response for AMI patients after PCI treatment.
Material and Methods: Blood samples and patient data were collected in the frame of the CardioSAVE study, a prospective 12-months longitudinal study, for risk stratification of AMI patients undergoing PCI, with a one year follow-up conducted at our Heart Center. Patients were selected according their LVEF < 40% or >50% at 6 months (M6) assessed by echocardiography. Plasma samples collected on day 3 (D3) after MI were analyzed for 92 biomarkers (BM) on the Proseek Multiplex CVD II (human cardiovascular and inflammatory markers) panel from Olink on the Biomark HD Platform. This innovative technology is based on a dual recognition of antibody-pairs and oligonucleotides called proximity extension assay.
Results: Six AMI patients with LVEF < 40% and 6 AMI patients with LVEF>50% at 6 months were analyzed. A differential expression was observed for 20 BM between both groups. Five BM exhibit an increase of the expression at D3 in the group with reduced ejection fraction at M6, whereas 15 BM decreased their expression at D3 in the group with reduced ejection fraction at M6.
Conclusion: The selected biomarker panel profile will be further investigated and developed on a diagnostic prototype. The reliability and accuracy of the novel diagnostic kit will be tested in a clinical setting to achieve Proof of Concept. Upon complete validation, this tool may serve as a personalized medicine device focusing on HF allowing the identification and risk stratification of AMI patients in low- and high risk groups after undergoing PCI.

P1211

Echocardiographic and neurohormonal correlations of plasma galectin-3 in adult patients with congenital heart disease.

A Alexandra Frogoudaki[1]; I Pantelakis[1]; D Birba[1]; V Bistola[1]; I Ikonomidis[1]; J Parissis[1]; D Alexopoulos[1]; G Filippatos[1]; J Lekakis[1]
[1]Second Cardiology Department, Athens University, ATTIKON University Hospital, Athens, Greece

Introduction: Galectin-3 is a β-galactoside–binding lectin and is best known for its role as a mediator of tumor growth and metastasis. In addition galectin-3 plays a role in inflammatory and immune-mediated disorders as well as in fibrogenesis, mechanisms involved in the progression of heart failure and cardiac remodelling. It has an important and significant prognostic value in identifying patients with heart failure at elevated risk for subsequent morbidity and mortality. However, no efficient data exist regarding the relationship of plasma galectin-3 levels and cardiovascular abnormalities in congenital heart disease.
Aim of the study was to look at echocardiographic and neurohormonal correlations of plasma galectin-3 in adult patients with congenital heart disease.
Methods: We studied 57 clinically stable patients (31 men, mean age 37.1 ± 16.9) with congenital heart disease. Fourty-nine had systemic left ventricle, 5 systemic right ventricle and 3 single ventricle physiology. All patients underwent echocardiographic study and NTproBNP and galectin-3 plasma levels were measured. For parameters with normal distribution Pearson correlation analysis was performed while for parameters withoutnormal distribution Spearman correlation analysis was performed.
Results: Mean galectin-3 value was 16,93 ± 6.39ng/ml. Mean NTproBNP value was 265.25pg/ml (range 18.7 pg/ml-3788pg/ml). Plasma galectin-3 levels correlated with LogNTproBNP (r=0.469, p = 0.001) and left atrial diameter (r=0.316 p = 0.025). Galectin-3 plasma levels didn't correlate with age, systemic ventricle ejection fraction, subpulmonary ventricle pressure, and subpulmonary ventricle function indices (annulus systolic excursion and systolic tissue Doppler velocity).
Conclusion: Galectin-3 plasma levels correlated with plasma NTpro BNP as well as left atrial diameter indicating that systemic ventricular fibrosis and/or left atrium may be included in the causes of increased systemic ventricle end-diastolic pressure in adult patients with congenital heart disease.

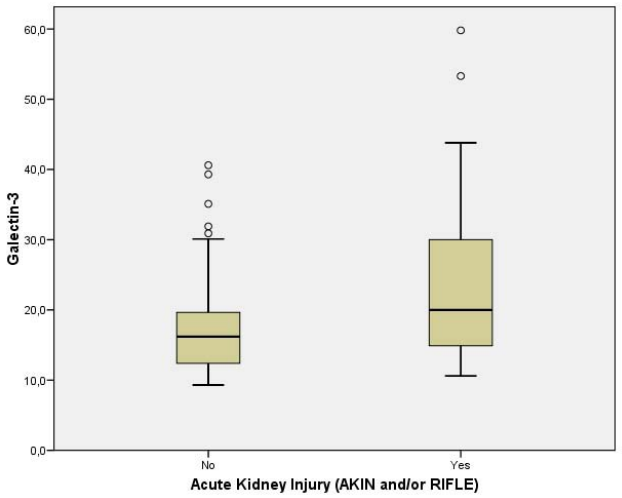
P1212

Prognostic value of Galectin-3 as predictor of acute kidney injury in acute heart failure hospitalization

J Juan Sanchez Serna[1]; M Navarro Penalver[1]; JJ Santos Mateo[1]; MT Perez Martinez[1]; A Lax[1]; MC Asensio Lopez[1]; J Sanchez Mas[1]; DA Pascual Figal[1]
[1]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiología, Murcia, Spain

Background: Elevated levels of Galectin-3 (Gal-3) have been associated with worse prognosis in acute heart failure (AHF). These may be influenced by the presence of

renal failure. However, it is unknown if Gal-3 can identify a worse renal prognosis.
Purpose: We intend to study whether Gal-3 concentrations in AHF admissions identify patients at higher risk of acute kidney injury (AKI).
Methods: We studied 111 patients admitted for AHF (61% men, 71 ± 11 years, LVEF 45 ± 15%). Gal-3 determinations were made on admission with a commercial assay (Biomerieux). Serum creatinine (Cr) value and glomerular filtration rate (GFR) during admission and baseline values before admission were collected. Two validated criteria were used to define AKI: RIFLE (increase ≥1.5 times of Cr or decrease of GFR ≥25% respect to baseline values or diuresis ≤0.5 mL/kg/h for 6 hours) and AKIN (increase ≥0.3mg/dl or ≥150% Cr within 48 hours of hospitalization or diuresis ≤ 0.5 mL/kg/h for 6 hours).
Results: Gal-3 levels at admission were 20.7 ± 11.9 ng/mL. During hospitalization, 24 (21.6%) patients presented AKI according to the AKIN criteria; 43 (38.7%) according to RIFLE criteria; and 46 (41.4%) according to AKIN and/or RIFLE. Based on the AKIN/RIFLE criteria, Gal-3 levels were higher in patients who developed AKI (18.79 vs 23.32, $p = 0.049$) (Figure). The ROC analysis showed an area under the curve of 0.66 (95% CI 0.55-0.76, $p < 0.01$). The best prediction point was 17.2 ng/mL. Considering this value, patients with higher levels had an increased risk of AKI (OR 2.83, 95% CI 1.28-6.23, $p < 0.01$). In the multivariate analysis taking into account age, sex, normal LVEF (> 55%) and preserved renal function (GFR> 30 ml/min/1.73m2), the predictive value of Gal-3> 17.2 ng/mL lost the statistical significance (OR 2.23, 95% CI 0.93-5.33, $p = 0.07$).
Conclusions: In patients admitted for AHF, Gal-3 on admission identified an increased risk of deterioration of renal function during hospitalization. After adjustment for known renal dysfunction factors, Gal-3 levels maintained a non-significant trend, suggesting the need for new studies with larger populations.



Figure

P1213

Biomarkers of systemic inflammation, hemodynamic stress, degradation of the extracellular matrix and adverse left ventricular remodelling in primary anterior STEMI patients

M Kercheva[1]; T Ryabova[1]; A Gusakova[1]; V Ryabov[2]
[1]Research Institute for ?ardiology, Emeregency cardiology department, Tomsk, Russian Federation; *[2]National Research Tomsk State University, Translational laboratory of cellular and molecular medicine, Tomsk, Russian Federation*

Purpose: to assess the impact of matrix metalloproteinases (MMP)-2, 3, 9, ST2, IL1β, hCRP, NTproBNP on the adverse left ventricular remodeling (LVR) in patients with acute primary anterior STEMI.
Methods: 21 pts with primary anterior STEMI (mean age 60.5 ± 7.4) were enrolled. Blood samples were determinated by the immunoassay - on the 1st (T1), 3d (T2), 7th (T3), 14th (T4) days of STEMI and 6 month after STEMI (T5). Echocardiography with 2D speckle tracking imaging was performed at the same period, without the point T1 ('Vivid E9'). Pts were divided into 2 groups: ST2>35 ng/ml and ST2 < 35 ng/ml at T1.
Results: All of them had urgent reperfusion therapy, in third of events it was during the first 3 hours. MMP-2 from T1 to T5: 224.9 ± 84.1→190.6 ± 63.9→224.5 ± 90.1→233.3 ± 70.3→262.9 ± 96.3 ng/ml ($p > 0.05$). MMP-3 increased from T1 to T3, then to T5: 14.2 ± 14.4→19.9 ± 14.9→23.3 ± 8.7 ng/ml ($p < 0.05$). MMP-9 decreased at the same terms: 905.9 ± 772.4→538 ± 520.6→365.5 ± 449.4 ng/ml ($p < 0.05$). IL1β decreased from T1 to T4:1.2 ± 0.4→0.9 ± 0.4 pg/ml ($p < 0.05$). NTproBNP and hCRP decreased from T1 to T5 and T1 to T4, respectively: 456.8 ± 359.3→198.8 ± 139.5 pg/ml ($p < 0.05$) and 7.1 ± 3.7→3.4 ± 2.8 mg/l ($p < 0.05$). ST2 decreased from T1 to T5: 90.5 ± 83→46.3 ± 35.4→30 ± 11.3→28.7 ± 7.8→28.7 ± 8.8 ng/ml ($p < 0.05$). Assessment of echocardiography shown, that in groups ST2>N and ST2<N:>
Conclusion: The dynamics of markers had the different directions. The level of MMP-2 was without significant dynamics. The level of MMP-3 increased to T3 and it have been continued to T5, however the level of MMP-9 had the reverse dynamics at the same period. IL1β and hCRP decreased to T4, as NTproBNP, but to T5. ST2 decreased at all observation period to T5. In addition, ST2 had the most predictive value. Its level more than 35 ng/ml at T1 was associated to the presence of the systolic dysfunction – the bigger value of wall motion score index, end-systolic volume, 2D global longitudinal strain and the smaller value of ejection fraction in the early post-infarction period.</N:>

P1214

Biomarkers of fibrosis, inflammation, renal dysfunction and its correlations in patients with HFpEF and HFmrEF

EA Medvedeva[1]
[1]Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation

There is extensive research on biomarkers in heart failure (HF) patients. However, only a few studies have reported an association between different biomarkers in HF with preserved and mid-range ejection fraction.
Objective: To evaluate concentrations of biomarkers of fibrosis, renal dysfunction, inflammation, and their correlation in patients with chronic heart failure (CHF) with prior myocardial infarction (MI) and ejection fraction (EF) ≥40%. Design and Methods. The study included 103 patients with HF with preserved (HFpEF, EF>50%) and mid-range ejection fraction (HFmrEF, EF: 40-49%). Criteria of inclusion were prior MI and primary PCI in history, NTproBNP level>125pg/ml. As a comparison group we included 51 patients with prior MI and PCI, without signs of HF and with level of NT-pro BNP < 125pg/ml. All patients underwent a comprehensive clinical assessment, echocardiography. There was valued the level of galectin-3, ST-2, hs-CRP and cystatin-C by immunoassay analysis. The estimated glomerular filtration rate (e-GFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. All statistical analysis was performed with Statistica 6.0. Continuous variables were described by median (1st -3rd quartile). 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: In the study group (1st), the level of NT-proBNP was 445.23 (245.9-896.93) pg/ml, in a comparison group (2nd) - 67.16 (40.17-86.61) pg/ml. The plasma level of ST-2 in the 1st and 2nd groups were 40.70 (33.45-49.27) ng/ml and 39.21 (32.64-46.38) accordingly, we did not observe significant difference between groups ($p > 0.05$). We found significant correlations between the level of biomarkers for fibrosis and myocardial stress only in patients with CHF: ST-2-NT-proBNP ($r1 = 0.36$, $p < 0.01$), galectin-3-NT-proBNP ($r1 = 0.38$, $p < 0.01$). Renal dysfunction was observed in both groups. The plasma concentration of cystatin C in the 1st group was 987.67 (854.68-1161.19) ng/ml, e-GFR - 58.5 ml/min/1.73m2 (44.0-79), there was not significantly different from 2nd group. The correlation analysis showed the following significant correlations: strong negative correlation in a pair of galectin-3-e-GFR ($r1 = -0.49$, $p < 0.01$) and positive between galectin-3 and cystatin C ($r1 = 0.62$, $p < 0.01$) in patients with CHF. Moreover, galectin-3 correlated with plasma level of hs-CRP ($r1 = 0.56$, $p < 0.01$), in the comparison group significant correlations were not observed.
Conclusions: The levels of biomarkers for fibrosis, inflammation and renal dysfunction in patients with prior MI and PCI were comparable in groups with HF with EF>40% and without HF. The plasma concentration of ST-2, galectin-3 correlated with the concentration of NTproBNP in HF patients. Galectin-3 also correlated with renal dysfunction and inflammation in HFpEF/HFmrEF patients with prior MI.

P1215

Lower platelet-to-lymphocyte and platelet-to-neutrophil ratios in ST-segment elevation myocardial infarction complicated with cardiogenic shock

A Scridon[1]; RC Serban[1]; L Hadadi[1]; I Sus[1]; EK Lakatos[1]; Z Demjen[2]; D Dobreanu[1]
[1]University of Medicine and Pharmacy of Tirgu Mures, Tirgu Mures, Romania; *[2]Institute of Cardiovascular Diseases, Targu Mures, Romania*

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Background: Low platelet-to-neutrophil (PNR) and platelet-to-lymphocyte (PLR) ratios have been associated with worse prognosis in patients with coronary artery

disease. However, it remains unknown if they are also able to predict more severe status at presentation with ST-segment elevation myocardial infarction (STEMI).
Purpose: We aimed to investigate whether PNR and PLR are associated with the presence of cardiogenic shock (CS) on admission for STEMI.
Methods: We evaluated data from 428 consecutive patients admitted for STEMI. Total and differential leukocyte and platelet count were obtained for all patients at hospital admission, within 24-h after symptoms onset, and PNR and PLR were evaluated. Association of these markers with the presence of CS on admission was assessed.
Results: CS was present at admission in 4.90% of STEMI patients. Patients with CS had more frequently a history of myocardial infarction ($p < 0.01$), heart failure ($p < 0.01$), and chronic kidney disease ($p = 0.02$). CS on admission was associated with higher leukocyte ($p < 0.0001$), lymphocyte ($p = 0.02$), and neutrophil ($p = 0.001$) counts and lower platelet count ($p = 0.02$). PNR (17.03 ± 7.82 vs. 31.61 ± 14.13, $p < 0.0001$) and PLR (90.68 ± 62.83 vs. 157.06 ± 129.44, $p = 0.001$) were both significantly lower in patients presenting with CS. In multiple regression analysis, both lower PNR (r=-0.20, $p = 0.0001$) and PLR (r=-0.14, $p < 0.001$) remained independent predictors of CS.
Conclusions: In patients with STEMI, the presence of CS on admission was associated with significantly lower PNR and PLR values. The potential of these readily available blood markers to predict the severity of hemodynamic impairment at presentation with STEMI deserves to be further studied.

P1216
Correlation between blood levels of S100b protein and incidence of heart failure or IMA in a cardiology unit

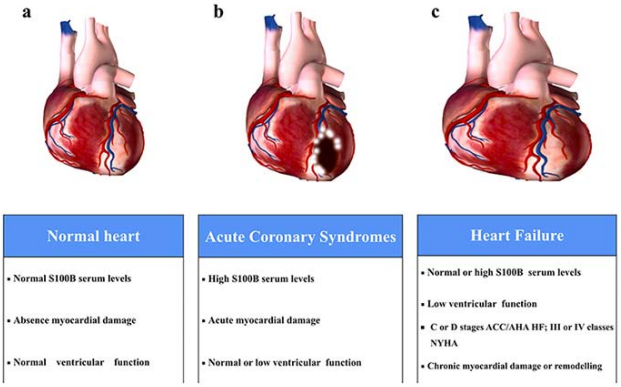
S Sebastiano Quartuccio[1]; E Imbalzano[1]; E Di Salvo[1]; G Trapani[1]; G Lizio[1]; M Casciaro[1]; S Gangemi[1]
[1]*University of Messina, Department of Clinical and Experimental Medicine, University of Messina, Italy, Messina, Italy*

Background/Introduction: Chronic heart failure is one of the most common consequence of myocardial infarction, and is characterized by a reduction of the heart ability to face peripheral blood distribution. Chronic heart failure (HF) and myocardial infarction (IMA) are often associated to the augmentation of inflammation markers. S100B is an alarmin secreted by damaged cardiomyocites. Serum S100B levels were increased in the pathogenesis of heart disease and involved their pathogenetic mechanisms. S100B is a tissue-specific protein (chondrocytes, adipocytes, skeletal myofibers, cardiomyocytes, dendritic cells, etc.); it was largely demonstrated to be released after a damage and the consequent remodelling involving cardiac tissue.
Purpuse: We examined the correlation between S100B protein serum levels and the incidence of acute heart failure and IMA in symptomatic patients.
Methods: We conducted a prospective study on 90 patients aged between 50 and 72 years accepted to our Unit referring cardiac associated symptoms (thorax pain, dyspnea, arrhythmic symptoms). They were divided in three groups: healthy subjects (group A), chronic heart failure patients (group B) and IMA patients (group C). CRP, NT-proBNP, and routine exam were performed in every patient. Moreover it was made a S100B dosage was made.
Results: Results demonstrated different levels among healthy subjects. However in chronic heart failure patients the alarmin levels were higher but not significantly augmented. Instead AMI patients had mean values of S100B doubled than the other two groups and significantly augmented.
Conclusions: According to our data S100B as the potential to be, in a near future, be considered as an acute myocardial infaction marker in addiction to the ones existing. However more studies are needed to identify possible byas elements in S100B serum dosage. This together with other elements are guiding us to a better understand of micro-structural changes in damaged heart in order to consider new therapeutic targets.

Tab. Groups

	Group A	Group B	Group C
Patients	30	30	30
Nt-pro-BNP	45 + 23	800 + 150	230 + 67
Crp	2 + 7	5 + 6	7 + 7
S100b	3,6 + 2,2	4,3 + 2,5	7,7 + 4,7

Serum levels of markers of inflammation in the different groups at the moment of access in cardiology unit



S100b and heart

P1217
The apelin relations with cardiac remodeling in the hypertension patients with type 2 diabetes

K Kostiantyn Yushko[1]; S Koval[1]; T Starchenko[1]
[1]*L.T.Malaya Institute of Therapy, NAMS of Ukraine, Kharkiv, Ukraine*

Purpose. The peptide apelin has antihypertensive and antidiabetic properties, but its role in the processes of cardiac remodeling in patients with hypertension and type 2 diabetes (T2D) isn't understood. The aim of the study was to investigate apelin levels in patients with hypertension and T2D and to determine its relations to heart structural parameters and types of cardiac remodeling.
Methods: We examined 63 hypertension patients grades 2-3 with concomitant T2D (33 men and 30 women), aged 43 to 70 years. The investigation complex included physical examination, standard transthoracic echocardiography and determination of apelin serum levels by ELISA. Types of cardiac remodeling we determined according to ESH/ESC 2013. Control group consisted of 16 volunteers.
Results: The apelin levels in patients with hypertension and T2D were significantly lower than in volunteers (0,882(0,788;0,924) ng/ml versus 1,097(0,944;1,171) ng/ml, $p < 0,001$). Negative correlation relations of apelin with septal wall thickness (r=-0,50, $p < 0,001$), posterior wall thickness (r=-0,46, $p < 0,001$), left ventricle (LV) mass (r=-0,39, $p < 0,01$), LV mass index (r=-0,42, $p < 0,001$) and left atrium size (r=-0,45, $p < 0,001$) have been observed. Among patients with hypertension and T2D concentric remodeling of LV was observed in 10 patients (16%), concentric LV hypertrophy was observed in 29 patients (49%) and eccentric LV hypertrophy was observed in 24 patients (38%). In patients with concentric remodeling of LV apelin levels were 0,918 (0,892; 0,984) ng/ml, with concentric LV hypertrophy – 0,855(0,722;0,899) ng/ml, with eccentric LV hypertrophy – 0,884(0,856;0,929) ng/ml ($p < 0,05$, $p < 0,001$, $p < 0,001$ versus control respectively). Patients with concentric LV hypertrophy had significantly lower apelin levels than patients with concentric remodeling of LV, $p < 0,05$.
Conclusion: In hypertension patients with T2D compared with healthy individuals the significant reduction of apelin blood levels has been found. Reduced blood levels of apelin are accompanied by the development of cardiac remodeling primarily concentric LV hypertrophy. Negative correlation of apelin with major heart structural parameters that characterize the LV remodeling and size of left atrium have been observed. The data allow us to consider apelin as an important prognostic marker of progression of hypertension with T2D, the development of pathological remodeling of the left ventricle and left atrium of the heart.

P1218
Can serum prolactin level determine the severity of acute decompensated heart failure?

M Chitsazan[1]; A Amin[1]; F Shioukhi[1]; M Chitsazan[2]
[1]*Rajaei Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Heart Failure and Trasnplantation, Tehran, Iran (Islamic Republic of)*;
[2]*Shahid Beheshti University of Medical Sciences, Tehran, Iran (Islamic Republic of)*

Background: Recent investigations have shown increased serum prolactin (PRL) level in chronic heart failure. However, data regarding PRL level and its prognostic implications in patients with acute decompensated systolic heart failure are lacking.
Purpose: The aim of this study was to evaluate the association between serum PRL level and functional, biochemical and echocardiographic indices of severity of heart failure in patients admitted with acute decompensated systolic heart failure.

Methods: All patients with advanced systolic heart failure [left ventricular ejection fraction (LVEF) of <30%) who were admitted for a recent acute decompensation were enrolled. The serum PRL level was measured on admission.
Results: A total of 86 patients (73% male), aged 48 ± 19 years with median LVEF of 15% (IQR, 10-20) were included. The median PRL level was 20.31 ng/mL (IQR, 14.77-33.53). The male and female patients had statistically similar PRL levels [18.80 ng/mL (14.38-28.90) versus 23.44 ng/mL (14.98-43.40)] (p = 0.21). The PRL levels were also statistically comparable among patients with NYHA function classes of II, III and IV (p = 0.07). No significant correlations were found between PRL level and LVEF (r=0.03, p = 0.75), NT-proBNP (r=0.07, p = 0.51), high-sensitivity C-reactive protein (r=-0.06, p = 0.67), erythrocyte sedimentation rate (r=0.05, p = 0.59), sodium (r=-0.04, p = 0.69), creatinine (r=0.04 , p = 0.66) uric acid (r=0.10, p = 0.39) and duration of hospitalization (r=-0.01, p = 0.89).
Conclusion: The serum PRL level does not seem to be an indicator of severity of acute decompensated systolic heart failure.

NURSING

P1219
Theoretical and practical training of students from vocational public high school to care for cardiac arrest: a prospective study in a developing country

VF Vanessa De Freitas Marcolla[1]; ER Santos[1]; LP Moura[1]; IPB Aragao[1]; DC Albuquerque[2]; E Ferreira[2]; ILPB Aragao[3]; AA Aragao[1]; CBOC Naves[2]; EPS Porto Neto[1]; ECS Peixoto[1]; AL Viana[1]
[1]Governo do Estado do Rio de Janeiro, Rio de Janeiro, Brazil; *[2]Rio de Janeiro State University (UERJ), Rio de Janeiro, Brazil*; *[3]Severino Sombra University, Vassouras, Brazil*

Cardiovascular diseases are the leading cause of death in the world, sudden cardiac arrest is a major contributor to this index. Training reduces the ignorance and fear, increasing safety to recognize that the victim is not breathing properly, so as to trigger the help and start CPR as soon as possible.
Objective: To apply a theoretical-pratical trainning of vocational public high school, to work correctly, quickly and safely before a cardiopulmonary arrest, resuscitation maneuvers running efficiently, in order to save lives.
Methods: This study was designed as a prospective investigation in more than 1800 students of vocational public high school, between 2012 and 2015. The program of theoretical and practical training lasts 2 hours. Each student attends a lecture with video on the subject for 30 minutes after 30 minutes of classroom practice. Then, using practical training mannequin, which are assessed through a performance checklist. A questionnaire was distributed before the start of training to see if the student had prior knowledge about a rescue in the event of cardiac arrest.
Results: A half of this students did not have any knowledge about the subject. This evaluation showed that after 2 hours of training and analyzed the performance checklists: 84% knew how to perform the procedures call for help effectively, 27% were able to recognize the absence of breathing, 31% positioned themselves and began of chest compressions recommended form.
Conclusion: Students from that school are represented by 90% of adolescents when trained are able to act in the scene of a cardiac arrest, multiply the knowledge to family and community and save lives. However, according to the international recommendations of retraining as an ideal that does not exceed two years.

P1220
Oral health assessment and referral guidelines: an evidence-based practice change

SJ Jasmine Demos[1]
[1]Sinai Hospital, Heart Failure Center, Baltimore, United States of America

Background: The World Health Organization (WHO) and the Institute of Medicine (IOM) have identified oral health disease as a growing epidemic of systemic disease burden on individuals and a cost burden onto the health care system. Significant correlations exist between improved oral hygiene and the reduction of morbidity and mortality from cardiovascular disease. The poor dental health status of outpatient clinic patients continues to be an unaddressed clinical concern encountered by health care providers. Individual barriers to obtaining dental health care include cost and the inability to access preventative dental services.
Purpose: Identify the incidence of oral health disease in an outpatient clinic setting, utilize an evidence-based practice (EBP) solution, and implement an effective intervention to address this concern.
Methods: A convenience sample of 36 adult English speaking outpatient clinic patients at an urban hospital in Maryland were included in the 6 week pilot study. The mean age of the participants was 53.5, 41.66% Males (n = 15), and 58.33% Females (n = 21), of which 66.6% were African Americans (n = 24), and 33.3% were Caucasians (n = 12). The Brief Oral Health Status Examination (BOHSE) tool was utilized as a valid and reliable oral screening tool to identify poor dental conditions needing urgent dental referral. A 10 item Dental Health Knowledge Questionnaire (DHKQ) was completed by participants prior to and after receiving dental education, and results were obtained via a comparative trend analysis.
Results: All participants, (100%, [n=36]) identified with oral health disease, received dental health education and were referred for low cost dental intervention. Statistical analysis of the effectiveness of the EBP change was determined by a paired-samples t-test. The mean dental knowledge scores improved from a pre DHKQ score of 78.3 % to a mean post DHKQ score of 98.4%. A significant increase in participant dental health knowledge, (p = 0.001) from the pre DHKQ to the post DHKQ, was demonstrated. The EBP change initiative was successful, providing participants with significantly improved dental health knowledge, promoting nursing staff education in the use of the BOHSE tool, and implementing dental referrals for patients with oral health disease identified by the BOHSE tool.
Conclusions: Outpatient clinic patients presenting with loose teeth, dental decay, and/or periodontal disease can successively receive dental education with dental health referral for disease intervention. The Maryland Dental Health Smiles Program and other local programs offer low cost dentistry to individuals with low incomes. Dental health education is critical for patients to understand the oral health and systemic health connection. Oral health assessments with referral guidelines are needed in all cardiac clinical settings to promote individual self-care management behaviors, improve patient health outcomes, and decrease health care costs.

P1221
Factors associated with the thirst distress in patients with heart failure

NP Kato[1]; N Waldreus[2]; MH Van Der Wal[1]; K Kinugawa[3]; T Jaarsma[1]
[1]Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden; *[2]Karolinska Institute, Department of Neurobiology, Care Sciences and Society, Stockholm, Sweden*; *[3]University of Toyama, Department of Cardiology, Toyama, Japan*

Background: Thirst distress can decrease quality of life in patients with heart failure (HF). To develop effective interventions to improve thirst distress, more information is needed on factors that are associated with thirst distress.
Purpose: To determine risk factors associated with the thirst distress in HF patients.
Methods: A cross-sectional survey was performed in the Netherlands, Sweden and Japan in stable HF patients. Thirst distress was evaluated by the 8-item thirst distress scale for HF patients (TDS-HF) which is a reliable and valid scale with higher scores indicating more thirst distress (range, 8-40). Demographic and clinical data were collected from the medical chart. Doses of loop diuretics were normalized to approximately equivalent doses of furosemide. Patients were divided into the three groups: non-usage, lower dose (less than 40 mg) and higher dose (40 mg or more) of loop diuretics groups. To determine risk factors associated with the thirst distress, firstly univariate analysis was performed using spearman's correlation coefficient, Mann–Whitney U test and Kruskal Wallis test. Afterwards, a multiple logistic regression analysis (cut-off value, TDS-HF score ≥16) was conducted, in which we included variables associated with the TDS-HF scores at p < 0.20 in the univariate analysis.
Results: Data from 232 HF patients (age 72 ± 11, male 70%; 28% NYHA class III/IV; LVEF 39% ± 15) were analysed (n = 99 the Netherlands, n=69 Sweden, n=64 Japan). In total 63% of the patients had fluid restriction and 65% was prescribed loop diuretics. The median of the TDS-HF score was 14.0 (Q1-Q3, 9.0-20.8) and 45% of patients (n = 104) had mild to moderate thirst distress (TDS-HF score ≥16). There were no significant differences in the TDS-HF scores among the three countries [the Netherlands 15.0 (9-21), Sweden 12.0 (8-19.5) and Japan 15.0 (10-20), p = 0.49,]. In univariate analysis, age (p = 0.17), NYHA class, dose of loop diuretics and fluid restriction (all p < 0.05) were associated with the TDS-HF score. A multiple logistic regression analysis showed that lower age [odds ratio (OR) = 0.97, p = 0.03], having NYHA class III/IV (OR=2.35, p = 0.01), higher dose of loop diuretics (40 mg or more in furosemide equivalent dose OR=2.12, p = 0.03) and fluid restriction (OR=2.06, p = 0.02) were independent risk factors for mild to moderate thirst distress (TDS-HF score ≥16).
Conclusions: Patients with lower age, higher dose of loop diuretics, more severe HF and fluid restriction might be in need of additional support to relieve their thirst distress. Re-assessment of the need to have a fluid restriction and the dose of loop diuretics might help to relieve the thirst distress in patients with HF.

P1222
Evaluation of a nurse-led cross intervention program in heart failure.

C Ortiz[1]; M Diaz[2]; MA Delgado-Nicolas[3]; L Moran-Fernandez[1]; J De Juan-Baguda[1]; I Ponz[1]; A Rodriguez-Chaverri[1]; D Lora-Pablos[2]; MD Garcia-Cosio[1]; MD Garcia-Cosio[1]; J Delgado-Jimenez[1]
[1]University Hospital 12 de Octubre, Cardiology, Madrid, Spain; *[2]University Hospital 12 de Octubre, Clinical Research Unit (I + 12), CIBER Epidemiology and Public Health (CIBERESP), Madrid, Spain*; *[3]Primary Health Care - Atención Primaria de Salud, MADRID, Spain*

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Background: Heart failure (HF) is one of the most important public health problems due to its associated morbidity, mortality and high health care cost, with more than two thirds of this cost attributed to medical expenditures. Several trials have evaluated the effect of disease management programs (DMPs) in HF, with diverse results. Although recent meta-analyses have shown a consistent reduction in hospital readmission, data concerning overall mortality reduction are inconclusive. Among DMPs, those based on multidisciplinary interventions have the highest evidence, while nurse-led interventions have insufficient evidence.
Objectives: The aim of this study was to develop a simple nurse-led clinic cross intervention program (health education and drug treatment optimization) for patients with heart failure and assess whether this intervention positively affects the prognosis of patients, their care costs (hospital readmissions) and perceived quality of life.
Methods and results: Between 2011 and 2013, 127 patients with reduced ejection fraction were prospectively randomly allocated (1:2) to standard care or intervention program. Primary composite endpoint was mortality and hospital readmissions from any cause. Secondary endpoints were mortality from any cause, hospital readmissions from any cause, readmissions for heart failure, time to first admission and quality of life improvements (assessed by Minnesota Living with Heart Failure Questionnaire). Mean age ± SD was 75 ± 12 years and 69% were males. An intention-to-treat analysis was performed and after 2-years median follow-up no differences were found in the primary composite endpoint (58% vs. 57%; p = 0.99). Likewise, there were no differences between groups in mortality from any cause or admissions from any cause (28% vs. 25%; p = 0.79 and 55% vs. 49%; p = 0.55 respectively). Time to first admission was similar in both groups (mean ± SD: 277 ± 235 days vs. 249 ± 224 days; p = 0.72). However, in the intervention group, admissions for heart failure were reduced (35% vs. 18%; p = 0.04) and quality of life related to health was higher (MLHFQ 23.46 vs. 19.8; p = 0.04).
Conclusions: Nurse-led cross intervention programs significantly improve perceived quality of life and reduce hospital admission for HF with no effect in all-cause mortality.

P1223

How does sacubitril/valsartan improve submaximal functional capacity measured through six-minute walk test?

M Mercedes Faraudo[1]; P Beltran[1]; R Freixa[1]; O Guri[1]; E Mena[1]; A Contra[1]; L Ceresuela[1]; J Masip[1]
[1]*Hospital de Sant Joan Despí-Moises Broggi, Haert Failure Unit, Sant Joan Despí, Spain*

Background: Sacubitril/Valsartan has been considered class I B in the recent 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (HF) for stable HF patients with left ventricular ejection fraction (LVEF) < 35%, who remain symptomatic after the standard therapy, based on the results of the PARADIGM trial. This study showed a significant reduction in the risk of cardiovascular death and hospitalization for HF in patients treated with Sacubitril/Valsartan compared to those treated with enalapril. Although the study reported to improve the quality of life and NYHA functional class, it was not tested the functional capacity with any functional test. The 6-minute walk test (6MWT) is a validated test and an easy method to objectively measure patients' submaximal functional capacity because of its reproducibilty, simplicity, and cost-effectiveness.
Purpose: To analyse the impact of Sacubitril/Valsartan on functional capacity in patients with chronic HF.
Methods: Since October 2016, when the drug was marketed, all the patients referred to our HF-Unit who accomplished the 2016 HF ESC guidelines criteria for Sacubitril/Valsartan were included in the study. A 6MWT was performed before starting the treatment and after three months of having optimized the dose. Physiological parameters and blood analysis were also measured during up-titration and at these time points.
Results: 41 patients were screened and 23 of them entered in the study. These patients had the following characteristics: mean age 71, 91% were males, mean LVEF was 31%, isquemic etiology of HF 56%, mean maximal tolerated dose 98mg/day. The results of the 6MWT, physiological parameters and blood samples are presented in the Table 1.
Conclusion: Patients treated with Sacubitril/Valsartan improved their submaximal functional capacity at three months of treatment. Safety criteria such as hypotension or impaired renal function were not observed. More studies are needed to confirm our data.

Table 1

	Baseline	After 3 months	p
6MWTmean (m)	274	335	< 0.05
patients walking < 300 m	52 %	30 %	< 0.05
SBPmean (mmHg)	128	119	n.s
patients with SBP < 100 mmHg	0 %	13 %	n.s.
GFR (ml/min/1.73m^2)	64	64	n.s.
patients with GFR < 60 ml/min/1.73m^2 (%)	49 %	39 %	n.s.

.6MWT: 6 minute walk test; m= meters; SBP: systolic blood pressure; GFR: glomerular filtration rate.

P1224

Health and community care utilization in patients hospitalized due to heart failure

E Emma Safstrom[1]; T Jaarsma[1]; A Stromberg[1]
[1]*Linkoping University, Linkoping, Sweden*

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Introduction: Patients with heart failure (HF) are often elderly and fragile, suffering from multiple illnesses leading to polypharmacy, frailty and increased need of community and health care. There is a lack of knowledge on HF patients' community- and health care utilization prior and post hospitalization.
Purpose: To describe health and community care utilization before and after hospitalization in patients hospitalized due HF.
Methods: The study had a cross-sectional design. Patients who had been hospitalized due to de novo or deteriorating HF were consecutively included. Data were collected by structured telephone interviews and medical chart review one week after discharge and review of health care utilization 30 days after discharge.
Results: A total of 121 patients were included in the study (mean age 82.5 ± 6.8 years, 49% women 2.6 additional co-morbidities, length of hospital stay 5.7 ± 4.8 days). Review of health care utilization before the index hospital admission revealed that a majority of the patients had not visited any health care facility the month preceding the hospitalization and 13% of the patients had been hospitalized. A total of 40% of the patients received assistance from community care or home health care prior hospitalization and 52% after discharge. At discharge, 10% of the patients had no documented plan for follow up, 48% were referred to the primary care and 36% to the outpatient medical clinic. Health care utilization seems to be increasing after hospitalization; review of health care utilization 30 days post discharge revealed that 55% of the patients had visited a health care facility and 35% of the patients had been hospitalized or visited the ER without being admitted.
Conclusion: This "real world" study from a non-academic hospital revealed that most patients had not visited any health care facility the month prior to the index hospital admission. The number of patients who received assistance at home increased after hospitalization and patients were most often referred for follow up in primary care. Health care utilization increased significantly after hospitalization.

P1225

The value of nurse-based patient education in the success of multidisciplinary heart failure programs in developing countries

B Bassam Atallah[1]; M Khalil[2]; ZG Sadik[1]; R Ferrer[3]; J Stapleton[3]; L Tbishat[4]; F Bader[2]
[1]*Cleveland Clinic Abu Dhabi, Pharmacy Services, Abnu Dhabi, United Arab Emirates*; [2]*Cleveland Clinic Abu Dhabi, Cardiovascular Medicine, Abu Dhabi, United Arab Emirates*; [3]*Cleveland Clinic Abu Dhabi, Nursing, Abu Dhabi, United Arab Emirates*; [4]*Hamad Medical Corporation, Doha, Qatar*

Background: Heart failure (HF) readmissions are associated with significant morbidity and mortality burdens. Adequate heart failure education on adherence and self-care behaviors can reduce readmission rates and nurses are at the frontline of patient education. Such education is valuable when establishing heart failure programs in developing countries, in light of the challenging socio-economic differences compared to the developed world. Purpose: This study aimed (a) to evaluate the level of heart failure knowledge that nurses have at a cardiac center; (b) to assess patients' baseline knowledge; and (c) to evaluate the effectiveness of structured nurse- driven education on knowledge acquired by patients.
Methods: A total of 131 cardiac center-based nurses and 30 chronic HF patients participated in the nurse and patient surveys, respectively. Patients were also surveyed a second time 3 to 6 months later, while being followed at an advanced heart failure clinic. Results: The majority of the nurses (80%) had not received heart failure

education previously and they did not know the NYHA functional classification (86%) even though they were able to recognize most of the heart failure symptoms (table 1). As for participating patients, significant improvement in knowledge has been noted between the initial and follow-up surveys (table 2). Conclusion: When establishing advanced heart failure programs caring for patients with mostly low levels of education, nurse-led educational efforts can still result in significant improvement on disease awareness and self-care behaviors. The success of such efforts and thus reducing readmissions can be enhanced through improving nursing knowledge beyond HF clinics.

Table 1

Symptom	Number (%)
Shortness of breath	129 (98)
Light Headedness	27 (21)
Leg swelling	115 (88)
Abdominal Swelling	61 (47)
Weight gain	112 (85)
Weakness, fatigue	116 (89)
Chest pain	71 (54)
Poor appetite	51 (39)
Poor sleep	82 (63)
Inability to lie flat	119 (91)

Knowledge of different HF symptoms by cardiac center nurses participating in the survey (total of 131).

Table 2: Responses of patients on the initial and follow up surveys to questions on adherence and self-care

Question	Choices	Initial	Follow up
How much salt should you approximately take per day?	2 grams or less	9	27
	5 grams	2	1
	Any amount of salt	3	0
	Don't Know	16	2
How many liters of fluid you can consume per day?	Up to 2 Liters or 2000ml	12	25
	2to 3 Liters (2000-3000ml)	3	3
	More than 3 Liters(3000ml)	0	1
	Don't Know	15	1
How often do you check your weight?	Every day early morning after passing urine and before breakfast	9	20
	Several times per week	0	3
	Once every week	4	5
	Whenever they find weighing scale	0	0
	Never	17	2
If your weight increases by 2 Kg or more over 2 days, what should you do?	Take extra water pill	6	5
	Call the heart failure nurse within 24 hours	4	23
	Wait until the next visit to tell the doctor	5	1
	Don't Know	15	1
Do you know who to contact if your heart failure symptoms (e.g. shortness of breath, weight gain, chest pain, palpitations) worsen?	Physician	15	12
	Nurse	3	24
	Dietician	0	0
	I don't know	13	2

P1226

Effective interventions to improve self-care in patients with heart failure

L Klompstra[1]; N Sedlar[2]; A Stromberg[3]; J Martensson[4]; M Lainscak[5]; J Farkas[5]; T Jaarsma[1]
[1]Linkoping University, Department of Social and Welfare studies, Linkoping, Sweden; [2]National Institute of Public Health, Ljubljana, Slovenia; [3]Linkoping University, Department of Medical and Health Science, Linkoping, Sweden; [4]Jonkoping University, School of Health and Welfare, Jonkoping, Sweden; [5]General Hospital Murska Sobota, Department of Cardiology, Murska Sobota, Slovenia

Background: Effective heart failure (HF) self-care is important for maintaining health and to prevent HF exacerbation. An increasing number of intervention studies to improve self-care are published and we aimed to systematically summarize outcomes of studies that measured self-care using the European Heart Failure Self-care Behaviour Scale (EHFScBS)

Methods: A literature search was undertaken between June 2003 (when the EHFScBS was first published) and November 2015 in the databases PubMed, Scopus and ScienceDirect, using search terms: ("self-care" OR "self-care behaviour" OR "self-care behavior" OR "European Heart Failure Self-care Behaviour Scale" OR EHFScBS OR "EHFScBS-9") AND ("chronic heart failure" OR "heart failure"). Articles were excluded if they were not focused on interventions increasing self-care or were not RCT studies. 2154 articles were initially found, 14 were included in the analysis.

Results: Of the 14 studies included, 7 interventions found a significant ($p < 0.05$) increase in the self-care in the intervention group compared to the control group. The average number of patients included in the studies was 225 (range 82-602) and the follow-up period ranged between 3 and 12 months. Of the 7 interventions with positive effects on self-care, 2 studies were telemonitoring interventions, 3 studies were nurse-led educational intervention and 2 studies were multidisciplinary educational interventions. One telemonitoring intervention included a system monitoring symptoms, knowledge and behaviour and the second study included monitoring of weight, diuretic medication and well-being. The nurse-led and multidisciplinary educational interventions included education, multiple home visits and telephone follow-up. The seven studies that were not effective to increase self-care were four nurse-led/multidisciplinary educational interventions, one pharmacist educational program, one educational program for general practitioners and one telemonitoring study.

Conclusion: There are several interventions that have shown to be effective to increase self-care in patients with HF, such as telemonitoring, nurse-led or multidisciplinary-led educational programs. However, at the same time there is a considerable amount of interventions, including the same components as the effective interventions, which did not work to increase self-care. Future research is needed to assess the difference in factors known to influence self-care between the effective and non-effective interventions, such as experience with the illness, physical functioning, depression and anxiety, social support, daytime sleepiness, and attitudes. Research is also needed to assess the effectiveness of interventions with follow-up longer than 12 months. Because the EHFScBS can pick up the benefits of different interventions, the scale can be used the for intervention effect assessment.

P1227

An end of year review of patients with left ventricular systolic dysfunction secondary to cardiotoxic cancer therapy in a cardiac tertiary centre

VJ Chambers[1]; H Pryse-Hawkins[1]; L Fallon[1]; RK Sharma[1]; SD Rosen[1]; AR Lyon[1]
[1]Royal Brompton Hospital , London, United Kingdom

Our Cardio-Oncology clinic provides cardiology management plans for patients with cardiac complications of cancer therapy and for patients with pre-existing cardiac conditions who receive cardiotoxic therapy. We present data regarding the patients diagnosed with left ventricular systolic dysfunction (LVSD) in whom the LV ejection fraction on echocardiogram is $< 55\%$.

Aim: To consider whether care provided by a Heart Failure Clinical Nurse Specialist (HFCNS) can be applied to patients with LVSD secondary to cardiotoxic cancer therapy.

Method: The HFCNS discusses symptom recognition, self-care and medication purpose and side effects with the patient in the clinic. An opportunity is provided to answer further questions and also contact numbers for the HFCNS are provided in case of symptom occurrence or problems with medications. Subsequent HFCNS review with up titration of heart failure medication in between cardiology appointments is arranged with the patient attending an in person consultation or a telephone consultation. In addition the HFCNS liaised with the oncology CNS or the patient's primary care physician.

Results: In 2016 169 new patients were referred and reviewed as new patients. Twenty-eight were diagnosed with LVSD. From this group of patients 22 (78%) received cardiotoxic cancer treatments for current disease. Table 1 demonstrates the cardiotoxic agents that this group of patients received, the way in which the patients were reviewed by the HFCNS and the cardiac medication prescribed. After their first consultation in the clinic 100% of patients continued with their oncology treatments as documented in table 1.

Conclusion: The role of the HFCNS is an established part of the heart failure team; however there is very limited literature on the role of HFCNS care for Cardio-Oncology patients. This is an evolving service and we hope that we have demonstrated that established heart failure nursing care can be applied to this group of patients with successful results as demonstrated by improved medication compliance, concordance and titration. The HFCNS, through effective collaboration with appropriate local services, may contribute to the optimal and holistic management of this care group.

Table 1

Tratuzumab/ Pertuzumab	Anthracylines	Tyrosine-Kinase Inhibitors	Other	
50%	27%	9%	14%	
Nurse Led Clinic	Telephone Contact	Referral Local Heart Failure CNS	Virtual Assesment via Oncology CNS	GP/Practice Nurse
21%	60%	43%	32%	17%
ACEI/ARB	Beta Blockers	MRA	Ivabradine	Max Titration
92%	75%	28%	21%	29%

P1228

B-type natriuretic peptide as a tool to increase the diagnostic accuracy of nursing in congestive heart failure patients

MELINA Trojahn[1]; SLS Barilli[1]; GB Aliti[1]; DS Bernardes[2]; LL Pedraza[3]; E Rabelo-Silva[1]

[1]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil; *[2]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil*; *[3]Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: Systemic congestion is the main factor related to decompensation of patients with heart failure (HF). The main clinical manifestations resulting from congestion are dyspnea, orthopnea, tiredness, distension of jugular vein, and edema. These signs and symptoms, are part of the diagnosis of Excess Fluid Volume (EFV) often established in congested patients. In the context of clinical congestion in patients with HF, the B-type Natriuretic Peptide (BNP) is a reliable tool for the diagnosis of dyspnea, becoming also an important clinical indicator to EFV ND. This study was planned in order to improve the accuracy of this nursing diagnosis.
Purpose: To clinically validate the blood marker BNP as a tool to diagnose EFV in patients congested with HF.
Methods: Cohort study conducted in the emergence of a public university hospital, of a Southern Brazilian University Hospital. We included patients with HF diagnosis, reduced or preserved systolic function, who were hospitalized by acute decompensation. The collection was systematized through a clinical evaluation at admission and discharge, containing the signs and symptoms already clinically validated for this diagnosis in patients with HF. Blood samples were also collected for BNP measurements.
Results: 64 patients were included, with mean age of 69 ± 13 years, and fraction ejection of the left ventricular of 50 ± 16%. The frequency of signs and symptoms of the EFV ND on admission (11,32 ± 2,8) and discharge (7,5 ± 3,2) were statistically significant $p < 0{,}001$. The median of the BNP values were reduced significantly:381(202-707) pg/ml in admission and 309(180-640) pg/ml in discharge, $p < 0{,}001$.
Conclusion: The results indicated a reduction in the congestive state observed by the decrease of frequency of the signs and symptoms of the EFV as well as in BNP values. These findings indicate that this blood marker can be used as a clinical indicator in congested patients, improving diagnostic accuracy.

P1229

Prevalence of depression and anxiety in "de novo" heart failure patients with reduced left ventricular ejection fraction and related factors

M J Maria Juana Oyanguren Artola[1]; P Latorre Garcia[2]; I Lekuona Goya[3]; J Torcal Laguna[1]; LL Garcia Garrido[4]; M Nebot Margalef[5]; C Arranz[1]; A Lopez Rodriguez[1]; B Fernandez Gonzalez[6]; MJ Perez Romero[6]; T Soria Gomez[7]; M Moure[8]; C Bravo Santiago[9]; Y Sanchez Paula[10]; R Sancho Garcia[11]

[1]Osakidetza- Basque Health Service, Bilbao, Spain; *[2]Unidad de Investigacion Atencion Primaria Bizkaia, Osakidetza, Bilbao, Spain*; *[3]Hospital Galdacano, Osakidetza, Galdacano, Spain*; *[4]University Hospital de Girona Dr. Josep Trueta, Girona, Spain*; *[5]Bellvitge University Hospital, Barcelona, Spain*; *[6]University Hospital of Burgos, Burgos, Spain*; *[7]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain*; *[8]University Hospital of Santiago de Compostela, Santiago de Compostela, Spain*; *[9]Hospital Santa María, LLeida, Spain*; *[10]Hospital Universitario Virgen de la Victoria, Malaga, Spain*; *[11]University Hospital Clinic of Valladolid, Valladolid, Spain*

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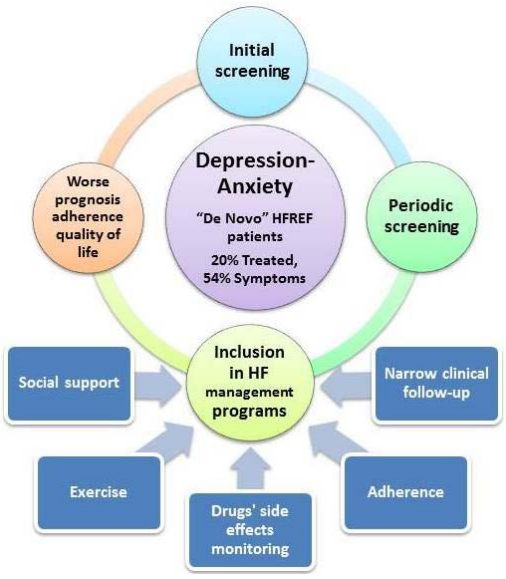
Background: Depression and anxiety are highly prevalent in HF patients, conditioning prognosis, adherence and quality of life. Treatment and symptoms prevalence are not well known in "de Novo" HF patients with reduced LVEF (HFREF)
Purpose: To evaluate antidepressant-anxiolytic treatment and self-reported symptoms in quality of life test prevalence in "De Novo" HFREF patients and clinical and sociodemographic factors related
Methods: Cross-sectional study, 174 HFREF patients of 18 hospitals (04-2015/11-2016). ETIFIC study. N (%) patients with antidepressant/anxiolytic treatment; with symptoms, Emotional Dimension>12 in Minnesota (MLWHF), 2-3 anxiety/depression in EQ-5D test; clinical and sociodemographic factors were evaluated. CEIC approved study. Categorical variables: %. Quantitative: mean +/-SD. Hypothesis Contrast: 1.-Chi2, 2.-Student t. Significant $p < 0.05$. Analysis with SAS v.9.4.
Results: 36(20.68%) patients treated with antidepressants / anxiolytics. Variables significantly related: women, NYHA III, 6-minute walking test, EQ-5D and Minnesota total score. 59(36.87%) in MLWHF and 86(53.75%) patients in Eq-5D, with self-reported symptoms
Conclusions: High prevalence of treatments with antidepressant / anxiolytics in the novo HF patients. Association with: female gender, dyspnea, 6-m. walking test and quality of life. Implications in Figure

	N 36 treated n(%)/n(Mean±SD)	N 138 no treated n(%)/ n(Mean±SD)	
Age	36(61.28±12.78)	138(61.12±11.44)	0.975
Female	19(52.78)	29(21.01)	0.001
Alcohol≥2Units	8(22.22)	37(26.81)	0.672
NYHA III	13(36.11)	17(13.49)	0.0008
Nt-proBNP	36(2589±2243)	116(2966±4586)	0.418
LVEF %	36(27.75±6.36)	126(27.83±7.23)	0.891
6 min test m.	36(303±96)	122(374±101)	0.001
AF/FL	8(22.22)	40(28.99)	0.531
AMI	5(13.89)	27(19.57)	0.629
Diabetes	6(16.67)	41(29.71)	0.142
G.F. < 60	8(23.52)	33(25.19)	0.841
Anaemia	8(22.22)	29(21.01)	0.875
MLWHF total	36(62.5±18.3)	124(45.1±22.1)	0.001
EQ-5D total	36(0.59±0.24)	120(0.77±0.22)	0.001



POPULATION STUDIES - EPIDEMIOLOGY

P1230

Mortality in ischemic heart failure patients with moderately reduced ejection fraction - A nationwide multicentre retrospective study.

F Fernando Montenegro Sa[1]; C Ruivo[1]; L Graca Santos[1]; A Antunes[1]; F Campos Soares[1]; J Morais[1]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*

On behalf of: National Acute Coronary Syndrome Registry Investigators

Introduction: Moderately reduced ejection fraction (mrEF) patients were recently defined by the European Society of Cardiology as a new subgroup of left ventricle systolic dysfunction to stimulate research on its particular characteristics and prognosis.
Aim: To compare, in post-acute coronary syndrome (ACS) patients, the in-hospital mortality (IHM) according to the ejection fraction (EF) and to identify, in mrEF patients, IMH predictors.
Population and methods: The authors analyzed a cohort of a multicentre national registry between 1/10/2010 and 30/09/2016. Patients with previously known heart failure or with no echocardiography EF evaluation were excluded. 9429 patients were included and classified in (1)EF>50%, (n = 6113, 65%), (2)EF 40-49% (n = 1922, 20%) and (3)EF < 40% (n = 1390, 15%). To determine IMH predictors for group 2, multivariate logistic regression was performed, including pre-hospital, clinical and laboratorial data, ACS classification, coronary anatomy when known and pharmacological treatment.
Results: Overall mortality was 2.8% (n = 263): 0.9% (n = 53) in group1, 2.4% (n = 37) in group2 and 11.4% (n = 159) in group3. IMH predictors are described in the enclosed table. Previous medication with aspirin, in-hospital beta blockers administration and coronariography had a positive impact in prognosis. The presented statistical model has a >80% sensitivity and specificity for event prediction in this population.
Conclusion: Patients with mrEF after an ACS are an intermediate risk group. The identified mortality predictors define a subgroup of patients with a higher risk, that similarly to reduced EF patients benefit the most of optimized therapeutic measures.

Table - In hospital mortality predictors

	OR	CI95%	P-value
Age>73 years	9.69	2.78-33.81	< .001
Severe valve disease	5.50	1.25-24.22	.024
Cardiac Arrest	23.46	1.86-296.31	.015
Heart rate > 109 bpm	4.82	1.75-13.11	.002
Platelet count > 192 000 /μL	3.70	1.30-10.50	.014
Previous medication: Aspirin	0.30	0.09-0.97	.044
Previous medication: Amiodarone	11.91	1.83-77.60	.010
In-hospital medication: Beta-blockers	0.28	0.12-0.64	.003
In-hospital medication: inotropics	14.98	5.95-37.74	< .001
Coronariography	0.09	0.04-0.22	< .001

P1231

ExTraHF survey. The european survey on implementation of exercise training in heart failure patients: regional differences.

A Verde[1]; SM Binno[1]; U Corra'[2]; P Seferovic[3]; GQ Villani[1]; T Jaarsma[4]; G Filippatos[5]; PP Ponikowski[6]; MF Piepoli[1]
[1]*Guglielmo da Saliceto Hospital, Heart Failure Unit, Department of Cardiology, Piacenza, Italy*; [2]*Fondazione Maugeri, Department of Cardiology, IRCCS Scientific Institute of Veruno, Veruno, Italy*; [3]*University Belgrade Medical School, Department of Cardiology, Clinical Center of Serbia, Belgrade, Serbia*; [4]*Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden*; [5]*Attikon University Hospital, Heart Failure Unit at the Department of Cardiology, Athens, Greece*; [6]*Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*

On behalf of: Committee on Exercise Physiology & Training of the Heart Failure Association and endorsed by the Cardiac Rehabilitation Section of the ESC

Background. In heart failure (HF), exercise training programmes [ETP] are well-recognised intervention to improve symptoms, but still poorly implemented. The Heart Failure Association promoted a survey to investigate whether and how cardiac centres in Europe are using ETP in their HF patients.
Methods: A 12-item web-based questionnaire was distributed using the coordinators of the HF working groups of the Countries affiliated to the ESC who distributed and promoted the survey in the key cardiac centres. Forty-one country coordinators out of 46 contacted replied to our questionnaire (89%). This accounted for 170 Cardiac Centres, in charge of 77,214 HF patients.
Results: The majority of the participating centres (82%) were general cardiology units and the rest were specialised rehabilitation units or local health centres. Sixty-seven (40%) centres (in charge of 36,385 [48%] patients) did not implement ETP. This was mainly attributed to the lack of resources (25%), largely due to lack of staff or of financial coverage. The lack of national or local pathway for such programme was the reason in 13% of the cases and in 12% the perceived lacks of evidence on safety or benefit were advocated. When implemented, in only 55% of the centres it was proposed to all HF patients, with restriction according to severity, or aetiology.
In the regional sub analysis: a larger implementation of ETP was observed in cardiac centres located in the North and Central Europe (69% and 67%) vs South and East Europe (59% and 45%) (P=0.5%)
No differences were observed between University, General or Community Hospitals (59%, vs 57%, vs 60%) (p = NS)
Conclusions: With respect to previous surveys, there is evidence of increased supply of exercise training programmes in HF in Europe, although still too many patients are denied a highly recommended therapy, mainly due to lack of resources or logistics, mainly in the South and East European Regions.

P1232

Clinical characteristics and in-hospital outcomes of HF with mid-range versus preserved and reduced ejection fraction: a subgroup analysis from Journey HF-TR study

M Zoghi[1]; U Y Umit Yasar Sinan[2]; DC Gurbuz[3]; O Celik[4]; HA Cakmak[5]; S Kilic[6]; S Inci[7]; G Gok[8]; MS Kucukoglu[2]
[1]*Ege University, Cardiology, Izmir, Turkey*; [2]*Istanbul University Cardiology Institute, Department of Cardiology, Istanbul, Turkey*; [3]*Izmir Katip Celebi University Ataturk Training and Research Hospital, Cardiology, Izmir, Turkey*; [4]*Hitit University School Medicine, Cardiology, Corum, Turkey*; [5]*Mustafakemalpasa State Hospital, Cardiology, Bursa, Turkey*; [6]*Nizip State Hospital, Cardiology, Gaziantep, Turkey*; [7]*Aksaray State Hospital, Cardiology, Aksaray, Turkey*; [8]*Goverment Hospital, Cardiology, Mardin, Turkey*

On behalf of: Journey HF-TR Study

Background: We aimed to investigate the clinical characteristic, concomitant conditions, and in hospital mortality of patients with HFmrEF in Turkish population.
Method: The patients who were hospitalized with the diagnosis of acute heart failure were compared based on new EF-related classification: HFrEF (EF < 40%), HFmrEF (EF 40-49%) and HFpEF (EF ≥50%).
Results: The 1606 patients (male: 57.2% mean age, 67.8 ± 13 years old) in 37 centers of Turkey were enrolled in this study. The age was similar between HFmrEF and HFpEF patients (p = 0.805). However, the patients with HFmrEF were older (p = 0.05) and a greater proportion were male compared to patients with HFrEF (p = < 0.001). The De novo clinical presentation was lowest in patients with low EF but similar between HFmrEF and HFpEF groups. The prevalence of anemia and hypertension were higher in HFmrEF and HFpEF groups than HFrEF group (p < 0.001 and 0.001 respectively). However, they were similar between HFmrEF and HFpEF groups. On the contrary, the CAD was more prevalent in HFrEF group than in HFpEF and HFmrEF groups (p < 0.001), but it was similar between HFpEF and HFmrEF groups. The mean length of stay was significantly longer (p < 0.001 and in-hospital mortality was lower (p = 0.01) in HFmrEF patients than the other study groups.
Conclusion: Not only the clinical characteristics but also in hospital clinical outcomes are different in patients with HFmrEF when compared with patients with low or preserved EF.

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Parameter	HFrEF	HFmrEF	HFpEF	P value
LVEF (%)	27.1 ÷ 7	42.5 ÷ 4.2	55.2 ÷ 4.8	< 0.001
Age (years old)	67.3 ÷ 12.5	69.1 ÷11.6**	71.5 ÷ 11.5*	* < 0.001 **0.05
De nova (%)	14.5	23	20.1	0.020
Male (%)	64.6	48.9	38.4	< 0.001
CAD (%)	65.2	56.7	41.4	< 0.001
HT (%)	62.2	78.7	73.1	< 0.001
DM Type 2 (%)	42	45	37	0.148
AF (%)	52	41.8	56.3	< 0.001
CKD (%)	29.8	25.5	25	< 0.167
Anemia (%)	41	62	63	< 0.001
PAD (%)	7.9	3.9	3.7	0.02
LOS (days)	11.7	22.5	10	< 0.001
In hospital mortality (%)	7.3	1.8	7.5	0.01

Comparison of baseline clinical characteristics, concomitant diseases and clinical outcomes of the studied groups.

P1233

Heart failure in intravenous drug users with infective endocarditis: etiology, clinical characteristics and outcomes

T S Getiya[1]; AS Pisaruk[2]; PV Lazarev[2]; EO Kotova[2]; I Merai[2]; GK Kiyakbaev[2]; VS Moiseev[2]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation; *[2]RUDN University, Moscow, Russian Federation*

Intravenous drug (IVD) use is a known risk factor for infective endocarditis (IE). The prevalence, clinical characteristics and prognostic implications of heart failure (HF) in IVD users with IE are not well studied.

Purpose: To study risk factors, clinical features and outcomes of HF in IVD users with IE.

Material and methods: The study included 53 IVD users hospitalised with IE (Duke criteria 2015). The numbers of patients with right-sided, left-sided and both-sided IE were 32 (60.4%), 15 (28.3%) and 6 (11.3%), respectively. HCV infection was present in 49 (92.5%) participants.

Patients: were divided into 2 groups: 29 patients with HF [group 1; median age 33.0 (28.5-40.0) years, 21 (72.4%) male] and 24 patients without HF [group 2; median age 33.5 (30.0-35.8) years, 21 (66.7%) male]. All patients underwent transthoracic and transesophageal echocardiography and laboratory investigation with measurement of NT-proBNP and markers of inflammation. Mortality and complication rates were calculated after 1-year follow-up.

Results: History of previous IE was more common in HF patients [8 (27.6%) vs. 4 (16.7%), p = 0,51]. They more often had dyspnea [28 (96.6%) vs. 14 (58.3%), p < 0.05] and edema [12 (41.1%) vs. 2 (8.3%), p < 0.05] than patients without HF. Patients in group 1 also had a higher frequency of hepatomegaly [27 (93.1%) vs. 18 (75.0%), p = 0.12] and splenomegaly [22 (75.9%) vs. 13 (54.2%), p = 0.15]. Systolic BP on admission was significantly lower in group 1 [105.0 (100.0-110.0) vs. 110.0 (100.0-120.0) mmHg, p < 0.05]. Glomerular filtration rate (CKD-EPI) was similar – 79.6 (55.5-106.4) ml/min/1.73 m^2 in group 1 and 86.0 (53.2-117.8) ml/min/1.73 m^2 in group 2 (p = 0.526). WBC and Hb values were comparable in both groups (p>0.05). However, platelet count was lower in HF patients [171.0 (61.5-199.5) vs. 228.0 (191.0-364.0) 10^9/l, p < 0.05]. Median NT-proBNP values were 1706.5 (280.3-4302.0) ng/ml in group 1 and 379.0 (58.0-998.8) ng/ml in patients without HF (p = 0.166). NT-proBNP positively correlated with inflammatory markers [CRP (rho=0.69), p = 0,05; rheumatoid factor (rho=0.75), p = 0.04]. Pulmonary artery systolic pressure was higher in group 1 [32.0 (23.0-50.5) vs. 25.0 (19.5-36.8) mmHg, p = 0.08], although left ventricle EF values were similar [58.0 (54.5-63.0) % in group 1 vs. 60.0 (58.0-62.0) % in group 2, p = 0.37]. IE caused by Staphylococcus spp. was diagnosed in 19 (65.5%) patients in group 1 and in 16 (66.7%) patients in group 2 (p>0.99), while the rate of S. aureus etiology was higher in HF group [19 (65.5%) vs. 10 (41.7%), p = 0.10]. The presence of HF conferred a higher risk of thromboembolic events [21 (72.4%) vs. 11 (47.8%), p = 0.09] and mortality [6 (20.7%) vs. 1 (4.2%), p = 0.11].

Conclusion: IE in patients with a history of IVD use is often complicated by HF that is associated with a higher rate of thromboembolism and 1-year total mortality. Risk factors for HF development could include S. aureus infection and higher degree of inflammation.

P1234

Younger heart failure population with higher in-hospital mortality

U Y Umit Yasar Sinan[1]; A Ekmekci[2]; B Ozbay[3]; F Akcay Ayyildiz[4]; L Bekar[5]; Y Koza[6]; I Bolat[7]; U Kocabas[8]; M Zoghi[3]
[1]Istanbul University Cardiology Institute, Department of Cardiology, Istanbul, Turkey; *[2]Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Center, Cardiology, Istanbul, Turkey*; *[3]Ege University, Cardiology, Izmir, Turkey*; *[4]Izmir Katip Celebi University Ataturk Training and Research Hospital, Cardiology, Izmir, Turkey*; *[5]Hitit University School of Medicine, Cardiology, Corum, Turkey*; *[6]Ataturk University, Cardiology, Erzurum, Turkey*; *[7]Fethiye State Hospital, Cardiology, Mugla, Turkey*; *[8]Soma State Hospital, Cardiology, Manisa, Turkey*

On behalf of: Journey-HF Study Group

Background: In this study, we aimed to evaluate the overall clinical characteristics, management and in-hospital outcomes of hospitalized patients with AHF in a large sample of Turkish population.

Methods: The Journey HF-TR study is a cross-sectional, multicenter, non-invasive and observational trial that was conducted in intensive/coronary care units and cardiology wards. The patients who were hospitalized with the diagnosis of acute heart failure in intensive/coronary care units between September 2015 and 2016 were included in our study.

Results: The 1606 patients (male: 57.2% mean age, 67.8 ± 13 years old) who were diagnosed with AHF (NYHA III-IV:75.2%) in 37 centers, in seven geographical regions of Turkey were enrolled in this study. Seventeen percent of patients were admitted to hospital with diagnosis of new onset AHF. Hypertension (67%) and coronary artery disease (59.6%) were the most frequent underlying diseases. Acute coronary syndrome accompanying to heart failure (14.7%), infection (29.3%), arrhythmia (25.1%), cardio-renal syndrome (23%) and non-compliance with medication (23.8%) were the precipitating factors. Biomarkers were used in 41% of patients at admission for diagnosis. The mean EF was 32.7 ± 14.1%. The median length of stay (LOS) in ICU was 3 days (IQR 1-72) and was 7 days (IQR 0-72) for in hospital's journey. The guideline recommended medications were less likely used (< 73%) before admission and were similar to European and US registers at discharge. In-hospital mortality rate was 7.6%.

Conclusions: Although our study population was younger than other registers, in-hospital mortality was high. Hypertension and coronary artery disease were the most frequent underlying diseases.

PSYCHOSOCIAL - ETHICAL CONCEPTS - EDUCATION

P1235

Imparting information to the HF patient; lessons learned from the cardiovascular ward round

G Gemma Reddin[1]; G O Carroll[1]; N Baroni[1]; C Keane[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Dublin, Ireland

Introduction: Inpatient ward rounds are an invaluable part of the hospital day allowing for daily assessment of each patient, evaluating treatment and basing clinical decisions on this information. Perhaps the most crucial role of the ward round is information transfer, which is particularly important in the management of chronic diseases such as heart failure, where poor lifestyle and treatment adherence directly impacts health outcomes. With the ward round being an important vehicle to transmit information to the patient, it is interesting that little objective analysis of the ward round has been undertaking.

Purpose: This study aimed to investigate inpatient's perception of the cardiology ward round, in order to identify strengths and weaknesses and in particular to assess how effective the ward round is in delivering information to the patient.

Methods: Initially, open interviews with in-patients were conducted to explore areas of concern and satisfaction surrounding the round. Repeated themes were identified and used to develop a relevant questionnaire which analysed four pertinent aspects of the ward round: Information-Giving & Communication, Emotional Reaction, Professionalism and Privacy.

Results: 98 cardiology inpatients completed the questionnaire. Patients had been admitted through the ER for a variety of cardiovascular emergencies including acute decompensated heart failure, ACS and arrhythmia. Professionalism and privacy were the highest scoring categories, with an average positive response rate of 79% and 81% respectively. Emotional reaction towards the ward round scored an average positive response rate of 69%. A considerable weakness was revealed under the category information giving and communication; the average positive response rate was only 60%. This low score was attributed to the use of medical jargon, apparent time constraints and patients perceived in-opportunity to ask questions; almost half of patients found the language used by staff difficult to understand, 58% felt that the ward round was rushed and 30% of patients felt they

did not have the opportunity to ask questions.
Conclusion: The presented data underlines a significant deficiency in knowledge transfer to the patient during the ward round. While other aspects of the round score scored satisfactorily, the noted deficiency in communication could potentially have a detrimental impact on post discharge morbidity especially in heart failure where understanding and treatment adherence is critical to effective self-care. Improving information-giving and communication is vital to establishing the ward round as a practice of significant importance in the hospital day in order to deliver superior, safe patient-centered care.

P1236

Depression and all-cause mortality in patients with congestive heart failure with implanted cardiac devices

GS Pushkarev[1]; VA Kuznetsov[1]; AM Soldatova[1]; TN Enina[1]; YA Fisher[1]
[1]Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Scienc, Tomsk, Russian Federation

Background: It is well known that depression is associated with high risk of cardiovascular mortality and morbidity. However the impact of depression on mortality in patients with implanted cardiac devices has not been fully evaluated. The purpose was to assess the association between depression and all-cause mortality in patients with congestive heart failure (CHF) and implanted cardiac devices.
Methods: The study enrolled 253 patients (mean age 56.8 ± 10.1 years, 83% men) with CHF and implanted cardiac devices (149 patients with implanted cardiac devices for resynchronisation therapy, 104 patients - with implantable cardioverter defibrillators). Mean duration of follow-up was 49.5 ± 31.7 months. The Beck Depression Inventory (BDI) was used to measure depressive symptoms. Depression was considered absent for a score between 0 and 9, mild to moderate between 10 and 18, significant – if more 19. Cox proportional hazards regression model was used to estimate hazard ratios (HR) with 95% confidence interval (95% CI) for impact of depression on all-cause mortality. HR was calculated after adjustment for the following confounders: age, gender, smoking status, hypertension, diabetes mellitus, body mass index, hypercholesterolemia, left ventricular ejection fraction, number of hemodynamically significant lesions of the coronary arteries and the type of the implanted cardiac devices.
Results: During follow-up period 37 patients died (11.4%). Adjusted HR for all-cause mortality on depression score was 1.04, 95% CI 1.01 – 1.08. Patients without depression were accepted as a reference group with HR=1.0 for analysis of categorical indicator. HR was 1.07, 95% CI 0.46 – 2.50 in patients with mild depressive symptoms and 2.72, 95% CI 1.14 – 6.47 in patients with significant depressive symptoms.
Conclusion: Increased depressive symptoms are associated with all-cause mortality in patients with CHF and implanted cardiac devices.

P1237

Understanding the symptoms and impacts of acute and stable heart failure patients: results from a concept elicitation study

K Benjamin[1]; O Moshkovich[1]; K Hall[1]; R Murphy[1]; B Boris Gorsh[2]; V Sikirica[2]; D Sprecher[3]; R Saini[3]; R Von Maltzahn[2]
[1]ICON Commercialisation & Outcomes, Clinical Outcomes Assessments, Dublin, Ireland; *[2]GlaxoSmithKline, Value Evidence and Outcomes, Collegeville, United States of America*; *[3]GlaxoSmithKline, Collegeville, United States of America*

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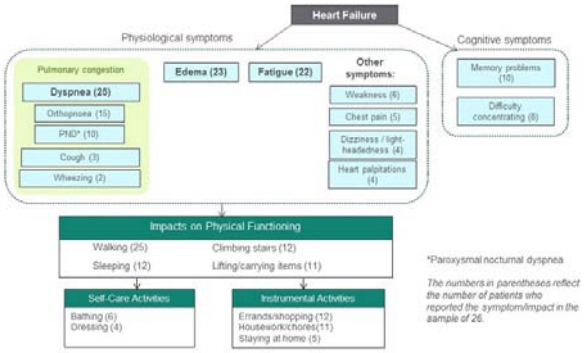
Purpose: To qualitatively elicit the important symptoms and impacts of HF directly from patients recently discharged after a hospitalization for acute decompensating heart failure (ADHF) and patients with HF without a recent ADHF hospitalization ("stable" patients). Elicitation was used to inform development or adaptation of a patient reported outcome (PRO) measure.
Methods: HF patients were recruited across three US clinical sites and patients provided informed consent. Acute patients had been discharged from an ADHF hospitalization≤ 45 days prior to enrolment; stable patients had no ADHF hospitalization in the past 6 months and no unplanned medical encounter due to HF in the past 3 months but had at least 2 HF encounters in the past 2 years. One-on-one telephone or in-person interviews were conducted to obtain patient perspectives on their HF experience. Interviews focused on the symptoms of chronic HF and ADHF, and how these symptoms affected patients' lives and functioning using a semi-structured open-ended interview guide. Interviews were recorded and transcribed for analysis. Data were analyzed in MaxQDA, a qualitative research software program.
Results: Twenty-six patients with HF participated, including 18 stable and 8 acute patients. The sample included patients from all NYHA classes, with most in Class II (46%) or Class III (34%). The majority were male (65%), mean age was 67 years (range 41-91), and 61% were non-Hispanic White. The majority of patients reported shortness of breath (SOB) (n = 25, 96%), fatigue (n = 22, 85%), and edema (n = 23, 88%) across both groups. Cognitive changes (memory problems / difficulty concentrating) were reported by 14 patients (54%).Other symptoms were less common (reported by≤ 6 patients). A subset of acute (n = 8) and stable (n = 6) patients, provided a description of their last acute HF episode. Of this subset, SOB was the symptom most frequently leading to hospitalization (n = 10, 71%). Patients reported impacts in physical functioning, including walking, climbing stairs, sleeping, and carrying items. These impacts were associated with difficulties with daily activities, including bathing, dressing, housework, running errands, and social outings. Patients reported curtailing recreational activities and fitness, and several stopped driving. Impacts to emotional well-being included frustration, worry about the future, depression, irritability, fear, and anxiety. Despite distinct subgroups, few differences in symptoms and impacts were identified across stable and ADHF patients. No new symptoms or symptom impacts were reported by the 18th interview, confirming concept saturation. A conceptual model of HF symptoms and impacts for the potential development or adaptation of a PRO measure is summarized in Figure 1.
Conclusion: Across a broad group of HF patients, three symptoms were consistently reported: SOB, fatigue, and edema. The conceptual model presented can serve as a starting point for further PRO development.

Figure 1. Conceptual Model of HF Symptom and Symptom Impacts



P1238

Influence of heart failure into quality of life of patients with heart rhythm disorders

R Mlynarski[1]; A Mlynarska[2]; KS Golba[2]
[1]Upper-Silesian Cardiology Center, Katowice, Poland; *[2]Medical University of Silesia, Katowice, Poland*

Influence of heart failure into quality of life was described many times, however no complex analysis in subpopulation of patients with serious heart rhythm disorders qualified for pacemaker implantation were performed.
Methods: 107 patients aged 70,72 ± 11,35 (47 women) with advanced heart rhythm disorders qualified for pacemaker implantation (ESC criteria) were included into the trial. Two subpopulations according symptoms of heart failure and ejection fraction were created: without heart failure (nHF) and with heart failure (HF). Ejection fraction was evaluated by echocardiography. In all quality of life was evaluated by using Minnesota Living with Heart Failure Questionnaire which describes self-assessment of how heart failure affects daily life. Analysis was performed in a two subgroups: related to the physical symptoms (physical domain) and related to the psychological distress (emotional domain). Fewer points mean better quality of life.
Results: General quality of life was statistically (p = 0,0255) lower in the group of heart failure (45,00 ± 10,68) if compare to these without heart failure group (40,48 ± 8,84). Similar relationship, however without significance, were noted in the physical group of quality of life: 20,47 ± 5,43 (HF) vs. 18,92 ± 4,22 (nHF); p = 0,1147, as well as emotional group 10,53 ± 4,43 (HF) vs. 8,86 ± 4,22 (nHF); p = 0,0686. Gender-dependent analysis did not show statistical differences – general quality of life in women (43,70 ± 9,47 (HF) vs. 39,48 ± 8,79 (nHF); p = 0,1926 and in men 45,59 ± 11,35 (HF) vs. 41,45 ± 3,97 (nHF); p = 0,1237. Quality of life domains-related exact results are presented in the table below.
Conclusion: Presence of heart failure worsen the quality of life patients with heart rhythm disorders qualified for pacemaker implantation.

	Women	Men				
	HF	nHF	p	HF	nHF	p
Physical domain	19,40±6,08	18,32±4,01	0,5056	20,95±5,19	19,50±4,39	0,3797
Emotional domain	11,60±4,45	8,81±4,33	0,0791	10,04±4,45	8,92±4,17	0,3297

HF - heart failure (HF); nHF - without heart failure

EXERCICE TESTING AND TRAINING

P1239

Monitoring changes of end-tidal pressure of carbon dioxide in patients with chronic heart failure and chronic obstructive pulmonary disease during six minute walk test

KA Kira Ageeva[1]; VN Abrosimov[1]; IB Ponomareva[1]; NN Peregudova[1]
[1]*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 CO2. Significance of end-tidal CO2 (PETCO2) 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 ± 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 ± 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 ± 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 PETCO2 in patients with CHF in NYHA class II was 38,2 ± 2,13 mm Hg, in patients in NYHA class III was 34,4 ± 2,22 mm Hg, in patients in NYHA class IV was 32,4 ± 1,14 mm mm Hg. Significance of PETCO2 in 1st group patients with COPD was 36,2 ± 2,43 mm Hg, in 2nd group patients was 34,1 ± 1,22 mm Hg. All patients performed 6MWT. The 6MWT distance in patients with CHF in NYHA class II was 384 ± 10,56 m, in NYHA class III was 290 ± 17,24 m, in NYHA class IV was 142 ± 3,51 m. The 6MWT distance in 1st group patients with COPD was 440 ± 15,48 m, in 2nd group was 384 ± 15,42 m. There is reduction PETCO2 in all patients with CHF during the 6MWT. PETCO2 in patients with CHF in NYHA class II was 33,34 ± 2,51 mm Hg, in NYHA class III was 31,75 ± 2,89 mm Hg, in NYHA class IV was 28,8 ± 1,32 mm Hg. 69,2% patients reported dyspnea as the main reason for a stop during the 6MWT. There is increase PETCO2 in all patients with COPD during the 6MWT. After the 6MWT the significance of PETCO2 in 1st group was 43,21 ± 2,81mm Hg, in 2st group was 45,05 ± 3,26 mm Hg. All patients reported dyspnea as the main reason for a stop during the execution 6MWT. When we analyzed the trend of PETCO2 we found that these patients showed signs of periodic breathing 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.

P1240

Cardiac rehabilitation: don't forget the ones that went away

H Helena Nascimento[1]; A Rocha[1]; M Braga[1]; G Pestana[1]; M Tavares-Silva[1]; R Pinto[1]; A Nunes[1]; P Araujo[1]; V Araujo[1]; F Parada[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Introduction: Cardiac rehabilitation program (CRP) is an intervention designed to promote a healthy lifestyle. In spite of a strong commitment from health-professionals, a significant number of patients (pts) leave the program. Our goal was to evaluate the socio-demographic and clinical features of pts not completing the CRP.
Methods: We analysed data from a prospective registry of 840 consecutive pts enrolled in a CRP after an acute coronary syndrome (ACS), between 2008 and 2016. Forty-two pts were excluded from the CRP due to medical reasons.
Results: From the total of 798 patients, 86% male and mean age 54.5 ± 9.9 years old. Most pts were actively working (55,4%) and married (92,8%). The prevalence of the classic cardiovascular risk factors was high with 59.9% dyslipidemic; 55.8% active smokers; 42.6% hypertensive; 24.9% obese and 18.5% diabetic. The dropout rate from CRP was 7,9% (63 pts). Main reasons for dropping out were lack of economic means or transportation constraints (23.8%), need to return to work (7.1%) and available exercise sessions schedules (2.9%). Women were slightly more prone to leave CRP ($p = 0.05$). Pts leaving the CRP were younger (51.2 ± 9.1 vs 54.3 ± 9.8 years old, $p = 0.011$), more often lived alone (38.1% vs 17.1%, $p < 0.001$) and were unemployed/retired (55.6% vs 41.8%, $p = 0.046$). Prevalence of active smokers (73.0% vs 54.3%, $p = 0.005$) and obese (42.9% vs 22.7%, $p = 0.001$) was also higher among these pts. Although there was no difference in functional capacity in baseline exercise testing (METs 8.9 ± 2.3 vs 8.4 ± 2.6, $p = 0.084$), at 1-year follow-up, those completing CRP showed better performance (METs 10.7 ± 2.3 vs 9.0 ± 2.2, $p < 0.001$). Independent predictors of non-completion of CRP by multivariate logistic regression modelling were obesity (OR 2.7, 95% CI 1.6-4.6, $p < 0.001$), smoking (OR 2.4, 95% CI 1.3-4.3, $p = 0.004$), unemployment (OR 1.9, 95% CI 1.1-3.2, $p = 0.017$) and living alone (OR 2.9, 95% CI 1.6-5.0, $p < 0.001$).
Conclusion: The benefits of CRP enrollment after an ACS are undeniable. However, dropout rates remain high and are a source of concern in CRP. Identifying those at higher risk of non-compliance, especially those with social and economic disadvantages might steer a redesign of CRP programs, and alternatives to reduce costs and inequities in access to this cost-effective treatment option.

P1241

The effects of long-term aerobic training designed with individualized method based on lactate threshold definition

T Tatiana Lelyavina[1]; MYU Sitnikova[1]; VL Galenko[1]; PS Kozlovps[1]
[1]*Almazov Federal Center of Heart Blood & Endocrinology, Saint Petersburg, Russian Federation*

Objective: to evaluate the effects of long-term aerobic training, designed with individualized method based on lactate threshold definition, on exercise capacity, HF severity and ergoreflex activity.
Methods: We evaluated 196 HF patients, mean age 51 +/-1.1, 132 men, with NYHA class III, LVEF 38,8 +/-0,8%. CPET performed on a treadmill ("Oxycon Pro") at baseline, in every 8 weeks and after 9 months. The cubital venous catheter was inserted before CPET. Blood samples were taken at baseline and at 1-minute intervals during test. Lactate concentration in blood was measured using analyzer i-STAT, cartridge CG4 (Abbot, USA). All patients were randomized into following groups: 109 patients of study group (SG), who underwent physical rehabilitation program (PRP), calculated due to lactate threshold; and 87 HF patients control group (CG), who underwent physical training, calculated based on VO2 percentage. Results: At baseline CPET results in both groups did not significantly differ. VO2 at lactate threshold and VO2peak were 8.7 +/-0,5; 13,5 +/-0,9 ml/min/kg and 8.9 +/-0.9; 13,6 +/-1,2 ml/min/kg in study group and control group, respectively (p1=0,08, p2=0,07, respectively). After 36 weeks of training VO2LT and VO2peak were better in the study group than in control group: the increase was 16% and 24% in the main group, and 4% and 7% in the control group, respectively ($p1 < 0,01$, $p2 < 0,01$). The ergoreflex activity at baseline did not significantly differ in two study groups. After long-term aerobic training we recorded a more marked reduction in the ergoreflex activity in study group: for DBP it was 35% and 20%, VE - 48% and 25%, VE/VCO2 - 39% and 12%, in the study group and control groups, respectively. By the 24th week of training in 91 (85%) patients of the study group the severity of HF was reduced to NYHA class II, and among the patients in the control group such dynamics was observed only in 43(50%) patients. Conclusions: aerobic exercise, designed with individualized method based on lactate threshold definition, increase exercise tolerance, reduces HF severity and ergoreflex activity more than aerobic training, calculated based on VO2peak percentage.

P1242

Endothelial and muscular alterations in a cardiometabolic obese rat model of heart failure with preserved ejection fraction (HFpEF)

V Volker Adams[1]; C Herz[1]; Z Schmederer[1]; TS Bowen[1]; NPL Rolim[2]; T Fischer[1]; S Werner[1]; A Linke[1]; U Wisloff[2]
[1]*University Leipzig, Heart Center, Leipzig, Germany*; [2]*Norwegian University of Science and Technology, Trondheim, Norway*

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Despite normal left ventricular ejection fraction patients with heart failure with preserved left ventricular ejection fraction (HFpEF) present exercise intolerance which can be attenuated by exercise training. Alterations in the peripheral skeletal muscle as well as in the vascular system have been described with conflicting results and the molecular mechanisms mediating the beneficial effects of exercise training after disease onset is still unknown. The present study, therefore, used a cardiometabolic rat model to further elucidate: 1) alterations in the skeletal muscle (EDL) and the

vascular system induced by HFpEF; and 2) the effects of exercise training during secondary prevention. After 20 weeks, obese Zucker diabetic fatty/spontaneously hypertensive heart failure F1 hybrid (ZSF1) rats (n = 12) were compared to their lean counterparts (n = 8), with a further 3 groups of obese ZSF1 rats assessed 8 weeks later following sedentary behavior (n = 15), moderate-continuous training (MCT; n=11) or high-intensity interval training (HIIT; n=11). Obese rats displayed signs of HFpEF including diastolic dysfunction, LV hypertrophy, exercise intolerance ($P < 0.05$) and preserved LVEF. Compared to leans, obese rats showed a significantly impaired endothelial-dependent vasodilation associated with reduced eNOS activation ($p < 0.05$) and a trend towards elevated expression of gp91phox ($p = 0.09$). Exercise, independent of modality, improved endothelial function, which was associated with a reduction in gp91phox expression (r=0.42, $p = 0.01$). Compared to controls HFpEF animals showed signs of skeletal muscle atrophy (lower muscle weight, lower CSA) and reduced maximal absolute force, but maximal specific force was elevated ($p < 0.05$). AT the molecular level a significant higher actin expression and creatine kinase activity was detected whereas xanthine oxidase activity was reduced ($p < 0.05$). Exercise training had no significant effect. To conclude, a cardiometabolic obese model of HFpEF was associated with impaired endothelial function and still preserved specific skeletal muscle force generation. Exercise training (independent of protocol) was able to reverse these alterations in the endothelium but had no significant effect on the skeletal muscle.

P1243

The combination of characteristics of exercise oscillatory ventilation is associated with the severity of chronic heart failure

N Panagopoulou[1]; E Karatzanos[1]; V Zarvalias[1]; P Ferentinos[2]; C Kapelios[3]; S Dimopoulos[1]; A Ntalianis[4]; I Chaveles[5]; S Nanas[1]; A Sideris[6]
[1]Cardiopulmonary Exercise Testing & Rehabilitation Laboratory, NKUA, Athens, Greece; *[2]Carnegie Faculty , School of Sport, Leeds Beckett University, Leeds, United Kingdom*; *[3]Laiko General Hospital of Athens, Cardiology Department, Athens, Greece*; *[4]National & Kapodistrian University of Athens, Department of Therapeutics, School of Medicine, Athens, Greece*; *[5]Evaggelismos General Hospital of Athens, 1st Cardiology Department, Athens, Greece*; *[6]Evaggelismos General Hospital of Athens, 2nd Cardiology Department, Athens, Greece*

Introduction: The pattern of exercise oscillatory ventilation (EOV) can be described by the length (λ) and amplitude (h) of cyclic fluctuations. The clinical significance of the severity of these characteristics has not been adequately described in chronic heart failure (CHF).
Purpose: To investigate the relationship between the combination of these EOV characteristics with indices of CHF severity.
Methods: 357 consecutive patients with systolic CHF were evaluated with maximum, symptom-limited exercise testing (CPET) of which 179 presented EOV (age:55 ± 13 years, VO2peak:17.9 ± 9.7 ml/kg/min). Cyclic fluctuations in ventilation with an amplitude during exercise ≥15% of the average resting amplitude, lasting ≥60% of total exercise duration, were considered as EOV. The average length (λ) and amplitude (h) of EOV for each patient was also calculated. Patients were divided into two severity groups (S: severe, M: mild) for each of these characteristics, based on their median value [Sλ: $\lambda \geq 41.4$sec, Mλ: $\lambda < 41.4$ sec; Sh: h≥6.5 L/min, Mh: h < 6.5 L/min]. Consequently, four subgroups resulted from the combination of characteristics and severity that were compared for CPET indices: VO2peak, VO2AT, VE/VCO2slope, PetCO2AT, PetCO2peak and VO2/t slope. Values are expressed as means ± SD.
Results: Significant between-group differences were observed for all indices examined ($p < 0.05$, Table 1). MλMh differed from MλSh and SλSh in some variables ($p < 0.05$) but not from SλMh (p>0.,05). MλSh differed from SλSh and SλMh ($p < 0.05$), while SλSh did not differ from SλMh (p>0.05).
Conclusions: The combination of different levels of length and amplitude, as characteristics of EOV -mainly the length- is related to the severity of CHF. Further investigation on larger sample is necessary to clarify these findings and define reference values for average length and amplitude of EOV in relation to CHF severity.

Table 1. Comparison within and between subgroups (based on EOV characteristics and severity) for parameters examined.

	Groups	p (ANOVA)			
Variables	$M_\lambda M_h$(n=59)	$M_\lambda S_h$ (n=30)	$S_\lambda S_h$ (n=60)	$S_\lambda M_h$ (n=30)	
VO_2peak (ml/kg/min)	19,0±13,0	21,7±8,7	16,1±7,5 #	15,3±3,7 #	0,02
VO_2AT (ml/kg/min)	11,6±4,5	14,1±6,3	10,3±5,5 #	10,6±3,3 #	< 0,01
VE/VCO_2 slope	33,8±7,3	32,8±5,4	37,3±9,4	34,3±5,4	0,09
PetCO_2AT (mmHg)	35,3±5,3	35,7±4,1	32,9±6,8	34,8±4,4	0,09
PetCO_2peak (mmHg)	32,5±5,2	32,6±5,2	29,6±7,1*	31,2±3,8	0,02
VO_2/t slope (L/min^2)	0,47±0,25	0,77±0,43 *	0,47±0,31#	0,38±0,22 #	< 0,01

*: compared to MλMh ($p < 0,05$), #: compared to MλSh ($p < 0,05$)

P1244

Different predictors of exercise capacity in HFpEF compared to HFrEF

A Batalli[1]; P Ibrahimi[1]; I Bytyci[1]; A Ahmeti[1]; E Haliti[1]; S Elezi[1]; M Henein[2]; G Gani Bajraktari[1]
[1]University Clinical Centre of Kosova (UCC), Service of Cardiology, Pristina, Kosovo Republic of; *[2]Heart Centre and Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden*

Background and Aim: Quality of life is as important as survival in heart failure (HF) patients. Controversies exist with regards to echocardiographic predictors of exercise capacity in HF, particularly in patients with preserved ejection fraction (HFpEF). The aim of this study was to prospectively examine echocardiographic parameters that correlate and predict functional exercise capacity assessed by 6 min walk test (6-MWT) in patients with HFpEF.
Methods: In 111 HF patients (mean age 63 ± 10 years, 47% female), an echo-Doppler study and a 6-MWT were performed in the same day. Patients were divided into two groups based on the 6-MWT distance (Group I: ≤ 300 m and Group II: >300 m).
Results: Group I were older ($p = 0.008$), had higher prevalence of diabetes ($p = 0.027$), higher baseline heart rate ($p = 0.004$), larger left atrium - LA ($p = 0.001$), longer LV filling time - FT ($p = 0.019$), shorter isovolumic relaxation time ($p = 0.037$), shorter pulmonary acceleration time - PAAT ($p = 0.006$), lower left atrial lateral wall myocardial velocity (a') ($p = 0.018$) and lower septal systolic myocardial velocity (s') ($p = 0.023$), compared with Group II. Patients with HF and reduced EF (HFrEF) had lower hemoglobin ($p = 0.007$), higher baseline heart rate ($p = 0.005$), higher NT-ProBNP ($p = 0.001$), larger LA ($p = 0.004$), lower septal s', e', a' waves, and septal MAPSE, shorter PAAT ($p < 0.001$ for all), lower lateral MAPSE, higher E/A & E/e', and shorter LVFT ($p = 0.001$ for all), lower lateral e' ($p = 0.009$), s' ($p = 0.006$), RV e' and LA emptying fraction ($p = 0.012$ for both), compared with HFpEF patients. In multivariate analysis, only LA diameter [2.676 (1.242-5.766), $p = 0.012$], and diabetes [0.274 (0.084 - 0.898), $p = 0.033$] independently predicted poor 6-MWT performance in the group as a whole. In HFrEF, age [1.073 (1.012 - 1.137), $p = 0.018$] and LA diameter [3.685 (1.348 - 10.071), $p = 0.011$], but in HFpEF, lateral s' [0.295 (0.099 - 0.882), $p = 0.029$], and hemoglobin level [0.497 (0.248-0.998), $p = 0.049$] independently predicted poor 6-MWT performance.
Conclusion: In HF patients predictors of exercise capacity differ according to severity of overall LV systolic function, with left atrial enlargement in HFrEF and longitudinal systolic shortening in HFpEF as the the main predictors.

PULMONARY HYPERTENSION

P1245

White blood cell count in pulmonary arterial hypertension: relation to pulmonary vascular resistance

H Gungor[1]; H Kaya[2]; M Meric[3]; YT Yaylali[4]; O Yazici[5]; AS Babu[6]
[1]Adnan Menderes University, Faculty of Medicine, Department of Cardiology, Aydin, Turkey; *[2]Cumhuriyet University, Cardiology, Sivas, Turkey*; *[3]19 May University, Cardiology, Atakum /SAMSUN, Turkey*; *[4]Pamukkale University, Cardiology, Denizli, Turkey*; *[5]Adnan Menderes University, Chest Disease, Aydin, Turkey*; *[6]Manipal University, Physiotheraphy, Karnataka, India*

AIM: Pulmonary vascular resistance (PVR) is an important hemodynamic variable used in the diagnosis and mangement of patients with pulmonary hypertension (PH). The positive relationship between WBC count and cardiovascular disease has been observed in several studies.
Methods: 20 patients (16 females) from four centers undergoing right heart catheterization having a mean age 56.20 ± 17.5 years, all belonging to group 1 PH [idiopathic

pulmonary arterial hypertension (PAH) (n = 11) and congenital heart disease (n = 9)] were retrospectively studied. Patients with associated PAH and anyone receiving anti-inflammatory treatment were excluded. All eligible patient records contained complete blood counts obtained using an automated blood counter. Parameters recorded were total white blood cells (WBC), neutrophils, lymphocytes and platelets, platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR) were. In addition, six minute walk distance (6MWD) was assessed and recorded.

RESULTS: The 6MWD mean pulmonary arterial pressure and mean PVR values were respectively 185.72 ± 121.10 meters, 41.79 ± 10.80 mmHg, 6.33 ± 3.00 WU (median=5.4) respectively. PVR showed significant correlation with WBC and neutrophil count. An inverse correlation was observed with PVR and age. However, ratios suggesting inflammation (i.e., NLR and PLR) were not correlated with PVR. When patients divided into two groups as PVR>5.4 WU and PVR < 5.4; age, platelet count, WBC and neutrophil count were significantly different between the groups. In a multivariate analysis only WBC count was found to be an independent predictor of PVR>5.4 WU (Table 1).

Conclusion: Our study suggests that high WBC count appears to be additive to predict higher PVR values in patients with PAH.

Table 1

		Univariate			Multivariate	
Statistically significant variables	p	OR	95%CI	p	OR	95%CI
White blood cell	0,038	2,042	1,042-4,002	0,029	5,198	1,187-22,771
Platelet	0,088	1,012	0,998-1,027			
Variables which correlated with PVR						
Age	< 0,001	0,972	0,958-0,986			
Neutrophil count	< 0,001	1,046	1,024-1,069			
SPAP	0,103	1,056	0,989-1,128			

Univariate and multivariate logistic regression analyses for predicting PVR>5.4 All the variables from Table 1 were examined and only those significant at P < 0.100 level and correlated with PVR are shown in univarite analysis.

P1246

Correlation betwen cardiac index and right ventricular sistolic function in pulmonary hypertension

HGSM Hector Gomez Santa Maria[1]; AF Alejandra Ferro[1]; GD Guido Damianich[1]; ALC Augusto Lavalle Cobo[1]; NG Nicolas Gonzalez[1]; GR Guadalupe Romero[1]; DC Diego Crippa[1]; MG Miguel Gonzalez[1]; HG Hugo Grancelli[1]; VD Victor Daru[1]; AL Adrian Lescano[1]

[1]Finochietto Clinic, Buenos Aires, Argentina

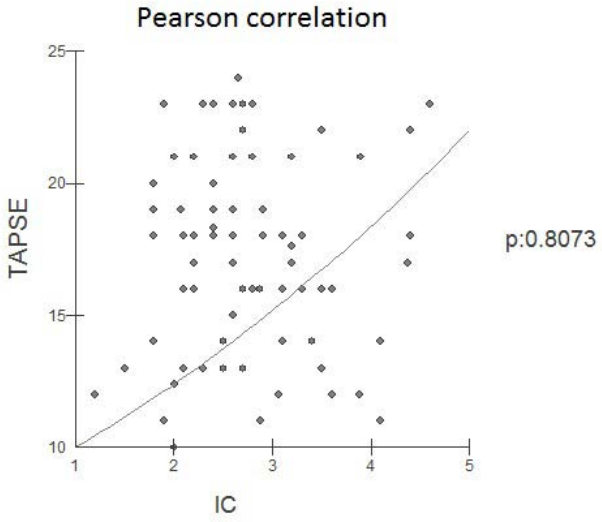
Pulmonary hypertension (PH) is a multifactorial desease defined as mean pulmonary arterial pressure ≥25 mmHg mesured by right heart catheterization.(RHC) International Guidelines recomend doppler ecocardiography as the method of screening to estimate the value of systolic pulmonary pressure and right ventricular systolic function (RVSF). The Tricuspid Annular Plane Systolic Excursion (TAPSE) is an indicator of RVSF, although it has been removed from the HP guidelines. The cardiac index (CI) is also an indicator of the right ventricular function and a marker of mortality. The question that arises is if there is a correlation between both techniques as indicators of RVSF.

Objective: To determinate the correlation between TAPSE and CI in our population, with the diagnosis of PH.

Material and methods: We conducted a multicenter, observational, prospective study that enrolled patients derived to our service with diagnosis of PH between March 2012 and Junary 2017. The following data were obtained: PH classification group, clinical features, hemodynamic variables, distance in the six minutes walk test (6MWT), functional class (FC), and echocardiographic measurements, according to guidelines. Echocardiographic variables were obtained by three experienced operators, with 2 ultrasound equipments (Vivid 5s) and a 3.5 mherz transducer, assessing: RVSF, TAPSE, pulmonary pressure and presence of pericardial effusion (EP). We performed RHC to confirm PH by measuring mean pulmonary artery pressure. We also recorded right atrium, systolic and diastolic pulmonary pressure (PP); wedge pressure, cardiac index (CI), pulmonary and systemic vascular resistance. Studies were performed with a difference of less than 24 hours and the physicians did not know echocardiography results. The results were incorpored into an Excel database. Bioestat 5.0 statistical package was used and linear correlation variables were analyzed.

Outcomes: We included 86 cases with hemodynamic diagnosis of HP. The average age of the population was 57.5 years (SD 19), 57.3 % were female. The diagnosis of HP was: Group (G) I 62.5%, G II 15%, G III 7%, and G IV and V 5% to 8%. In relation to clinical features 79% of p presented heart failure (HF) and 26% had syncope. Direct hemodynamic mean measurements were: systolic PP 76 mm Hg, MPP mean 46 mm Hg (SD 15.2), diastolic PP 32 mm Hg, right atrial pressure 9.1 mm Hg and cardiac index 2.86 (4.6-1.2) l / min / m2. The TAPSE average was 17.9 mm (30-10). The Pearson correlation coefficient between TAPSE and CI was: r 0.02 (95% CI 0.20-0.25), with a p = 0.08.

Conclusion: In our study population with established diagnosis of PH we observed a bad correlation between TAPSE and CI. This data support the need of cardiac catheterization to quantify right ventricular systolic function.



Pearson correlation

P1247

Prevalence and predictors of pulmonary hypertension in a general community based population

S Sebastiano Quartuccio[1]; E Imbalzano[1]; G Mandraffino[1]; G Trapani[1]; A Lo Gullo[1]; A Saitta[1]; M Vatrano[2]; VA Ciconte[2]; R Ceravolo[2]

[1]University of Messina, Department of Clinical and Experimental Medicine, University of Messina, Italy, Messina, Italy; *[2]Civil Hospital of Pugliese, UTIC and Cardiology , Catanzaro, Italy*

Background/Introduction: The exact prevalence of PH in Italy is not known. Echocardiography is useful in the screening of patients with suspected PH by estimation of the pulmonary artery systolic pressure (PASP) by regurgitant tricuspid flow velocity evaluation, according to the simplified Bernoulli equation.

PURPOSE: We conducted a retrospective study to estimate the prevalence of PH in 7005 patients who underwent echocardiography.

Methods: Clinical data and echocardiographic results were used to determine etiological group of PH. Clinical data and echocardiographic results were used to determine etiological group of PH. PH causality was coded using criteria and subcategories of the ESC classifications.

Results: The mean age of the study population was 57.1 ± 20.5 years with 55.3% male. The prevalence of intermediate probability of PH was 8.6%, with nearly equal distribution between men and women (51.3 vs 48.7 %; P=NS) whereas the prevalence of high probability of PH was 4.3%, with slightly but not significant higher prevalence in female patients (43.2 vs 56.8; p = ns); PH is more prevalent in patients with chronic obstructive pulmonary disease (COPD) or left ventricle (LV) systolic dysfunction. PH prevalence increased with age. Also, sPAP was significantly associated with left atrial enlargement, left ventricular ejection fraction and, in addition, an increased sPAP was related to an enlargement of the right atrium and right ventricle.

Conclusion(s): PH as measured by echocardiography has low prevalence in our general population, but the estimates may be higher in specific subgroups. Analysis of the registry data could be an instrument for quality control and might help identify weak points in assessment and treatment of these patients.

P1248

New insights into inpatient symptom burden in pulmonary arterial hypertension

MA Mahesh Chandrasekhar[1]; C Barnett[1]; G Ruiz[1]; K Walker[1]; H Groninger[1]
[1]*Washington Hospital Center, Cardiology, Washington, United States of America*

BACKGROUND: Despite the high symptom burden in patients with pulmonary arterial hypertension, there is a relative paucity of research in the inpatient palliative care needs of this population. The aim of this study was to assess the palliative care needs of a pulmonary arterial hypertension cohort by retrospective review.
Methods: Patients with PAH receiving PC consultation were retrospectively evaluated from a large single center advanced heart failure (AHF) center in the United States. The PC team (specially trained physician, nurse practitioner, pharmacist, social worker, chaplain) is embedded within the AHF clinical program. Data on symptom burden was collect via a modified Edmonton Scale. Data on length of stay, palliative care interventions, and final disposition were evaluated using descriptive statistics.
Results: Consultations were performed on 11 PAH (median hospital length-of-stay 6 days) from January to December in 2015. Two patients developed PAH secondary to scleroderma, one patient developed PAH secondary to systemic sclerosis, and the rest of the cohort had idiopathic PAH. In all cases, reason for PC consultation was either goals of care (4 patients), pain control (6 patients) or non-pain symptom management (1 patient). In regard to pain control, 64% reported moderate to severe pain at time of consult; at 48 hours after consult, pain was resolved or reduced to mild pain in only 43% of patients. In regard to non-pain symptom management, 27% of patients were evaluated for moderate or severe dyspnea, 9 % moderate or severe depression, and 9% moderate or severe constipation. As a result of PC evaluation, 73% of patients received psychological counseling, 64% of patients received spiritual counseling, 27% participated in discussions that facilitated a change in resuscitation status, and 9% of patients were referred to hospice.
Conclusions: Patients with Pulmonary Arterial Hypertension have a unique and significant symptom burdens and palliative care needs in the inpatient setting.

P1249

Invasive and non-invasive characteristics of heart failure patients, related to pulmonary hypertension due to left heart disease, in qualification process for heart transplantation

J Migaj[1]; MI Marta Izabela Kaluzna-Oleksy[1]; M Dudek[1]; E Straburzynska-Migaj[1]
[1]*Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland*

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 (HF). 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: Characterization of patients with heart failure with reduced ejection fraction (HFrEF) considered for heart transplantation (HTX)with and without PH. Evaluation of the role of non-invasive tests in diagnosis of PH in HFrEF patients.
Methods: This was a prospective analysis of 211 patients with HFrEF (left ventricular ejection fraction $<40\%$), with ischemic(ICM) and non-ischemic cardiomyopathy(NICM) undergoing qualification process for HTX. Following items were analyzed:epidemiological data, laboratory results (including BNP), and chosen parameters obtained in echocardiography, cardiopulmonary exercise testing (CPET) and RHC (thermodilution method). PH was diagnosed according to the ESC guidelines.
Results: The mean age of the analyzed patients was 52 ± 10 years, and most were men(88%); 72% had NYHA class 3 and 4. There were 141 patients(70%) with PH, including 138 with post-capillary PH and 3 with combined pre- and post-capillary PH. The patients with PH did not differ significantly from those without as to age, gender or cause for HF. They had more often NYHA class 3 and 4 (79%vs56%;$p = 0.002$) and showed significantly higher BNP (992vs361 pg/mL;$p < 0.001$), larger right ventricle in echocardiography (36 mmvs32 mm;$p < 0.001$) and higher right ventricular systolic pressure (RVSP) (47vs36;$p < 0.001$). There were no significant differences as to left ventricle and EF. There were no significant differences in CPET, but PH patients tended to show worse results: pVO2(14vs20 ml/kg/min;$p = 0.112$) and VE/VCO2 slope 40vs37;$p = 0.077$). BNP showed significant positive correlations with mean pulmonary arterial pressure (mPAP) (r=0.21), mean right atrial pressure (r=0.28), and pulmonary capillary wedge pressure (PCWP) (r=0.27). There was no significant correlation between BNP and transpulmonary gradient (TPG), pulmonary vascular resistance(PVR) and mean right ventricular pressure. RVSP measurement in echocardiography correlated positively with mPAP, diastolic PAP, mean right atrium pressure (mRAP), RVP, PCWP, TPG and diastolic pressure gradient(DPG) measured in RHC. There were also significant correlations between RVSP and pulmonary vein resistance (PVR) (r=0.44).
Conclusions: Non-invasive test results like BNP, echocardiographic and CPET parameters correlate with invasive RHC parameters in patients with HFrEF. Patients with HFrEF and PH present higher NYHA class and higher BNP levels, despite similar LVEF or LV size in comparison to those without PH. Combined non-invasive parameters provide a useful and feasible tool for evaluation of HFrEF patients to differentiate those with PH and without.

P1250

The impact of pulmonary hypertension on post-transplant outcomes

M Maria Simonenko[1]; P Fedotov[1]; K Malikov[2]; Y Sazonova[3]; A Bautin[4]; V Rubinchik[5]; O Moiseeva[6]; M Sitnikova[7]; G Nikolaev[3]; M Gordeev[3]; M Karpenko[2]
[1]*Federal North-West Medical Research Centre, Cardiopulmonary test, Saint-Petersburg, Russian Federation*; [2]*Federal Almazov North-West Medical Research Centre, Saint-Petersburg, Russian Federation*; [3]*Federal Almazov North-West Medical Research Centre, Thoracic Surgery and Transplantation Laboratory, Saint-Petersburg, Russian Federation*; [4]*Federal Almazov North-West Medical Research Centre, Pulmonary Hypertension Department, Saint-Petersburg, Russian Federation*; [5]*Federal Almazov North-West Medical Research Centre, ICU department 4, Saint-Petersburg, Russian Federation*; [6]*Federal Almazov North-West Medical Research Centre, Non-coronary disease department, Saint-Petersburg, Russian Federation*; [7]*Federal Almazov North-West Medical Research Centre, Heart Failure Department, Saint-Petersburg, Russian Federation*

Puprose: The aim of study was to evaluate the impact of pulmonary hypertension (PHT) on early and late results after heart transplantation (HTx).
Methods: From 2010 to 2016 we performed 80 HTx (57 – male, 23 – female). Causes of heart failure were ischemic heart disease (47,5%; n=38), dilated cardiomyopathy (32,5%; n=26), non-compacted myocardium (11,3%; n=9) and others (9%; n=7). Recipients separated into 2 groups according to right heart catheterization results: 1st group - patients with PHT ($n = 54$; mean PAP $>$ 25 mm Hg) and 2nd group - without PHT ($n = 26$; mean PAP $<$ 25 mm Hg). Mean age of recipients in 1st group was $45,6 \pm 15,0$ yrs, pulmonary vascular resistance (PVR) – $3,6 \pm 1,4$ WU, PVR after reduction test (Iloprost 20 mkg, NO 80ppm) – $2,7 \pm 1,0$ WU, pulmonary artery systolic pressure (PASP) – $49,3 \pm 12,7$ mm Hg, pulmonary artery wedge pressure (PAWP) – $20,5 \pm 7,0$ mm Hg. In 2nd group mean age of patients was $46,9 \pm 11,9$ yrs, PVR – $2,1 \pm 0,8$ WU, PASP – $28,2 \pm 4,8$ mm Hg, PAWP – $11,9 \pm 4,3$ mm Hg. Outcomes were estimated by the time in ICU, results of TTE, frequency of right heart failure (RHF) and vasodilator indications.
Results: After HTx there was no significant difference in how much time patients with PHT or without spent in ICU (8 [4;49] days vs. 7 [4;36] days). But time spent in ICU in 1st group was more complicated: RHF occurred in 9% cases due to they were implanted extracorporeal membrane oxygenation (ECMO) support, 7% - underwent tricuspid valve repair due to severe tricuspid regurgitation. There was no indications in 2nd group to implant ECMO. Levosimendan treatment was successfully used in patients with PHT and without (41% ($n = 22$) vs. 15% ($n = 4$), $p < 0,05$). During 6 months after HTx 13% ($n = 7$) of recipients from 1st group treated by Sildenafil. Six months after HTx TTE results got to normal values in both groups: PVR (1st group - $1,8 \pm 0,5$ WU vs. 2nd group – $1,6 \pm 0,4$ WU, $p>0,05$), PASP ($34,8 \pm 6,7$ mm Hg vs. $35,1 \pm 4,4$ mm Hg, $p>0,05$), PAWP ($12,2 \pm 5,9$ mm Hg vs. $11,1 \pm 3,9$ mm Hg, $p>0,05$). Six months after HTx PASP significantly decreased in 1st group from $49,3 \pm 1,8$ mm Hg to $34,8 \pm 1,0$ mm Hg ($p < 0,001$), the same as PVR – from $3,6 \pm 0,2$ WU to $1,8 \pm 0,9$ WU ($p < 0,001$). There was no significant difference in TTE results in 6 months and in 1 yr after HTx.
Conclusions: Time in ICU of patients with PHT is complicated and development of RHF is more frequent what require specific treatment. After HTx PHT full regressed.

P1251

Clinical and echocardiographic correlates of pulmonary hypertension in heart failure patients

O A Kushimo[1]; AC Mbakwem[1]; JNA Ajuluchukwu[1]
[1]*Lagos University Teaching Hospital, Lagos, Nigeria*

Background: Pulmonary hypertension (PH) is highly prevalent amongst heart failure (HF) subjects and now recognized as an independent predictor of poor prognosis. Not much is known presently in our environment about the frequency and correlates of PH in HF, its effect on management and impact on outcomes. Studies on this subject will help us in better risk stratification, management and prognostication of our heart failure patients.
Purpose: To determine the frequency of PH in an academic hospital in our environment and assess its correlates using echocardiography.
Methods: Heart failure patients, 219, in New York Heart Association (NYHA) class II-IV were consecutively recruited from the emergency room and the cardiology out-patient clinic. Those with other co-morbidities that could cause PH were excluded. Data on demographic parameters, clinical features and

echocardiography were obtained. Correlation between elevated pulmonary artery systolic pressure (PASP), mean pulmonary artery pressure (mPAP) and selected clinical/echocardiographic parameters were further interrogated.
Results: The frequency of PH was determined by two criteria. PH using a PASP cut off of >36mmHg was present in 85 (38.8%) of subjects. However, using the mPAP criterion of ≥ 25mmHG, PH was present in 135 (61.6%) of subjects. Heart failure subjects with PH were more likely to be male ($p = 0.03$) with a lower body mass index ($p < 0.01$), lower systolic blood pressure ($p < 0.01$) and a worse NYHA functional class ($p < 0.01$) compared with subjects without pulmonary hypertension. Heart failure subjects with PH also had significantly higher left ventricular (LV) filling pressures, (higher left atrial volume index and E/e'ratio), more severe mitral regurgitation (higher mitral regurtitant volume), poorer LV systolic function, and worse parameters RV structure and function compared with those without PH. Echocardiographic variables that correlated significantly PASP include parameters of LV filling pressures ($p < 0.001$ for all), mitral regurgitant volume ($r = 0.269$, $p < 0.001$) LV and ejection fraction ($r = -0.239$, $p > 0.001$). Similar correlations were obtained with mPAP. On multivariate analyses, the left atrial volume index and E/e' ratio were independently associated with PASP, while the LV ejection fraction, E/e' ratio and the left atrial volume index were independently associated with mPAP.
Conclusion: PH is quite common amongst heart failure subjects in our environment with a variable frequency depending on the assessment method employed. It is associated with higher LV filling pressure, more severe MR, poorer LV systolic function and worse RV remodeling. Routine screening for PH amongst heart failure patients is recommended for better risk stratification and management.

P1252
How different responses of total pulmonary vascular resistance to exercise can influence right ventricular inotropic reserve and functional capacity in post pulmonary endarterectomy patients?

A R Ana Rita Almeida[1]; MJ Loureiro[1]; L Lopes[1]; D Repolho[1]; F Ferreira[1]; S Alegria[1]; AR Pereira[1]; P Fazendas[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Almada, Portugal

Introduction: After pulmonary endarterectomy (PEA) there is an abnormal pulmonary hemodynamic response to exercise, even in patients (pts) with near normal resting hemodynamics, causing excessive afterload of the right ventricle (RV) and exercise limitation.
Purpose: Determine if different responses of total pulmonary vascular resistance (TPVR) to exercise can affect RV inotropic reserve and functional capacity during exercise echocardiography (EE) in pts after PEA.
Methods: EE was done using treadmill ergometer and modified Bruce protocol until exhaustion. During exercise pts went symptoms, arterial pressure and ECG monitoring. To evaluate RV function we used right ventricle stroke volume indexed to body surface area (RVSVI); tricuspid annular plane systolic excursion (TAPSE); free RV wall S wave (S wave) and RV fractional area change (RVFAC). To evaluate total pulmonary vascular resistance (TPVR) = mean pulmonary artery pressure (mPAP)/cardiac output (CO); for this we have to evaluate mPAP = systolic pulmonary artery pressure (PSAP)x0.6 + 2, where PSAP=RV/RA (right atrium) gradient + RA pressure estimate and CO=LVSV(left ventricular stroke volume) (LVOT VTI x LVOT area) x heart rate. We used test duration to define functional capacity. We defined 2 groups of pts according to variation of TPVR during exercise, one in which TPVR increased and other in which TPVR decreased and compared variables of RV function and test duration between them using t'student test for independent samples.
Results: The group of post' PEA pts consisted of 13 patients at least 6 months after PEA, with mean age of 57.0 ± 11.7 years, 7 females. When compared the 2 groups, we verified that pts in whom TPVR increased with exercise (3 pts) had significant lower functional capacity (test duration of 606.7 ± 46.5 vs 777.6 ± 179.6 sec. ($p = 0.02$)), significant lower increase in TAPSE (1 ± 2.6 mm vs 6.2 ± 3.1 mm ($p = 0.02$)) and significant lower increase in RVSVI (3.4 ± 2.5 mL/m2 vs 11.2 ± 4.6 mL/m2 ($p = 0.02$)). We didn't verify significant differences in variation of RVFAC and S wave between the 2 groups.
Conclusions: Pts in whom TPVR increased with exercise had lower functional capacity and lower RV inotropic reserve than pts in whom it decreased with exercise. Perhaps different responses of TPVR to exercise can be used to differentiate post' PEA pts with different prognosis.

P1253
Pulmonary hypertension in end-stage renal disease patients undergoing haemodialysis via arterio-venous access

A Amin[1]; M Chitsazan[1]; H Navid[1]; M Chitsazan[1]
[1]Rajaei Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Heart Failure and Trasnplantation, Tehran, Iran (Islamic Republic of)

Background: Pulmonary hypertension (PH) has been described in a considerable proportion of end-stage renal disease (ESRD) patients on hemodialysis and has been associated with worse prognosis. Our objective was to determine the right heart catheterization-derived hemodynamic data in ESRD patients on regular hemodialysis.
Methods: Fifty-five patients with ESRD who were on maintenance hemodialysis through an arteriovenous fistula underwent screening for PH with trans-thoracic echocardiography (TTE). Patients who were found to have PH on screening TTE (i.e., pulmonary arterial systolic pressure of >25 mmHg and tricuspid regurgitant velocity of >3.8 m/s) underwent diagnostic right heart catheterization (RHC) for evaluation of their hemodynamic status.
Results: Out of 55 patients, 30 (54%) patients had PH in initial screening with TTE (mean age of 39 ± 11 years). Of these 30 patients, 24 patients (80%) had post-capillary pulmonary hypertension (Class II PH) and 6 patients had pre-capillary pulmonary hypertension (Class I PH); based on the RHC findings. The RHC findings are demonstrated in Table1.
Conclusion: ESRD patients on maintenance hemodialysis therapy have a substantial risk of developing PH which in the vast majority of cases appears to be post-capillary.

Table 1

Table 1. Right Heart Catheterization Findings

	Class I PH(N=6)	Class II PH (N=24)
MVO2 (%)	77.83±4.79	71.78±8.63
CI (l/min/m^2)	5.13±2.10	6.15±4.45
PAP (mmHg)SystolicDiastolicMean	41.66±15.70 18.00±11.22 26.38±12.18	49.87±15.92 25.45±6.99 33.57±9.43
PCWP (mmHg)	12.66±2.33	24.04±5.26
PVR (dyn · sec · cm^{-5})	1.21 (0.54-3.24)	1.07 (0.36-1.70)

Data are presented as mean ± standard deviation or median (interquartile range). Abbreviations: CI; cardiac index, MVO2; mixed venous O2 saturation, PAP; pulmonary artery pressure, PCWP; pulmonary capillary wedge pressure, PVR; pulmonary vascular resistance.

P1254
Prevalence and determinants of pulmonary arterial hypertension (PAH) in acute and chronic heart failure (CHF).FRESH study from GICC

T Thibaud Damy[1]; R Isnard[2]; M Saval[3]; C Tribouilloy[4]; F Picard[5]; JC Eicher[6]; F Roubille[7]; JN Trochu[8]; G Roul[9]; P De Groote[10]; E Berthelot[11]; V Bataille[12]; N Naccache[12]; F Bauer[13]; D Logeart[14]
[1]AP-HP - University Hospital Henri Mondor, Creteil, France; *[2]Hospital Pitie-Salpetriere, Cardiology, Paris, France*; *[3]University Hospital of Grenoble, Cardiology, Grenoble, France*; *[4]University Hospital of Amiens, Cardiology, Amiens, France*; *[5]University Hospital of Bordeaux, Cardiology, Bordeaux, France*; *[6]University Hospital of Dijon, Cardiology, Dijon, France*; *[7]University Hospital of Montpellier, Montpellier, France*; *[8]University Hospital of Nantes, Cardiology, Nantes, France*; *[9]University Hospital of Strasbourg, Cardiology, Strasbourg, France*; *[10]CHRU Lille, Cardiology, Lille, France*; *[11]Hospital Bicetre, Cardiology, Bicetre, France*; *[12]French Society of Cardiology, Paris, France*; *[13]University Hospital of Rouen, Rouen, France*; *[14]Hospital Lariboisiere, Cardiology, Paris, France*

On behalf of: GICC

Objectives: To investigate the prevalence and the determinants of pulmonary arterial hypertension (PAH) in acute and chronic heart failure (CHF) in France.
Background: The epidemiology of PAH in France in CHF is poorly described.
Methods: FRESH is an on-going multicenter survey collecting exhaustive data in both acute and chronic HF (NCT01956539). Estimate of systolic pulmonary artery pressure(SPAP) was attempted routinely by echocardiography and was divided in three classes: ≥45mmHg (Gr3), <45mmHg (Gr2) and not measured/able (Gr1). The diagnosis of CHF was based on symptoms, signs, echocardiography NT-proBNP. Comparisons were performed using chi^2 tests for categorial variables and ANOVA or non-parametric Kruskal Wallis test for continuous variables. Logisticregression-wasused to identify factors associated with PAPS≥45mmHg (Gr3).
Results: 2093 patients were included in FRESH. 1690 (81%) had an echocardiography of whom 596 (35%) were in AHF, of whom 29%, 34%% and 37% were respectively in Gr1, Gr2 and Gr3 and 1094 (65%) were in CHF of whom 31%, 48%, 21% were respectively in Gr1, Gr2 and Gr3. Independent factors associated with Gr3 (vs Gr1 and Gr2 pooled) were mitral insufficiency, High grade NYHA (III/IV), increased BNP, increased LVEDD and reduced TAPSE.
Conclusion: Using a definition of PASP>45mmHg, 37% of patients with AHF and 21% of CHF had pulmonary hypertension, which was associated with LV remodeling and mitral insufficiency leading to right ventricle failure. Whether PAH a target for therapy in these populations remains to be elucidated.

Variables		AHF		p		CHF		p
	Gr1	Gr2	Gr3		GR1	GR2	GR3	
Age, yrs *	71 (14)	70 (13)	73 (12)	0.11	63 (15)	65 (14)	66 (14)	0.07
Male, %	64	64	68	0.56	75	74	71	0.55
SBP, mmHg *	131 (31)	132 (29)	128 (27)	0.25	124 (20)	122 (21)	120 (21)	0.13
Ischemic Heart disease **, %	37	30	35	0.33	38	35	41	0.36
Class of HFHFref (<40)HFmref (40-49)HFpef (50+)	47	18	35	49	13	38	53	14	33	0.47	52	27	21	53	22	25	71	12	17	<0.001
LVEDD, mm *	59 (13)	57 (11)	61 (13)	0.04	60 (11)	61 (13)	64 (11)	< 0.01
IVSTD, mm ***	12 (9-14)	11 (9-13)	11 (9-13)	0.24	10 (8-12)	10 (8-12)	10 (8-12)	0.68
Mitral insufficiency,%	7	8	26	< 0.001	6	4	14	< 0.001
TAPSE *	16 (5)	17 (5)	15 (5)	0.11	18 (5)	19 (5)	17 (6)	< 0.01

* Mean (SD)** Previous PCI, CABG or MI*** Median (IQ)

* Mean (SD)** Previous PCI, CABG or MI*** Median (IQ)

RIGHT VENTRICULAR FUNCTION

P1255

Persistent right ventricular dysfunction in patients with acute pulmonary embolism: does it have effect on prognosis?

J Simoes[1]; J Bicho Augusto[1]; M Borges Santos[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal*

Background: Right ventricular (RV) dysfunction is found in at least 25% of patients with acute pulmonary embolism (PE). The presence of RV dysfunction at diagnosis of acute PE is a determinant of the severity and early clinical outcome and its detection is useful for risk stratification of the disease. However, the effect on prognosis of persistent RV dysfunction after the standard treatment for acute PE has not been defined so well.
Purpose: To evaluate the effect of persistent RV dysfunction, at the time of discharge, in patients hospitalized for acute PE. The effect was measured by post-discharge all-cause mortality.
Methods: Retrospective review of 428 consecutive patients admitted for acute PE in a single-center hospital for two years until October 2016. We identified those who underwent transthoracic echocardiogram and who were found to have RV dysfunction at the moment of hospital admission (n = 103, 24.1%). RV dysfunction was defined as the presence of either RV dilatation, TAPSE < 16 mm, S' tricuspid < 10 cm/s or maximum tricuspid velocity regurgitation > 2.6 m/s. A second transthoracic echocardiogram was performed at discharge in 45 patients (43.7%) and the persistence of RV dysfunction was looked for. Patients were categorized in one of two groups: group 1 - those in whom RV dysfunction was present at the moment of their hospital admission, but not at discharge (n = 19; 42.2%); and group 2 - those in whom RV dysfunction was present at the moment of hospital admission and persisted at discharge (n = 26; 57.8%). Primary outcome was defined as the occurrence of all-cause mortality after discharge.
Results: We included 45 patients with acute PE and RV dysfunction at admission who were successfully discharged (mean age 66.2 ± 17.8 years, 28.9% males). Median follow-up time was 495 (interquartile range (IQR) 417) days. Mortality rate after discharge was 8.9%. Median proBNP was significantly superior in group 2 than in group 1 (median 12.597 vs. 293 pg/mL; p = 0.029). Similarly, patients in group 2 had significantly higher mortality rate than patients in group 1 (0.0 vs. 21.1%; p = 0.026).
Conclusions: In patients admitted for acute PE, mortality seems to be higher in those who have persistent RV dysfunction before discharge. Although these results must be confirmed by better-designed, prospective study cohorts, we believe our study may point to the relevance of further risk stratification of patients whose RV dysfunction is present at the initial echocardiographic evaluation and persists before discharge from the hospital.

P1256

Short-term prognostic value of shock index in normotensive oncologic patients with pulmonary embolism: keep it simple

S Moura Ferreira[1]; J Ferreira[2]; V Marinho[2]; P Marques[2]; N Silva[3]; R Baptista[2]; MJ Ferreira[2]; M Pego[2]
[1]*Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal*; [2]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; [3]*University Hospitals of Coimbra, Internal Medicine, Coimbra, Portugal*

INTRODUCTION: The Shock Index (SI), although not included in the standard risk assessment of PE, showed better performance than the ESC model in normotensive patients suffering for acute PE. The value of SI to predict short-term mortality in normotensive oncologic patients with symptomatic PE is currently unknown. In this study, we aimed to assess the value of SI to predict 30-day all-cause mortality in normotensive oncologic patients with acute symptomatic PE.
Methods: Retrospective, observational study that included all normotensive cancer patients with acute PE diagnosed during emergency room stay by MDCT between January 2010 and December 2011. Demographic and clinical data, MDCT variables and blood tests results were collected for all patients. The primary endpoint of this study was 30-days all-cause mortality. We used a t test to compare means of SI between patients that died at 30-days and those that have survived. A receiver operating characteristics (ROC) curve was used to test SI as a predictor of the primary endpoint and to obtain the best cut-off value. Then we transformed SI into a categorical variable with 2 groups and conducted a Cox regression survival analysis to test the strength of prediction for 30-days overall mortality.
RESULTS: Between January 2010 and December 2011, 69 normotensive patients (42 males, median age 73 years) were diagnosed with acute PE by MDCT during emergency room stay. 19 (27.5%) patients died at 30 days of FU. There were significant differences in Mean Arterial Pressure (100.15 ± 2.55mmHg vs 88.37 ± 3.24mmHg, p = 0.01), Log Lactates (0.18 ± 0.03mmol/L vs 0.34 ± 0.06mmol/L, p = 0.02) and SI (0.68 ± 0.03 vs 0.83 ± 0.04, p < 0,01) between survivors and non-survivors at 30 days of follow-up. There were no other significant differences between the 2 groups, including cardiac biomarkers and a sPESI score≥2. As there was a significant interaction between SI, Log Lactates and Mean Arterial Pressure, only SI was included in cox regression analysis. The area under the curve (AUC) for SI was 0,71 (p < 0,01), yielding moderate discriminative power. We considered the best cut off point to be a SI of 0.62 (sensitivity 94,7 and specificity 42,0). In a cox regression analysis a SI equal or greater than 0.62 was strongly associated with a worse prognosis during the first month of follow-up (unadjusted OR 10.37 with a 95% confidence interval 1.38 – 77.71, p = 0,02).
Conclusion: SI is simple and strong independent predictor of 30-day all-cause mortality in normotensive cancer patients admitted in the emergency room with acute PE. In our population, a sPESI≥2 was not a predictor of fatal outcome at 30 days of FU.

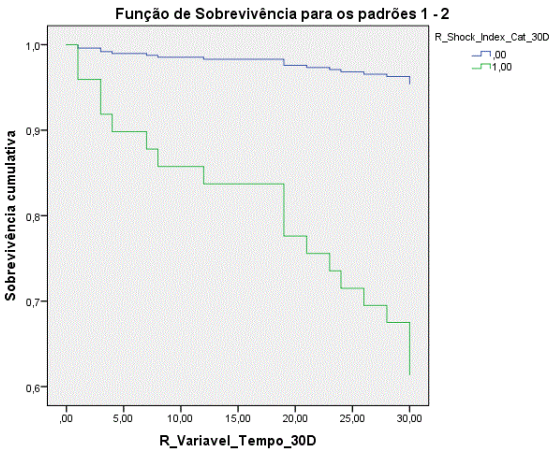


Figure 1

P1257

Late ventricular potentials in patients with arterial hypertension and coronary artery disease

VA Kuznetsov[1]; LG Evlampieva[1]; EI Yaroslavskaya[1]; EA Gorbatenko[1]
[1]*Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Tyumen, Russian Federation*

Background: Late ventricular potentials (LVPs) recorded by signal-averaged electrocardiography (ECG) are used as a prognostic factor for ventricular arrhythmias in patients with arterial hypertension (AH) and with coronary artery disease (CAD). However, the impact of combination of both diseases on LVPs has not been fully studied.
Purpose: To reveal factors influencing on LVPs in patients with AH and CAD.
Methods: The study enrolled 190 patients: 85 with AH, 39 with CAD and 66 with combined CAD and AH. All patients were divided into 2 groups: 41 subjects (mean age 44.3 ± 13.2 years) with LVPs (group I) and 149 subjects (mean age 44.6 ± 12.6 years) without LVPs (group II). Signal-averaged ECG was recorded using the standard Simson method. ECG signal averaging has been applied for 300 complexes using three orthogonal leads system. Enhanced, averaged and filtered with a bandwidth of 40-250 Hz signals were combined into vector amplitude of these orthogonal leads. Based on the automatic algorithm the quantitative evaluation of three parameters was performed with the following criteria for LVPs: filtered QRS complex duration (F QRS d) longer than 120 milliseconds; duration of low amplitude signals lower than 40 μV (LAS40) >38 ms, and less than 20 μV of the root mean square signal amplitude in the last 40 milliseconds of the filtered QRS complex (RMS40). A patient was considered to show LVPs if at least two criteria were present.
Results: Group I patients were higher than patients of group II (175.6 ± 6.84 vs 171.1 ± 8.02 cm, p=0.001). Significant differences were detected in group I compared to group II in the number of men (40 (97.6%) vs 124 (83.2%), p = 0.018); previous myocardial infarction (18 (43.9%) vs 40 (26.8%), p = 0.036); right ventricular (RV) dimension (25.00 ± 2.94 vs 23.45 ± 4.35 mm, p = 0.049); aorta size (34.37 ± 4.20 vs 32.93 ± 3.73 mm, p = 0.037); left ventricular ejection fraction (LVEF) (56.76 ± 6.98 vs 59.95 ± 7.23%, p = 0.003), as well as the tendency for difference in left ventricular size was observed (51.17 ± 3.92 vs 49.68 ± 4.44 mm, p = 0.057). No difference between the groups was found in age, smoking status, AH, angina and circulatory insufficiency. LVPs recorded in patients with AH was 15 (17.6%) vs 7 (17.9%) in patients with CAD and 19 (28.8%) in patients with CAD and AH. Logistic regression showed the association of probability of LVPs with RV enlargement (OR 1.16, 95% CI 1.01 to 1.34; p = 0.042) and with reduced LVEF (OR 0.953, 95% CI 0.909 to 0.999, p = 0.049).
Conclusion: LVPs were independently associated with RV dimension and LVEF in patients with AH and CAD.

P1258

Shock Index is an independent predictor of long-term mortality in normotensive oncologic patients with pulmonary embolism

S Sara Moura Ferreira[1]; J Ferreira[2]; V Marinho[2]; P Marques[2]; N Silva[3]; R Baptista[2]; MJ Ferreira[2]; M Pego[2]
[1]*Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal*; [2]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; [3]*University Hospitals of Coimbra, Internal Medicine, Coimbra, Portugal*

Introduction: The Shock Index (SI), although not included in the standard risk assessment of PE, showed better performance than the ESC model in normotensive patients suffering for acute PE in a recently published study. The value of SI to predict long-term mortality in normotensive oncologic patients with symptomatic PE admitted in the emergency room is currently unknown. In this study, we aimed to assess the value of SI to predict 1-year all-cause mortality in normotensive oncologic patients with acute symptomatic PE.
Methods: Retrospective, observational study that included all normotensive cancer patients with acute PE diagnosed during emergency room stay by MDCT between January 2010 and December 2011. Demographic and clinical data, MDCT variables and blood tests results were collected for all patients. The primary endpoint of this study was 1-year all-cause mortality. We used a t test to compare means of SI between patients that died at 1 year of follow-up and those that have survived. A receiver operating characteristics (ROC) curve was used to test SI as a predictor of the primary endpoint and to obtain the best cut-off value. Then we transformed SI into a categorical variable with 2 groups and conducted a Cox regression survival analysis to test the strength of prediction for 1-year overall mortality.
Results: Between January 2010 and December 2011, 69 normotensive patients (42 males, median age 73 years) were diagnosed with acute PE by MDCT during emergency room stay. 38 (55.1%) patients died at 1 year of FU. There were significant differences in Mean Arterial Pressure (103.31 ± 3.39mmHg vs 91.68 ± 2.44mmHg, p < 0.01), Log Lactates (0.16 ± 0.05mmol/L vs 0.34 ± 0.060.27 ± 0.04mmol/L, p < 0.05) and SI (0.65 ± 0.04 vs 0.77 ± 0.03, p = 0,02) between survivors and non-survivors at 1 year of follow-up. There were no other significant differences between the 2 groups, including cardiac biomarkers and a sPESI score≥2. As there was a significant interaction between SI, Log Lactates and Mean Arterial Pressure, only SI was included in cox regression analysis. The area under the curve (AUC) for SI was 0,66 (p = 0,02), yielding fair discriminative power. We considered the best cut off point to be a SI of 0.73 (sensitivity 71.1 and specificity 65.5). In a cox regression analysis a SI equal or greater than 0.73 was strongly associated with a worse prognosis during the first year of follow-up (unadjusted OR 3.11 with a 95% confidence interval 1.54 – 6.30, p < 0,01).
Conclusion: SI is simple and strong independent predictor of 1 year all-cause mortality in normotensive cancer patients admitted in the emergency room with acute PE. In our population, a sPESI≥2 was not a predictor of fatal outcome at 1 year of FU.

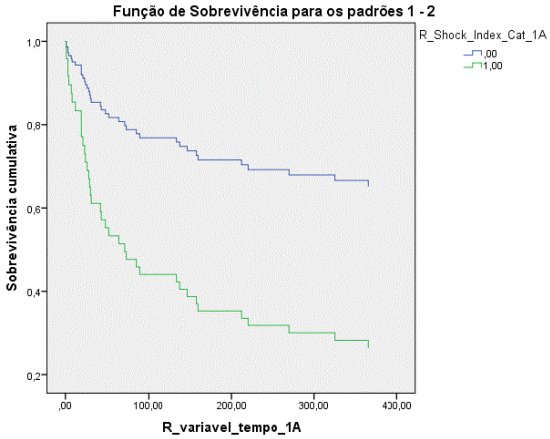


Figure 1

P1259

Does fibrinolytic therapy improves right ventricular function in acute pulmonary embolism?

J Simoes[1]; J Bicho Augusto[1]; M Borges Santos[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal*

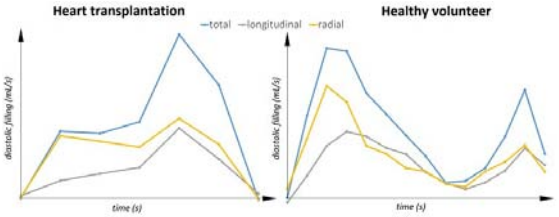
Background: Right ventricular (RV) dysfunction is found in at least 25% of patients with acute pulmonary embolism (PE). The presence of RV dysfunction at diagnosis of acute PE is a determinant of the severity and early clinical outcome and its detection is useful for risk stratification of the disease. However, it is not well known whether RV dysfunction at diagnosis of acute PE is improved by fibrinolytic therapy.
Purpose: To evaluate the effect of fibrinolytic therapy on RV function in patients with acute PE and echocardiographic signs of RV dysfunction.
Methods: Retrospective review of 428 consecutive patients admitted for acute PE in a single-center hospital for two years until October 2016. We identified those who underwent transthoracic echocardiogram and who were found to have RV dysfunction at the moment of hospital admission (n = 103, 24.1%). RV dysfunction was defined as the presence of either RV dilatation (defined as RV end-diastolic diameter >30 mm in parasternal long-axis or short-axis views, right-to-left ventricular end-diastolic diameter >0.9 in apical or subcostal 4-chamber views, or hypokinesis of the right ventricular free wall), tricuspid annular plane systolic excursion (TAPSE) <16mm, velocity of the tricuspid annular systolic motion (S') <10 cm/s or tricuspid regurgitant jet systolic velocity >2.6 m/s. Patients found to have RV dysfunction at the moment of hospital admission were further categorized in one of two groups: those who have undergone fibrinolysis (group 1) and those who have not undergone fibrinolysis (group 2). A second transthoracic echocardiogram was performed at discharge and the persistence of RV dysfunction was looked for.
Results: We included a total of 45 patients with acute PE and RV dysfunction at admission who had a reevaluation echocardiogram at discharge (mean age 66.2 ± 17.8 years, 28.9% males). Among these, 14 patients underwent fibrinolysis (31.1%). We found no differences in terms of RV dysfunction persistence between patients in group 1 and group 2 (42.9 vs. 41.9%, respectively; p = 0.954). There were no differences in proBNP values between the two groups (mean 9973 vs. 8694pg/mL; p = 0.901).
Conclusions: In acute PE, fibrinolytic therapy seems not to improve RV function in patients found to have RV dysfunction at admission. Given the fact that fibrinolytic therapy is not devoid of risk, these results may stress the current recommendation of restricting fibrinolysis to carefully selected patients.

P1260

Functional shift in right ventricular longitudinal versus radial contribution to diastolic fillling in heart transplant recipients

B K Balint Karoly Lakatos[1]; Z Toser[2]; M Tokodi[1]; A Assabiny[1]; B Sax[1]; A Kosztin[1]; B Merkely[1]; A Kovacs[1]
[1]*Semmelweis University Heart Center, Cardiovascular Imaging Group, Budapest, Hungary*; [2]*Eötvös Loránd University, Department of Software Technology and Methodology, Budapest, Hungary*

Previous studies reported the altered contribution of radial versus longitudinal motion to right ventricular (RV) global systolic function in patients underwent heart transplantation (HTX). However, the diastolic wall motions of the RV may be of high interest as well. Our aim was to quantify the longitudinal and radial components of diastolic RV wall motion in HTX patients compared to healthy volunteers. 47 heart transplant recipients (HTX, median of 258 days after HTX) were enrolled in the study, and 35 age- and gender matched healthy volunteers (CTL) served as the control group. Full volume datasets of the RV were acquired and 3D beutel models were created and exported volume-by-volume. Beyond conventional echocardiographic parameters, such as RV end-diastolic volume (EDV) we have determined the early (E) and late (A) diastolic filling volumes as well. Using our custom method, we were able to decompose the motion of the RV along the three orthogonal axes and quantify the relative contribution of radial and longitudinal motion to the two phases of diastolic filling (Erad, Elong, Arad, Along) and also the overall contribution of these components (Diarad and Dialong). Compared to CTL, HTX patients have significantly higher EDV (HTX vs. CTL 96 ± 28 vs. 79 ± 26 mL, $p < 0.01$). In the CTL group, the early diastolic filling volume was significantly higher, while in HTX patients the late diastolic filling was more dominant (E: 21 ± 9 vs. 28 ± 10 mL A: 20 ± 12 vs. 11 ± 5 mL, both $p < 0.01$) suggesting impaired relaxation. By decomposing the wall motions contributing to RV filling, we found that the two groups have different patterns: in early diastole, the HTX group has significantly lower Elong (5 ± 3 vs. 11 ± 4 mL, $p < 0.0001$) with comparable Erad (14 ± 6 vs.14 ± 7 mL, p = NS), and in late diastole both the Along and Arad are significantly higher compared to CTL (Along: 6 ± 4 vs. 3 ± 2 mL, Arad: 9 ± 7 vs. 4 ± 3 mL, both $p < 0.01$). The overall effect of longitudinal motion to diastolic filling is significantly lower in the HTX group, however, an increased radial contribution is present (Dialong: 10 ± 8 vs. 14 ± 4 mL; Diarad: 23 ± 8 vs. 17 ± 7 mL, both $p < 0.001$). Based on these findings, HTX results in a complex change in right ventricular diastolic function with an altered contribution of longitudinal and radial motion in early and late diastole as well.



HTX vs. CTL in diastole

LEFT VENTRICULAR FUNCTION

P1261

Changes in systolic and diastolic function in gestational hypertension and reversibility of these changes after delivery

A Ilic[1]; S Stojsic[1]; K Pavlovic[1]; A Stojsic-Milosavljevic[1]; T Miljkovic[1]; M Bjelobrk[1]; D Grkovic[1]; B Radisic[1]; S Tadic[1]; M Stefanovic[1]; DJ Ilic[2]; J Papovic[3]; A Milovancev[3]
[1]*Institute of CVD Vojvodina, Sremska Kamenica, Serbia*; [2]*Clinical Center of Vojvodina, Department of Gynecology and Obstetrics, Novi Sad, Serbia*; [3]*Institute of pulmology Vojvodina, Sremska Kamenica, Serbia*

Background: It was well known that diastolic function changed during pregnancy complicated by hypertension. The data about systolic function in gestational hypertension (GH) are more contradictory. Purpose: The purpose of this study was to establish whether systolic function was also impaired in GH and to determine the reversibility of these changes after delivery.
Methods: This study included 90 pregnant women, 60 with GH (defined as blood pressure ≥140/90 mmHg that was appeared after 20th week of gestation and disappeared within six weeks postpartum) and 30 normotensives as control. All participants underwent a complete echocardiography that was used to assess diastolic function: the left ventricular (LV) filling index E/e', IVRT, E, A, E/A, DTE; systolic function: EF, IVCT, ET, stroke volume index (SVi), cardiac output index (COi), Vcf, longitudinal systolic velocity at septal and lateral mitral annulus: s's and s'l; and global cardiac function: Tei index. The echo was performed in the third trimester and 6 weeks after delivery. Results: Participants with GH had more impaired systolic and global LV function. Tei index was higher in women with GH (0,48 ± 0,06 vs 0,36 ± 0,02; $p < 0,0005$), also IVCT was longer (61,13 ± 9,88 vs 49,9 ± 6,04; $p < 0,0005$). Hypertensive women had lower EF (62,8 ± 2,79 vs 64,3 ± 1,83; $p = 0,002$), shorter ET (289,28 ± 14,42 vs 300,17 ± 16,15; $p = 0,002$), reduced s's (0,088 ± 0,009 vs 0,098 ± 0,014; $p = 0,001$) and s'l (0,09 ± 0,015 vs 0,11 ± 0,01; $p < 0,0005$). There weren't significant differences in Vcf, COi and SVi between groups. Diastolic function was also more impared in GH compared to normotensives with high statistically differences. IVRT was longer (78,15 ± 12,42 vs 60,07 ± 4,55; $p < 0,0005$), also as DTE (176,72 ± 23,45 vs 157,6 ± 18,44; $p < 0,0005$), E/e' was higher (8,0395 ± 1,3035 vs 7,151 ± 1,252; $p = 0,003$), while women with GH had reduced E/A ($p < 0,0005$). There weren't significant differences between groups in the following parameters after delivery: EF, longitudinal systoloc velocity, IVCT, ET, E/e' and DTE. Also all changed echocardiographic parameters became improved six weeks after delivery, the difference persisted in women who had GH compared to normotensives in IVRT (62,1 ± 4,54 vs 57,9 ± 2,92; $p < 0,0005$), Tei index (0,38 ± 0,02 vs 0,36 ± 0,02; $p < 0,0005$) and E/A ($p = 0,004$). Conclusions: Both systolic and diastolic function changed in gestational hypertension. After delivery differences still remained present in global and diastolic cardiac function, while in systolic function there wasn't significant differences between women with gestational hypertension and controls.

P1262

Association of subclinical left ventricular dysfunction in type-2 diabetic patients with nighttime blood pressure pattern

A Angelina Stevanovic[1]; M Dekleva[2]
[1]*Railway Health Care Institute, Belgrade, Serbia*; [2]*University Clinical Center Zvezdara, Department of Cardiology, Belgrade, Serbia*

The authors aimed to discover subclinical left ventricular (LV) dysfunction in diabetic patients, and estimate risk stratification of patients according to LV dysfunction and nocturnal blood pressure (BP) pattern.
Methods: A total of 109 asymptomatic normotensive diabetic patients were divided into two groups according of ambulatory BP pattern: group of dippers (n = 71) and group of non-dippers (n = 38). Conventional and Tissue Doppler (TDI) echocardiography as well as Global longitudinal strain (GLS) was performed in all patients. Comparisons between two study groups in clinical, laboratory and echocardiographic parameters were assessed. Follow up period for all patients was three years for adverse cardiac events.
Results: Value of GLS was significantly lower (-17,0 ± 2,55 vs -18,1 ± 1,56, $p = 0.009$) and ratio of early diastolic velocities from mitral inflow and from annular TDI (E/Em) significantly higher (11,2 ± 3,34 vs 9,4 ± 2,37; $p = 0.001$) in non-dipping group. Using the GLS cut-off value of -17% as index of LV systolic dysfunction in 29% of whole patients (32/109) decreased GLS values were found, even 45% in non-dippers (17/38) ($p < 0.001$). By multivatiate model analysis, peak GLS and E/Em were two independent predictors for cardiac outcome.
Conclusions: Subclinical LV systolic dysfunction in non-dipping group is significantly common than in dipping group. GLS is a powerful parameter in early detection of subclinical systolic dysfunction and stratification of patients at higher risk for the future cardiac events.

P1263

Left ventricular-arterial uncoupling is associated with early cardiac remodeling in patients with myocardial infarction treated with percutaneous coronary intervention

E Zharikova[1]; S Villevalde[1]; ZH Kobalava[1]
[1]*RUDN Univercity, Moscow, Russian Federation*

Objective: Left ventricular (LV) remodeling is the precursor to developing heart failure and an important prognostic factor after myocardial infarction (MI). The value of modern non-invasive indices of LV and arterial system function in contemporarily treated patients with MI is not established. The aim of the study was to determine the relationship of adverse remodeling with the left ventricular-arterial coupling (VAC) in patients with MI treated with percutaneous coronary intervention (PCI).
Methods: In 112 patients with MI (64 (57.2%) with STEMI) and PCI (68% male, age 61.1 ± 9.5 years (M ± SD), smokers 35%, diabetes 7%, arterial hypertension 83%) 2-dimentional echocardiography was performed to assess arterial elastance (Ea) and end-systolic LV elastance (Ees) on admission and in 4 weeks and 6 months. VAC was assessed as the ratio Ea/Ees. Cardiac adverse remodeling was defined by ratio [follow up - initial LV end diastolic volume (LVEDV)] / initial LVEDV more than 20%.

Results: Baseline LV ejection fraction (LVEF) was 48.2 ± 4.6%, Ea 1.7 ± 0.3 mmHg/ml/m2, Ees 2.1 ± 0.3 mmHg/ml/m2, VAC 0.88 ± 0.2. At baseline all patients had LVEF >40% and VAC in optimal (0.5-1.2) range. In 4 weeks after PCI VAC >1.2 was revealed in 24 (29%) patients (33% STEMI), adverse LV remodeling - in 12 (10%) patients, all of them with VAC >1.2. After 6 months VAC ≥1.2 was found in 67 (75%) patients (68.6% STEMI), adverse LV remodeling - in 81 (90%) patients (71.6% with VAC >1.2). Achieved VAC >1.2 was associated with adverse cardiac remodeling (odds ratio 6.16; 95% confidence interval 2.47-15.37; p < 0.0005). In patients with achieved VAC >1.2 Ees significantly decreased (from 1.9 ± 0.3 to 1.3 ± 0.2 mmHg/ml/m2, p < 0.001) and Ea significantly increased (1.7 ± 0.3 to 2.1 ± 0.5 mmHg/ml/m2, p < 0.001). Conclusions: In patients with MI treated with PCI impairment of functioning of cardio-vascular system assessed by increased value of VAC >1.2 was revealed 75% of patients in 6 months. Increase of VAC was associated with decrease of Ees and increase of Ea. Increased VAC index >1.2 indicating LV-arterial uncoupling may be considered as early marker of adverse LV remodeling.

P1264
Longitudinal and circumferential myocardial strain in patients with STEMI with various types of left ventricular remodeling

V Valentin Oleinikov[1]; V Galimskaya[1]; E Melnikova[1]; N Burko[1]
[1]Penza State University, Penza, Russian Federation

Aim: to explore the changes of global longitudinal and circumferential deformation of the heart at 6 months after STEMI by two-dimensional Strain in patients with various types of left ventricular (LV) remodeling.
Methods: The study included 53 subjects with STEMI (53,2 ± 9,7 years). Inclusion criteria were the absence of hemodynamically significant stenoses of the coronary arteries except the infarct-related, previous myocardial infarction and other cardiovascular diseases. Echocardiography was performed on the ultrasonic scanner MyLab 90 (Esaote, Italy) at 7 days and 6 months from the onset of the disease. Global longitudinal (GLS) and global circumferential strain (GCS) were determined using X-Strain ™ software. Among the traditional indicators the end-diastolic volume index (EDV index) was analyzed.
Results: According to the degree of LV dilatation at 6 months 2 groups of patients were allocated conditionally: group 1 (N=23; 43,4%) which was characterized by rapidly progressive remodeling with an increase of EDV index on 8% or more; Group 2 (N=30; 56,6%), without remodeling when EDV index increased less than 8% since STEMI. GLS initially in groups 1 and 2 had the value (-14,6) ± 8,4 and (-15,7) ± 4,7%; GCS - (-17,2) ± 8,6 and (-20,4) ± 8,3%. After 6 months, these values corresponded to GLS (-16,7) ± 6,5 and (-17,8) ± 5,1%, GCS - (-19,02) ± 8,3 and (-22 4) ± 6,7%. And GLS dynamics in groups 1 and 2 was 12.6 and 11,8%, respectively, GCS - 9,6 and 8,9%.
Conclusion: In groups of patients with STEMI rapidly progressive LV remodeling and absence of remodeling the global longitudinal and circumferential deformation does not have significant differences, and after 6 months of follow-up their values have not changed significantly.

P1265
Determination of minimal allowable hemoglobin level in patients undergoing CABG surgery

NA Beley[1]; OA Loskutov[1]; OM Druzhyna[1]; DO Loskutov[2]; BM Todurov[3]
[1]National Medical Academy of Postgraduate Education, Anesthesiology and Intensive Care, Kiev, Ukraine; *[2]National O.O. Bohomolets Medical University, Kiev, Ukraine*; *[3]Heart Institute of the Ministry of Healthcare of Ukraine, Kiev, Ukraine*

Background. The research proved that the reduction of gas transport function of the blood caused by low level of hemoglobin has a significant negative effect on myocardial contractility. But there is no clear minimal Hb level which would help to balance between myocardial contractility and blood gas transport function.
Purpose: Determination of the minimal level of Hb for providing functional myocardium state in accordance to oxygen transport blood function.
Methods: The explorations have been conducted on 72 patients who underwent isolated CABG with the imposition of three aorto-coronary grafts. The average age of the patients was 66,96 ± 1,81 years, average weight – 86,5 ± 1,44kg. In our study we took into consideration Hb, cardiac index (CI), contractility index (ΔS), left ventricular stroke work index (LVSWI), oxygen delivery index (ODO2). In order to calculate the minimum permissible level of Hb we used the method of least squares and linear programming. Unknown quantities were identified in the following manner: Hb - z, CI - x1, ΔS - x2, LVSWI - x3, IDO2 - x4.
Results: After the calculating of dependence z=a0 + a1x1 + a2x2 + a3x3 + a4x4 with the least squares method we obtained the next variables' coefficients: a0=9,250213; a1=0,2195560; a2=0,4048034; a3=0,1035031; a4=2,831839 10-3. Resulting equation was as follows: z=9,250213 + 0,2195560x1 + 0,4048034x2 + 0,1035031x3 + 2,831839 10-3x4. The coefficient of determination was d=R2=0,90012; correlation coefficient R=0,948747. The closeness of the correlation coefficient to 1 showed that the mathematical model shows the relationship between the parameters. For calculating minimal Hb level we used simplex method with the following limitations: x1≥3; x2≥32; x3≥27; x4≥400 for solving the linear programming task. As a result, the following figure of zmin=89,7583 was obtained.
Conclusions: To sum up, in observed group of patients, minimum allowed level of Hb is 90g/l providing myocardial contractility function needed for marinating normal systemic hemodynamics.

HYPERTENSION - LV HYPERTROPHY - RENAL DENERVATION

P1266
Orthostatic hypertension is associated with masked hypertension in the very elderly treated hypertensives

N Ezhova[1]; YV Kotovskaya[2]; SV Villevalde[2]; ZD Kobalava[2]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation; *[2]RUDN University , Moscow, Russian Federation*

Objective: Masked hypertension (MHT) and isolated nocturnal HT are associated with increased risk of target organ damage and cardiovascular events. We investigated prevalence and predictors of those blood pressure (BP) phenotypes in very elderly treated hypertensives. Methods. Office BP evaluation (simultaneous bilateral brachial BP measurement in supine position and then after 2 minutes of standing) and 24-h ambulatory BP monitoring (ABPM) were performed in 67 treated hypertensive subjects older than 80 years (age 84.1 ± 3.1 (M ± SD) years, 25.5% male, mean office brachial systolic BP 134.8 ± 23.2 mm Hg) with a validated oscillometric cuff-based device. Patients with left ventricular ejection fraction < 40% and severe comorbidities were not included. Orthostatic hypotension (OH) was defined as a decrease in systolic BP of at least 20 mm Hg upon standing and orthostatic hypertension (OHT) as a corresponding increase.
Results: The prevalence of MHT was 47.7 % in the entire study population and 71.1% among patients with office-controlled hypertension (BP < 150/90 mm Hg). 78.2% patients with MHT had isolated nocturnal HT. Orthostatic reaction was abnormal in 34.3% subjects: 22.4% had OH while incidence of OHT was 11.9%. OHT was significantly associated with MHT (odds ratio 1.7, 95% confidence interval 1.14-2.78).
Conclusion: OHT is predictive for MHT in the very elderly treated hypertensives. Evaluation of orthostatic reaction in very elderly may help to detect a population that would benefit from ABPM.

P1267
Gene polymorphism ABCB1 polymorphic marker C3435T, antihypertensive efficacy and safety of amlodipine in hypertensive patients

T Tatiana Morozova[1]; NV Shikh[1]; DA Sychev[2]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation*

Purpose: To explore the relationship of polymorphism ABCB1 gene polymorphic marker C3435T, antihypertensive efficacy and safety of amlodipine in patients with arterial hypertension (AH) I-II degree.
Methods: 100 patients with hypertension I-II art. (M.- 36, w.- 64) between the ages of 47 to 73 years (av. age 53 ± 4 years) with various gene polymorphisms ABCB1 evaluated parameters efficacy and safety of amlodipine in a daily dose of 5 mg. Genotyping of polymorphic marker C3435T ABCB1 gene was performed by polymerase chain reaction. Antihypertensive efficacy is excellent at lowering blood pressure < 140/90 ; good - with a decrease in blood pressure of 10 mm Hg, but without achieving the target values.; satisfactory - with a decrease in blood pressure of 10 mm Hg; unsatisfactory - in the absence of blood pressure dynamics. Safety was assessed by the incidence of adverse drug reactions (ADR) according to the survey. The duration of observation - 3 months. Statistical processing was performed on the basis of IntelPentium 4 processors using package 'INSTAT' statistical programs.
Results: Excellent and good antihypertensive efficacy in patients with genotype TT polymorphic marker C3435T ABCB1 gene was 76.1%, SS - 47.1%, CT - 67.0%. Significant group differences in the Mann Whitney SSvsCT p = 0.06; CCvsTT p = 0.04; CTvsTT p = 0.5; ANOVA p = 0.04. According to the office BP measurement SBP decreased in patients with the CC genotype at 7,36 ± 2,9%, CT - on 9,07 ± 3,1%, the TC - on 8,40 ± 3,1%; DBP to 4,12 ± 1,2%; 5,46 ± 2,7% and 4,98 ± 2,4% respectively (p < 0.05 in all cases). ADR rate with genotype SS was 35.3%, CT - 6.7%, CT - 11.3%. On multivariate ANOVA analysis revealed significant differences CC and TT genotypes in the degree of decrease in SBP (p = 0.02), antihypertensive

efficacy parameter (p = 0.02), an increase in dose requirements (p = 0.04) and the incidence of ADR (p = 0.05).
Conclusions: Thus, in patients with genotype TT marked the highest efficiency of amlodipine on the background of the least amount arising ADR.

P1268

Renal sympathetic denervation improves LV filling pressures in patients with resistant hypertension and LV diastolic dysfunction

K Cerlinskaite[1]; A Berukstis[2]; D Zakarkaite[2]; J Celutkiene[2]; A Laucevicius[2]
[1]*Faculty of Medicine of Vilnius University, Vilnius, Lithuania*; [2]*Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*

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Background: Renal sympathetic denervation (RSD) is a procedure aimed at treating resistant arterial hypertension (RAH) by ablating and thus lowering sympathetic activation of renal artery wall nerves. Current clinical trials are evaluating the potential effect of RSD on other diseases associated with an overactive sympathetic drive. It is known that abnormally activated sympathetic tone can alter diastolic function of the heart and worsen prognosis of heart failure patients. The aforementioned activation particularly increases during exercise. We performed the present study to examine RSD effect on diastolic function of the left ventricle (LV) during stress.
Purpose: To investigate the RSD effect on LV filling pressures during stress in patients with RAH and LV diastolic dysfunction.
Methods: Prospective study enrolled 15 patients with RAH (age 56 ± 7 years, 8 male, using 5.7 ± 1.2 antihypertensive drugs, mean 24-hour ambulatory blood pressure (BP): systolic 161.92 ± 16.78 mmHg, diastolic 99.25 ± 11.08 mmHg), who underwent bilateral RSD. All 15 patients had diastolic LV dysfunction (13 patients had impaired relaxation, 2 – pseudonormal diastolic function) and preserved systolic LV function, confirmed by echocardiography. LV filling pressures during stress were determined by performing exercise echocardiography at workload of 50 Watts and assessing indirect estimates of LV filling pressures: estimated pulmonary capillary wedge pressure (PCWP, mmHg) by Nagueh equation (1.24×(E/e'lateral) + 1.9) and the difference between the duration of pulmonary venous atrial reversal wave and the duration of the mitral valve A-wave (ARdur-Adur, ms) before and 6 months after the procedure. Continuous variables were checked for normal distribution by Shapiro-Wilk statistic. Normally distributed variables were compared by paired Student's t-test, while non-normally distributed variables were compared using the Wilcoxon signed rank test. A p value <0.05 was considered statistically significant. Data was analysed using SPSS v22 statistical package.
Results: Mean ambulatory BP decreased significantly 6 months after RSD: systolic BP decreased to 151.58 ± 20.32 mmHg (p = 0.039), diastolic BP to 91.75 ± 8.92 mmHg (p = 0.009). Peak stress systolic, diastolic BP and heart rate were 201.5 ± 25.5 and 198.7 ± 24.9 mmHg, 100.5 ± 14.5 and 102.7 ± 14.3 mmHg, 103.3 ± 13.4 and 104.5 ± 10.4 bpm at baseline and after 6 months, respectively (p>0.05 for comparison). Estimated PCWP reduced significantly at six months after the procedure (from 16.16 ± 4.17 to 12.19 ± 3.27 mmHg, p = 0.007), as well as ARdur-Adur (from 18.23 ± 25.78 to -9.62 ± 24.98 ms, p = 0.002).
Conclusions: In addition to lowering 24-hour ambulatory BP, our study revealed that renal sympathetic denervation reduces LV filling pressures during stress in patients with resistant arterial hypertension and LV diastolic dysfunction. This effect could be of benefit in halting the progression of heart failure in patients with resistant hypertension.

P1269

Fixed dose combination nebivolol/hydrochlorthiazide improve diastolic function in elderly hypertensives with heart failure with preserved ejection fraction and high pulse pressure

L Livia Popescu[1]; H Balan[1]
[1]*University of Medicine and Pharmacy Carol Davila , Bucharest, Romania*

BACKGROUND: Heart failure with preserved ejection fraction (HFpEF) is common, increasing in prevalence, and unfortunately, no disease-specific therapy exists to improve prognosis. Hypertension is worldwide spread and represents the leading cause of death and of HFpEF. High blood pressure is associated with left ventricular hypertrophy and diastolic dysfunction. Epidemiological evidence suggests increasing proportion of elderly people. Hypertension occurs in one half/two thirds of them. High pulse pressure is a marker of central arterial stiffness and a predictor for mortality. Old people are in high risk, have high pulse pressure and comorbidities. ESC/ISH guidelines suggest the use of fixed dose combination from the beginning in the therapy of hypertensives at high risk because fixed dose combination ensures a better and quicker therapeutic effect, a better compliance, with diminished adverse effects and simplification of therapy.
PURPOSE: The aim of our study was to evaluate the efficacy of the fixed dose combination nebivolol/hydrochlorthiazide 5/12.5 mg (N/H) on BP, pulse pressure, left ventricular hypertrophy and diastolic dysfunction in elderly hypertensives (over 65 years old) with HFpEF, and high pulse pressure.
Methods: We performed a prospective study, lasting 3 months, in which 56 never-treated elderly hypertensives, with high pulse pressure (≥ 60 mmHg), and HFpEF (EF ≥50%), medium age 72 ± 4.5 years, received once a day fixed combination N/H. The assessment of echocardiographic parameters of left ventricle was performed at baseline and after 3 months of treatment. Office blood pressure and pulse pressure ware monitored every month.
Results: Blood pressure was significantly reduced by treatment, both systolic (167.5 ± 22.5 vs 134 ± 11.5 mmHg, $p<0.01$) and diastolic (95 ± 10 vs 83 ± 12 mmHg, $p<0.01$). Pulse pressure decreased from 67 ± 15 mmHg to 58 ± 19 mmHg ($p<0.03$). LVMI decreased from137.5 ± 17 to 113.5 ± 14.3 g/m^2 ($p<0.001$). E/A ratio increased from 0.98 ± 0.05 to 1.19 ± 0.04 ($p<0.05$). Treatment was well tolerated.
Conclusions: Treatment with fixed dose combination nebivolol/hydrochlorthiazide in elderly hypertensives with HFpEF and high pulse pressure ensured a good control of BP, and already after 3 months, a regression of cardiac hypertrophy with improvement in LV diastolic function.

P1270

Effects of antihypertensive treatment on ventricular-arterial coupling in hypertensive patients

A Bogomaz[1]; Y Kotovskaya[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Objective: To evaluate left ventricular-arterial coupling in hypertensive patients after therapy with a beta-blocker and its fixed dose combination (FDC) with amlodipine.
Design and methods: 28 patients (age 53,9 ± 7,2 (M ± SD), 20 males, blood pressure (BP) 149 ± 13/97 ± 14 mmHg, heart rate (HR) 83 ± 10 bpm, abdominal obesity in 56%, dyslipidemia in 53%, smoking in 42%) with untreated uncomplicated hypertension underwent simultaneous echocardiography and BP measurement at baseline, after 4 weeks of bisoprolol 5-10 mg monotherapy and after 8 weeks after switching to bisoprolol 5-10/amlodipine 5-10 mg FDC. Doses were titrated to reach BP <140/90 mmHg. Arterial elastance (Ea) and LV elastance (Ees) at rest were calculated as end-systolic pressure (ESP)/stroke volume and ESP/end-systolic volume. Ventricular-arterial coupling (VAC) was assessed as Ea/Ees. VAC optimal range is considered as 0,5-1,2. Mechanical efficiency of left ventricle (ELV) and peripheral arterial resistance (PAR) were evaluated. $p<0,05$ was considered significant.
Results: After monotherapy with bisoprolol BP decreased to 146 ± 15/85 ± 11 mmHg (p>0,05 vs baseline), HR decreased to 60 ± 8 bpm ($p<0,05$ vs baseline), after FDC – to 132 ± 11/76 ± 11 mmHg and 65 ± 7 bpm, respectively ($p<0,05$ vs baseline). Bisoprolol decreased Ees from 4,45 ± 1,9 to 3,67 ± 0,98 mmHg/ml/m2 ($p<0,05$) whereas Ea (1,88 ± 0,39 vs 1,92 ± 0,38 mmHg/ml/m2), PAR (137,1 ± 35,3 vs 128,9 ± 36 dyn·s·cm−5) did not change significantly. Ea/Ees increased significantly from 0,47 ± 0,16 to 0,55 ± 0,14 ($p<0,05$). Switching to bisoprolol/amlodipine FDC resulted in decrease of Ea to 1,48 ± 0,17 mmHg/ml/m2, PAR – to 105,6 ± 28 dyn·s·cm−5. Ees did not change from that on bisoprolol. Ea/Ees returned to baseline values (0,45 ± 0,1). ELV did not change significantly throughout a study.
Conclusions: In untreated patients with uncomplicated arterial hypertension monotherapy with bisoprolol reduces initially increased Ees without negative effect on Ea and PAR. Switching to bisoprolol/amlodipine FDC results in additional Ea reduction. Thus the study confirms potential benefits of bisoprolol/amlodipine combination in arterial hypertension in terms of cardiovascular.

HFPEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

P1271

Another look at heart failure based on the study of ESPVR

R M Rachad M Shoucri[1]
[1]*Royal Military College of Canada, Mathematics and Computer Science, Kingston, Ontario, Canada*

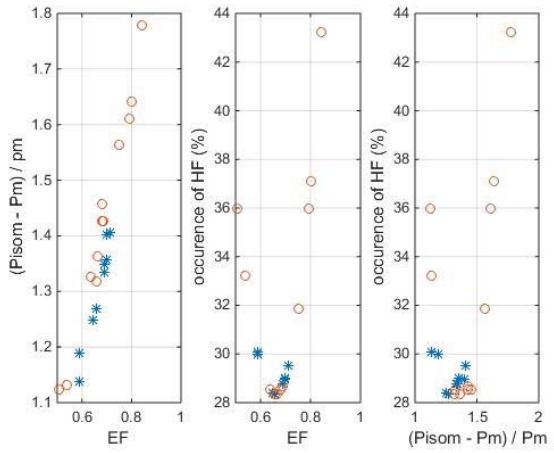
Background: Another look at the problem of heart failure with normal or preserved ejection fraction (HFpEF) was made possible by the study of new relations derived between the ejection fraction (EF) and the parameters describing a non-linear model of the end-systolic pressure-volume relation (ESPVR), the relation between ventricular pressure Pm and volume Vm when the myocardium reaches its maximum state of activation during contraction.

Purpose: A relation between percentage of heart failure (HF) and EF is extended to obtain other new relations between percentage of HF and indexes derived from the parameters of the non-linear ESPVR.
Methods: The approach used is based on the theory of large elastic deformation of the myocardium, the active pressure Pisom generated by the myocardium is included in the formula describing the ESPVR. Ratios of pressures can be calculated in a non-invasive way, which allows non-invasive clinical applications.
Results: Application to clinical data is shown in the Figure. From a relation between EF and the percentage occurrence of HF (Figure center), and between EF and the ratio (Pisom – Pm)/Pm (Figure left), the relation between percentage of HF and (Pisom – Pm)/Pm was derived (Figure right); data are for cases of aortic stenosis (o) and normal group (*). Notice the minimum of the curve of percentage of HF around the normal group for EF $\asymp$ 0.67 and (Pisom – Pm)/Pm $\asymp$ 1.3, while the cases of aortic stenosis appear more scattered into three subgroups in and around the normal group. Calculations indicate optimal value of SW/SWx $\asymp$ 0.8 (SW = stroke work, SWx = maximum stroke work), and optimal value of tang/eam $\asymp$ 4 (tang = slope of the tangent to the ESPVR, eam = max. arterial elastance). SWR = SWx – SW measures the stroke work reserve and TW is the total area under the ESPVR curve, the quantities SWR/SW $\asymp$ 0.25 and SW/TW $\asymp$ 0.5 were also calculated; estimated optimal values of some indexes (minimum of the percentage of HF curve) are summarized in the Table. These indexes can be used for classification of clinical groups into normal, mildly depressed and severely depressed state of the ventricle.
Conclusion: The EF is commonly used to assess the performance of the heart ventricles. Many indexes derived from the ESPVR can also be calculated in a non-invasive way and can be used for the same purpose. Bivariate (or multivariate) analysis of indexes is a better approach for studying HFpEF. The curve of the percentage of HF can easily be implemented for classification of clinical groups in a non-invasive way.

Estimated optimal value of some indexes

EF	$(P_{isom} - P_m)/P_m$	SW/SWx	SWR/SW	SW/TW	tang/eam
0.67	1.3	0.8	0.25	0.5	4

Symbols are defined in text.



EF, % of HF and (Pisom-Pm)/Pm relations

P1272
The association of cardiac autonomic neuropathy and left ventricular diastolic dysfunction. : from Korean women's chest pain registry (KoROSE)

MN Kim[1]; DH Cho[1]; HL Kim[2]; SM Park[1]; MS Shin[3]; MA Kim[2]; KS Hong[4]; KJ Shin[5]; WJ Shim[1]
[1]Korea University, Anam Hospital, Seoul, Korea Republic of; *[2]Boramae Hospital, Cardiology, Seoul, Korea Republic of*; *[3]Gachon University, Cardiology, Incheon, Korea Republic of*; *[4]Hallym University, Chuncheon, Korea Republic of*; *[5]Ewha University, Seoul, Korea Republic of*

On behalf of: KoRean wOmen'S chest pain rEgistry

Background: The clinical implications of cardiac autonomic neuropathy (CAN) had been repeatedly studied in patients of heart failure with reduced ejection fraction and diabetes mellitus. But the association between diastolic dysfunction (DD) and CAN has not been well investigated. The aim of this study is to evaluate the relation of CAN with DD in patients who presented with exertional dyspnea and chest tightness but had no significant coronary stenosis
Methods: 347 patients (F/M=268/81, 58.5 ± 10.5yrs) who had ≥50% of left ventricular ejection fraction and no significant coronary stenosis were included from KoRean wOmen'S chest pain rEgistry. Treadmill exercise test (TET) and transthoracic echocardiography were performed in all patients. The diastolic function was classified as normal, indeterminate and DD by 2016 ASE/EACVI guideline. Autonomic dysfunction was assessed by heart rate recovery (HRR1min: maximal heart rate - heart rate at 1minute after exercise) and blood pressure response (BPR3min: systolic blood pressure (SBP) at 3 minute after exercise / maximal SBP)
Results: Among 347 patients, DD was present in 21 patients (6%) and 52 patients (14.9%) were belonged to indeterminate group. The presences of diabetes and hypertension were more common in patients with DD (diabetes: 28.6% vs 7.7 % in indeterminate vs 8.8% in normal, P=0.03, and hypertension: 57.1% vs 55.8% in indeterminate vs 36.5% in normal, P=0.004 respectively). HRR1min was progressively disminished from normal, indeterminate and to DD group. BPR3min also progressively decreased from DD to normal group. (Figure1). During TET, exercise duration was lower in DD group than that of indeterminate and normals (6.54 ± 2.3 vs indeterminate: 8.23 ± 2.0 vs normal: 8.68 ± 2.3 minute, P < 0.001). There was significant relation between HRR1min and exercise duration (R=0.283, P < 0.001), but BPR3min was not (R=-0.46, P=0.428). HRR1min was independently related with DD after adjusting age, sex, hypertension, diabetes, body mass index by multivariate analysis (RR=0.93, 95% CI=0.88-0.99, P=0.02).
Conclusion: The patients with DD had impaired cardiac autonomic function. These association was irrelevant to age, diabetes, hypertension and was related with decreased exercise tolerance. It could be concluded that CAN may be one of contributors for developing and worsening symptoms of heart failure with preserved ejection fraction.

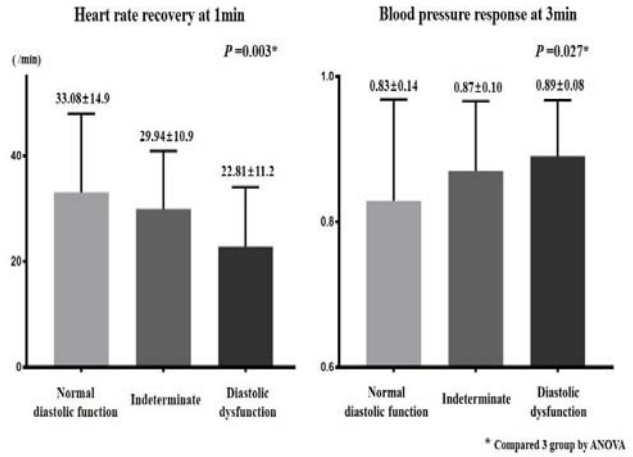


Figure 1

P1273
Effect of obesity on left ventricular longitudinal myocardial strain using speckle tracking echocardiography in patients with heart failure with preserved left ventricular ejection fraction

L Ljubica Georgievska-Ismail[1]; P Zafirovska[2]; Z Hristovski[3]
[1]University clinic of cardiology, Skopje, Macedonia The Former Yugoslav Republic of; *[2]Special Hospital for Surgical Diseases Filip II, Skopje, Macedonia The Former Yugoslav Republic of*; *[3]Acibadem Sistina Clinical Hospital, Skopje, Macedonia The Former Yugoslav Republic of*

Background. Obesity has been shown to be an important risk factor for the development of heart failure irrespective of the presence of other cardiovascular risk factors.
Purpose: The aim of this study was to determine the direct role of obesity in the subclinical impairment of left ventricular (LV) systolic function in patients with heart failure with preserved left ventricular ejection fraction (HFpEF).
Methods: We assessed myocardial systolic and diastolic function in 252 patients (62.2 ± 9.7 y; 39.7% men and 60.3% women) with unexplained dyspnea and/or exercise intolerance who fulfill clinical and/or echocardiographic criteria of HFpEF presence using 2D echocardiography and tissue Doppler imaging. Myocardial deformation was assessed using 2D speckle tracking software (STE). All the

patients were divided into three groups according to their body mass index (BMI): normal-weight patients (BMI < 25 kg/m2; n=28, 11.1%), overweight patients (BMI 25-29.9 kg/m2; n=110, 43.7%), and obese patients (BMI ≥ 30 kg/m2; n=113, 44.8%).
Results: Obese patients were significantly younger (p = 0.001), but despite higher percentage of hypertension, dyslipidaemia and/or diabetes there was lack of any significant difference in comparison to the overweight and those with normal BMI. We couldn't find more pronounced diastolic dysfunction in overweight/obese groups compared to the normal BMI group. However, patients who were obese showed significantly reduced global LV longitudinal strain (GLS) in comparison to those either overweight or with normal weight (-16.1 ± 4.3%;-17.9 ± 3.3%-18.9 ± 2.8%;p = 0.0001, respectively) as well as there was significant correlation between GLS and BMI (r=0.230, p = 0.0001). Multivariate regression analysis adjusted for age, hypertension and diabetes presence, showed a direct and independent effect of BMI on GLS (β= 0.311; 95%CI: 0.210-0.412; p = 0.0001).
Conclusion: Obesity is independently related to more pronounced subclinical LV systolic dysfunction expressed as reduced GLS in patients with HFpEF; thus may implicated increased risk and/or worse prognosis.

P1274
Quantitative assessment of myocardial stiffness using transthoracic shear wave imaging in healthy and hypertrophic cardiomyopathy adults

O Villemain[1]; M Correia[1]; E Mousseaux[2]; JEROME Baranger[1]; S Zarka[3]; I Podetti[1]; G Soulat[2]; T Damy[4]; M Tanter[1]; E Messas[3]; MATHIE Pernot[1]
[1]Waves and Acoustics Laboratory Institute Langevin, Paris, France; *[2]European Hospital Georges Pompidou, Radiology, Paris, France*; *[3]European Hospital Georges Pompidou, Cardiology, Paris, France*; *[4]University Hospital Henri Mondor, Cardiology, Creteil, France*

Objectives: Myocardial stiffness is an important prognostic and diagnostic parameter in heart failure. Up to now, there is no noninvasive tools for quantitative evaluation of this parameter. We introduced recently a new ultrasound based technique called Shear wave imaging (SWI) to quantitatively assess the intrinsic tissue stiffness. The goal of our study was to investigate the potential of Myocardial SWI to quantify non-invasively the diastolic myocardial stiffness (MS, kPa) in healthy adult volunteers (HV) and in hypertrophic cardiomyopathy populations with heart failure with preserved ejection function (HCM-HFpEF).
Methods: We included prospectively 80 adults: 60 HV (divided into three groups: 20-40 yo (n = 20); 40-60 yo (n = 20); 60-80 yo (n = 20)) and 20 HCM-HFpEF. An echocardiography, a cardiac magnetic resonance imaging (CMR) and a biological exploration were achieved in all the study population. The MS estimation was performed using an ultrafast ultrasound scanner with cardiac phased array, on the basal antero-septal segment during the end-diastole, in long and short axis views. Fractional anisotropy (FA) of shear wave speed was also estimated.
Results: For 20-40, 40-60, and 60-80 yo group respectively, the mean MS was 2.59 ± 0.58 kPa, 4.70 ± 0.88 kPa, 6.08 ± 1.06 kPa (p < 0.01 between each group). MS strongly correlated with age (r=0.88). For the HCM-HFpEF group (mean MS=12.68 ± 2.91 kPa), the MS was significantly higher than in the healthy volunteer (p < 10-4), with a cut-off identified at 8 kPa (AUC=0.993, Se=95%, Sp = 100%). The FA was lower in HCM-HFpEF (mean=0.170 ± 0.082) than in HV (0.289 ± 0.073), p < 0.01. Positive correlations were found between the MS and parameters in echocardiography (E/e', r=0.783; E/Vp, r=0.616; left atrial volume index, r=0.623) and CMR (late gadolinium enhancement, r=0.804).
Conclusion: Quantitative assessment of MS was shown feasible non-invasively in healthy and HCM-HFpEF adults using shear wave imaging. MS was found to increase with age in healthy population. A MS cut-off of 8 kPa was found to differentiate healthy and HCM-HFpEF patients. This new noninvasive parameter could help to better diagnose the diastolic function and its prognosis in clinical practice. (Non-Invasive Evaluation of Myocardial Stiffness by Elastography: NCT02537041)

P1275
Impact of changes in consensus diagnostic recommendations on the echocardiographic prevalence of diastolic dysfunction

O Huttin[1]; A Fraser[2]; S Coiro[3]; E Bozec[1]; C Selton-Suty[4]; Z Lamiral[1]; Z Frikha[1]; P Rossignol[1]; F Zannad[1]; N Girerd[1]
[1]INSERM, Centre d'Investigations Cliniques 9501, Université de Lorraine, CHU de Nancy, Institut Lorrain du cœur et des vaisseaux, Nancy, France and INI-CRCT F-CRIN Network, Vandoeuvre-les-Nancy, France; *[2]Cardiff University, Wales Heart Research Institute, Cardiff University, Cardiff, UK., Cardiff, United Kingdom*; *[3]University of Perugia, Division of Cardiology, University of Perugia, School of Medicine, S. Andrea delle fratte, Perugia, Perugia, Italy*; *[4]Hospital Brabois of Nancy, Department of Cardiology, Vandoeuvre les Nancy, France*

AIMS: Evaluation and scoring system for preclinical and symptomatic diastolic dysfunction are still under debate due to the lack of evidence-based grading systems. 2016 ASE/EACVI guidelines considerably changed the diastolic grading system. However, the impact of these changes on the prevalence and severity of diastolic dysfunction in healthy patients has not been studied.
Methods and Results: Participants from the community-based prospective STANISLAS Cohort France underwent 2-dimensional transthoracic echocardiography with comprehensive diastolic function evaluation. Patients without a history of heart failure and with LVEF >50% were classified according to the presence and degree of diastolic dysfunction following the 2016 ASE/EACVI guidelines scoring system and compared with previously published diastolic dysfunction evaluation systems. Of the 1485 study participants, (47 ± 14 years), 20 (1.3%) had diastolic dysfunction according to 2016 criterias, and the proportion of diastolic dysfunction significantly increased with higher age. The prevalence of diastolic dysfunction using previous guidelines were respectively of 8.8%, 5.7% and 5.9% according to Appleton definition, 2007 consensus statement and 2009 ASE/EACVI guidelines (when only considering 2 and 3rd grade of diastolic dysfunction). When considering the subset of participants aged >60, the proportion of diastolic dysfunction was 3.1% using the 2016 criterias vs 9.1%, 10.2% and 12.9% according to Appleton definition, 2007 consensus statement and 2009 ASE/EACVI guidelines.
Conclusion: The choice of published algorithms used for diastolic dysfunction identification has a wide impact on the proportion classified as having diastolic dysfunction. Outcome based studies might help identify a consistent, evidence-based and clinically useful definition of diastolic dysfunction in the future.

P1276
The value of combined cardiopulmonary end stress-echocardiography testing in discovering latent hfpef in patients with hypertension and normal LV systolic and diastolic function at rest

M Marko Banovic[1]; I Nedeljkovic[1]; J Stepanovic[1]; V Giga[1]; M Nedeljkovic[1]; M Petrovic[1]; N Dikic[1]; B Beleslin[1]
[1]University Institute for Cardiovascular Diseases, Belgrade, Serbia

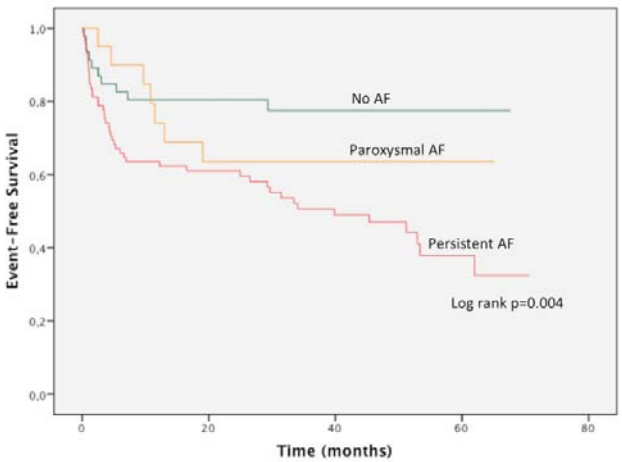
Background/Aim: Heart failure with preserved ejection fraction (HFpEF) is often associated with hypertension (HTA). Exercise stress-echocardiography (ESE) and cardiopulmonary exercise-testing (CPET) appear to be useful in assessment of HFpEF. The aim of our study was to assess the value of combined ESE-CPET in discovering exertional dyspnea and latent HFpEF in patients with HTA and normal LV systolic and diastolic function at rest
Method: 101 patients underwent combined ESE-CPET testing (supine bicycle, Ramp 15 protocol, 15W/min with 3min of unloaded pedalling). Echocardiography measurements were performed at rest and at peak load. The E/E' >15 at peak exercise was a marker for latent HFpEF. Expiratory gases were collected on breath by breath analysis and analysed by metabolic card (Schiller CS 200, Germany).
Results: The mean age was 55.9 years, 62 males (61.38%). There were no differences in echocardiographic parameters at rest (LVEF 68.1vs 65.7%, E/E' 6.01 vs 6.74, deceleration time 198.7vs 166.6, p = ns). Increase in E/E' > 15 during ESE-CPET occurred in 10 patients (9.9%). Those patients also had lower peak VO2 (14.67 vs 20.39; p = 0.005), lower workload (123 vs 159W, p = 0.01), and higher VE/VCO2 slope (35.25 vs 26.55, p < 0.001). Patients with Increase in E/E' > 15 during ESE-CPET were more often diabetic (50% vs 15.4%, p = 0.008).
Conclusion: Combined ESE-CPET testing is reliable and useful tool in discovering latent HFpEF in patients with HTA and normal LV systolic and diastolic function at rest.

P1277
Persistent atrial fibrillation in heart failure with preserved ejection fraction - Association with extracellular volume accumulation, invasive hemodynamics, and outcome

R Schoenbauer[1]; F Duca[2]; A Kammerlander[2]; S Aschauer[2]; C Binder[2]; C Zotter-Tufaro[2]; M Koschutnik[2]; L Fiedler[1]; FX Roithinger[1]; D Bondermann[2]; J Maschauerbauer[2]
[1]Landesklinikum Wiener Neustadt, Cardiology, Wiener Neustadt, Austria; *[2]Medical University of Vienna, AKH – Vienna, Cardiology Clinic, Vienna, Austria*

Background and Objectives: Heart failure with preserved ejection fraction (HFpEF) and atrial fibrillation (AF) frequently occur together. However, data on AF subtype and its association with comorbidities, extracellular volume (ECV) by cardiac magnetic resonance imaging (CMR), hemodynamics, and relation to outcome in HFpEF are sparse.
Methods: and Results: From 2011 to 2015 152 consecutive HFpEF patients were enrolled in our prospective observational registry. All patients underwent echocardiography, left and right heart catheterization (RHC), and CMR including T1 mapping with the modified Look-Locker inversion recovery (MOLLI) sequence.

Patients with significant coronary artery disease were excluded. 105 patients (69%) suffered from AF, 85 (56%) had persistent and 20 (13%) had paroxysmal AF. Patients with persistent AF were in worse New York Heart Association functional class (p = 0.006), and more often suffered from chronic obstructive pulmonary disease (p = 0.018) than patients with paroxysmal AF or sinus rhythm. They had higher levels of N-terminal pro-brain natriuretic peptide (NTproBNP) (p = < 0.001), and worse renal function (p = 0.041). Invasive hemodynamics showed higher right atrial pressures (p = 0.014) and pulmonary capillary wedge pressures (p = 0.050). Echocardiography revealed more pronounced atrial dilatation (p = < 0.001) as well as a more dilated right ventricles (p = 0.001) and higher systolic pulmonary artery pressures (p = 0.037). By CMR left and right atria as well as the right ventricle were more dilated (p = 0.001, 0.002, and 0.001, respectively) and left and right ventricular ejection fractions were lower in patients with persistent AF (p = 0.002, < 0.001 and 0.005 respectively). Furthermore, these patients had higher levels of ECV by T1 mapping (p = 0.018). After a median follow-up of 46 months (13-71) 63 patients (41%) reached the combined endpoint defined as hospitalization for HF and/or cardiovascular death. By multivariate Cox regression analysis only persistent AF (p = 0.039, HR 2.013, 95% CI 1.035-3.915) and six-minute walk distance (p = 0.013, HR 0.997, 95% CI 0.994-0.999) were independently associated with outcome.
Conclusion: More than 50% of HFpEF patients suffer from persistent AF. Persistent but not paroxysmal AF is significantly related with markers of disease severity, extracellular volume accumulation, and worse cardiovascular outcome.

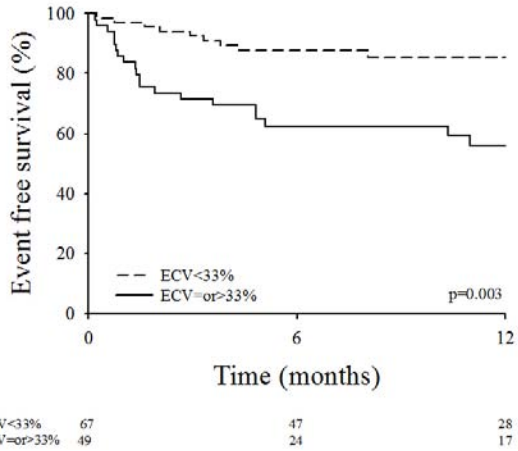


Kaplan-Meier plot, event-free survival

P1278
Prognostic significance of diffuse myocardial fibrosis evaluated by cMR in patients with heart failure with preserved ejection fraction.

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

Background: Myocardial fibrosis is known as one of the potential pathophysiologic mechanisms in heart failure with preserved ejection fraction (HFpEF). The aim of this study was to evaluate the prognostic significance of diffuse fibrosis estimated by extra cellular volume (ECV) in HFpEF patients.
Methods: Between January 2015 and October 2016, we prospectively enrolled 118 consecutive patients with HFpEF (78 ± 8 years, 63% women) defined by ESC guidelines. Diffuse myocardial fibrosis was estimated by ECV quantified by 3 Tesla cMR with the Modified Look-Locker Inversion Recovery sequence. High level of diffuse fibrosis was determined by an ECV age- and sex-adjusted cutoff value (cutoff = 33%) corresponding to mean + 2 standard deviations in 26 age- and sex-matched volunteers (76 ± 5years, 65% women) without previous cardiac history. Patients were followed up for overall survival and a composite outcome of all-cause mortality and first HF hospitalization.
Results: Mean ECV value in HFpEF patients was 32.9 ± 4.8%. During a mean follow-up of 11 ± 6 months, we observed 43 events (11 all-cause deaths and 32 first HF hospitalizations). Cox analysis identified hemoglobin level (HR=0.62 [0.44-0.89], p = 0.009), ECV ≥33% (HR= 14.18 [1.78-112.7], p = 0.012) and BMI (HR= 0.86 [0.76-0.97], p = 0.015) as significant predictors of all-cause mortality.
Thirty eight patients (32%) reached the combined end point. Presence of diabetes (HR= 1.98 [1.04-3.76], p = 0.038) and hemoglobin (HR= 0.81 [0.67-0.98], p = 0.028) were significantly associated with the composite outcome even after adjusting for important clinical and imaging covariables. The ability of ECV≥33% to improve this model was then tested and added significant prognostic information (χ^2 4.457, p = 0.035). Kaplan Meier event free survival curves showed that HFpEF patients with ECV≥33% have poorer 1-year prognosis than those with ECV<33% (56 ± 8% vs 82 ± 5%, p = 0.001, Figure).
Conclusion: Among HFpEF patients, high level of fibrosis defined by ECV ≥33% was associated with all cause mortality and poor prognosis with higher rate of all cause death and first HF hospitalization, suggesting that the evaluation of diffuse myocardial fibrosis could be useful for the risk stratification. Besides, hemoglobin level was a strong predictor of short term composite outcome, as often demonstrated in HFrEF.



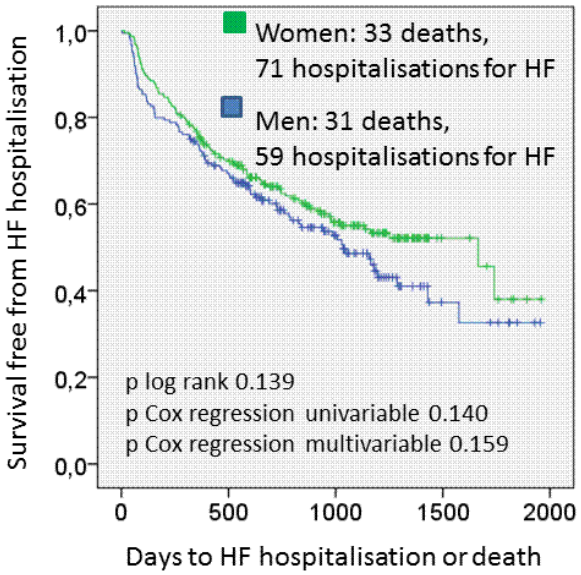
Event free survival in HFpEF patients

P1279
Sex specific differences in quality of life and diastolic function in HFpEF

U Ljung Faxen[1]; C Hage[1]; ED Donal[2]; CD Daubert[2]; C Linde[1]; LH Lund[1]
[1]*Karolinska Institutet, Department of Medicine, Stockholm, Sweden*; [2]*University Hospital of Rennes, Département de Cardiologi & CIC-IT U 804, Rennes, France*

Funding Acknowledgements: Société Française de Cardiologie, Medtronic Bakken Reseach Center, Swedish Research Council, Swedish Heart and Lung Foundation

INTRODUCTION: Heart failure with preserved ejection fraction (HFpEF) is relatively more common in women. However, sex differences within HFpEF remain poorly characterized.
PURPOSE and Methods: In the Karolinska-Rennes (KaRen) Study of HFpEF, we performed a comprehensive assessment of gender differences in clinical, biomarker, echocardiography, quality of life, therapy and prognostic data.
Results: Among 425 patients, 241 were women (57%). Women were older, median (IQR), 79 (73-84) vs. 77 (68-82) years, p = 0.011, had higher heart rate, 70 (60-70) vs. 65 (60-75), p = 0.027, and lower diastolic blood pressure (mmHg), 70 (63-80) vs. 75 (67-85), p = 0.011. NT-proBNP (ng/L) levels were similar, 1409 (509-2443) vs. 1376 (517-2802), p = 0.438. Prevalence of atrial fibrillation/flutter (AF) (62 vs. 64%), hypertension (80 vs. 79%), diabetes type 2 (DM2) (27 vs. 31%), history of myocardial infarction (12 vs. 18%) and stroke (10 vs. 12%), were similar; while coronary artery disease (CAD) was less common in women, 28% vs. 38% (p = 0.028). Despite similar New York Heart Association class, women rated lower quality of life (QoL) than men in ED-Q5, 50 (45-70 vs. 60 (50-75), p = 0.011. Female gender predicted ED-Q5D below 50 independent of age and NTproBNP, OR 1.90, 95% CI 1.08-3.35, p = 0.026. There was no difference in use of heart failure medication or diuretics. Ejection fraction was higher in women; median (IQR), 64 (57-68) compared to men, 62 (57-66), p = 0.020. Female gender was associated with diastolic dysfunction measured as E/e', OR 1.11 (95% CI 1,06 -1.17), p < 0.001 but not LAVI, nor E/A ratio. Over a median follow-up of 893 (515-1208) days, there was no difference in survival free from HF hospitalization (Figure 1) in univariable (HR 0.81, 95% CI 0.610-1,072, p = 0.140) or multivariable (HR 0.79, 95% CI 0.57-1.10, p = 0.159) analyses, adjusted for age, NTproBNP, eGFR, AF, DM2 and CAD.
Conclusion: In this un-selective HFpEF cohort, men and women were similar in most regards, including prognosis, with the notable distinction of worse quality of life and more pronounced diastolic dysfunction in women.



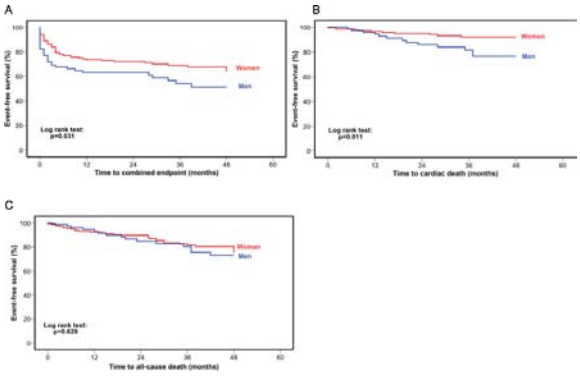


Figure 1

P1280

Gender differences in heart failure with preserved ejection fraction-insights from a prospective registry

F Franz Duca[1]; C Zotter-Tufaro[1]; AA Kammerlander[1]; S Aschauer[1]; C Binder[1]; B Koell[1]; J Mascherbauer[1]; D Bonderman[1]
[1]Medical University of Vienna, Cardiology, Vienna, Austria

Background: Approximately half of all heart failure (HF) patients present with a near normal ejection fraction (HFpEF). It is known that more women than men suffer from HFpEF, but studies investigating further gender differences in this disease are scarce.
Methods: Between December 2010 and November 2016, 260 consecutive patients with HFpEF were included in our study. Patients underwent clinical assessment including 6-minute walk test (6-MWT), left and right heart catheterization and spirometry. Study participants were prospectively followed for up to 48 months. The primary outcome was a composite endpoint of HF hospitalization or cardiac death.
Results: Median age of the total cohort was 73.0 years (IQR: 76.0 - 77.0), 181 (69.6%) were female, median NT-proBNP was 1169 pg/mL (IQR: 557 – 2072) and 170 (65.4%) study participants were in NYHA class ≥III. Men had lower percentages of their predicted 6-MWT distance (66.7% versus 78.1%, $p = 0.036$). With regards to co-morbidities, men had higher incidences of atrial fibrillation (69.6% versus 54.7%, $p = 0.024$), anemia (73.4% versus 60.8%, $p = 0.050$), sleep apnea (20.3% versus 5.0%, $p < 0.001$), COPD (46.8% versus 27.1%, $p = 0.002$) and smoking history (46.8% versus 27.1%, $p = 0.009$). No differences with respect to concomitant medication could be found. Among invasive hemodynamic parameters men had a higher diastolic pressure gradient (3.0 versus 1.0, $p = 0.010$). Amidst spirometry parameters men had lower forced expiratory volumes (65.0 versus 78.0, $p < 0.001$) and had more often a severely impaired diffusion capacity for carbon monoxide (3.8% versus 2.8%, $p = 0.028$). During a median follow-up of 17.0 months, 87 events occurred, of which 24 were cardiac deaths. Men had a worse event-free survival, both for the combined endpoint (Fig. 1A, $p = 0.031$) and cardiac death (Fig. 1B, $p = 0.011$). No difference could be detected for all-cause death (Fig. 1C, $p = 0.629$). Also, men were more likely to die from cardiac death as compared to women (16.5% versus 6.1%, $p = 0.008$) and less likely die from non-cardiac death (2.5% versus 10.5%, $p = 0.030$).
Conclusion: Among a well-characterized typical HFpEF study population we could detect several differences among clinical, hemodynamic and spirometry parameters between men and women. Additionally, we could show that men rather die from HFpEF as compared to women, who rather die with HFpEF.

P1281

Analysis of pathological features in elderly patients with heart failure with preserved ejection fraction

JF Yang[1]; H Hua Wang[1]; KE Chai[1]; YY Li[1]; FANG Fang[2]
[1]Beijing Hospital,National Center of Gerontology, Beijing, Department of Cardiology, Beijing, China People's Republic of; *[2]Beijing Hospital,National Center of Gerontology, Department of Pathology, beijing, China People's Republic of*

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Background Heart failure with preserved ejection fraction (HFpEF) is the dominant form of heart failure in the older population.
PURPOSE: To summarize the cardiac pathological features of elderly HFpEF patients , analyze pathological changes associated with coronary heart disease (CHD) and coronary artery lesion characteristics by autopsy, and evaluate the differences between clinical diagnosis and pathological diagnosis.
Methods: We retrospectively analyzed 1485 patients'autopsy reports from April 1969 to October 2013. Each autopsy was approved by signing the consent forms by relatives of the deceased. 154 elderly patients aged from 60 to 99 years old were diagnosed HFpEF. The diagnostic criteria of HFpEF were: 1) Clinical history of previous hospital discharge diagnosis included heart failure or last hospitalization were diagnosed with heart failure; 2) the last echocardiography at the end of patients' lifetime indicated that LVEF≥50%.. All P values < 0.05 were accepted as statistically significant.
Results: Among 154 elderly patients with HFpEF aged from 60 to 99 years old, there were 142 male(92.2%) and 12 female(7.8%) with mean age of 85.7 ± 7.4 years old. According to pathological criteria, the incidence of CHD among HFpEF cases was 68.2% (105/154), incidence of AMI was 12.3% (19/154), incidence of OMI was 50.6% (78/154), incidence of chronic myocardial ischemia was 18.2% (28/154) (Figure 1). Grade III and more severe stenosis of left anterior descending branch were very common, reaching 51.9%(Figure 1).Clinical diagnosis of CHD were 81.8%(126/154) among HFpEF patients, missed diagnosis rate of CHD was 9.5% and misdiagnosis rate was 63.3%. Missed diagnosis rates of AMI and OMI were 57.9%, 57.7% respectively, misdiagnosis rates were 10.4% and 23.7% respectively.(Table1)
Conclusions: The incidence of CHD was high in the elderly patients with HFpEF and severe stenosis of anterior descending branch was common. Misdiagnosis rate of CHD in HFpEF was high and missed diagnosis rates of AMI and OMI were high. Further coronary artery evaluation should be emphasized in elderly patients with HFpEF.

Differences between clinical and autopsy

Differences between clinical diagnosis and pathological diagnosis in HFpEF with CHD

	Both clinical diagnosed and pathological diagnosed	missed diagnosis (%)	misdiagnosis (%)	diagnosed neither by autopsy nor clinical
CHD	95	109.5%	3163.3%	18
AMI	8	1157.9%	1410.4%	121
OMI	33	4557.7%	1823.7%	58

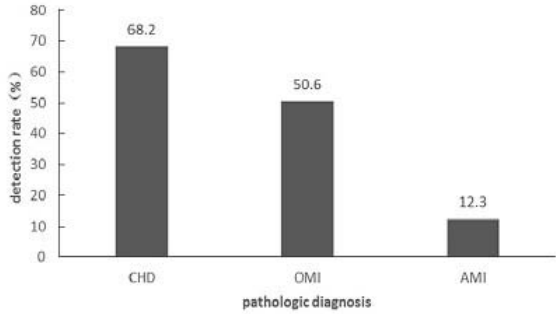


Figure 1.Incidence of CHD by autopsy in HFpEF patients

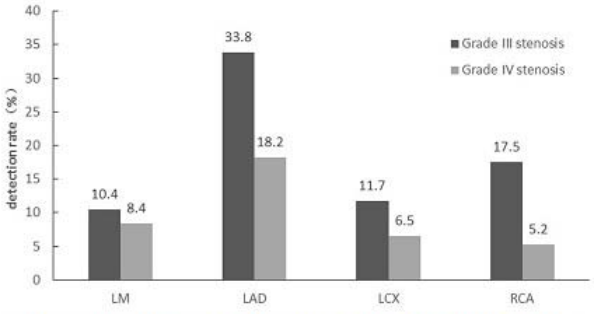
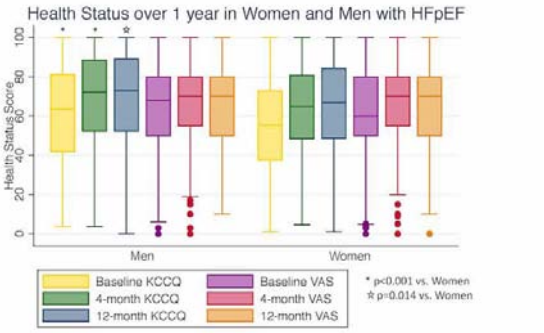


Figure 2.Grade III and IV stenosis in coronary artery branches in HFpEF patients
LM: Left main coronary artery; LAD: Left anterior descending artery; LCX: Left circumflex; RCA: Right coronary artery

Incidence of CHD by autopsy in HFpEF

Patient characteristics			
N=1767	Women	Men	p-value
Age	72.1± 9.9	71.0± 9.5	0.0209
Atrial fibrillation (afib)	348 (39.5%)	395 (44.7%)	0.027
Coronary artery disease (CAD)	336 (38.1%)	479 (54.3%)	<0.0001
Hypertension (HTN)	807 (91.5%)	781 (88.5%)	0.039
Peripheral vascular disease	87 (9.9%)	120 (13.6%)	0.018
Dyslipidemia	596 (67.5%)	654 (74.1%)	0.003
Diabetes	354 (40.1%)	434 (49.2%)	<0.0001
Thyroid disease	243 (27.6%)	90 (10.2%)	<0.0001
Bone fracture	160 (18.2%)	106 (12.0%)	<0.0001
Estimated glomerular filtration rate (eGFR)	63.0± 22.3	66.0± 20.5	0.0032
Body Mass Index (BMI)	34.4± 8.8	33.2± 7.4	0.0030
Comorbidity count *	5.5± 1.9	5.4± 1.8	0.4816
PHQ score (N=1427)	8.4± 6.6	7.4± 6.3	0.0019

* sum of the following comorbidities: afib, CAD, stroke, COPD, asthma, hypertension, PAD, dyslipidemia, diabetes, thyroid disease, fracture, obesity (BMI ≥ 30), depression (PHQ-9 ≥ 9), CKD (GFR ≤ 60)



Health Status Box Plot

P1282

Sex differences in long-term health status in heart failure with preserved ejection fraction

K Kelsey Flint[1]; M Merrill[1]; D Kao[1]
[1]*University of Colorado, Cardiology, Aurora, United States of America*

Background: Little is known about sex differences in health status over time in heart failure with preserved ejection fraction (HFpEF).
Purpose: 1. Describe longitudinal sex-specific patterns of global- and heart failure-specific health status 2. Identify factors associated with reduced health status in women with HFpEF.
Methods: Data source: TOPCAT trial. Health status was measured at 0 and 12 months. Health status measures were Kansas City Cardiomyopathy Questionnaire (heart failure-specific; KCCQ) and visual analog scale (global; VAS). Analysis was restricted to Americas due to very low event rates in Russia/Georgia.
Results: Compared to men, women with HFpEF were older, and had more non-cardiac comorbidities. Men had more CV risk factors and CV disease. Overall comorbidity burden was similar (Table). KCCQ was moderately reduced in women compared to men at each time point (Figure) despite a greater increase in KCCQ in women over time. VAS did not differ by sex at any time point. The relationship between sex and 12-month KCCQ was attenuated ($p = 0.543$) when controlling for BMI ($p < 0.001$), depression ($p < 0.001$) and eGFR ($p < 0.001$).
Conclusion: Women with HFpEF have worse KCCQ but not VAS scores. Further study is needed to evaluate the relationship between health status and obesity, depression, and renal function in women with HFpEF.

P1283

Determinants of heart failure in patients with arterial hypertension and type 2 diabetes mellitus

A Vintila[1]; M Dobrovie[2]; D Vasiliu[2]; C Tudorica[2]; V Vintila[3]
[1]*University of Medicine and Pharmacy Carol Davila, Coltea Clinical Hospital, Internal Medicine and Cardiology, Bucharest, Romania*; [2]*Coltea Clinical Hospital, Bucharest, Romania*; [3]*University of Medicine and Pharmacy Carol Davila, University Emergency Hospital of Bucharest, Cardiology, Bucharest, Romania*

Background: The association between arterial hypertension and type 2 diabetes mellitus is frequent and determines synergistic alterations in myocardial properties. This leads to subclinical cardiac remodeling, which may evolve into heart failure, worsening the prognosis of these patients.
Purpose: We aimed to investigate the prevalence of heart failure and factors correlated to its development in a cohort of hypertensive patients with type 2 diabetes mellitus.
Methods: We evaluated 60 consecutive patients with arterial hypertension and type 2 diabetes mellitus, mean age 68± 9 years, hospitalized for hypertension related problems. We recorded demographic data, clinical characteristics, resting ECG and transthoracic echocardiography with Tissue Doppler imaging at the level of the lateral and septal mitral annulus. Blood tests have been performed as clinically indicated.
Results: Heart failure was diagnosed in 28 out of 60 patients (46.7%). 18 patients (64.3%) were in NYHA class III, while 10 (35.7%) were in NYHA class II. Left ventricular ejection fraction was preserved in 19 out of 28 patients with heart failure (67.9%). Presence of heart failure was correlated with age ($r = 0.373$, $p < 0.001$), diagnosis of atrial fibrillation ($r = 0.420$, $p = 0.001$), left atrial diameter ($r = 0.506$, $p < 0.001$) and volume ($r = 0.526$, $p < 0.001$), right atrial diameter ($r = 0.466$, $p < 0.001$), right ventricular diameter ($r = 0.307$, $p = 0.017$), E/E' ratio ($r = 0.391$, $p = 0.004$), lateral MAPSE ($r = -0.478$, $p < 0.001$), septal MAPSE ($r = -0.461$, $p = 0.001$), TAPSE ($r = -0.502$, $p < 0.001$) and myocardial systolic velocities at the level of the lateral

mitral annulus (r = -0.302, p = 0.032) and septal mitral annulus (r = -0.362, p = 0.013). It was also correlated with glomerular filtration rate estimated by MDRD formula (r = -0.425, p = 0.001), plasma HDL-cholesterol (r = -0.285, p = 0.033), thrombocyte count (r = -0.269, p = 0.037) and mean platelet volume (r = 0.277, p = 0.032). Using stepwise linear regression, we computed a model for prediction of heart failure, with 3 independent predictors: left atrial diameter, plasma HDL-C level and mean platelet volume (R2 = 0.866, p < 0.001).
Conclusions: Development of heart failure is frequent in patients with arterial hypertension and type 2 diabetes mellitus. Left ventricular ejection fraction is preserved in the majority of patients. Prediction of heart failure in this population could be realized based on three independent predictors: left atrial diameter, plasma HDL-cholesterol level and mean platelet volume.

P1284
Hypertensive left ventricular hypertrophy is a risk factor for the development of a HFPEF but not a depressed left ventricular ejection fraction within eight years

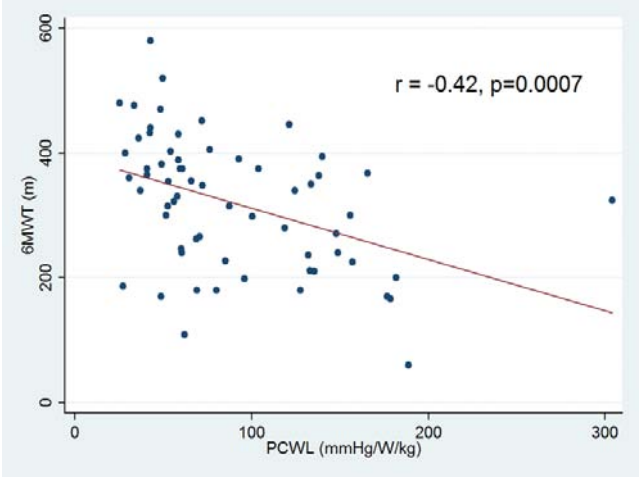
AG Artem Ovchinnikov[1]; MV Ojerelyeva[1]; FT Ageev[1]
[1]Russian Cardiology Research and Production Complex, Moscow, Russian Federation

Background. Hypertensive heart disease is a major cause of the development of heart failure with preserved ejection fraction (HFPEF). However, rate and determinants of the transition from asymptomatic left ventricular hypertrophy (LVH) to HFPEF and whether LVH is a common precursor to depressed LVEF is poorly understood.
Purpose: to determine rate and predictors of the transition from asymptomatic hypertensive LVH to HFPEF and whether LVH is a risk factor for the development of a reduced LVEF.
METHODS AND RESULTS. From 2002 through 2010, 350 patients at our Out-Patient Department underwent echocardiography and had asymptomatic hypertensive concentric LVH and normal LVEF. Of these, 223 had a follow-up clinical and echocardiographic assessment by March 2016. The primary outcomes were the development of HFPEF or depressed LVEF. After a median follow-up of 8.1 years, the most of patients with asymptomatic concentric LVH (161, or 72%) developed HFPEF. Transition from asymptomatic LVH to HFPEF was associated with deterioration of LV diastolic dysfunction (DD): increase of DD grade occurred in 51% patients, and an increase of DD grade provided 100% sensitivity for predicting HFPEF. Multivariable analysis identified three independent predictors of the development of HFPEF namely, an old age, an increase of LV mass index >10% during follow-up, and an absence of taking of statins (P < 0.05 for all). Yet, 34 (15%) patients developed low LVEF, but only in 16 of them (7% of whole group) it occurred without interval myocardial infarction (MI). All these 16 patients had only mild systolic dysfunction (LVEF >40%) and all but only one patient had concentric LVH. Independent predictors of the development of low LVEF by this 'internal' mechanism were chronic atrial fibrillation and high mass body index (P < 0.05 for both).
Conclusions: In hypertensive heart disease, the transition from asymptomatic LVH to HFPEF was very frequent (72%) after long-term follow-up, and was related to deterioration of LVDD and an absence of taking of statins. The transition from a normal LVEF to a low LVEF, however, was infrequent (7%) in the absence of interval MI and did not result in a change in the LV geometry from a concentric to an eccentric phenotype.

P1285
Exercise hemodynamics and 6 minute walk distance in patients with HFpEF: importance of workload corrected pulmonary capillary wedge pressure

E Wolsk[1]; D Kaye[2]; BA Borlaug[3]; D Burkhoff[4]; DW Kitzman[5]; J Komtebedde[6]; CSP Lam[7]; P Ponikowski[8]; SJ Shah[9]; F Gustafsson[1]
[1]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; *[2]Baker IDI Heart and Diabetes Institute, Melbourne, Australia*; *[3]Mayo Clinic, Rochester, United States of America*; *[4]Cardiovascular Research Foundation, New York, United States of America*; *[5]Wake Forest University, Winston-Salem, United States of America*; *[6]Corvia Medical, Inc, Boston, United States of America*; *[7]Duke-NUS Graduate Medical School Singapore, Singapore, Singapore*; *[8]Military Hospital of Wroclaw, Wroclaw, Poland*; *[9]Northwestern University, Chicago, United States of America*

BACKGROUND: Patients with heart failure (HF) and preserved ejection fraction (HFpEF) are characterized by an abnormal hemodynamic response to exercise and varying degrees of functional impairment. The 6-minute walk test (6MWT) serves as a standardized test for functional capacity quantification in HF patients, and is associated with cardiovascular outcomes. However, the association between 6MWT and hemodynamic parameters at rest and during exercise in HFpEF patients is unknown.
Objective: Identify invasive hemodynamic variables at rest, light to moderate exercise, and peak exercise associated with 6MWT in patients with HFpEF.
Methods: We studied 64 patients enrolled in the REDUCE LAP-HF trial who completed a 6-minute walk test (6MWT) at baseline and cardiac catheterization with measurement of hemodynamic variables at baseline, light to moderate exercise (20 W), and at peak supine exercise. Univariate linear regression models were used to assess the associations between 6MWT and measured or derived hemodynamic variables at baseline, light to moderate exercise (20 W), and at peak supine exercise. Variables were added to multivariable models with stepwise forward selection (p < 0.1).
Results: The average 6MWT distance was 318 ± 106 meters. At rest, only pulmonary capillary wedge pressure (PCWP) was associated with 6MWT (p = 0.033) in a multivariable model. During light to moderate exercise, mean pulmonary artery pressure (mPAP) was associated with 6MWT in a multivariable model (p = 0.033). During peak exercise, central venous pressure (CVP), cardiac index (CI), and PCWP/CI correlated with 6MWT, however the workload corrected PCWP (PCWL) was the only variable independently associated with 6MWT (Figure; r=-0.42, p < 0.001, multivariable, p = 0.002). Changes in CI and mPAP from baseline to peak exercise were associated with 6MWT after multivariable adjustment (p = 0.0027 and p = 0.052, respectively).
Conclusion: Workload corrected PCWP correlated best with 6MWT performance. While non-cardiac factors clearly play a role in determining 6MWT distance, this study suggests that workload corrected PCWP could be an important target for intervention when aiming at improving functional capacity in HFpEF.



Figure

ISCHEMIA - REPERFUSION - PRECONDITIONING - POSTCONDITIONING

P1286
Gender differences in left ventricular remodeling features in patients with stent restenosis following primary percutaneous coronary intervention

N Nino Sharashidze[1]; B Tsinamdzgvrishvili[1]; G Saatashvili[1]; N Mamamtavrishvili[1]; R Abashidze[1]; D Trapaidze[1]; N Chanturidze[1]; A Kordzadze[1]; Z Gachava[1]
[1]Iv.Javakhishvili Tbilisi State University, Tbilisi, Georgia Republic of

We aimed to compare Left Ventricular (LV) remodeling and function between genders in patients with in stent re-stenosis who underwent primary percutaneous intervention (PCI) due to acute coronary syndromes (ACS).
Methods: Patients who developed in stent re-stenosis during 12 months after PCI due to acute coronary syndromes were studied. Study subject (total number 70) were included in groups according gender (52 males and 18 females). Gender differences in rate of LV hypertrophy (LVH), systolic and diastolic dysfunction and Heart Failure (by Killip I-III and chronic HF II-III by NYHA). LV remodeling and function were assessed using ultrasound-Doppler modality. Statistics: Student T –test, Fisher's exact test and regression analysis were performed.
Results: rate of LVH was 0.50 in women and 0.46 in men (P=0.79). Rate of reduced EF (< 40%) was 0.38 in women and 0.17 in men (P=0.06). Diastolic dysfunction rate measured by mitral flow velocities was 0.44 and 0.28 in females and males respectively (P=0.21). Rate of heart failure in acute settings I-III by Killip was found in women and men 0.11 and 0.14 respectively (P=0.73).Rate of Chronic HF II-III by NYHA was

0.50 in females and 0.21 in males (P= 0.019.)Regression analysis showed association of chronic HF with stent re-stenosis in women OR 3.67 (95% CI 1.19-11.27).
Conclusions: Differences in rates of LVH, reduced EF, diastolic dysfunction and HF in acute settings did not differ significantly between female and male patients who developed in stent re-stenosis after primary PCI due to ACS. However, statistically significant difference was revealed by prevalence of chronic HF between genders and association of chronic HF with in stent re-stenosis in women was found.

P1287
Hepatitis-c virus infection is a risk factor for coronary artery disease in egypt

A M Abdelmohsen Moustafa Abdou Aboualia[1]; MO Kayed[1]; MS Rehan[1]; M Abood[2]; M Attia Mohamed[3]
[1]Al-Azhar University, cardiology department, cairo, Egypt; *[2]Al-Azhar University, Radiology department, Cairo, Egypt*; *[3]Al-Azhar University, clinical pathology, Cairo, Egypt*

Aim of the work: is to study the presence of atherosclerotic coronary artery disease in patients with chronic hepatitis C virus infection.
Patients and methods: This study included two main groups of patients with symptomatic ischemic heart disease (according to HCV serology), presented as Acute coronary syndrome or for elective or emergent coronary angiography : Group 1: 100 HCV seropositive patients as a test group and group 2: 32 HCV seronegative patients as a control group. All patients were studied along the following scheme: informed consent, full history taking, complete physical examination, full routine labs, HCV rapid test, resting twelve lead ECG, transthoracic echocardiography, pelvi-abdominal ultrasound and coronary angiography.
Results: the two groups were matched in age after exclusion of diabetes, hypertension, chronic renal diseases, clinical liver cirrhosis and history of ischemic heart disease. There was male predominance in group I with statistical significance. In this study 99% of patients with HCV seropositive had abnormal coronary angiography while 65.6% of HCV seronegative had abnormal coronary angiography and this difference showed statistical significance (< 0.001). The number of the affected vessels was higher in HCV seropositive than seronegative groups (1 vessel disease (49% versus 56.3%, 2 vessel disease 25% versus 6.3% and multivessel 25% versus 3.1% in HCV seropositive and seronegative respectively) with $p < 0.001$. LM was present in 5 patients in group I and no patient in group II. In this study univariate logistic regression analysis the predictors of coronary artery disease were sex ($P < 0.0001$), smoking ($P = 0.037$) and HCV seropositivity ($P = 0.041$). Also in multivariate logistic regression analysis the predictors of coronary artery disease were smoking ($P = 0.011$) then HCV seropositivity ($P = 0.032$) and lastly age ($p = 0.40$).
Conclusion: Hepatitis C virus is a risk factor for coronary artery disease and associated with increased angiographic burden of coronary artery disease in patients with HCV seropositivity.

P1288
34 minutes is the mean door to needle time in Egyptian patients with first attack of STEMI who showed myocardial recovery after receiving thrombolytic therapy

A Ahmed Al-Habbaa[1]; M El-Abbady[1]; M Mostafa[1]; ABD Shereidah[1]; W Attia[1]
[1]Al-Azhar University, Department of Cardiology, Cairo, Egypt

Objectives: We aimed to assess the time table of patient care who presented with acute first attack of STEMI.
Patients and methods: The study included 42 patients with first attack of STEMI admitted to our CCU unit who showed symptoms and signs of successful reperfusion after pharmacological thrombolytic therapy, the patients were classified into two groups; group I included 28 patients with with improvement of RWMA score, group II included 14 patients without improvement of RWMA score. All patients had been subjected to the following: informed consent, personal, demographic data collection, time table from ER entrance till beginning of thrombolytic therapy, reperfusion therapy by streptokinase I.V., baseline conventional transthoracic echocardiography evaluation, 2D speckle tracking echocardiographic study within 72 hours after the successful reperfusion, medical follow-up for 3 months and follow-up conventional transthoracic echocardiography for RWMA score assessment.
Results: The baseline clinical characteristics were matched in both groups. Group I who showed myocardial recovery had mean door to needle time of 34.28 ± 7.9 minutes while group II who showed no myocardial recovery had a mean door to needle time of 51.42 ± 17.3 minutes.
Conclusion: The shorter the door to needle time the more was the recovery of myocardial function in patients with first attack of STEMI. We are getting more to the ideal door to needle time of 30 minutes, as we still have thrombolytic therapy as the wide used option in Egypt.

P1289
Primary coronary percutaneous intervention in diabetic versus nondiabetic patients. Outcome and follow-up. independent predictors of survival and event free survival

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[1]; ILPB Anjos[2]; VF Marcolla[1]; AAB Aragao[1]
[1]Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil; *[2]Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

Background: 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).
Objectives: 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 $\geq$ 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 $\geq$ 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

MULTIVARIATE COX ANALYSIS - INDEPENDENT PREDICTORS OF DEATH 1 YEAR			
INDEPENDENT VARIABLE	P	HAZARD RATIO	IC 95%
FEMALE GENDER	0,050	2,617	0,999 – 6,852
AGE ≥ 65 YEARS	0,035	3,391	1,091 – 10,543
FAILURE OUTCOME	0,023	3,364	1,182 – 9,578
MULTIVARIATE COX ANALYSIS - INDEPENDENT PREDICTORS OF MACE 1 YEAR			
INDEPENDENT VARIABLE	P	HAZARD RATIO	IC 95%
MULTIVESSEL DISEASE	0,034	1,854	1,048 – 3,280

P1290

One-step or two-step myocardial revascularisation in patients with ACS without ST-segment elevation with multivessel coronary artery disease

Z Shugushev[1]; D A Maximkin[1]; T Chernigina[1]; R Goloshchapo-Aksenov[1]; A Faibushevich[1]; N Sturov[1]; R Bachoo[1]; A Nikitin[2]
[1]RUDN University, Moscow, Russian Federation; [2]Central Clinical Hospital Russian Academy of Science, Moscow, Russian Federation

Aims: to evaluate the results of endovascular treatment of patients with acute coronary syndrome without ST-segment elevation with multivessel coronary artery disease.
Methods: AND RESULTS: 346 patients were enrolled in the study and initially randomized into 3 groups. Group 1 included 100 patients in whom complete myocardial revascularization was performed during initial PCI. Group 2 consisted of 124 patients, in whom complete myocardial revascularization was performed during initial hospitalization and group 3 included 122 patients in which complete revascularization was performed at different periods after the initial hospitalization. Criteria: patients with ACS without ST-segment elevation with multi-vessel coronary artery lesion (SYNTAX score=23-32); high and medium risk on GRACE scale; no history of myocardial revascularization. Long-term results were assessed in 192 patients. After 12 months in patients of group 3 had significantly more often cardiovascular complications and re-intervention on the target vessel was needed. It was revealed that the implementation of complete myocardial revascularization later than 30 days from a day of diagnosed acute coronary syndrome, adversely affects the prognosis of the disease (r=0,58, p < 0,05). Risk factors that adversely affect the prognosis of patients with ACS without ST-segment elevation with multi-vessel coronary artery lesion include: Subtotal stenosis in asymptomatic arteries, circulatory insufficiency- Killip class III, history of myocardial infarction, high risk on the GRACE scale, the extent of lesions in the asymptomatic arteries more than 20mm, diabetes, the degree of risk on a SYNTAX scale score>25, overweight/obesity and hypercholesterolemia>6.5 mmol/L.
Conclusions: when performing PCI in patients with ACS without ST-segment elevation with multi-vessel coronary bed lesion, the implementation of complete myocardial revascularization later than 30 days from a day of diagnosed acute coronary syndrome, adversely affects the prognosis of the disease.

P1291

Incidence, timing, predictors and impact of acute heart failure complicating an acute coronary syndrome

PM Pedro Azevedo[1]; J Bispo[1]; D Carvalho[1]; D Bento[1]; T Mota[1]; J Guedes[1]; S Pereira[1]; W Santos[1]; J Mimoso[1]; N Marques[1]; P Gago[1]; I Jesus[1]
[1]Faro Hospital, Cardiology, Faro, Portugal

Introduction: Acute heart failure (AHF) is a common complication of an acute coronary syndrome (ACS), resulting in higher costs of treatment and poor prognosis. This study pretends to evaluate the incidence, timing, predictors and impact of AHF in a population with an ACS.
Methods: Retrospective, descriptive and correlational study with all patients admitted with an ACS in a Cardiology department between the 1st of October 2010 and 31st of August 2015. Patients with AHF (Killip Class > 1) were compared to patients without AHF, and between patients with AHF at presentation and those who developed in-hospital AHF. The 1-year follow-up was made through phone call by a Cardiologist. We performed a univariate and multivariate statistical analysis of in-hospital mortality, mortality and hospitalization rate at 1-year using SPSS.
Results: 3319 patients with an ACS were included, 2465 (74,3%) men with a mean age of 65,8 ± 13 years. There were 1478 (44,5%) patients with an ST-segment elevation myocardial infarction (STEMI), 1607 (48,4%) with NSTEMI, 116 (3,5%) with unstable angina and 118 (3,6%) had acute MI of unknown location.
AHF was observed in 495 (14,9%) patients. 352 (10,6%) had AHF at admission and 143 (4,3%) only developed AHF in the hospital. AHF was significantly associated with age, female sex, non-smokers, hypertension, diabetes, and several other comorbidities. AHF was also associated with STEMI, anterior wall myocardial infarction, atrial fibrillation and dyspnea on admission.
Patients with AHF had higher heart rate at admission (86,8 vs74,9 bpm, p < 0,01), lower systolic blood pressure (129 vs 141 mmHg, p < 0,01), lower left ventricular ejection fraction (LVEF) (44,9% vs 59,1%, p < 0,01), less coronary catheterization (53,9% vs 78,9%, p < 0,001) and percutaneous coronary intervention (41,2% vs 60,9%) and longer delay between symptoms and revascularization (303,6 vs 256,4 minutes, p < 0,01) in STEMI.
The independent predictors of AHF were female sex (OR 1,7, p < 0,01), higher age, past history of stroke (OR 2,2, p < 0,01) or HF (OR 1.92, p < 0,01), diabetes mellitus (OR 1.3, p = 0,04), STEMI (OR 1.67, p < 0,01), atrial fibrillation (OR 2.2, p < 0,01) and lower LVEF.
The in-hospital mortality rate was higher in patients with AHF (19,9% vs 1,2%, p < 0,01), as was the 1-year mortality (28,6% vs 6,2%, p < 0,001) and hospitalization rate (38% vs 19,2%, p < 0,001).
On multivariate analysis, AHF was the strongest independent predictor of in-hospital mortality (OR 7.89, p < 0,01), and also independently associated with 1-year mortality (OR 2.6, p < 0,001) and hospitalization (OR 1.81, p < 0,01). The timing of AHF had no impact on outcome.
Conclusion: AHF commonly complicates ACS and is independently predicted by older age, female sex, diabetes, STEMI, atrial fibrillation and lower LVEF. In this study, AHF, regardless of its timing, was an independent predictor of in-hospital death and 1-year mortality or hospitalization.

BASIC SCIENCE: ANIMAL EXPERIMENTATION

P1293

The status of cerebral arteries, leptin levels and postprandial hypertriglyceridemia in patients with coronary heart disease with preserved systolic function combined with non-alcoholic fatty liver di

M Mariya Grechanyk[1]; NM Grechanyk[2]; YV Filippova[2]; AV Kuryata[1]
[1]Dnepropetrovsk Medical Academy, Dnepropetrovsk, Ukraine; [2]Dnipropetrovsk Regional Hospital Mechnikov, Dnepropetrovsk, Ukraine

Objective: to estimate the frequency of atherosclerosis of cerebral arteries, leptin levels and postprandial hypertriglyceridemia (PPG) in patients with coronary heart disease (CHD) with preserved systolic function combined in combination with non-alcoholic fatty liver disease (NAFLD), depending on the body mass index (BMI).
Methods: The study involved 24 men (mean age 56,2 ± 1,3 years) with CHD with preserved systolic function combined with NAFLD, the control group consisted of 14 patients with coronary artery disease without NAFLD. The study group was divided into 3 subgroups according to BMI (subgroup 1 (33%) - patients who are overweight, 2 (41%) - obesity 1 degree, 3 (25%) - obesity grade 2). Evaluated atherosclerotic changes of the neck vessels, endothelial function, PPG, leptin levels.
Results: In the group of patients with CHD with preserved systolic function and NAFLD point plaques found significantly more often (31%, p = 0,01) when significantly more abuse on the part of endothelial function (47% lower, p = 0,01), than in the control group. In patients with grade 2 obesity identified the highest leptin levels (43,6 ± 20,2, p < 0,05), which is 44% higher than in the subgroup with obesity 1 degree (24,4 ± 14,6, p < 0.05) and 63% greater than in the subgroup with overweight. The greatest increase in triglycerides after fat loading test with fixed subgroup 1 (70%) and in the control group (125%).
Conclusion: Thus, in patients with CHD with preserved systolic function combined with NAFLD leptin and PPG have different levels change depending on body weight. Increasing body weight was not associated with further development of atherosclerotic changes in the cerebral arteries. There was correlation between the endothelial dysfunction and level of leptin (r=0,74, p = 0,04) in a group 2 however in a group 1 and 3 such connection was not observed.

P1294

Acute myocardial dysfunction after ionizing radiation exposure

L Napolitano[1]; A Franco[2]; J Gambardella[3]; A Fiordelisi[3]; D Sorriento[3]; M Ciccarelli[1]; G Iaccarino[1]
[1]University of Salerno, Dept. of Medicine and Surgery, Salerno, Italy; [2]University of Naples Federico II, Dpt of Clinical Medicine, Cardiovascular & Immunological Science, Naples, Italy; [3]Federico II University, Scienze Biomediche Avanzate, Napoli, Italy

In time of programming interstellar journeys, the study of the effect of ionizing radiation (IR) exposition on human physiology and health is relevant. IR causes cardiac dysfunction due 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. To evaluate the possible involvement of mitochondria to mediate the effects of IR exposure on cardiac function, 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. At 3 h post-IR, we observed increased left ventricle diastolic diameter (LVDd: 39.5 0.3 vs 35 0.15 mm; p < 0.05 vs Basal) with reduced ejection fraction (EF: 45% 2 vs 66% 4; p < 0.05 vs Basal). At 24h post IRI, we found a recovered LVDd (36.2 0.4 vs 35 0.15 mm; ns) and ameliorated cardiac contractile function (EF: 60% 3 vs 66% 4; ns). Morphological analysis by TEM (Fig 1) reveled 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. A recently described modulator of mitochondrial survival, GRK2, was investigated in a related in vitro model. In H9C2, over-expression of GRK2, induced a rightward shift in time for mitochondrial alterations and ROS production, which occurred after 8 hours after IR. Opposite, GRK2 silencing lead to anticipated mitochondrial impairment and no recovery occurred at 8h. Mechanistically, IR exposure produced interaction of GRK2 with MFN1 and 2, key molecules of mitochondrial recovery process, at 3h post IR. IR induces an acute cardiomyopathy that is associated to an altered mitochondrial morphology and function.

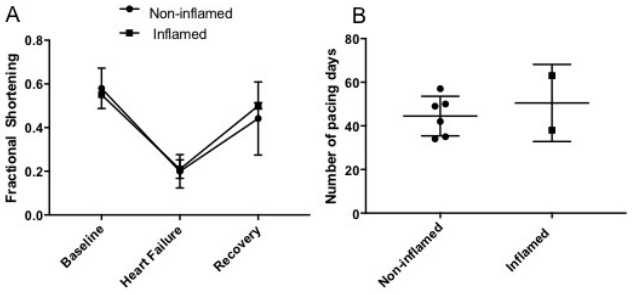
P1295

Pre-existing systemic inflammation does not influence onset or severity of heart failure

P Parminder Chaggar[1]; A Watkins[2]; W Critchley[3]; M Mohamud[3]; P Foden[4]; R Venkateswaran[1]; N Yonan[1]; A Trafford[2]; JE Fildes[3]
[1]University Hospital of South Manchester NHS Foundation Trust, The Transplant Unit, Manchester, United Kingdom; *[2]University of Manchester, Division of Cardiovascular Sciences, Manchester, United Kingdom*; *[3]University of Manchester, Manchester Collaborative Centre for Inflammation Research, Manchester, United Kingdom*; *[4]University Hospital of South Manchester NHS Foundation Trust, Department of Medical Statistics, Manchester, United Kingdom*

Funding Acknowledgements: The Transplant Unit, University Hospital of South Manchester

Background: The immune system is considered integral to the development of left ventricular (LV) failure. However, whilst inflammation can induce cell death in native tissue, it is also required for repair and therefore may have a bi-directional effect in heart failure. This is supported by trials of anti-inflammatory therapy in heart failure that demonstrate, at best, a neutral effect on clinical outcomes and at worst, an increase in mortality. The relationship between inflammation and heart failure development and recovery is poorly understood and warrants further investigation.
Purpose: This study was conducted to examine if baseline asymptomatic inflammation in healthy sheep would affect the time to development of, the severity of or the recovery from heart failure induced by tachycardic pacing. We hypothesised that pre-existing inflammation would increase susceptibility to the development of heart failure and lead to a more severe disease phenotype.
Methods: 8 healthy Welsh mountain sheep underwent VVI pacemaker implant and paced at 210bpm until they developed overt clinical signs of heart failure when pacing was terminated and the animal was allowed to recover. A panel of cytokines was quantified via a protein array at baseline to determine the degree of asymptomatic inflammation. The severity of LV dysfunction was assessed by serial measurements of fractional shortening on echocardiography at baseline, heart failure and recovery. Fractional shortening has previously been validated as an accurate measure of LV function in sheep. Sheep with high levels of baseline inflammation (upper quartile of cytokine concentrations) were compared to the non-inflamed sheep with regards to the time taken to induce clinical heart failure and changes in fractional shortening.
Results: Of the 8 healthy sheep, the 2 sheep in the upper quartile of inflammation had significantly higher baseline levels of all pro-inflammatory cytokines interferon-gamma, CXCL9, IP10, IL17A and IL21 compared to the remaining 6 sheep. Compared to sheep with low baseline inflammation, sheep with high baseline inflammation demonstrated no difference in fractional shortening (Figure 1A) at any time point or the number of days of pacing required to induce heart failure (Figure 1B).
Conclusion: In this study systemic inflammation had no impact on susceptibility to or severity of heart failure in sheep exposed to tachycardic pacing. This challenges the widely accepted dogma that inflammation would negatively impact heart failure disease progression and severity. These findings need to be confirmed in a larger population and expanded to other models of myocardial injury.



Inflamed versus non-inflamed sheep

P1296

Effect of candesartan cilexetil and extract of polygonum sp. on the number of endothelial progenitor cells in vivo

A Aliaksandra Beliayeva[1]; V Afonin[1]
[1]National Academy of Science, Institute of Bioorganic Chemistry, Minsk, Belarus

Background: Cardiovascular diseases are widespread in many countries of the world, therefore development and formulation of new drugs and their combinations, as well as characterization of new properties of available medicines appears extremely relevant.
Purpose: To study the effect of candesartan cilexetil, which is an angiotensin-II receptor blocker, and extract of Polygonum sp. on the contents of endothelial progenitor cells in vivo.
Methods: Male C57Bl/6 mice (n = 80) were selected for the study. They were divided into 8 groups (10 test animals in each). Mice of 7 groups received daily intragastrically candesartan cilexetil and extract of Polygonum sp. for 7 weeks. The substances were dissolved/suspended in 1% starch solution. Group 1 was supplied candesartan cilexetil at 1.5 mg/kg dose, groups 2 – 4 were administered extract of Polygonum sp. at 1 mg/kg, 10 mg/kg and 50 mg/kg doses, respectively, groups 5 – 7 received candesartan cilexetil at 1.5 mg/kg dose coupled to extract of Polygonum sp. at 1 mg/kg, 10 mg/kg and 50 mg/kg doses, respectively. The control group was provided with 1% starch solution. Quantitative evaluation of endothelial progenitor cells (CD117 +) in bone marrow and blood of C57Bl/6 mice was performed by flow cytometry.
Results: In this study we investigated the effect of candesartan cilexetil and extract of Polygonum sp. in different dosages on the number of endothelial progenitor cells. Cell surface marker CD117 (or c-kit) was chosen for analysis. It's a cytokine receptor, KIT gene product. CD117 is expressed on the surface of stem cells, including endothelial progenitor cells. It was shown in this study that candesartan cilexetil at 1.5 mg/kg dose resulted in a significant rise of CD117 + stem cell ratio in blood as compared to the control. Extract of Polygonum sp. at 10 mg/kg and 50 mg/kg doses stimulated generation of CD117 + cells in bone marrow and blood of C57Bl/6 mice in comparison with the control ($p < 0.05$). The first evidence was recorded that concerted application of candesartan cilexetil at 1.5 mg/kg dose and extract of Polygonum sp. at 10 mg/kg and 50 mg/kg doses promoted considerably production of CD117 + cells in bone marrow and blood of C57Bl/6 mice ($p < 0.05$), with the resulting values higher than those obtained for individual substances. The largest increment of the number of endothelial progenitor cells in bone marrow and blood was observed in variant with combination of candesartan cilexetil at 1.5 mg/kg dose and extract of Polygonum sp. at 50 mg/kg dose. Conclusion: It was originally demonstrated that combination of candesartan cilexetil and extract of Polygonum sp. was effective to induce mobilization of endothelial progenitor cells in bone marrow and to increase their ratio in blood of C57Bl/6 mice. The experimental data may be used in formulation of new complex drug for the treatment of cardiovascular diseases, capable to promote the mobilization of endothelial progenitor cells in the body.

P1297

Exercise preconditioning increases serotonin vasoconstriction of isolated pulmonary artery in ovariectomy female rats with hypoxic pulmonary hypertension

N Nadezda Pankova[1]; N Medvedeva[1]; N Terentyeva[1]; A Terentyev[1]
[1]M.V. Lomonosov Moscow State University, Biological, Moscow, Russian Federation

Introduction: Endothelial dysfunction is one of reason of hypoxia pulmonary hypertension (hPAH). There is an imbalance between vasodilators and vasoconstrictors

with the development of this disease. Serotonin is involved in triggering pulmonary hypertension. Exercise training (ETr) may have protective effects in the cardiovascular system. Experiments in the animals have shown that Etr induces endothelium-dependent vascular relaxation via the nitric oxide, prostacyclin, and hyperpolarization pathways. There are conflicting data on the effect of ETr on the development of hPAH.
The aim of the study was to test the hypothesis that ETr will decrease serotonin-dependent constriction of pulmonary vessels and reduce the degree of pulmonary hypertension.
Methods and design. Female Wistar rats were used. They were divided into 7 groups: four were with hPAH (H) and three without (C). Two groups from (H) and (C) rats were gonadectomized (HG and CG) and two were with ovaries (HN and CN). One group from HG,CG,HN,CN were with exercise preconditioning (groups HGEx, CGEx,HNEx) and one group were without exercise (groups HGC,CGC,HNC,CNC) 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 (10 h a day, 2 wk.,O2 concentration reduced to 10%). For exercise preconditioning rats were subjected to exercise training (aerobic swimming during 30 min/day.) for a period of 2 weeks to hypoxia. Systolic right ventricle pressure (SRVP) was measured. Right ventricular (RV) hypertrophy was calculated as RV weight /heart w. Perfusion pressure of isolated pulmonary and systemic (popliteal) artery to vasoconstrictor serotonin (3,3*10-8 – 10-5M) was measured.
Results Two weeks after chronic hypoxia exposure all (H) groups of rats developed hPAH with different extent of the disease. SRVP was lower by 24% in group HGEx compared with group HGC($p < 0,05$). There are no differences between other hypoxic groups.. Pulmonary artery response to serotonin 3*10-7M in HGC group was less by 59% than in HNC group ($p < 0,05$) without effect in systemic vessels. Pulmonary vessels of gonadectomized rats with hPAN, which had exercise preconditioning demonstrated the increase of vasoconstriction in response to the 3*10-7M serotonin in 4 times $p < 0,05$) than HGC. However, response to serotonin (3*10-6M) in systemic vessels was less by 65% in HGEx group compared with HGC ($p < 0,05$).
Conclusions: Aerobic exercise preconditioning (30 min. swimming) causes a protective effect in isolated systemic vessels without effect in pulmonary vessels. Decreasing SRVP by gonadectomy do not connect with change response vessels to serotonin.

P1298
Myosin protein kinases in signaling in heart failure and hypertrophy and in the development of the heart

T Tatiana Kulikova[1]; O Stepanova[1]
[1]*Russian Cardiology Research and Production Complex, cardiology department, Moscow, Russian Federation*

Mechanical forces - play a significant role in signaling in hypertrophy and heart failure (HF), but the link between physical stimuli and biological responses remains not well understood. Various concepts have been introduced to explain signaling at the molecular level, including myosin activating protein kinases participation. Cardiac myocytes differ from other cells in that they contain sarcomeres which are essential for the generation of forces. Sarcomerogenesis is activated in cardiac hypertrophy and HF and is characteristic for development of the heart too. There are hypertrophy changes in HF due to dilated cardiomyopathy (DCM). The phosphorylation of myosin – main protein of cardiomyocyte contractile machinery plays an important role in the sarcomerogenesis regulation. Myosin activating protein kinases can directly phosphorylate myosin - nonmuscle/smooth muscle myosin light chain kinase (MLCK 108), skeletal MLCK and such kinases as Rho-associated protein kinase (ROCK), zipper-interacting protein kinase (ZIPK) and integrin-linked kinase (ILK) with broader specificity. In our study the expression levels of protein kinases ROCK-1, ROCK-2, ILK were determined in endomyocardial biopsies of patients with HF due to DCM using real time PCR. Ten biopsies of patients with HFdue to DCM and five myocardial samples of patients without cardiovascular pathology were analyzed. Significant ILK expression level increase was detected in the myocardial samples of patients with HF due to DCM in comparison with expression level of this kinase in the myocardial samples without cardiovascular pathology. ROCK-1 and ROCK-2 expression levels did not differ from expression levels in the myocardial samples of patients without cardiovascular pathology. The localization of myosin activating protein kinases has been studied by us in cardiomyocytes isolated from human fetal myocardium (8-9 and 13 weeks gestation). It has been established by immunofluorescense approach that MLCK 108, MLCK 210, skeletal MLCK and death associated protein kinase (DAPK) are colocalized with nonmuscle myosin IIB in premyofibrils at 8-9 weeks gestation. These data allow us to propose that nonmuscle myosin IIB may be the substrate for these kinases at this heart development stage, these kinases are likely to jointly regulate the myofibrils formation. MLCK 210 was found in the heart at different gestation stages, MLCK 108 and MLCK 210 relationship was first established at different gestation stages. The approximate time period was revealed when the ratio of MLCK 108 and MLCK 210 varies (between 8-9 and 13 weeks), which may be associated with increased load in heart development. Our results demonstrate that in the postnatal heart ILK serves dual function not only as a mechanoreceptor but also as a nodal regulator of adaptive, prohyperthrophic signaling. MLCK 108, MLCK 210, skeletal MLCK and DAPK jointly regulate sarcomerogenesis in heart development.

P1299
AKIP1 promotes physiological cardiac hypertrophy

BD Daan Westenbrink[1]; KT Nijholt[1]; RA De Boer[1]; CWA Van De Kolk[1]; WH Van Gilst[1]; HHW Sillje[1]; HG Booij[1]
[1]*University Medical Center Groningen, Groningen, Netherlands*

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Background: Overexpression of A Kinase Interacting Protein 1 (AKIP1) promotes physiological hypertrophy in cultured cardiomyocytes by activating AKT-mediated growth pathways. Whether AKIP1 regulates physiological cardiac hypertrophy in vivo is unknown.
Methods and results: Mice with cardiomyocyte-specific overexpression of AKIP1 (AKIP1-TG) and their wild type (WT) littermates were subjected to 4 weeks of voluntary wheel running, whereas control mice remained sedentary. While running time and distance were comparable between AKIP1-TG and WT mice, the induction of physiological hypertrophy after voluntary exercise was markedly increased in AKIP1-TG mice compared to wild type mice (Heart Weight / tibia length 9.5 ± 0.3 mg/mm in AKIP1-TG vs. $8,7 \pm 0.2$ mg/mm in WT mice, $p < 0.05$). The augmentation of exercise-induced cardiac hypertrophy was associated with a 6-fold increase in AKT-phosphorylation and the activation of its down-stream pathways ribosomal rpS6 and translation elongation factor eEF2.
Conclusion: Cardiomyocyte-specific overexpression of AKIP1 promotes physiological cardiac hypertrophy after voluntary exercise by activating AKT. These findings suggest that AKIP1 may serve as a nodal point to induce beneficial reprograming of hypertrophic heart disease.

P1300
Cardiopulmonary characterization of a feline HFpEF model induced by slow progressive pressure overload

M Wallner[1]; RM Berretta[1]; DM Eaton[1]; G Borghetti[1]; J Wu[2]; ST Baker[2]; CD Troupes[1]; TE Sharp[1]; EA Feldsott[1]; M Oyama[3]; PR Fox[4]; MR Wolfson[2]; SR Houser[1]
[1]*Temple University School of Medicine, Cardiovascular Research Center, Philadelphia, United States of America*; [2]*Temple University School of Medicine, Physiology; Thoracic Medicine and Surgery; CILR, Philadelphia, United States of America*; [3]*University of Pennsylvania, School of Veterinary Medicine, Section of Cardiology, Philadelphia, United States of America*; [4]*The Animal Medical Center, Cardiology, New York, United States of America*

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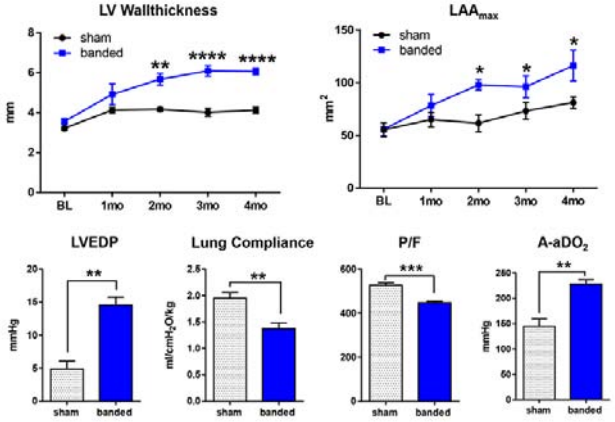
Background: Heart Failure with preserved Ejection Fraction (HFpEF) represents a major public health problem. Little is understood about the causative mechanisms and there are no proven effective treatments for HFpEF, partially attributable to the lack of well-established animal models for HFpEF.
Purpose: To establish a feline HFpEF model induced by slow progressive pressure overload and to characterize structural and functional cardiopulmonary consequences in this model.
Methods: Male domestic short hair cats ($n = 17$; 2 months), underwent either sham (S) procedures ($n = 8$) or aortic constriction ($n = 9$) with a customized pre-shaped band (B), resulting in slow progressive pressure overload during growth in contrast to immediate pressure overload. Terminal pulmonary function, gas exchange, and invasive hemodynamic studies before and after dobutamine infusion (5µg/kg/min), were performed 4 months post-banding. Data is presented as mean ± SE.
Results: Terminal 4-month echocardiography revealed preserved global systolic function (fractional shortening: (S) $32.8 \pm 1.3\%$ vs (B) $31.8 \pm 0.70\%$, $p = 0.99$), significant concentric left ventricular hypertrophy (Fig.: LV Wallthickness) and left atrial (LA) enlargement (Fig.: LAAmax) with impaired LA function. Diastolic function was significantly impaired post-banding reflected by inversion of E/A ratio. ProBNP and left ventricular end diastolic pressure (Fig.: LVEDP) were significantly ($p < 0.01$) greater in (B) compared to (S) cats. While cardiac output and dp/dtmax did not differ significantly between groups at baseline, after dobutamine infusion the increase in dp/dtmax was significantly attenuated in (B) (6310 ± 1157mmHg/s) vs (S) cats (9508 ± 430mmHg/s, $p < 0.05$), indicating impaired inotropic reserve. Terminal in vivo measurements of pulmonary function and gas exchange demonstrated marked impairment in (B) cats, reflected by a significant reduction in respiratory compliance, reflective of increased lung stiffness, decrease in the PaO2/FIO2 (P/F) reflective of impaired oxygenation, and an increase in alveolar-arterial oxygen gradient (A-aDO2)

reflective of an increase in intrapulmonary shunt. (B) cats showed a significant increase in the percentage of LV fibrotic and myocyte cross-sectional area.
Summary and Conclusion: Slow progressive pressure overload in cats induces severe LV concentric hypertrophy, LA enlargement and dysfunction without causing LV dilation or systolic dysfunction. The cardiac findings mimic some discriminating clinical hallmarks of HFpEF patients. In addition, this study presents seminal observations of the impact of LA impairment on pulmonary function and gas exchange, which are in agreement with clinical observations of dyspnoea at rest and exercise-induced reduction of diffusion capacity in humans with HFpEF. Collectively, these data support the translational efficacy and potential utility of this novel feline HFpEF model to explore therapeutic options (HDAC inhibition) for humans.



Cardiopulmonary Impairments

P1301
Targeting the nitric oxide-unresponsive soluble guanylate cyclase in a rat model of pressure overload induced left ventricular myocardial hypertrophy and heart failure

M Ruppert[1]; T Radovits[1]; S Korkmaz-Icoz[2]; S Li[2]; P Hegedus[2]; BT Nemeth[1]; A Olah[1]; CS Matyas[1]; K Benke[1]; B Merkely[1]; M Karck[2]; G Szabo[2]
[1]Semmelweis University Heart Center, Budapest, Hungary; [2]University of Heidelberg, Department of Cardiac Surgery, Heidelberg, Germany

Background: Chronic pressure overload of the left ventricle induces the manifestation of pathological left ventricular myocardial hypertrophy (LVH) that entails gradual deterioration of cardiac function. Recently, preclinical studies have indicated that the impairment of the soluble guanylate cyclase (sGC) - cyclic guanosine monophosphate (cGMP) – protein kinase G signaling contributes to the development of LVH associated cardiac dysfunction.
Purpose: Therefore we investigated the effect of the sGC activator cinaciguat in a rat model of pressure overload-induced LVH and heart failure.
Methods: Abdominal aortic banding (AB) was carried out to induce pressure overload for 6 or 12 weeks. Sham operated animals served as controls. The experimental groups were treated from the 7th to the 12th postoperative week, with 10 mg/kg/day cinaciguat (Cin) or with placebo (Co) p.o., respectively. The temporal development of LVH and its progression to heart failure was investigated by serial echocardiography. Cardiac function was assessed by pressure-volume analysis. In addition, histological and molecular biological measurements were also performed.
Results: In the cinaciguat treated aortic banded group decreased heart weight-to-tibial length ratio (HW/TL ratio: 0.57 ± 0.02 vs. 0.48 ± 0.02g/cm, $p < 0.05$ AB 12th week-Co week vs. AB 12th week-Cin) decreased cardiomyocyte diameter (CD: 23.94 ± 0.59 vs. $20.02 \pm 0.20 \mu$m, $p < 0.05$ AB 12th week-Co week vs. AB 12th week-Cin) and reduced myocardial expression levels of atrial natriuretic peptide and β/α-myosin heavy chain ratio were detected. Furthermore, we observed, that chronic activation of the sGC by cinaciguat provided protection against the increased interstitial fibrosis (Masson's score: 1.7 ± 0.2 vs. 1.2 ± 0.1, $P < 0.05$ AB 12week-Co vs. AB 12week-Cin) and nitro-oxidative stress. The prevention of the pathological structural alterations was accompined by improved cardiac function (ejection fraction: 47.4 ± 2.7 vs. $63.7 \pm 2.4\%$, $P < 0.05$ AB 12week-Co vs. AB 12week-Cin).
Conclusion: Our results demonstrate that chronic activation of the sGC enzyme prevents the transition from pressure overload-induced LVH to heart failure.

P1302
Sympathetic renal denervation after acute myocardial infarction results in increased myocardial salvage in pigs

L E Pastormerlo[1]; S Burchielli[1]; M Ciardetti[1]; C Grigoratos[1]; F Bernini[1]; A Pucci[1]; E Benelli[1]; G Acquaro[1]; A Giorgetti[1]; P Marzullo[1]; M Franzini[1]; C Passino[1]; M Emdin[1]
[1]Gabriele Monasterio Foundation-CNR Region Toscana, Pisa, Italy

Background: Despite advances in treatment of acute myocardial infarction (AMI), many patients still suffer significant myocardial damage and are at increased risk of cardiac dysfunction following AMI. Sympathetic renal denervation may represent an innovative approach to reduce adverse neurohormonal activation following AMI and its contribution to increased myocardial damage and adverse long term remodeling.
Methods: and Results: Sixteen male farm pigs underwent a 90 minutes left anterior descending artery occlusion followed by reperfusion. They were randomized (1:1) to percutaneous sympathetic renal denervation (RD) procedure immediately after reperfusion. Global and regional LV function, extent of myocardium at risk, and myocardial necrosis were quantified by cardiac magnetic resonance imaging studies performed 5 and 30 days after coronary occlusion. No adverse haemodinamic effects were reported in pigs that underwent RD immediately after AMI. RD and control pigs did not differ in the extent of myocardium at risk (63 and 61% of left ventricle, P=NS). At 30 days, RD significantly reduced the amount of gadolinium delay enhancement (17 versus 31 % of LV, $p < 0.001$) with improved myocardial salvage index (74% vs 44%, $p < 0.001$). Cardiac output in RD pigs was significantly higher than control at 30 days (3.7 ± 0.8 versus 2.66 ± 0.7 L/min, $p < 0.001$), with a trend for lower LV end diastolic volume (98 ± 16 versus 113 ± 31 ml, $p = 0.14$).
Conclusions: RD performed immediately after AMI results in increased myocardial salvage and better cardiac remodeling. The reduction of neurohormonal activation following AMI warranted by RD, may be in cause.

P1303
Interest of colchicine in the treatment of acute myocardial infarct responsible for heart failure in a mouse model

M Akodad[1]; J Fauconnier[2]; P Sicard[2]; F Huet[1]; F Blandel[2]; P De Santa Barbara[2]; S Aguilhon[1]; A Lacampagne[2]; F Roubille[1]
[1]University Hospital Arnaud de Villeneuve, Interventional Cardiology, Montpellier, France; [2]University of Montpellier, U1046, Montpellier, France

BACKGROUND: Inflammation is deeply involved in the pathophysiology of ischemia-reperfusion (I/R) lesions and ventricular remodeling due to an acute myocardial infarction (AMI). Colchicine as a pleiotropic anti-inflammatory molecule may exert cardioprotective effects under acute ischemia. Here, we aimed to evaluate the impact of colchicine on reperfusion injury in a mouse model.
Method: Myocardial ischemia/reperfusion (I/R) injury were induced in C57BL/6 male mice, after 45 min ligation of the left coronary artery followed by reperfusion. 400 µg/kg of colchicine or the vehicle was administrated intraperitoneally (i.p) 25 minutes before the reperfusion (blinded administration). Mice were sacrificed at 24 hours after the acute myocardial ischemia (AMI) and the area at risk (AAR) and the infarcted area (IA) were evaluated after Evans blue/TTC staining. Circulating level of troponin and cytokines profile were assessed 4 hours after the AMI. An echocardiography was performed in a follow-up group mice, 48 hours and 8 weeks after the AMI.
Results: The AAR/total area ratios were similar in the colchicine and the vehicle group ($52.6\% \pm 1.1\%$ versus $50.6\% \pm 0.8\%$ respectively, $p > 0.05$, n=13 per group). The infarct size was reduced in Colchicine treated mice in comparison to control mice with IA/AAR ratios respectively at $39.8\% \pm 3.5$ versus $52.9\% \pm 3.2$, $p < 0.05$. Troponin was significantly lower in the Colchicine treated mice (7015.7 ± 1423.7 pg/mL, n= 5 vs 30723.7 ± 7959.9 pg/mL in the placebo group, n=6; $p < 0.0001$). Fibrosis was decreased in the Colchicine group (24.51 ± 3.13 % vs 11.38 ± 2.46 % in the colchicine group, $p = 0.03$). In the follow-up group mice ($n = 8$), there were no differences between mice treated with placebo ($n = 9$) and mice treated with colchicine ($n = 9$) regarding to cardiac remodelling parameters but outflow approximated by the ITV was higher in the Colchicine group.
Conclusion: In conclusion, colchicine allowed a significant reduction of infarct size in mice, improves haemodynamic parameters and decrease cardiac fibrosis.

P1304
Characterization of the antioxidant effect of eplerenone on adverse cardiac remodeling. Implication of enzyme nitric oxide synthetic (enos)

MC Asensio-Lopez[1]; MC Sanchez-Perez[1]; MT Perez-Martinez[2]; IP Garrido-Bravo[2]; DA Pascual-Figal[2]; AM Antonio Manuel Lax[2]
[1]Biosanitary Research Institute of Murcia (IMIB-Arrixaca)., Cardiology, Murcia, Spain; [2]University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain

Background: Oxidative stress is related to the evolution of cardiac remodeling to heart failure (HF). Although eplerenone (Eple) decreases morbidity and mortality in patients with HF, the molecular mechanisms underlying this protection have not been studied. The aim of this study is to characterize the effect of Eple on the enzymatic system endothelial nitric oxide synthase (eNOS).
Methods: Human left ventricular (LV) explants from patients undergoing transplantation, LV of healthy donors as well as the infarcted LV area of animals from a rat model of myocardial infarction (MI), were analyzed. MI was induced by ligation of the left anterior descending coronary. The animals (n = 10 / group) were distributed within two groups: untreated or treated with Eple from the day of ligation up to 4 weeks (100 mg/kg/day). The control group underwent the same surgery but without ligation. The eNOS expression and activity were evaluated by RT-qPCR and Western blot, respectively. The levels of BH4 and MDA were assessed by colorimetry. The activities of catalase (CAT), glutathione peroxidase (GPx-3) and ROS were measured by fluorimetry. Each value has been referred to the control group and has been expressed as mean ± standard error.
Results: Compared to healthy donors, the failed VIs showed decreased levels of eNOS (32 ± 12) and BH4 (21 ± 9), as well as an accumulation of eNOS in its monomeric (inactive) form and a significant increase in oxidative damage: ROS (4.5 ± 1), MDA (21 ± 3), CAT (34 ± 12%) and GPx-3 (36 ± 8%). In an experimental study, in relation to control, animals submitted to MI showed decreased levels of eNOS (49 ± 13), BH4 (35 ± 9), and an accumulation of eNOS in its monomeric (inactive) form. Besides, this analyzed tissue showed oxidative damage characterized by an increase in ROS (3 ± 0.5), MDA (12 ± 4) and a decrease in CAT (32 ± 12%) and GPx-3 (43 ± 14%). Treatment with Eple increased eNOS expression (89 ± 15) and BH4 levels (78 ± 21), as well as homodimeric levels of eNOS (active). Furthermore, treatment with Eple reduced oxidative damage by decreasing ROS (1.5 ± 0.9) and MDA (3 ± 0.3) and increasing CAT (67 ± 12%) and GPx-3 (78 ± 17%).
Conclusions: Eplerenone, through overexpression and increased activity of eNOS and its cofactor BH4, prevents post-IM adverse cardiac remodeling.

P1305
Cardiac bone marrow-derived cell-based therapy associated with scaffold for heart regeneration

I Ines Borrego[1]; A Frobert[1]; J Valentin[1]; G Ajalbert[1]; V Roth[2]; B Fellay[2]; S Cook[1]; MN Giraud[1]
[1]University of Fribourg, Department of Medicine - Cardiology, Fribourg, Switzerland; *[2]Laboratory HFR - Tafers, Hospital Fribourgeois, Fribourg, Switzerland*

Purpose: The development of patched associating of bone marrow derived cells (BMDC) and a substrate/scaffolds provided evidence of beneficial outcomes and optimal delivery approaches on myocardial infarction (MI). Preclinical trials are usually performed with BMDC isolated from healthy donor. However, for clinical application, BMDC isolated from infarcted patients are favoured as an autologous cell source. We hypothesized that the therapeutic capacity of the implanted biological patch may vary with BMDC origin. To test this hypothesis, we compared the regenerative potential of a biological patch composed of BMDC isolated from healthy or infarcted donor as a treatment of MI in a rat model.
Methods: MI was induced by Left Anterior Descending Artery ligation. BMDC were isolated from healthy and infarcted Lewis male rats. MI was induced in 52 female Lewis rats; two weeks post MI, 34 rats with an ejection fraction (EF) between 35-60% were selected and randomised in different treatment groups, sham operation (Sh, n=9), epicardial application of the biological patches obtained with 2 million cells isolated from healthy donors (HD, n=12), or from infarcted donors (ID, n=7) or substrate only (S, n=6). Four weeks post treatment, cardiac function and regional contractility (strain imaging) were measured by high-resolution echocardiography, the infarct expansion was quantify using systematic sampling of total heart and image analyses of trichrome-stained histological sections.
Results: Four weeks post MI, heart function decreased in control groups (ΔEF.Sh=-1.21 ± 3.2% and ΔEF.S=-7.4 ± 6.4%). Cells and substrate significantly induced stabilizations of heart function compared to substrate alone (ΔEF.HD=1.1 ± 5.6%,p = 0.02 and ΔEF.ID=0.99 ± 4.9%,p = 0.4). Nevertheless, it is important to underline that heterogeneity in response to the treatments was observed, 42% responded positively to the treatment (ΔEF≥3%). In addition, the regional LV myocardial contractility showed that the LV non-contractile region decreased significantly for HD group from 10.8 ± 3.3mm to 8.3 ± 4.0mm (p = 0.02). Furthermore, the index expansions (EI) decreased with the implantation of the biological patches, and were respectively EI.Sh=0.21 ± 0.11 vs. EI.HD=0.08 ± 0.04(p = 0.05) vs. EI.ID=0.15 ± 0.07(p = 0.47). Interestingly, the LV volume significantly increased 4 weeks post ID patch implantation. These results suggested that although ΔEF for both biological patches are comparable, LV dilatation observed with infarcted cells may be detrimental in long term.
Conclusion: Our study demonstrated that independent of the cell origin, patches stabilized heart function. However, only healthy donor cells showed a regenerative capacity. Noticeably, LV dilatation following infarcted cell implantation questioned the long-term safety. Heterogeneity of outcomes revealed the presence of respondent and non-respondent subjects to the treatment.

P1306
Rodent heart failure models do not reflect the human circulating microRNA response in heart failure

E L Eline Vegter[1]; E S Ovchinnikova[1]; H Sillje[1]; L M G Meems[1]; A R Van Der Velde[1]; E Berezikov[2]; A A Voors[1]; R A De Boer[1]; P Van Der Meer[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands; *[2]European Research Institute for the Biology of Ageing, Groningen, Netherlands*

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Introduction: We recently identified a set of plasma microRNAs (miRNAs) that are downregulated in patients with heart failure in comparison with control subjects.
Purpose: To better understand their meaning and function, we sought to validate these circulating miRNAs in two different well-established rat and mouse heart failure models, and correlated the miRNAs to parameters of cardiac function.
Methods: The miRNAs let-7i-5p, miR-30e-5p, miR-16-5p, miR-18a-5p, miR-223-3p, miR-652-3p, miR-423-3p, miR-423-5p, miR-26b-5p, miR-27a-3p and miR-199a-3p were measured by means of quantitative real time polymerase chain reaction (qRT-PCR) in plasma samples of 8 homozygous TGR(mREN2)27 (Ren2) transgenic rats and 8 (control) Sprague-Dawley rats, as well as in 6 mice with angiotensin II-induced heart failure (AngII) and 6 control mice. Circulating miRNA levels were compared between the heart failure animals and healthy controls.
Results: Ren2 rats and AngII mice showed clear signs of heart failure, exemplified by increased left ventricular and lung weights, elevated end-diastolic left ventricular pressures, impaired contractility and increased left ventricular relaxation time. All miRNAs except mir-423-5p were detectable in plasma from rats and mice. No significant differences were observed between the circulating miRNAs in the Ren2 rats and AngII-treated mice when compared to the healthy control animals (all P>0.05), and no robust associations with cardiac function could be found.
Conclusions: The previous observation that miRNAs circulate in lower levels in patients with heart failure could not be validated in well-established rat and mouse heart failure models. This should be taken in consideration in the study of circulating miRNAs in heart failure.

P1307
Eplerenone prevents adverse cardiac remodeling through modification of enzymatic NADPH oxidase 4 activity

AM Antonio Manuel Lax[1]; MC Sanchez-Perez[2]; MT Perez-Martinez[1]; F Pastor[1]; DA Pascual-Figal[1]; MC Asensio-Lopez[2]
[1]University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain; *[2]Biosanitary Research Institute of Murcia (IMIB-Arrixaca)., Cardiology, Murcia, Spain*

Background: The prevalence of heart failure (HF) has increased worldwide in recent decades. Although eplerenone (Eple) is used to treat patients with left ventricular (LV) systolic dysfunction following myocardial infarction (MI), the mechanisms involved have not been studied. In this study, we evaluate whether Eple, through the modulation of the NADPH oxidase 4 (mitoNox) activity, prevents adverse cardiac remodeling and development to HF.
Methods: Myocardial infarction (MI) was induced by ligation of the left anterior descending coronary in male Wistar rats. The animals (n = 10/group) were distributed within two groups: untreated and treated with Eple, from the day of ligation up to 4 weeks (100 mg/kg/day). The control group underwent the same surgery but without ligation. In parallel, explants from transplanted human LV, LV from healthy donors as well as the infarcted LV zone of an animal model of MI, were analyzed. The expression levels of mitoNox and gp22phox was evaluated by RT-qPCR and Western blot, while mito-NOX activity was assessed by luminescence. MDA and GSH levels were evaluated by colorimetry. The glutathione peroxidase (GPx-3) activity was assessed by fluorimetry. Each value has been referred to the control group and has been expressed as mean ± standard error.
Results: Regarding healthy donors, the failed LV showed high levels of mRNA and protein for mitoNox (27 ± 8; 5 ± 0.3) and gp22phox (25 ± 9; 4 ± 0.2), mitoNox activation (19 ± 4) and an increase in oxidative damage: MDA (45 ± 15), GSH (40 ± 9), and GPx-3 (36 ± 8). In an experimental analysis, compared to control group, rats with MI showed elevated levels of mitoNox mRNA and protein expression (49 ± 13; 4.6 ± 0.2) and gp22phox (35 ± 9; 4 ± 1); mitoNox activation (21 ± 7) and increased oxidative damage: MDA (55 ± 20), GSH (35 ± 13), and GPx-3 (43 ± 14). Treatment with Eple was associated with a decrease in mitoNox (10 ± 4, 1.2 ± 0.2) and gp22phox (9.5 ± 2, 2.1 ± 0.14) mRNA and protein levels, and a mitoNOX inhibition (5.32 ± 1.4). In addition, Eple reduced oxidative damage by decreasing MDA (12 ± 4) and increasing GSH (85 ± 20) and GPx-3 activity (80 ± 17).
Conclusions: This study demonstrates that Eple through inhibition of mitoNox activity exerts a modulatory role in adverse cardiac remodeling induced by MI.

P1308

Myocardial fibrosis and fat infiltration in obese and streptozotocin-induced diabetic Gottingen minipigs

S Simone Krog[1]; OL Nielsen[1]; JE Moller[2]; TP Ludvigsen[3]; HD Pedersen[1]; LH Olsen[1]
[1]*University of Copenhagen, Department of Veterinary and Animal Sciences, Copenhagen, Denmark*; [2]*Odense University Hospital, Department of Cardiology, Odense, Denmark*; [3]*Novo Nordisk A/S, Insulin Pharmacology II, Måløv, Denmark*

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Background: Diabetes mellitus and obesity are associated with cardiovascular disease, and cardiovascular complications are the most common cause of death in diabetic patients. Diabetes related myocardial fibrosis and fat infiltration has been associated with the development of heart failure.
Purpose: The present study aimed to assess the effect of high-fat/high-cholesterol diet and streptozotocin-induced diabetes on left ventricular (LV) myocardial fibrosis and fat infiltration in Göttingen minipigs.
Methods: Twenty-nine castrated male Göttingen minipigs (5-6 months) were divided into three groups. A control group fed standard pig chow: C (n = 7); and two groups fed high-fat/high-cholesterol diet: HFD (n = 14) and HFD-D (n = 8), the latter group with superimposed streptozotocin-induced diabetes. To avoid severe hyperglycemia, fasting blood glucose was maintained at 12-15mM by treating animals with insulin glargine. After 58 weeks all pigs were euthanized, body and heart weight measured, and myocardial samples from the LV free wall were collected. For each animal the degree of myocardial interstitial fibrosis and fat infiltration as well as perivascular fibrosis and fat infiltration was semi-quantitatively scored as 0/+/++/+++. In addition, degree of epicardial fat infiltration and vascular tunica media fibrosis was evaluated. Vascular changes were reported as an average of evaluated myocardial arterioles and small arteries.
Results: Total plasma cholesterol and triglycerides were higher in HFD [11.82 (9.09-13.18)mM (median and quartiles); P=0.0003; and 0.64 (0.54-0.88)mM; P=0.0004] and HFD-D [17.45 (14.01-27.00)mM; P=0.0022; and 1.22 (0.75-1.64)mM; P=0.0014] compared to C [1.69 (1.36-2.18)mM; and 0.34 (0.29-0.35)mM]. Heart weight was higher in HFD [199 (181-208)g; P < 0.0001] and HFD-D [175 (138-205)g; P=0.02] compared to C [131 (115-142)g]. No differences between groups were found when heart weight was normalized to body surface area. No differences between groups were found in degree of myocardial interstitial fibrosis [C: 7/0/0/0; HFD: 12/2/0/0; HFD-D: 6/2/0/0; P=0.55] or fat infiltration in myocardium [C: 4/2/1/0; HFD: 1/7/3/3; HFD-D: 5/2/1/0; P=0.09]. Likewise, no differences were observed in perivascular [C: 1.00 (0.50-2.00); HFD: 1.58 (1.00-2.29); HFD-D: 1.00 (0.00-1.75); P=0.39] or epicardial [C: 4/1/0/0; HFD: 2/5/6/0; HFD-D: 3/3/2/0; P=0.16] fat infiltration, or in tunica media fibrosis [C: 0.00 (0.00-0.33); HFD: 0.17 (0.00-1.00); HFD-D: 0.00 (0.00-0.25); P=0.32]. The degree of perivascular fibrosis was lower in HFD-D [0.00 (0.00-0.00)] compared to C [0.50 (0.00-0.75); P=0.03] and HFD [0.13 (0.00-0.50); P=0.04]. No difference in perivascular fibrosis was found between C and HFD (P=0.39).
Conclusion: Obesity and diabetes did not increase myocardial fibrosis and fat infiltration in Göttingen minipigs. Further studies are needed to determine the possible influence of breed, sex and exposure time; and the significance of the vascular changes.

P1309

Impact of intracoronary allogeneic cardiac progenitor cell administration on myocardial edema and functional recovery in sub-acutely infarcted swine

C Baez-Diaz[1]; FM Sanchez-Margallo[1]; I Palacios[2]; V Blanco-Blazquez[1]; J Maestre[1]; B Sanchez[2]; R Rosado[2]; MT Mangas-Ballester[1]; JG Casado[1]; A Bernad[3]; V Veronica Crisostomo[1]
[1]*Jesus Uson Minimally Invasive Surgery Centre, Caceres, Spain*; [2]*Coretherapix (Tigenix Group), Madrid, Spain*; [3]*National Center of Biotechnology (CSIC), Madrid, Spain*

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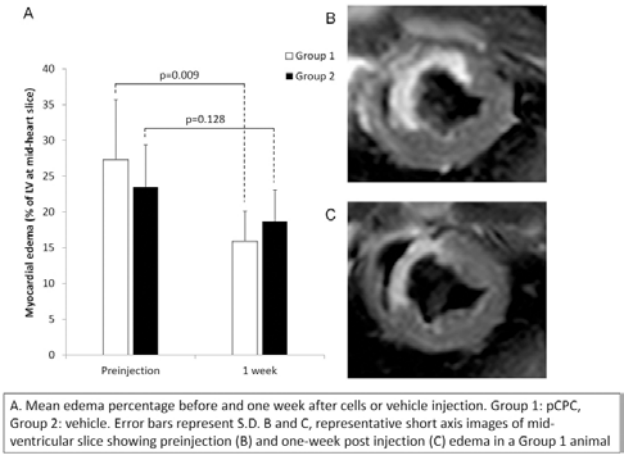
Background: Myocardial edema is associated to impaired regional function and conductivity and as such has been proposed as a therapeutic target, since it. On the other hand, intracoronary (IC) allogeneic cardiac progenitor cell (CPC) administration has been recently used for MI therapy in experimental models, and is currently being evaluated in clinical trials.
PURPOSE: We undertook this study to evaluate the effects of IC porcine CPC (pCPC) administration on myocardial edema and its relationship to cardiac function after experimental infarction in swine.
Methods: Female domestic pigs surviving a 90 minutes balloon occlusion of the mid-LAD were subjected to an IC injection of 50x106^ pCPC (n = 7, group 1) or vehicle (n = 7, group 2) one week after AMI. Cardiac MR was performed before injection and one and 10 weeks after. Myocardial edema/area-at-risk (AAR) was calculated as a percentage of the left ventricle in a mid-heart slice using T2-weighted imaging. Other parameters studied included Ejection Fraction (EF), End Diastolic Volume (EDV), End Systolic Volume (ESV) and infarct size. Myocardial Salvage Index (MSI) was then computed as AAR at mid-heart slice minus final infarct size (FIS) in an equivalent slice divided by AAR (MSI=(AAR-FIS)/AAR).
Results: No differences were seen between groups in any MR-derived parameter before pCPC or vehicle injection, thus confirming that both AAR and infarct sizes, and their effects on functional parameters (EF, EDVi and ESVi) were comparable. Injection was successful in all cases, in absence of major adverse cardiac events. There was a significant decrease in edema in the treated group one week after pCPC injection (from 27.29 ± 8.44% to 15.00 ± 4.24%, p = 0.009), while no significant change in this parameter was seen in Group 2 (from 23.43 ± 5.94% to 18.71 ± 4.35%, p = 0.128). At ten weeks there were no significant differences in scar sizes, despite a trend towards smaller scars in treated animals (5.86% ± 4.14% versus 8.29% ± 2.81%). However, MSI was significantly higher in the treated group (MSI=0.63 ± 0.17 in Group 1 and MSI=0.35 ± 0.20 in Group 2, p = 0.01), evidencing a cardioprotective effect of the cells. In terms of cardiac function, a clear trend towards EF recovery was seen in Group 1, that was absent in non-treated animals. Ventricular volumes were also significantly smaller in Group 1 (EF was 50.23 ± 4.92% and 42.14 ± 10.00%, EDVi was 94.01 ± 11.42mL/m2 and 119.03 ± 24.84mL/m2 (p = 0.018) and ESVi was 46.96 ± 8.19mL/m2 and 70.45 ± 25.53mL/m2 (p = 0.018) in Groups 1 and 2, respectively).
Conclusion: The Intracoronary injection of 50x10^6 pCPC one week after experimental infarction could be able to exert a beneficial decrease in myocardial edema, which after 10 weeks is associated to improved cardiac function and a two-fold increase in MSI. The exact mechanisms by which pCPC are related to myocardial edema decrease need to be further clarified, but it could represent another therapeutic target for early cell therapy.



A. Mean edema percentage before and one week after cells or vehicle injection. Group 1: pCPC, Group 2: vehicle. Error bars represent S.D. B and C, representative short axis images of mid-ventricular slice showing preinjection (B) and one-week post injection (C) edema in a Group 1 animal

Evolution of myocardial edema after pCPC

P1310

Lower dietary fat intake increases cardiac hypertrophy and left ventricular remodelling in a hypertensive rat model

E Mc Namara[1]; C Watson[2]; L Shiels[1]; A Russell-Hallinan[1]; M Ledwidge[3]; J Baugh[1]
[1]*University College Dublin, Conway Institute, Dublin, Ireland*; [2]*Queen's University of Belfast, Belfast, United Kingdom*; [3]*St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*

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Background: Much attention has been paid to the clinical effects of lipid intake on the development of coronary heart disease, however, the effects of dietary fats on the development and progression of heart failure have been largely ignored. The present study compares the effect of a high-fat diet (HFD) versus a low-fat diet (LFD) on left ventricular remodelling in the presence of hypertension.
Methods: Experiments were performed with approval from the local animal ethics committee. Adult, male Wistar-Kyoto (WKY, n=10) and spontaneously hypertensive rats (SHR, n=20) were fed low (10 kcal% fat) or high (45 kcal% fat) saturated fatty acid-based diets for 16wks. Cardiac structure and function were determined in vivo using 2D M-mode echocardiography. Excised hearts were weighed, dissected and formalin-fixed. Left ventricular collagen deposition and cardiomyocyte hypertrophy were assessed using a digital image analysis system (Aperio) following Picrosirius red and H&E staining, respectively.

Results: No change in final bodyweight was recorded among groups. SHR exhibited increased arterial pressure vs. normotensive WKY controls (systolic pressure ˜151mmHg vs. 131mmHg). Following 16wks of dietary intervention SHR-LFD displayed left ventricular (LV) remodelling with significantly increased: LV mass, myocyte cross-sectional area, perivascular and interstitial fibrosis compared WKY. These effects were not seen in the SHR-HFD. Correspondingly, echocardiography revealed significantly increased LV anterior and posterior wall dimensions in SHR-LFD.
Conclusion: These results demonstrate that in the presence of hypertension, low dietary fat intake leads to increased cardiac growth and structural remodelling of the left ventricle, effects that are attenuated by high dietary fat intake. Future work aims to elucidate the role of inflammatory mediators in these phenomena.

P1311
Erythropoietin reduces collagen deposition after myocardial infarction but does not improve cardiac function in male rats

F Fernanda Pessoa[1]; C Mady[1]; KCB Fonseca[1]; ON Ribeiro[1]; VMC Salemi[1]; MR Jordao[1]; F Fernandes[1]; FJA Ramires[1]
[1]Heart Institute of the University of Sao Paulo (InCor), Cardiomyopathy Unit, Sao Paulo, Brazil

Funding Acknowledgements: FAPESP

Background: Myocardial remodeling includes inappropriate collagen deposition in the interstitium. Erythropoietin (EPO) may have cardioprotective effects. We aimed to assess the role of EPO on myocardial remodeling.
Methods: We studied 60 Wistar rats divided into: Control (CT), Control + EPO (CT + EPO), Infarcted (MI) and Infarcted + EPO (MI + EPO). The interstitial collagen volume fraction (ICVF) and infarct size were quantified. Echocardiography was performed for geometry and ventricular function. Western Blotting was used to evaluate inflammatory proteins (TNFα, TGFβ1) and tissue inhibitors of metalloproteinases 1 and 2 (TIMP-1 and TIMP-2). Zymography was applied for MMP-2. Parametric and non-parametric analysis was performed according to normality test. Results: ICVF was greater in MI groups ($p < 0.001$) and was attenuated by EPO ($p = 0.05$). We did not observe any difference in infarct size, with or without EPO treatment (MI = 30.93 ± 13.26 %, MI + EPO = 34.12 ± 16.21%, $p = 0.65$). In this model, EPO did not show protective effects on ventricular dilatation LVDD (MI vs MI + EPO, $p = 0.79$), LVSD (MI vs MI + EPO, $p = 1.00$) or dysfunction (EF (MI): 41% ± 15, EF (MI + EPO): 40% ± 12, $p = 1.00$). The infarcted groups showed lower values of ejection fraction (EF) and larger LVDD and LVSD compared to the controls. Relative wall thickness did not showed any difference between MI vs MI + EPO ($p = 1.00$) neither Tei index ($p = 0.78$). The inflammatory proteins studied were increased in the infarcted groups but without statistical significant. Again the EPO did not modulate these protein synthesis after 4 weeks of MI (TNF, $p = 0.08$ and TGF, $p = 0.15$). The TIMP-1 had increased amount in the MI + EPO group but with no statistical significance, $p = 0.16$. The TIMP-2 also had no statistical difference, $p = 0.55$. The activity of MMP-2, did not show any difference between groups after 4 weeks of MI, $p = 0.79$. We found a strong positive correlation between EF and TIMP-1 ($p < 0.05$ and $r = 0.95$) and TIMP-2 ($p < 0.05$ and $r = 0.95$) in MI + EPO group. Conclusions: We concluded that EPO attenuated interstitial collagen accumulation, but did not protect from heart dilation or dysfunction. This protection seems to be not related to those studied inflammatory proteins modulation neither to collagen degradation pathways.

P1312
Cyclic GMP deficiency and cardiorenal fibrosis in diabetic cardiomyopathy: an experimental model of type 2 diabetic cardio-nephropathy

S-H Siu-Hin Wan[1]; S Ameenuddin[1]; HH Chen[1]
[1]Mayo Clinic, Rochester, United States of America

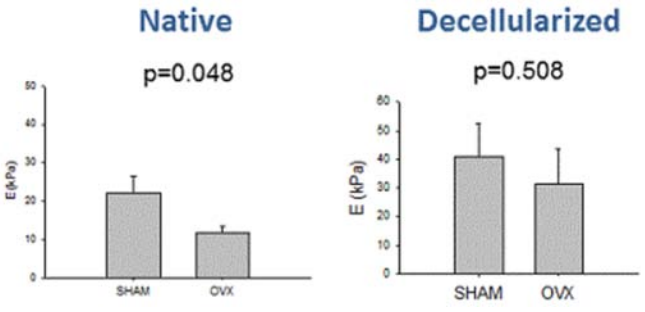
Background and Purpose: Cyclic guanosine 3',5'-monophosphate (cGMP) is important in the preservation of cardiorenal function and disruption of this signal transduction process contributes to cardiorenal dysfunction. In type 2 diabetes mellitus (DM), we defined neurohormonal dysregulation leading to cardio-nephropathy.
Methods: Ten genetically designated Zucker diabetic ZDFO rats and ten nondiabetic ZDFL control rats received echocardiography with strain imaging, vital sign monitoring and neurohormonal blood and urine collection over 32 weeks. At conclusion, cardiac and renal tissues were harvested for fibrosis assessment.
Results: DM in the ZDFO rats was confirmed by glucose and HbA1c measurements. There was increased fibrosis in both the left ventricle (LV) and kidney with cardiorenal dysfunction in the DM vs control rats. There was increased 24 hr proteinuria and a trend for worsened early diastolic strain rate in the DM rats. Despite similar plasma BNP levels, plasma cGMP was significantly attenuated in the diabetic vs control rats.
Conclusion: In this Zucker type 2 DM rat model, there was cGMP deficiency with evidence of cardiorenal fibrosis and dysfunction. Future studies are warranted to determine if enhancing the cGMP system with neprilysin inhibition or administration of exogenous natriuretic peptide would improve cardiorenal function.

Characteristics at 32 weeks	ZDFL (Controls, n=10)	ZDFO (Type 2 DM, n=10)	P value
Blood glucose (mg/dL)	176±7	445±16	< 0.01
HbA1c (%)	5.1±0.1	12.7±0.2	< 0.01
Mean Arterial Pressure (mmHg)	95±2	106±4	0.01
Plasma Insulin (ng/mL)	0.50±0.06	0.38±0.03	0.3
Ejection Fraction (%)	78.0±0.7	78.1±0.6	0.87
Early Diastolic Strain Rate (%)	-11.6±0.9	-9.6±0.7	0.13
Plasma BNP (pg/mL)	18.4±2.6	24.6±5.5	0.76
Plasma cGMP (pmol/mL)	8.9±1.7	2.8±0.7	0.01
24h Urine Volume (mL)	8.5±0.7	146±2	< 0.01
24 h Urine Excretion Protein (mg/dL/min)	0.77±0.06	31.2±4.3	< 0.01
24 h Urine Glucose (mg/dL)	1.8±0.4	304±40	< 0.01
LV Mass : Body Weight (mg:g)	2.06±0.03	2.34±0.36	< 0.01
LV Interstitial Fibrosis (%)	10.8±1	21.6±3	0.01
Renal Cortex Fibrosis (%)	26.2±1.2	39.8±3.0	< 0.01
Renal Medulla Fibrosis (%)	25.4±1.2	32.7±2.3	0.04

P1313
Ovariectomy reduces the passive stiffness of left ventricular myocardial tissue in a post-menopause mouse model

N Farre[1]; I Jorba[2]; M Torres[3]; R Farre[2]; I Almendros[2]; D Navajas[2]
[1]Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; *[2]University of Barcelona, Unitat Biofísica i Bioenginyeria, Facultat de Medicina, Barcelona, Spain*; *[3]Hospital Clinic de Barcelona, Department of Pneumology; CIBER de Enfermedades Respi, Barcelona, Spain*

Backgraound: Heart failure (HF) is usually associated with diastolic dysfunction. Although post-menopause women are at increased risk of HF and diastolic dysfunction, poor attention has been paid to clinically and experimentally investigate this group of patients. In particular, whether myocardial stiffness is affected by the loss of sex hormones after menopause is unknown.
Purpose: To characterize the passive stiffness of left ventricular myocardial tissue in a mouse model of ovariectomy (OVX).
Methods: After 6 months of bilateral OVX, 8 mice (C57BL/6J) were sacrificed and passive tension-length curves were measured (Aurora Scientific, 300C-LR) in fresh left ventricular myocardial strips (˜8x1x1 mm). Data were fitted to a constitutive model and tissue stiffness (E) was computed at 20% stretch. To assess the relative contribution of cellular and extracellular matrix components in OVX-induced changes, E was measured in the tissue strips decellularized using a SDS protocol. Tissue stiffness was also measured in a control group of 8 same-age sham-OVX mice.
Results: E (in kPa; m ± SE) in OVX mice was ˜50% lower than in controls (11.7 ± 1.8 and 22.1 ± 4.4, respectively; $p < 0.05$). A lower decrease in E was found in the decellularized tissue (31.4 ± 12.05 and 40.9 ± 11.5, respectively; $p = 0.580$) (Figure 1).
Conclusion: Loss of female sexual hormones in an OVX model induces a reduction in the passive stiffness of myocardial tissue, suggesting that active relaxation should play a counterbalancing role in systolic dysfunction in postmenopausal women with HF.



P1314

The role of air pollution upon chagas cardiomyopathy

KCB Fonseca[1]; F Fernanda Pessoa[1]; C Mady[1]; V Hotta[1]; ON Ribeiro[1]; F Fernandes[1]; RS Nascimento[2]; PHN Saldiva[2]; FJA Ramires[1]
[1]Heart Institute of the University of Sao Paulo (InCor), Cardiomyopathy Unit, Sao Paulo, Brazil; *[2]University of Sao Paulo, Sao Paulo, Brazil*

Funding Acknowledgements: FAPESP

Background: Chagas' disease is one of the major cause of cardiomyopathy and heart failure in Latin America. It is characterized by intense myocardial fibrosis which is directly related to a complex cascade of pathways, such as inflammation, oxidative stress and apoptosis. As well air pollution leads to intense activation of these same pathways wich would amplify the response against the infection. We aimed to assess the role of air pollution upon progression of Chagas cardiomyopathy in the acute phase (60 days) of the disease.
Methods: 100 females Sirius Hamsters were divided into 4 groups: Control (Ct), Control + Pollution (Ct + P), Infected (Inf) and Infected + Pollution (Inf + P). The animals were exposed to pollution by inhalation of particulate matter produced by burning diesel fuel. Echocardiography and electrocardiogram (ECG) were performed. Survival curve was analyzed during the acute phase. Results: We observed ventricular dilatation (left ventricular diastolic diameter and left ventricular systolic diameter) in infected groups compared to controls, $p = 0.04$ and $p = 0.002$, respectively. However, the pollution did not increase it. The infected groups showed lower values of ejection fraction compared to controls ($p = 0.004$). Again the air pollution did not decrease it. The ECG showed that heart rate (HR) was different between groups ($p = 0.0008$). We observed that infected groups had higher HR than controls, mainly Ct + P vs Inf and Inf + P. Sinus rhythm was similar among groups, and ventricular arrhythmias were the same in all groups at 60 days. Survival analysis showed a high mortality in infected groups (68%) compared to the controls (4%) and air pollution did not increase mortality (Inf=68%, Inf + P=68%). Conclusions: We observed that air pollution at the acute phase of Chagas disease did not worsened ventricular dilatation or function neither increased mortality.

BASIC SCIENCE - CELLULAR BIOLOGY & CELL SIGNALLING

P1315

TRPV4 channel in the TGF-beta1 mediated differentiation of ventricular fibroblasts

BS Byungsu Yoo[1]; MS Ahn[1]; YW Um[1]; JW Lee[1]; YJ Youn[1]; JW Son[1]; JH Yoon[1]; SH Lee[1]; MC Cho[2]
[1]Wonju College of Medicine, Yonsei University, Division of Cardiology, Department of Internal Medicin, Wonju, Korea Republic of; *[2]Chungbuk National University Hospital, Cheongju, Korea Republic of*

Cardiac fibroblasts (CFs) are the predominant cell types that reside in the interstitial space of the heart. In response to pathological stimuli, CFs are stimulated to undergo phenotypic modulation and become myofibroblasts that are hypersecretory and highly contractile and which deposit excessive extracellular matrix proteins. Ca2 + signals are essential to a diversity of cellular functions, including differentiation, gene expression, cell proliferation, and growth. CaV1.2-mediated L-type Ca2 + current (ICa,L) is a fundamental myocardial calcium entry channel, but CFs do not typically express the voltage-gated Ca2 + channel. Transient receptor potential (TRP) channels are nonselective calcium entry channels, and their function has been studied in many cell types. TRP is expressed in a cell-specific manner, and its role has not been evaluated in human ventricular fibroblasts. Here, we evaluate the role of the TRP channel in the differentiation of human ventricular fibroblasts into myofibroblasts. Concordant with previous studies, Ca2 + was found in the current study to be an essential component in fibroblast differentiation. Intracellular chelation inhibited p-ERK expression and fibroblast differentiation. TRPV4 mRNA was expressed in human ventricular fibroblasts and increased on account of TGF-β1 (2 ng/mL). TRPV4 agonist (GSK1016790A) treatment induced the robust differentiation of fibroblasts into myofibroblasts. TRPV4 antagonist (RN-9893) significantly inhibited TGF-β1-induced p-ERK expression and the differentiation of CFs. Using ratio Ca2 + imaging measurements, we found a robust increase in Ca2 + influx after fibroblasts were treated with TRPV4 agonist (GSK1016790A). These results demonstrate that TRPV4 has a role as a Ca2 + -permeable channel in the differentiation of human ventricular fibroblasts into myofibroblasts, through the ERK signaling pathway.

P1316

Intercalated discs in human dilated cardiomyopathy: molecular and ultrastructural remodeling and its relationship to left ventricular function

E Esther Rosello-Lleti[1]; A Ortega[1]; E Tarazon[1]; C Gil-Cayuela[1]; F Lago[2]; JR Gonzalez-Juantey[2]; L Martinez-Dolz[1]; M Portoles[1]; M Rivera[1]
[1]Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain; *[2]Instituto de Investigación Sanitaria de Santiago, Cellular and Molecular Cardiology Research Unit, Santiago de Compostela, Spain*

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Background: Dilated cardiomyopathy (DCM) is characterized by chamber dilation and contractile dysfunction. Alterations in myocardial structure and reduced cardiomyocyte adhesions have been previously implicated.
Purpose: We have studied the transcriptomic changes of cell adhesion molecules and the potential relationships with left ventricular (LV) function in DCM patients. We also visualized the intercalated disc (ID) structure and organization.
Methods: Twenty-three explanted LV samples were analysed using RNA sequencing (13 DCM, 10 control [CNT]), to compare the transcriptomic profile, focusing on cell adhesion genes.
Results: We found 29 differentially expressed genes, including a broad set of genes belonging to the ID structure. We further analysed the relationship between the mRNA levels and LV dysfunction and found that the expression of GJA3, DSP and CTNNA3 was directly associated with LV ejection fraction (r=0.741, P=0.004; r=0.674, P=0.011 and r=0.565, P=0.044, respectively), LV systolic (r=−0.746, P=0.003; r=−0.753, P=0.003; r=−0.605, P=0.028, respectively) and diastolic (r=−0.712, P=0.006; r=−0.801, P=0.001; r=−0.616, P=0.025, respectively) diameters. Electron microscopy micrographs showed a reduction in the ID convolution index in DCM patients.
Conclusions: We report a high number of expression changes in cell adhesion genes and found that the ID components GJA3, DSP and CTNNA3 were highly related to LV function of patients. Microscopic observations indicate that ID is structurally compromised in these patients.These findings offer new data for understanding the ventricular depression that characterizes DCM, which may occur as a result of alterations in cell adhesion integrity and machinery, leading to new therapeutic perspectives on these, until now, non-specifically treated patients.

P1317

Expression of golgi genes are related to the degree of ventricular remodeling in heart failure

E Esther Rosello-Lleti[1]; E Tarazon[1]; A Ortega[1]; C Gil-Cayuela[1]; F Lago[2]; JR Gonzalez-Juanatey[2]; L Martinez-Dolz[1]; M Portoles[1]; M Rivera[1]
[1]Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain; *[2]Instituto de Investigación Sanitaria de Santiago, Cellular and Molecular Cardiology Research Unit, Santiago de Compostela, Spain*

Funding Acknowledgements: National Institute of Health [PI13/00100; PI14/01506], CIBERCV [CB16/11/00261], the European Regional Development Fund (FEDER), RETICS [12/0042/0003].

Background. The size and complexity of the Golgi apparatus in cardiomyocytes increase during heart failure. Recently, we have observed morphological changes in human Golgi vesicles that are associated with poorer functional status in patients with dilated cardiomyopathy (DCM).
Purpose: In this study, we examined mRNA expression of Golgi components and it relationship with left ventricular remodeling in patients with DCM and ischemic (ICM) cardiomyopathy.
Methods: We performed RNA-sequencing analysis in patients with DCM ($n = 12$) and ICM ($n = 12$) and healthy controls ($n = 8$) focused on the Golgi apparatus.
Results: We found one hundred thirty-four genes deregulated, of which fifteen and thirteen , respectively, were involved in vesicular secretion in DCM and ICM. Of these, STX5 and AP1M1 mRNA levels related to left ventricular end-systolic and diastolic diameters (both $P < 0.01$) and, more importantly, to systolic function (ejection fraction, $P < 0.05$). Conclusions: In this study we found that changes in expression of some Golgi transport genes in DCM and ICM, STX5 and APM1, are significantly related to the degree of ventricular remodeling and to the left ventricular function. This relationship may lead to an alternative therapeutic approach for a syndrome that currently has no specific treatment; through the manipulation of these genes that may have an important role in ventricular maladaptation to changes in heart wall stress to which the left ventricle is subjected to.

P1318

Role of AQP1 in the left ventricular remodeling

V Montiel[1]; HE Esfahani Hrag[1]; DD De Mulder Delphine[1]; JPD Deglasse Jean-Philippe[2]; OD Devuyst Olivier[3]; JCJ Jonas Jean-Christophe[2]; JLB Balligand Jean-Luc[1]
[1]*Universite Catholique de Louvain, FATH - IREC, Brussels, Belgium*; [2]*Universite Catholique de Louvain, EDIN -IREC, Brussels, Belgium*; [3]*Universite Catholique de Louvain, NEFR - IREC, Brussels, Belgium*

Aquaporins are a family (AQP0-12) of transmembrane water channels known to mediate rapid water movements following osmotic gradients, as created under a variety of tissular stresses. Some isoforms may be permeable to additional small molecules (e.g. H2O2 in plants) although such function in mammalian Aqp's is undefined. We clearly identified Aqp1 in peripheral membranes of both capillary endothelial and cardiac muscle cells by immunohistochemistry. Aqp1 co-segregated with caveolin and other caveolar residents in lipid rafts/caveolae. Surprisingly, we observed that genetic deletion of Aqp1 in mice produces a striking microcardia, with smaller cardiac myocytes (transverse section area by histological analysis). This was not associated with changes in blood osmolality or free water balance. Moreover, isolated adult myocytes from Aqp1 KO mice failed to build a normal hypertrophic response to phenylephrine. By analogy with plant aquaporins, we hypothesized that Aqp1 mediates transmembrane transport of extracellular H2O2 generated by, and mediating the hypertrophic response to alpha1-adrenergic activation. Indeed, genetic deletion of Aqp1 reduced the intracellular detection of ROS (by H2-DCFDA) or H2O2 (with the specific roGFP2-Orp1 sensor) in cardiac myocytes exposed to graded concentrations of extracellular H2O2, demonstrating a role for Aqp1 in transmembrane transport of H2O2. Notably, incubation of wild-type myocytes with phenylephrine increased ROS/H2O2 signals, but co-treatment with phenylephrine and cell-impermeable (i.e. non-PEGylated) catalase abrogated both the intracellular ROS signals and the hypertrophic response. Similarly decreased ROS/H2O2 signals were observed upon exposure of myocytes from Aqp1 KO mice to phenylephrine (normalized fluorescence, X103: 102 + /-34 vs 400 + /-16 in WT; $P < 0.05$), suggesting that Aqp1 mediates the import of H2O2 produced extracellularly upon alpha1-adrenergic stimulation. To test the functional importance of Aqp1 deletion on cardiac remodeling, we treated Aqp1 KO mice (and WT littermate) with minipump infusion of angiotensin II for 14 days. To control for loading conditions, blood pressure was continuously measured in all mice by implanted telemetry. Ang II resulted in similar increases in BP in both genotypes (SBP in WT: 164 + /-8; Aqp1 KO: 174 + /-13 mmHg; P: ns). WT mice developed cardiac myocyte hypertrophy and fibrosis, which were significantly attenuated in Aqp1 KO (myocyte area (WGA): 462 + /-13µ2 vs 702 + /-23 µ2 in WT; $P < 0.01$). Similar reductions in hypertrophy and fibrosis were observed in Aqp1 KO mice after TAC (myocyte area (WGA): 454 + /-15µ2 vs 762 + /-14 µ2 in WT; $P < 0.01$). We conclude that cardiac aquaporin-1 mediates transmembrane transport of H2O2 and critically modulates the development of myocardial hypertrophy and fibrosis in response to physiologic and pathologic stimuli. Pharmacologic inhibition of AQP1 could be exploited therapeutically to attenuate stress-induced myocardial remodeling.

P1319

Notch3 modulates the cardiac adaptation to physiological cardiac growth

C Clement Delacroix[1]; H Ragot[1]; S Guinemer[1]; I Da Costa[1]; E Polidano[1]; R Merval[1]; C Chatziantoniou[2]; J-L Samuel[1]
[1]*Hospital Lariboisiere, Inserm UMR-S942, Paris, France*; [2]*Hospital Tenon, Inserm UMR-S 1155, Paris, France*

Background – The Notch3 receptor plays an important role in differentiation, migration and signal transduction of vascular smooth muscle cells (VSMCs). Notch3 signaling has been recently demonstrated to be essential for the coronary adaptation to pressure overload and in turn prevented acute heart failure (Ragot Hypertension 2016). The objective of the present study was to determine whether Notch3 signaling plays a role in cardiovascular remodeling in response to 2 physiological growth signals: the physical exercise and pregnancy.

Methods: – Male and female mice knocked out for the Notch3 gene (Notch3-/-) or Wild-Type (WT) mice were respectively submitted to treadmill physical-training program for 5 weeks or mated,. Methods included echocardiography, qPCR, western-blot, immuno- and histo-morphometry.

Results: – At baseline, Notch3-/- females exhibited similar cardiac phenotypes than males characterized by an arteriolar rarefaction (-60%, $p < 0.001$) and increased oxidative stress. Pregnancy decreased shortening fraction in Notch3-/- females (-25%, $p < 0.01$ vs post-partum WT). Interestingly, a microvascular adaptation occurred with increase in the capillary density (+25%, $p < 0.05$ vs Notch3-/-). Conversely, moderate physical training did not alter cardiac function in WT and Notch3-/- males. However, the analyses of coronary compartment showed an increased in capillary density (+12%, $p < 0.05$) in the WT mice after training only, these parameters being unmodified in the Notch3-/- mice. The angiogenesis pathway analysis revealed an increased expression in the anti- angiogenic soluble receptor, sFLT1, in the Notch3-/- mice after training (+40%, $p < 0.05$ vs WT + training) whereas it was not induced by the pregnancy in the Notch3-/- females. Conclusion– We provided lines of evidence suggesting that the Notch3 signaling pathway could mediate unique effect according to volume overload stimuli and/or gender which may be due to unique modulation of sFLT1 expression.

P1320

Extracellular signaling regulation of ABCA1 expression

H Hong Yang[1]; ZM Guo[1]
[1]*Meharry Medical College, Nashville, United States of America*

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While increase in cellular cholesterol is able to upregulate ATP-binding cassette transporter A1 (ABCA1) expression, the increased ABCA1 level by this stimulation is insufficient for prevention of foam cell formation. Using a mouse macrophage cell line, we demonstrated a signaling cascade independent of cellular cholesterol level for upregulation of ABCA1 expression. Specifically, activation of very low-density lipoprotein receptor (VLDLR) and apolipoprotein E receptor 2 (apoER2) with apoE, reelin or a reelin subregion containing its receptor binding domain significantly increased ABCA1 mRNA and protein levels. These VLDLR/apoER2 ligands also increased phosphorylation of disabled-1 (Dab1), phosphatidylinositol 3-kinase (PI3K), protein kinase C-ζ (PKC-ζ), and specificity protein 1 (Sp1), and increased PKC-ζ binding with Sp1. Sequential knockdown or inhibition of VLDLR/apoER2, Dab1, PI3K, PKC-ζ and Sp1 diminished the upregulatroy activity of apoE and reelin on ABCA1 mRNA and protein expression. Mutation of the Sp1 binding site in the ABCA1 promoter and inhibition of Sp1 DNA binding suppressed the ABCA1 promoter activity and reduced the ABCA1 mRNA expression level. In addition, VLDLR/apoER2 ligand treatment enhanced phosphorylation of Akt1 and Akt2, but not Akt3. PI3K inhibitors weakened Akt phosphorylation. Inhibition of Akt or knockdown of Akt2 only reduced ABCA1 protein but not its mRNA. Suppression of protein synthesis did not erase the ability of apoE to increase ABCA1 protein level. Further, apoE increased the resistance of ABCA1 protein to calpain-mediated degradation without affecting calpain activity. These data support a model in which activation of VLDLR and apoER2 by reelin and apoE induces ABCA1 transcription via a signaling cascade involving Dab1, PI3K, PKCζ and Sp1, and inhibition ABCA1 protein degradation via a signaling cascade involving PI3K and Akt2. We also observed that apoE, reelin and its subregion accelerated apoAI-mediated cholesterol efflux and inhibited foam cell formation. Thus, upregulation of ABCA1 expression via mechanisms additional to increasing cellular cholesterol level might inform interventions to inhibit foam cell formation and atherosclerosis.

P1321

Identification of upstream kinases that regulate p38-MAPK in cardiomyocytes: H2O2 signals to p38-MAPK via ASK1 whereas interleukin-1-beta signals via TAK1

D N Daniel Nathan Meijles[1]; K A Rostron[1]; A Clerk[1]
[1]*University of Reading, School of Biological Sciences, Reading, United Kingdom*

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Introduction. Pathophysiological stresses including oxidative stress (e.g. H2O2) and proinflammatory cytokines (e.g. interleukin 1β, IL1β) activate the stress-regulated mitogen-activated protein kinases (MAPKs), p38-MAPKs and c-Jun N-terminal kinases (JNKs) in cardiomyocytes. They also cause cardiac dysfunction and cardiomyocyte death, so components of the pathways are potential therapeutic targets for treatment of heart failure. MAPKs are final components of cascades in which MAPK kinases (MKKs) phosphorylate and activate MAPKs. JNKs are activated by MKK4/7 whilst p38-MAPKs are activated by MKK3/6. MKKs are phosphorylated and activated by upstream protein kinases, MAP3Ks, but the MAP3Ks for activation of p38-MAPKs and JNKs under different conditions are not well defined. Purpose. We aim to identify the MAP3Ks that activate p38-MAPKs and JNKs in cardiomyocytes. Our hypothesis is that different pathological stimuli signal through specific MAP3Ks to MKK4/7 and MKK3/6. Methods and results. Proteomics analysis of neonatal and adult rat ventricular myocytes (NRVMs and ARVMs) detected significant expression of MAP3Ks 1-7 and MAP3K11. MAP3K9, MAP3K12 and MAP3K14 were also detected at the mRNA level. Only MAP3K5 (ASK1) was expressed at a higher relative level in ARVMs, although others including MAP3K7 (TAK1) remained relatively highly expressed in ARVMs. We compared the effects of H2O2 and IL1β on phosphorylation (i.e. activation) of ASK1 and TAK1 in cardiomyocytes by immunoblotting extracts with antibodies to phosphorylated and total kinases. H2O2 promoted phosphorylation of ASK1, but not TAK1 (maximal activation with 1 mM H2O2, 5 min). In contrast, IL1β (25 ng/ml) stimulated phosphorylation of TAK1, but not ASK1 (maximal activation at 5 min). Similar results were obtained in Langendorff perfused adult rat hearts. Phosphorylation of MAP3K3 results in the appearance of a reduced mobility

band on immunoblots. Such a band shift was detected in cardiomyocyte extracts in response to either H2O2 (1mM) or IL1β. To dissect the role of ASK1 in activation of stress-regulated MAPKs, we examined the effects of a small molecule inhibitor of ASK1, selonsertib, on phosphorylation (i.e. activation) of p38-MAPKs and JNKs by immunoblotting cardiomyocyte extracts with antibodies to phosphorylated and total kinases. Selonsertib selectively inhibited activation of p38-MAPK by H2O2 with no effect on activation of p38-MAPK by IL1β and no effect on activation of JNKs by either agonist. Conclusions: Several MAP3Ks are expressed in cardiomyocytes and can signal to stress-regulated MAPKs. Our data identify selective signalling through specific MAP3Ks in response to different stimuli. Thus, oxidative stress signals through ASK1 to p38-MAPKs, not JNKs, whereas IL1β does not activate ASK1, but activates TAK1 instead. It will therefore be important to target different MAP3Ks under different conditions to manipulate p38-MAPK and/or JNK signalling for the management of heart failure.

P1322

In vivo silencing of histone deacetylase 1 displays anti-atherosclerotic effects in hypercholesterolemic apolipoprotein E deficient mice

S-A Simona-Adriana Manea[1]; ML Antonescu[1]; MI Fenyo[1]; A Manea[1]
[1]*Institute of Cellular Biology & Pathology Nicolae Simionescu, Bucharest, Romania*

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Background - The beneficial effects of several pan-histone deacetylase (HDAC) inhibitors have been demonstrated in various experimental models of heart failure and hypertension. However, the role of HDACs in atherosclerosis and the rationale of using HDAC inhibitors as therapeutic strategy are not established. HDAC1 is an essential isoform of the HDAC family and control a large number of physiological activities. Up-regulation of HDAC1 induces histone deacetylation resulting in transcriptional repression of genes that normally function in cellular proliferation, differentiation, and apoptosis. In addition, HDAC1 may act on and modulate the function of multiple non-histone proteins such as transcription factors to induce/repress the gene expression.
Purpose: - To establish the specific contribution of HDAC1 isoform in mediating oxidative stress and inflammation in atherosclerosis.
Methods: - A nanotechnology-based procedure was employed for in vivo siRNA delivery in hypercholesterolemic apolipoprotein E deficient (ApoE-/-) mice. Male ApoE-/- mice were randomized to receive normal (ND) or high-fat cholesterol-rich diet (HD) for 10 weeks (intermediary lesions). Aged-matched C57BL/6J mice maintained on normal diet were used as controls. Atherosclerotic ApoE-/- mice (HD) were treated with 0.5 mg/kg of non-targeted (control) or HDAC1 siRNA. One week after siRNA administration, the animals were sacrificed and aorta was analysed by Oil Red O staining and Western blot. To set-up the optimal conditions for systemic siRNA delivery, FITC-labelled siRNA and in vivo imaging (IVIS Caliper, Perkin Elmer) were used. The fluorescence signal was detected at different time points after FITC-siRNA administration to assess the biodistribution and the uptake efficiency of the FITC-siRNA (blood and various organs).
Results: - We found that HDAC1 protein level was significantly elevated in the aorta of ApoE-/- mice fed a HD compared to ApoE-/- mice maintained on ND. Ex vivo imaging revealed that FITC-siRNA was abundant in the blood and several organs (liver, lungs, and pancreas) and to a lesser extent in the kidneys. Systemic delivery of HDAC1 siRNA resulted in a significant decrease in HDAC1 protein expression level in the aorta of atherosclerotic ApoE-/- mice (HD). In vivo silencing of HDAC1 correlated with significant decreases in the expression of NADPH oxidase, a reactive oxygen species-generating enzyme complex (Nox1, Nox2, and Nox4), vascular inflammation (NOS2, MMP9, CD45), matrix deposition and remodeling (fibronectin, MMP9), and cell proliferation (PCNA) markers.
Conclusion: - Our preclinical study indicates that selective targeting of a specific HDAC isoform (e.g., HDAC1) rather than pan-HDAC inhibition may be a novel therapeutic strategy to counteract vascular oxidative stress and inflammation in atherosclerosis.

P1323

Protein expression profiling of histone acetyltransferases and histone deacetylases in human and experimental atherosclerosis

A Adrian Manea[1]; S-A Manea[1]; ML Antonescu[1]; IM Fenyo[1]; M Raicu[1]; M Simionescu[1]
[1]*Institute of Cellular Biology & Pathology Nicolae Simionescu, Bucharest, Romania*

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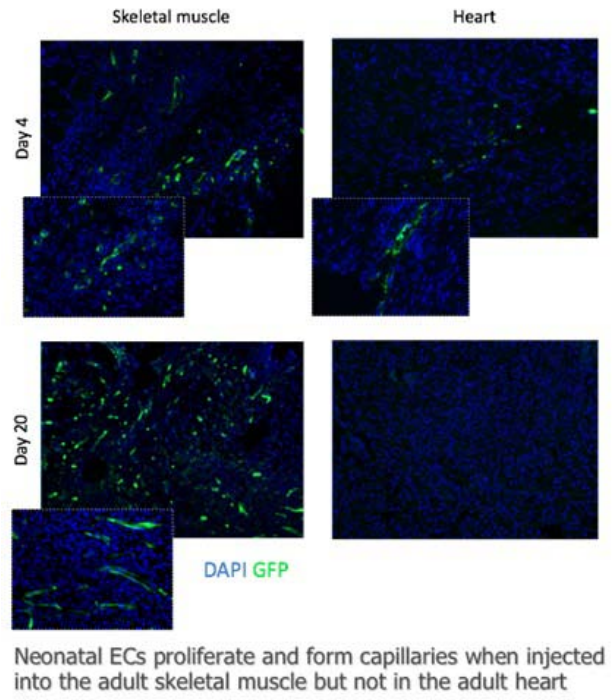
Background. Changes in chromatin conformation due to histone acetylation play a major in epigenetic regulation of gene expression. Histone acetylation is regulated by the activities of two major enzyme families, namely histone acetyltransferases (HAT) and histone deacetylases (HDAC). As general principle, histone acetylation induces chromatin relaxation, a condition that facilitates the accessibility of transcription factors to their cognate DNA elements in the genome. Thus, histone acetylation is associated with active gene expression. Several non-histone proteins such as transcription factors may be the substrates of HAT/HDAC activity. The beneficial effects of various pan-HDAC inhibitors were demonstrated in several experimental models of cardiovascular diseases. Hitherto, the regulation of HAT/HDAC and their implication in atherogenesis and also the rationale of using HDAC inhibitors are not completely understood.
Purpose: The aim of this study was to investigate the protein expression profile of representative HAT (type A: p300, type B: HAT1) and HDAC (class I: HDAC1, HDAC2, class IIa: HDAC4, class IIb: HDAC6, class III: Sirt1, class IV: HDAC11) isoforms and to estimate the overall histone acetylation status in human and mouse atherosclerosis.
Methods: Non-atherosclerotic (superior thyroid artery) and atherosclerotic (carotid artery) samples obtained as discarded tissues from patients undergoing carotid endarterectomy and apolipoprotein E deficient (ApoE-/-) mice were used. At 7 weeks of age male ApoE-/- mice were distributed into experimental groups to receive normal or high-fat cholesterol-rich diet for 10 weeks. Aged-matched C57BL/6J mice maintained on normal diet were used as controls. Oil red O staining was employed to assess lipid deposition within atherosclerotic lesions. The expression/localization of HAT and HDAC subtypes, the level of H3K27ac, oxidative stress and inflammatory markers were determined by Western blot/microscopy.
Results: We found that p300, HAT1, HDAC1, HDAC2, HDAC4, Sirt1, and HDAC11 isoforms were significantly up-regulated in atherosclerotic plaques derived from human carotid artery compared to non-atherosclerotic samples. A similar expression pattern of HAT and HDAC proteins was found in the aorta of atherosclerotic ApoE-/- mice. Interestingly, the increased expression of HAT and HDAC subtypes correlated with the severity of atherosclerotic lesions and plasma cholesterol level in ApoE-/- mice. An overall increase in H3K27ac (marker of active gene expression) level was detected in both human and mouse atherosclerotic lesions as compared to the corresponding non-atherosclerotic controls. Conclusion. Our study provides the first evidence that the histone acetylation system is altered in atherosclerosis. Both HAT and HDAC subtypes are up-regulated in atherosclerosis suggesting the existence of a feed-back mechanism whereby increased expression of HATs is compensated by up-regulation of HDACs and vice versa.

P1324

Understanding the poor angiogenic capacity of the mammalian heart

A Ambra Cappelletto[1]; YQ Tang[1]; M Rehman[1]; C Pierro[1]; S Zacchigna[1]
[1]*International Centre for Genetic Engineering and Biotechnology (ICGEB), Cardiovascular Biology, Trieste, Italy*

Purpose: The reason why a hypoxic tumor forms its own vasculature, mainly through the secretion of the Vascular Endothelial Growth Factor (VEGF), whereas an ischemic heart cannot, still remains obscure. We hypothesize that cardiac endothelial cells (ECs) loose their capacity to proliferate soon after birth, similar to what happens to mammalian cardiomyocytes.
Methods and Results: The injection of an adeno-associated vector (AAV) encoding for VEGF into either the adult skeletal muscle or the embryonic heart induced a massive formation of capillaries and arterioles. In contrast, the same vector injected into an adult heart did not result in any increase in endothelial cell proliferation. To understand whether the different angiogenic potential of the three organs depends on intrinsic properties of ECs or rather on the presence of some inhibitory factors within the adult heart, we purified ECs using CD31 magnetic beads. By flow cytometry we could detect the presence of an EC sub-population characterized by high expression levels of VEGFR2 and CD105, two tip cell markers, in the embryonic/neonatal but not in the adult heart ECs. Consistently, the formation of filopodia by tip cells and vessel-like tubular structures in response to VEGF was much more evident for embryonic/neonatal than for adult cardiac ECs. RNAseq data from the three EC types reveal a differential expression profile for coding genes, miRNAs and lncRNAs. ECs purified from the heart of EGFP transgenic pups formed capillaries and integrated into the vascular network of the skeletal muscle but not of the adult heart, suggesting the presence of an anti-angiogenic factor in this latter organ. The expression of VEGFR1 and its soluble isoform sFlt1 was significantly increased in adult compared to embryonic hearts, consistent with the role of sFlt1 in keeping the cornea completely avascular. Cancer cells injected into the heart of adult syngeneic mice grew much less compared to the same number of cells injected into the skeletal muscle, possibly indicating that the impaired angiogenic potential of the heart inhibited tumor growth. Conclusions: Collectively, these results indicate that both cell-autonomous and non autonomous mechanisms halt the proliferation of ECs in the post-natal heart and pave the way to novel therapeutic opportunities to promote angiogenesis in cardiac ischemia and, possibly, to control tumor progression.



GFP + Endothelial Cells injected in vivo

BASIC SCIENCE - ANIMAL AND TRANSLATIONAL

P1325

Pharmacological evaluation of the agonists of nuclear and G protein coupled estrogen receptors in arterial hypertension associated with estrogen depletion

G Gisele Zapata-Sudo[1]; JSS Jaqueline Soares Da Silva[1]; AMS Ananssa Maira Da Silva[1]; TLM Tadeu Lima Montagnoli[1]; HW Hao Wang[2]; XS Xuming Sun[2]; LG Leanne Groban[2]; RTS Roberto Takashi Sudo[1]
[1]Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; *[2]Wake Forest University, Winston-Salem, United States of America*

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Background - In the presence of premenopausal hypertension it may intensify a cardiac dysfunction when estrogen depletion occurs, this study aimed to evaluate the estrogen receptor agonists in the estrogen depletion in normotensive (WKY) and spontaneously hypertensive (SHR) rats.
Methods: Protocols were approved by Animal Care and Use Committee at Universidade. Females WKY or SHR (12 weeks old) were divided into groups, Sham and oophorectomized (OVX) treated subcutaneous with vehicle, G1, PPT or DPN, 24 μMol/kg, 28 days. Diastolic function was determinate by the ratio between early transmitral filling velocity (E) and rapid mitral annular velocity (e') and left ventricular end diastolic pressure (LVEDP). In addiction was analyzed mean blood pressure (MBP). Results - There was uterine atrophy in OVX. There was weight gain in the OVX, WKY and SHR and reduced in WKY-OVX-PPT. The heart/tibia increase in OVX, WKY and SHR compared to Sham, and reduction in WKY-OVX-PPT and SHR-OVX treated with G1 or PPT. The E/e' was elevated in the SHR-OVX compared to SHR-Sham and the SHR-OVX G1 treatment reversed. MBP were increased in SHR-Sham compared to WKY-Sham, from 107.8 ± 14.72 to 112.7 ± 7.54 mmHg ($P < 0.05$), in SHR-OVX was intensified to 143.7 ± 7.66 mmHg ($P < 0.05$). Treatment with G1, DPN and PPT promoted partial reduction of MBP in SHR-OVX. OVX in WKY increased from PVEDF when compared to WKY-Sham from 2.05 ± 0.66 to 8.12 ± 1.7 mmHg ($P < 0.05$), which was not reduced with treatments. We observed that SHR-Sham presented increased PVEDF in relation to WKY-Sham 7.38 ± 0.88 mmHg ($P < 0.05$) and increased in SHR-OVX to 13.81 ± 2.10 mmHg compared to SHR-Sham ($P < 0.05$). SHR-OVX-DPN presented PVEDF reduction to 5.70 ± 0.92 mmHg, ($P < 0.05$) compared to SHR-OVX. Conclusion - We observed improvements in cardiac structure and functional parameters with the different estrogen agonists in equimolar doses.

P1326

Pharmacokinetics of ubiquinol, administered intravenously.

O Oleg Medvedev[1]; O Kulyak[1]; E Gorodetskaya[1]; V Makarov[2]; E Kalenikova[1]
[1]M.V. Lomonosov Moscow State University, Pharmacology, Moscow, Russian Federation; *[2]Institute of Pharmacy, Pharmacy, Saint Petersburg, Russian Federation*

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Introduction: Coenzyme Q10 (CoQ10) plays an important role in the generation of the cell energy – ATP, being part of the electron transport chain in process of oxidative phosphorylation in the internal membrane of mitochondria. Many diseases of the cardiovascular system and congestive heart failure, in particular, depend on decreased content of Coq10 and myocardial CoQ10 content tends to decline as the degree of heart failure worsens. Additionally, CoQ10, through its antioxidant effects, may reduce oxidative stress, which is known to adversely affect left ventricular ejection fraction and alter disease outcomes. The long-term supplementation of CoQ10 in patients with HF seems safe, appears to produce symptomatic improvements, and, more importantly, has been found to significantly reduce major adverse cardiovascular events and mortality. Ubiquinol is the reduced form of coenzyme Q10. This drug is expected to complement coenzyme Q10, which is naturally found in the organism, helping the cells to produce more energy y and thus relieve the symptoms of this disease.
Purpose: – investigation of the pharmacokinetics of ubiquinol, administered intravenously, for the urgent increase of its concentration in blood and myocardium.
Methods: Solution (1%) of solubilized ubiquinol (dose 10 mg/kg) was administered intravenously to male Wistar rats. Samples of blood and myocardium were taken in 0, 0.25, 0.5, 1, 2, 4, 8, 24, 32, 48h after i.v. injection. 5 rats were used for each time point that means 50 rats were used for the study. Levels of ubiquinol were measured by HPLC with an electrochemical detector.
Results: High levels of ubiquinol were detected in blood during the whole period of observation, and it was 10-fold higher than baseline level 48 h after iv administration. The significant increase in the myocardial level of ubiquinol was detected in 15 min after iv injection. The maximal increase in the myocardial level of ubiquinol by 50-80% maintained during 24 h and reached the initial level in 48 h.
Conclusion: Intravenous administration of the solubilized ubiquinol is followed by the fast increase in its concentrations in blood and myocardium that could be used for the treatment of acute heart failure as well as ischemia/reperfusion conditions.

P1327

Repetitive obstructive respiratory events favors the development of an atrial arrhythmogenic substrate in a novel rat model for sleep apnea

M Mathias Hohl[1]; B Linz[1]; S Khoskhish[1]; AG Nickel[1]; C Maack[1]; M Boehm[1]; D Linz[1]
[1]Saarland University Hospital, Dept. of Internal Medicine III,Cardiology, Angiology & Intensive Care , Homburg, Germany

Table 1: P1324 Animal characteristics

	WKY	SHR								
	Sham	OVX	Sham	OVX						
	Vehicle	Vehicle	G1	PPT	DPN		Vehicle	G1	PPT	DPN
Utero/tibia(mg/mm)	22.21± 4,59	3.23 ± 0.54*	3.19 ± 0.17*	5.17 ± 1.02*	3.68 ± 0.66*	17.80 ± 3.10	3.50 ± 0.48#	5.07 ± 2.0#	4.07 ± 0.55#	4.49 ± 1.30#
Body weight(g)	249.0 ± 4.9	334.0 ± 21.6*	300.6 ± 7.3*	290.3 ± 7.5*	264.4 ± 12.3$	224.2 ± 4.3	286.0 ± 18.5#	291.8 ± 4.9#	287.0 ± 7.9#	280.5 ± 9.5#
Heart/tibia(mg/mm)	25.84 ± 0.87	32.64 ± 0.65	31.11 ± 0.68	26.81 ± 1.82	31.05 ± 1.08	28.74 ± 1.01	33.13 ± 1.49#	30.73 ± 0.81	30.76 ± 1.25#	38.18 ± 3.14
Filling pressure (E/e')	19.39 ± 5.57	20.82 ± 1.00*	22.16 ± 4.61*	21.82 ± 1.48*	23.55 ± 3.41$	23.02 ± 1.42	31.15 ± 2.02#	23.37 ± 2.39&	24.53 ± 1.61	28.71 ± 4.21

E/e' Rapid filling transmitral velocity/rapid mitral annular velocity. Data were expressed as mean ± EPM. *$p < 0.05$ compared to WKY-Sham; $$p < 0.05$ compared to WKY-OVX; #$p < 0.05$ compared to SHR-Sham; $p < 0.05$ compared to SHR-OVX. n=5

Background: Obstructive sleep apnea (OSA) is associated with increased occurrence of atrial fibrillation (AF) and dysregulation of the circadian rhythm. Repetitive obstructive respiratory events as appearing in OSA are characterized by intermittent hypoxia and hypercapnia. Ineffective breathing attempts against the occluded upper airways result in intrathoracic pressure changes increasing transmural pressure gradients in the heart. Yet it is unknown, whether intermittent hypoxia (IH) per se or negative intrathoracic pressure changes in combination with hypoxia (NTP-H) during obstructive respiratory events are responsible for the development of an arrhythmogenic substrate in the atrium.
Method: In anaesthetized rats, either IH or NTP-H was applied repetitively for one minute via a customized mask by a negative pressure device. In an acute-test-series (ATS), rats had a rest period of four minutes between every maneuver. Eight IH-rats and eight NTP-H-rats were sacrificed instantly after four hours. In a chronic-test-series (CTS), we applied one minute of IH or NTP-H with a rest period of nine minutes for four hours every second day. After three weeks, rats were sacrificed with a recovery period of 24 hours after the last maneuver. Rats with comparable anesthesia without application of IH or NTP-H were used as controls (CTR). Invasive left ventricular pressure measurements were performed and inducible AF-duration by atrial burst stimulation was determined.
Result: In ATS-rats, acute application of four hours repetitive NTP-H resulted in a substantial decrease of atrial anti-oxidative capacity indicated by diminished glutathione-ratio (GSH/GSSG: $p = 0.02$ vs. CTR). However, IH did not influence atrial anti-oxidative capacity. In CTS-rats, chronically applied NTP-H but not IH induced an increase in LA and RA interstitial fibrosis formation (LA: +135% vs. CTR, $p = 0.01$; RA: +125% vs. CTR, $p = 0.04$). Additionally, enlarged LA-myocyte diameters indicated developing hypertrophy in NTP-H-rats (LA: +107%, $p = 0.03$ vs. CTR). This was associated with significantly prolonged inducible AF-duration in rats with chronically applied NTP-H ($p = 0.02$ vs. CTR; NTP-H: 11.65 seconds; CTR: 0.98 seconds) but not with IH ($p = 0.31$ vs. CTR; IH: 1.28 seconds).
Conclusion: During acute obstructive respiratory events, NTP-H but not IH per se results in a transient and rapidly reversible increase in atrial oxidative stress. In the long term, chronically applied NTP-H results in an atrial arrhythmogenic substrate, characterized by increased interstitial fibrosis formation, atrial myocardial hypertrophy and AF-vulnerability.

P1328

An investigation of ca2+ regulation abnormalities underlying hypertrophic cardiomyopathy in cat hearts

A E Messer[1]; J Chan[2]; A Daley[2]; O Copeland[1]; D J Connolly[2]; S B Marston[1]
[1]Imperial College London, Myocardial Function, London, United Kingdom; *[2]The Royal Veterinary College, Small Animal Medicine and Surgery Group, London, United Kingdom*

Background: Hypertrophic cardiomyopathy (HCM) is the most common cardiac disease affecting 1 in 500 humans. HCM is even more prevalent in cats and affects 16% of the outbred population and up to 26% in pedigree breeds such as Maine Coon and Ragdoll. Homozygous MYBPC3 mutations have been identified in these breeds but the mutations in other cats are unknown. At the clinical and physiological level, feline HCM is closely analogous to human HCM, but little is known about the primary causative mechanism.
Purpose: The aim of this project is to compare troponin regulation by Ca2+ and phosphorylation in HCM and wild-type cats with human HCM and to ascertain if treatments that reverse the abnormalities in human samples also work in HCM cats.
Methods/Results: Quantitative in-vitro motility assays were performed with troponin extracted from post-mortem hearts of 8 cats diagnosed with HCM including one Ragdoll cat with a homozygous MYBPC3 R820W mutation and 5 wild-type (WT) unaffected cats. Two cats showed MyBP-C haploinsufficiency, but genotypes are currently unknown. All the HCM cats have a higher Ca2+-sensitivity than the WT cats (EC50 of 0.057 ± 0.003 μM, n=44 compared to 0.092 ± 0.006 μM, n=24) with an average increase of $x2.05 \pm 0.13$. This is equivalent to that found in many studies of Ca2+-regulation in HCM mutations (1.87 ± 0.07 fold, n=71: Marston, Front physiol. 2016; 7(242), 415). This differs from human myectomy samples, where Ca2+-sensitivity is the same as donor, probably due to secondary changes.
A major phenotype of human HCM is that the relationship between troponin I phosphorylation and Ca2+-sensitivity is uncoupled. This uncoupling is also observed in all the HCM cats examined ($EC50P/EC50unP = 1.05 \pm 0.02$, n=25) whereas all the WT cats tested show normal coupling ($EC50P/EC50unP = 1.83 \pm 0.11$, n=8). We showed previously that in myectomy samples the uncoupling was due to an abnormality of troponin T and we have likewise been able to restore coupling in cat HCM by replacing TnT with wild-type (human) protein. Similarities between cat and human HCM are further emphasised by the observation that the enhanced Ca2+-sensitivity and uncoupling due to HCM mutations can be reversed by 100 μM Epigallocatechin-3-gallate (EGCG) in the cat as has been previously demonstrated in human heart muscle ($EC50P/EC50unP$ cat HCM + EGCG $= 2.13 \pm 0.17$, n=12).
Conclusion: To conclude, our result further demonstrate that feline HCM is an excellent model for the human disease both at the fundamental cellular level with respect to Ca2+ regulation of sarcomeric proteins and at the clinical level in disease expression.

P1329

Functional mini-gene analysis reveals aberrant splicing due to an infrequent intronic mutation in the cardiomyopathy-associated MYBPC3 gene

M Torrado[1]; E Maneiro[2]; D Salvado[2]; L Monserrat[2]; A Mikhailov[1]
[1]Institute of Health Sciences, University of La Coruna, La Coruna, Spain; *[2]Health in Code Ltd., La Coruna, Spain*

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Background: Mutations in the myosin-binding protein (MYBPC3) gene are the most common cause of hypertrophic cardiomyopathy (HCM). There is evidence to suggest that MYBPC3 point mutation localized in the donor splice site of intron 32 (MYBPC3 c.3627+1G>A) is associated with a severe HCM phenotype in patients. Purpose: The aim was to functionally analyze MYBPC3 c.3627+1G>A mutation, as a first step towards understanding whether this mutation could account for a HCM phenotype in vivo.
Methods: Mutation screening of the MYBPC3 gene was performed by bidirectional Sanger sequencing of genomic DNA from a heterozygous patient with HCM undergoing genetic testing at our molecular diagnostic facility. Both MYBPC3 splice-site consensus (control) and c.3627+1G>A mutated regions were amplified from this genomic DNA by PCR and cloned into mini-gene dual tagged (N-terminal FLAG and C-terminal c-Myc) expression plasmids. The resulting plasmids were amplified, endotoxin-free purified, confirmed by DNA sequencing, and transfected into COS-7 cells. The expression of mini-gene plasmids was analyzed in transfected COS-7 cells at the protein (Western blot) and transcript (RT-PCR) level. Results: To verify the potential role of the MYBPC3-c.3627+1G>A mutation identified by genetic screening, we used the multi-algorithm software suite: all five algorithms showed that this mutation impairs the consensus splice-donor site of intron 32 and is expected to lead to disruption in MYBPC3 transcription. Consensus and mutated MYBPC3 allelic mini-genes (900 bp and 1928 bp) were generated using the patient genomic DNA as template. Western blot and RT-PCR analyses at different time points after transfection revealed that: (1) consensus mini-gene constructs were processed as predicted by computer analysis generating intronless transcripts which were translated into the protein detected by both anti-FLAG and anti-Myc antibodies, (2) neither the normally processed transcripts nor FLAG/Myc-tagged proteins were detected in COS-7 cells transfected with mini-gene constructs carrying the c.3627+1G>A mutation, and (3) the length of the mini-gene sequence did not significantly influence the expression response of COS-7 cells transfected by either consensus or mutated plasmids. Conclusions: The results strongly suggest that the intron c.3627+1G>A mutation of the MYBPC3 gene could result in haploinsufficiency, potentially modifying the disease phenotype.

P1330

Insights into disease mechanisms of cardiomyopathy in the presence of the CSRP3 C58G mutation

M Ehsan[1]; M Kelly[1]; C Hooper[1]; J Beglov[1]; B Davies[2]; C Redwood[1]; H Watkins[1]; K Gehmlich[1]
[1]University of Oxford, Radcliffe Department of Medicine, Cardiovascular Division, Oxford, United Kingdom; *[2]University of Oxford, Transgenic Core, Wellcome Trust Centre for Human Genetics, Oxford, United Kingdom*

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Purpose: Missense mutations in CSRP3, the gene coding for Muscle LIM Protein (MLP), are known to cause Hypertrophic Cardiomyopathy (HCM). MLP is not localised to the myofilaments and this challenges the paradigm of HCM being a disease of the sarcomere. We hypothesise that HCM mutations in signalling proteins such as MLP can cause perturbations in hypertrophic signalling cascades in the heart, resulting in cardiomyopathy. Supporting this hypothesis, MLP has recently been identified as an endogenous inhibitor of protein kinase C and reduction of inhibition may contribute to cardiomyopathy and heart failure.
Methods: A knock-in mouse model was generated by homologous recombination, introducing the C58G mutation into the mouse MLP protein. Heterozygous and homozygous knock-in mice were generated and their cardiac function assessed in vivo by echocardiography and invasive haemodynamic measurements. Tissues harvested from these animals were analysed for molecular markers of hypertrophy and heart failure as well as aberrant activation of protein kinase C alpha signalling (by quantitative PCR, Western blotting and Phos-Tag electrophoresis).
Results: Heterozygous MLP C58G knock-in mice display no overt phenotype and

show a similar hypertrophic response to trans-aortic constriction when compared to wildtype littermates. Homozygous MLP C58G knock-in mice have a phenotype resembling dilated cardiomyopathy, with compensatory activation of hypertrophy. At the molecular level, markers of heart failure and hypertrophic signalling are induced in these mice. Total MLP protein is significantly reduced (approximately 20 % of wild type levels), consistent with previous studies suggesting the mutation causes protein destabilisation. The mutant protein lacks phosphorylation (compared with MLP being 30-50 % in mono-phosphorylated state in wildtype) although protein kinase C alpha activity is elevated.
Conclusion: The mouse model recapitulates aspects of human Hypertrophic Cardiomyopathy caused by MLP missense mutations (such as protein destabilisation) and is a valuable tool to study molecular mechanisms resulting in cardiomyopathy, in particular how MLP integrates protein kinase C signalling into hypertrophic signalling cascades.

P1331
Myocardial and peripheral gene expression profile modulations in both acute cellular and antibody-mediated rejection of cardiac allograft

D Diane Bodez[1]; N Tchitchek[2]; G Coutance[3]; N Benhaiem[4]; R Gallet[1]; S Guendouz[1]; JP Couetil[5]; E Teiger[1]; JL Dubois-Rande[1]; L Hittinger[1]; T Damy[1]; Y Levy[6]; H Hocini[7]
[1]*University Hospital Henri Mondor, Department of Cardiology, Creteil, France*; [2]*CEA, DSV/iMETI, UMR1184, IDMIT infrastructure, Fontenay-aux-Roses, France*; [3]*Hospital Pitie-Salpetriere, Department of Cardiac Surgery, Paris, France*; [4]*University Hospital Henri Mondor, Department of Pathology, Creteil, France*; [5]*University Hospital Henri Mondor, Department of Cardiac Surgery, Creteil, France*; [6]*University Hospital Henri Mondor, Department of Clinical Immunology, Creteil, France*; [7]*Mondor Biomedical Research Institute, Genomic platform, Creteil, France*

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Background. Heart transplantation is the last treatment in case of terminal heart failure. Acute rejection after heart transplantation raises several issues due to its occurrence despite immunosuppressive therapies and the requirement of invasive and repeated endomyocardial biopsies (EMB) that have several histological grading limitations. Non-invasive diagnostic and predictive criteria are needed.
Purpose: Characterize acute cellular (ACR) and antibody-mediated rejections (AMR) of cardiac allograft using a molecular approach, in myocardium and peripheral blood.
Methods: We characterized myocardial and peripheral blood gene expression profiles (GEP) during ACR and AMR by mean of microarray analyses. By a retrospective study conducted on a historical EMB collection, we first showed a strong myocardial immunologic modulation during ACR. For the same ACR histological grading, two transcriptional profiles were identified corresponding to distinct inflammation profiles. Moreover, myocardial GEP modifications were observed one month before the occurrence of ACR, while histological characteristics showed no abnormality. A second study conducted on a prospective collection of both EMB and peripheral blood samples confirmed the results obtained on EMB and showed peripheral blood GEP modulations during both ACR and even one month earlier. Finally, we have also shown for the first time in heart transplantation, myocardial and peripheral GEP modulations in AMR, including common pathways between ACR and AMR.
Conclusion: Identification of modulated pathways in both ACR and AMR indicates intricate pathophysiological mechanisms, and should allow for the determination of common rejection biomarkers.

P1332
Novel nesprin-1 mutations in dilated cardiomyopathy cause nuclear envelope disruption and defects in myogenesis

C Can Zhou[1]; C Li[1]; B Zhou[2]; L Rao[3]; V Koullourou[1]; EM Mcnally[4]; S Shackleton[5]; CM Shanahan[1]; QP Zhang[1]
[1]*King's College London, Cardiology, London, United Kingdom*; [2]*The Second People's Hospital of Chengdu, Chengdu, China People's Republic of*; [3]*West China Hospital Sichuan University, Cardiology, Chengdu, China People's Republic of*; [4]*University of Chicago Medicine, Chicago, United States of America*; [5]*University of Leicester, Leicester, United Kingdom*

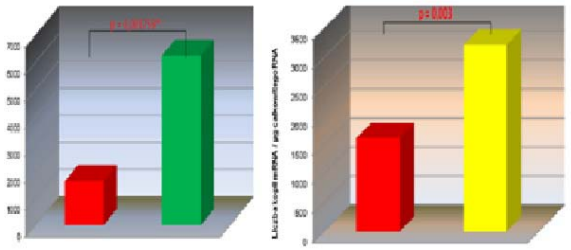
On behalf of: Catherine Shanahan
Funding Acknowledgements: British heart foundation

Nesprins 1 and 2 are highly expressed in skeletal and cardiac muscle and together with SUN (Sad1p/UNC84)-domain containing proteins and lamins form the Linker of Nucleoskeleton and Cytoskeleton (LINC) bridge complex at the nuclear envelope (NE). Mutations in nesprin-1 and -2 have previously been found in patients with autosomal dominant Emery–Dreifuss muscular dystrophy 4 (AD-EDMD 4, OMIM 612998) and 5 (AD-EDMD5, OMIM 612999) as well as dilated cardiomyopathy (DCM). In this study, three novel rare variants (R8272Q, S8381C, N8406K) in the C-terminus of the Syne-1 gene (nesprin-1) were identified in 7 DCM patients by mutation screening. Expression of these mutants caused nuclear morphology defects and reduced lamin A/C and SUN2 staining at the NE, and GST-pull down indicated that SUN/lamin/nesprin-1 interactions were disrupted. Nesprin-1 mutations were also associated with augmented activation of the ERK pathway in vitro and in hearts in vivo. During C2C12 muscle cell differentiation nesprin-1 levels are increased concomitantly with kinesin light chain (KLC1/2), and immunoprecipitation and GST-pull down showed that these proteins interacted via an LEWD domain in the C-terminus of nesprin-1. Expression of nesprin-1 mutants in C2C12 cells caused defects in myoblast differentiation and fusion associated with dysregulation of myogenic transcription factors and disruption of the nesprin-1/KLC-1/2 interaction at the outer NE. These findings support a role for nesprin-1 in myogenesis and muscle disease, and uncover a novel mechanism whereby disruption of the NE-LINC complex may contribute to the pathogenesis of DCM.

P1333
Transforming growth factor beta 1 - new chronic ischaemic heart failure decompensation marker?

J Dabek[1]; M Piechota[2]; M Majewski[1]
[1]*Medical University of Silesia in Katowice, School of Health Sciences, Chair and Department of Cardiology, Katowice, Poland*; [2]*City Hospital in Tychy, Department of Cardiology, Tychy, Poland*

Introduction: Cardiovascular diseases remain important cause of morbidity and mortality in developed countries. Atherosclerosis of coronary arteries is dominant element and often leads to ischemic heart failure (HF). Transforming growth factor beta 1 (TGF-β1) is one of the crucial cytokines in atherosclerosis development and progression as well as in HF formation. Accurate knowledge of its role in these processes may allow for early implementation of appropriate management in order to improve the prognosis of patients with ischemic HF.
Purpose: The aim of the study was to compare TGF-β1 transcriptional activity in patients with ischemic decompensated HF, after their compensation as well as in patients with advanced coronary artery disease without HF, constituting control group.
Methods: Studied group involved all consecutively admitted to the cardiology department patients with HF in the course of coronary artery disease in III and IV NYHA class (n = 52). The control group consisted of patients with advanced coronary artery disease without HF coexistence (n = 23). RNA was obtained from peripheral blood mononuclear cells. Transcriptional activity of TGF-β1 using QRT-PCR method in patients with advanced HF due to coronary artery disease and in patients with coronary heart disease without coexisting HF as well as their expression in the stage of both: decompensation and in compensated period was assesed. Enrolled patients were evaluated within first 24 hours and then after 4-8 weeks since admission, when HF compensation was achieved.
Results: Obtained dada are presented in figure below. To the left, transcriptional activity of TGF-β1, statistically significantly lower in patients with advanced heart failure in the course of coronary artery disease (red color) compared with controls – ischaemic subjects without HF (green) has been shown. To the right side transcriptional activity of TGF-beta 1 in patients with decompensated ischemic HF (red) and during their compensation (yellow) has been presented.
Conclusions: Statistically significant reduction of TGF-β1 transcriptional activity in patients with congestive heart failure and their further reduction during decompensation suggest importance of that gene in the development and decompensation of heart failure, making it useful diagnostic and prognostic clinical marker identifying subjects with coronary coronary heart disease and high risk for HF developing, its decompensation and compensation.



TGF beta 1 transcriptional activity

P1334

The relevant role of SR Ca leak in the development of heart failure

BA Mohamed[1]; L Kattner[2]; K Guan[1]; SE Lehnart[1]; S Luther[3]; S Sossalla[1]; G Hasenfuss[1]; K Toischer[1]
[1]University clinic, Cardiology and Pneumology, Goettingen, Germany; *[2]ENDOTHERM GmbH, ENDOTHERM, Germany*; *[3]Research Group Biomedical Physics, Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany*

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Purpose: Increased sarcoplasmic reticulum (SR) Ca2 + leak via the cardiac ryanodine receptor (RyR2) has been suggested to have a mechanistic role in the development of heart failure (HF). So we tested the hypothesis whether inhibiting or inducing SR Ca2 + leak modulates HF progression.
Methods: Wild-type C57BL/6J mice, subjected to transaortic constriction (TAC)-induced pressure overload (PO) or permanent coronary artery ligation-induced myocardial infarction (MI), were treated with a selective RyR2 stabilizing Rycal S36. Moreover, Ryr2RS/WT knock-in mice with the patient catecholaminergic polymorphic ventricular tachycardia (CPVT)-associated RyR2 mutation (R2474S) were subjected to shunt-induced volume overload (VO).
Results: In the TAC model, SR Ca2 + leak was significantly reduced in S36- versus placebo-treated mice. However, both treatment groups exhibited comparable contractile deterioration. Interestingly, S36-treated mice exhibited an improved survival after TAC. Implanted ECGs showed a markedly decreased arrhythmia score by ≍ 42%. Arrhythmia inducibility in perfused hearts was dramatically reduced by ≍ 72% post-TAC. Consistently, MI mice, treated with Rycal S36, experienced improved survival and reduced arrhythmias vulnerability. However both MI S36 and MI placebo hearts developed similar pump dysfunction. In the VO model, although SR Ca2 + leak was massively increased in Ryr2RS/WT mice, both WT and Ryr2RS/WT mice had a similar depressed pump function post-shunt.
Conclusions: These results suggest that SR Ca2 + leak may not primarily influence contractile remodeling in three different HF models, whereas ventricular arrhythmias were significantly reduced and survival was improved by Rycal S36 treatment. Thus selective SR Ca2 + leak inhibition via the Rycal S36 might be a promising option for treatment of cardiac arrhythmias in patients with HF and CPVT.

P1335

Autonomic regulation of cardiac activity in patients with prehypertension

BG Hojakuliyev[1]; BN Orayeva[1]; MB Muhammedov[2]
[1]Turkmen State Medical University, Ashgabat, Turkmenistan; *[2]Mary Regional Multi-field Hospital, Myocardial infarction, Mary, Turkmenistan*

Hypertensive disease (HD) is a disease dysregulation, and at the stage of formation of the disease the clinical picture is dominated by manifestations of autonomic dysfunction. The purpose of research - study of heart rate variability (HRV) and to assess the relationship between the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS) in patients with HD and prehypertension (preHTN) emissions during the orthostatic test. The study involved 30 patients with HD (20 men, 10 women), average age 46,6 ± 1,4 years and 25 with preHTN (16 men and 9 women), average age 34,8 ± 2,1 years. The control group consisted of 12 healthy people, the average age of 26,1 ± 3,2 years.All patients conducted daily Holter ECG. The total capacity of the spectrum of neurohumoral modulation in patients with HD was 1253 ± 470 ms2 / Hz, preHTN 2.4 times higher - 3032 ± 978 ms2 / Hz in the control group - 3778 ± 1022 ms2 / Hz. In 55.7% of patients with HD and y 17.3% of patients with preHTN has been a transition to the system of regulation of autonomic reflex level to a lower humoral-metabolic, who is able to quickly provide the homeostasis of the cardiovascular system. In the analysis of the balance of ANS at 71.1% HD patients prevailed activity of the sympathetic division, at 28.8% - with preHTN and 26.9% - the control group. Balanced type of autonomic modulation of cardiac rhythm was observed in 50% of cases with preHTN, in 55.8% - healthy and 25.1% - with the HD; parasympathetic predominance was seen in 21.1% of patients with preHTN and in only 3.8% of HD patients. Thus, in patients with preHTN notes balanced type of autonomic modulation of cardiac rhythm without changing the spectral parameters.

Rapid Fire 4 - Therapy and management

1377

Age and effect of implantable cardioverter-defibrillator (ICD) in patients with non-ischemic systolic heart failure.

M B Elming[1]; JC Nielsen[2]; J Haarbo[3]; L Videbaek[4]; E Korup[5]; LL Olesen[6]; FH Steffensen[7]; NE Bruun[3]; H Eiskjaer[2]; A Brandes[4]; JH Svendsen[1]; D Hoefsten[1]; S Pehrson[1]; L Koeber[1]; JJ Thune[8]
[1]Rigshospitalet - Copenhagen University Hospital, Dept. of Cardiology, Copenhagen, Denmark; [2]Aarhus University Hospital, Cardiology, Aarhus, Denmark; [3]Herlev Hospital, Cardiology, Herlev, Denmark; [4]Odense University Hospital, Cardiology, Odense, Denmark; [5]Aalborg University Hospital, Cardiology, Aalborg, Denmark; [6]University Hospital, Cardiology, Roskilde, Denmark; [7]Lillebaelt Hospital, Cardiology, Vejle, Denmark; [8]Bispebjerg University Hospital, Cardiology, Copenhagen, Denmark

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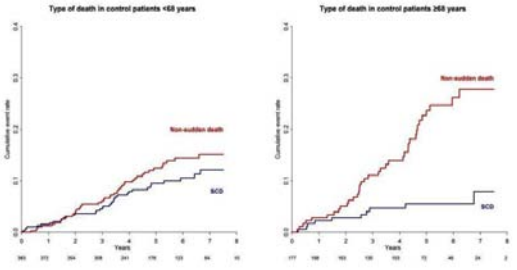
Background: Systolic heart failure carries an increased risk of sudden cardiac death. However, no single study has demonstrated a prophylactic effect of implantable cardioverter-defibrillator (ICD) implantation in patients with non-ischemic systolic heart failure. The recent Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality (DANISH) study did not demonstrate an overall effect on all-cause mortality. However, there was a significant interaction between age and implantation of an ICD with a significant mortality reduction in the youngest patients.
Purpose: Further investigation of the relationship between age and the effect of primary prophylactic ICD in patients with non-ischemic systolic heart failure.
Methods: In the DANISH study 1116 patients with non-ischemic symptomatic systolic heart failure and left ventricular ejection fraction (LVEF) ≤35% were randomized to ICD implantation or control. Assessment of interaction between age and ICD implantation was done with age as a continuous variable. Causes of death were divided into sudden cardiac death and non-sudden death (a composite of non-cardiovascular death and non-sudden cardiac death), and compared between the two youngest tertiles and the oldest tertile. Incidence rates were calculated as events per 100 patient years.
Results: There was a linear correlation between the effect of an ICD on all-cause mortality and decreasing age, p = 0.03. Causes of death differed significantly for patients not treated with an ICD and respectively below and above 68 years, p = 0.01. For patients younger than 68 years the rate of sudden cardiac death was 2.0 (1.4 – 2.7) events/100 patients years and the rate of non-sudden death was 2.6 (2.0 – 3.5) events/100 patients years, and for patients older than 68 years the incidence rate of sudden cardiac death was 1.3 (0.7 – 2.4) events/100 patients years and the rate of non-sudden deaths was 4.7 (3.4 – 6.5). Expressed in percent, sudden cardiac death occurred in 12% of patients younger than 68 years, whereas 15% in this age group died from a different cause. In contrast, patients ≥68 years old only 8% died of sudden cardiac death compared to 28% who died in a different way.
Conclusion: In patients with systolic heart failure not caused by ischemic heart disease the effect of ICD implantation decreased with increasing age. Patients younger than 68 years had roughly equal incidence rates of sudden cardiac death and non-sudden death and had a significant reduction in all-cause mortality when treated with an ICD. Patients older than 68 years were relatively more likely to die from other causes than sudden cardiac death which may explain why implantation of an ICD did not benefit survival in this age group.



Type of death by age group

1378

Use of mineralocorticoid receptor antagonists in a real-world population with heart failure and reduced ejection fraction: an analysis of 24,529 patients from the swedish heart failure registry

G Savarese[1]; JJ Carrero[2]; B Pitt[3]; S Anker[4]; U Dahlstrom[5]; LH Lund[1]
[1]Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden; [2]Karolinska Institute, Division of Renal Medicine, CLINTEC, Stockholm, Sweden; [3]University of Michigan, Ann Arbor, United States of America; [4]University Medical Center Gottingen (UMG), Innovative Clinical Trials, Department of Cardiology and Pneumology, Gottingen, Germany; [5]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden

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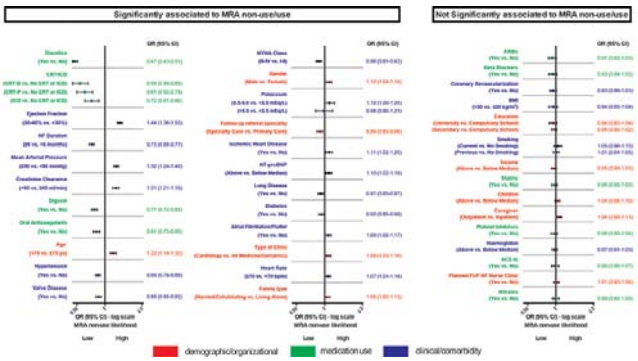
Background: Mineralocorticoid receptor antagonists (MRAs) improve outcomes in heart failure with reduced ejection fraction (HFrEF), but may be under-utilized in contemporary clinical practice.
Purpose: To assess predictors of MRA non-use in a large unselected cohort of patients with HFrEF.
Methods: In the nationwide Swedish Heart Failure registry (SwedeHF), we all included patients with HFrEF (EF < 40%) during years 2000-2012. Logistic regression analysis was performed to identify the predictors of MRA non-use among 38 variables (demographical, clinical, treatments). Missing data were managed by multiple imputation.
Results: Of 24,529 patients, 29% were female; mean age was 72 + 12 years; Only 8,102 (33%) patients were receiving MRAs. Demographic, clinical characteristics and concomitant treatments independently associated with MRA non-use are shown in the figure. Notable characteristics were, in descending order of magnitude, no need for diuretics, absence of implantable cardioverter or cardiac resynchronization device, higher ejection fraction, shorter HF duration, higher blood pressure, estimated glomerular filtration rate, older age, lower NYHA class, male gender, followed-up in primary rather than in specialized care, history of ischemic heart disease, higher NT-proBNP levels, concomitant atrial fibrillation/flutter, being registered in internal medicine/geriatrics rather than in cardiology department and being married/cohabitating rather than living alone. There was a trend toward underuse of MRAs in patients with mid-range potassium serum levels (3.5-5.0 mEq/L) vs. those with low (< 3.5 mEq/L) and high (>5.0 mEg/L) levels.
Conclusions: MRAs remain underused in HFrEF. MRAs may be used to supplement diuretics and for K-sparing. Their use does not appear to decrease with elevated K. The underuse may be linked to non-specialist care and follow-up and non-use of other HF interventions, suggesting specialized referral, a better education and understanding of the indications and benefits of MRAs in guideline appropriate HFrEF patients should be encouraged.



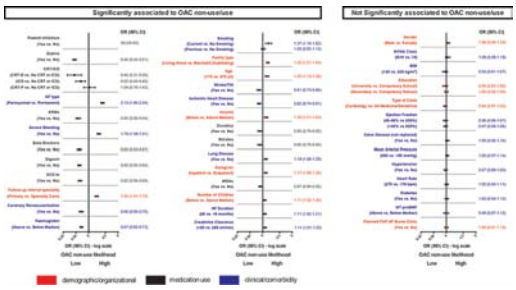
1379

Oral anticoagulant use in patients with atrial fibrillation and concomitant heart failure: an analysis of 22,719 patients from the swedish heart failure registry

G Savarese[1]; L Friberg[2]; U Dahlstrom[3]; LH Lund[1]
[1]Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden; *[2]Danderyd University Hospital, Department of Clinical Sciences, Stockholm, Sweden*; *[3]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*

Funding Acknowledgements: The County Council of Stockholm, The Swedish Heart and Lung Foundation and The Swedish Research Council.

Background. Atrial fibrillation (AF) is common in patients with heart failure (HF). HF is considered a risk factor for both thromboembolic and bleeding risk in patients with AF.
Purpose: To assess oral anticoagulants (OACs) use in a large unselected cohort of AF patients with concomitant HF and to identify patient characteristics associated with their non-use.
Methods: We included patients with AF, HF and no previous valve replacement enrolled in the Swedish Heart Failure Registry. Multivariable logistic regression analysis was performed to identify independent predictors of OAC non-use among 39 variables (demographical, clinical, treatment). Missing data were managed by multiple imputation.
Results: Of 22,719 included patients, 37% were female. The mean age was 76 + 10 years. Approximately half of the patients enrolled (52%) had HF with reduced ejection fraction (EF), while the 22% had HF with mid-range EF and 26% had HF with preserved EF. In total, 13,153 patients (58%) were receiving OACs at baseline. The demographic and clinical characteristics and concomitant treatments associated with OAC non-use are shown in the figure. Notable characteristics were, in descending order of magnitude, treatment with platelet inhibitors, absence of implantable cardioverter or cardiac resynchronization device, paroxysmal (vs. permanent) AF, history of severe bleeding, followed-up in a primary rather than in specialized care, low haemoglobin levels, current smoking, living alone (vs. being married/cohabitating), older age (>75 years), no history of stroke/transient ischemic attack or ischemic heart disease, low income, concomitant lung disease, being an inpatient (vs. outpatient), having fewer children, longer HF duration and lower creatinine clearance.
Conclusions: In this nation-wide registry, we found low utilization of OACs among patients with AF and concomitant HF. Platelet inhibitors appeared inappropriately used in lieu of OACs. Some characteristics associated with OAC underuse were linked to older age, history of severe bleeding, lower haemoglobin levels and less use of HF therapy suggesting a generalized fear of OACs in frailer patients, despite their greater stroke risk. Furthermore, there were additional unwarranted predictors of non-use, such as paroxysmal AF and socio-economic conditions.



1380

SGLT2 inhibition differentially reduces extracellular fluid volume relative to blood volume: a hypothesis for heart failure protection

K Melissa Hallow[1]; G Helmlinger[2]; PJ Greasley[3]; DW Boulton[2]
[1]University of Georgia, School of Chemical, Materials, and Biomedical Engineering, Athens, GA, United States of America; *[2]Astrazeneca, Waltham, MA, United States of America*; *[3]Astrazeneca, Mölndal, Sweden*

Introduction. In the EMPA-REG cardiovascular outcomes trial, treatment with the sodium glucose cotransporter 2 inhibitor (SGLT2i) empagliflozin significantly reduced heart failure hospitalization and cardiovascular death. This result was unexpected, and there is currently no consensus understanding of the mechanism for this protective effect. Improvements were apparent very early in the trial, suggesting treatment may have "rescued" individuals who were on the verge of cardiac decompensation.
Purpose: SGLT2i causes osmotic diuresis due to glucosuria. We hypothesize that SGLT2i-induced osmotic diuresis, a distinctly different mechanism than other diuretic classes, results in greater electrolyte-free water clearance, which in turn causes greater clearance of fluid from the extracellular fluid (ECF) space than from the circulation. In heart failure patients, this may result in greater clearance of congestion with minimal impact on arterial filling and organ perfusion.
Methods: 24-hour urinary volume and sodium and plasma sodium data from a previously conducted study in healthy subjects (N=42) administered either the SGLT2i dapagliflozin or the loop diuretic bumetanide for seven days were coupled with a 3-compartment mathematical model of blood, ECF, and peripheral sodium and water, to simulate the effect of each drug on ECF and blood volume. Drug-induced water and sodium excretion with either dapagliflozin or bumetanide were applied as model inputs, with the magnitude and time profile determined by fitting to the clinically measured 24-hour urinary sodium and urine volume. The model was constrained by fitting measured plasma Na + concentration, and ECF volume and blood volume changes were simulated.
Results: With dapagliflozin, the reduction in ECF volume was predicted to be 2-fold greater than the reduction in blood volume, while with bumetanide, the reduction in ECF volume was 22% less than the reduction in blood volume. Model-based analyses further illustrated that, in general, as electrolyte-free water clearance increases, there is a greater reduction in ECF volume relative to blood volume, and that this effect may be mediated by peripheral sequestration of sodium in order to buffer ECF sodium concentration.
Conclusions: These results support the hypothesis that by increasing electrolyte-free water clearance, SGLT2i reduces ECF volume with a smaller effect on blood volume, compared to loop diuretics. Heart failure is often characterized by excess fluid accumulation in both the blood and interstitial space, yet many heart failure patients actually experience arterial underfilling due to low cardiac output, and treatment must balance the need to relieve congestion while maintaining arterial filling. SGLT2i may reduce interstitial congestion without deleterious effects of arterial underfilling, hypotension, reduced organ perfusion, and neurohormonal activation that can accompany excess blood volume depletion with other forms of diuretics.

1381

Chronic oral study of myosin activation to increase contractility in heart failure (COSMIC-HF): dose-escalation phase

J R Teerlink[1]; GM Felker[2]; JJV Mcmurray[3]; SD Solomon[4]; ML Monsalvo[5]; R Palaparthy[5]; J Johnston[5]; J B Kim[5]; FI Malik[6]
[1]University of California San Francisco, Veterans Affairs Medical Center, San Francisco, United States of America; *[2]Duke University School of Medicine, Durham, NC, United States of America*; *[3]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom*; *[4]Brigham and Women's Hospital, Boston, United States of America*; *[5]Amgen, Inc., Thousand Oaks, United States of America*; *[6]Cytokinetics, Inc., South San Francisco, United States of America*

On behalf of: COSMIC-HF Investigators
Funding Acknowledgements: Amgen, Inc

Background: Omecamtiv mecarbil (OM), a novel cardiac myosin activator, has improved cardiac function in patients with acute and chronic heart failure (HF). OM is absorbed rapidly when dosed orally, resulting in high peak-trough fluctuation (PTF). Three modified release formulations were developed to slow absorption and reduce PTF.
Purpose: To select an oral formulation of OM to advance into the dose-expansion phase of COSMIC-HF.
Methods: The COSMIC-HF (NCT 01786512) dose-escalation phase was a randomized, placebo-controlled, multicenter, sequential-cohort, phase 2 study. In each cohort, subjects were randomized to receive 1 of 3 oral formulations BID (M-F1, M-F2, and SCT-F2), or placebo BID for 7 days. Pharmacokinetic (PK) and safety data were reviewed before enrollment into the next dose cohort. Eligible patients were 18-85 years of age, LVEF≤40%, heart failure with 4 weeks of stable optimal medical therapy, NYHA class I-III, and NT-proBNP ≥200 pg/mL (≥1200 pg/mL with atrial fibrillation). PK sampling was performed on days 1 and 7.
Results: Two cohorts were enrolled; Cohort 1 (n = 48) at 25 mg BID and Cohort 2 (n = 46) at 50 mg BID. The mean (SD) age was 65.1 (9.3) years; 21% of patients were women; 87% were white. The PK of the 3 formulations were similar (Table). However, the Cmax and AUC12 of M-F1 had the lowest variability (CV) and PTF (Cmax/Cpredose ratio) at 50 mg BID. The terminal half-life was 24.6 ± 8.7 h (25 mg BID) and 28.6 ± 7.4 h (50 mg BID). Excessive concentrations of OM occurred in one patient (50 mg M-F1) at day 7 (Cmax 1320 ng/mL) compared to the other subjects (n = 9, Cmax: 349 to 654 ng/mL) which was associated with myocardial infarction. This outlier informed the implementation of PK-based titration in the expansion phase of COSMIC-HF.
Conclusions: The M-F1 formulation was selected for additional evaluation in the expansion phase of COSMIC-HF, with further optimization of plasma concentrations using PK-guided dose titration.

1381: PK Parameters on Day 7, Mean ± SD (CV%)

Parameter	M-F1 OM 25 BID (n = 10)	M-F2 OM 25 BID(n = 14)	SCT-F2 OM 25 BID(n = 13)	M-F1 OM 50 BID(n = 10)	M-F2 OM 50 BID(n = 11)	SCT-F2 OM 50 BID(n = 14)
Cpredose	157±63.7 (41)	137±56.8 (42)	134±54.7 (41)	376±170 (45)	395±108 (27)	476±234 (49)
Cmax	193±59 (31)	201±94 (47)	171±54 (32)	492±115 (23)	502±138 (28)	601±204 (34)
AUC12	2030±658 (32)	2000±1020 (51)	1740±586 (34)	5070±1060 (21)	5010±1160 (23)	6550±2340 (36)
Cmax/Cpredose Ratio	1.28±0.18 (14)	1.37±0.21 (15)	1.27±0.15 (12)	1.14±0.12 (11)	1.28±0.15 (11)	1.17±0.07 (6)

Cpredose = plasma concentration prior to an OM dose (ng/mL); Cmax = maximum observed plasma concentration (ng/mL); AUC12 = Area Under the Curve for a dosing interval of 12h (ng*hr/mL); SD = standard deviation, CV = coefficient of variation.

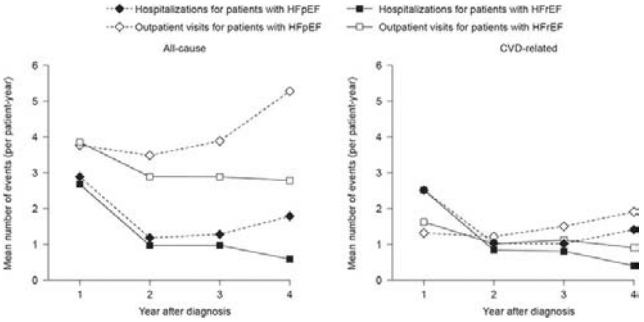
1382

Healthcare resource utilization associated with heart failure with preserved versus reduced ejection fraction: a retrospective population-based cohort study in Sweden

K Boman[1]; K Lindmark[2]; M Olofsson[1]; J Stalhammar[3]; G J Bergman[4]; M Tornblom[4]; S Bruce Wirta[5]; M Costa-Scharplatz[5]; F Calado[6]; G Wikstrom[7]
[1]Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden; *[2]Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[3]Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*; *[4]QuintilesIMS, Solna, Sweden*; *[5]Novartis Sweden AB, Stockholm, Sweden*; *[6]Novartis Pharma AG, Basel, Switzerland*; *[7]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*

Background and purpose: To estimate healthcare resource utilization among patients with heart failure (HF) with preserved (HFpEF) versus reduced (HFrEF) ejection fraction using population data from two Swedish counties.
Methods: Patients with HF were identified via electronic medical records (EMRs) from primary and/or secondary care in Uppsala and Västerbotten, linked via unique identifiers to data from the National Patient Register and Swedish Prescribed Drug Register. Local echocardiography data were used to identify HFpEF (defined as ejection fraction ≥50%) and HFrEF (defined as <50%). Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. Patients were followed from date of first diagnosis (index date) to end of study period or EMR collection, date of death or loss to follow-up for other reasons, whichever came first. Unadjusted all-cause and cardiovascular disease (CVD)-related hospitalization rates were assessed using a Cox proportional hazards model, accounting for age, sex, setting of first diagnosis (primary vs secondary care), HF phenotype and NT-proBNP level.
Results: In total, 8702 patients with HF were identified. HF phenotype was known in 3167 patients; 64.6% had HFrEF, 35.4% had HFpEF. Patients with HFrEF were younger (mean ± SD: 69.9 ± 13.7 vs 74.2 ± 12.6 years) with a lower Charlson comorbidity index (1.65 vs 1.83) than those with HFpEF. All-cause hospitalization rates were marginally lower for HFrEF than for HFpEF (mean [95% CI] proportion of patients hospitalized within 1 year of diagnosis, 72.5 [70.1–74.8]% vs 73.8 [70.7–77.0]%; hazard ratio [HR] over whole follow-up period, 0.87 [0.79–0.97], p = 0.0093). The proportion of patients hospitalized was higher for those diagnosed in secondary care than in primary care, particularly within 1 year of diagnosis (1-year rate, 69.6 [68.3–71.0]% vs 59.1 [56.8–61.4]%; HR, 1.15 [1.07–1.23], p = 0.0002). Similar trends were observed for CVD-related hospitalization rates for HFrEF vs HFpEF (1-year rate, 69.5 [67.1–71.9]% vs 70.7 [67.5–74.0]%; HR, 0.89 [0.81–0.99], p = 0.0309) and for patients diagnosed in secondary vs primary care (1-year rate, 66.6 [65.3–68.0]% vs 56.2 [53.8–58.5]%; HR, 1.15 [1.07–1.24], p = 0.0001). Numbers of hospitalizations and outpatient visits decreased with time after diagnosis for HFrEF, but increased slightly for HFpEF after 2 years (Figure). The mean ± SD total number of all-cause days of hospitalization during the first year after diagnosis was lower in patients with HFrEF vs HFpEF (19.9 ± 26.1 vs 26.3 ± 34.5 days), while the number of HF-related days of hospitalization was similar (16.0 ± 22.4 vs 17.2 ± 24.0 days).
Conclusions: Number and duration of hospital stays were significantly lower over time in patients with HFrEF than HFpEF; this may be explained by the comorbidity burden in the latter group.

All-cause and cardiovascular disease-related hospitalizations and outpatient visits after diagnosis of heart failure with preserved (HFpEF) versus reduced (HFrEF) ejection fraction in Sweden



1383

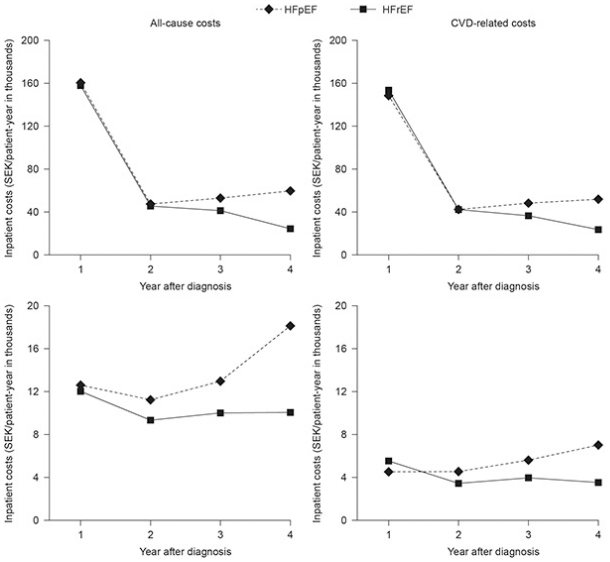
Costs associated with heart failure with preserved versus reduced ejection fraction: a retrospective population-based cohort study in Sweden

K Boman[1]; K Lindmark[2]; J Stalhammar[3]; G Wikstrom[4]; G J Bergman[5]; M Tornblom[5]; M Costa-Scharplatz[6]; S Bruce Wirta[6]; M Olofsson[1]
[1]Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden; *[2]Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[3]Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*; *[4]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*; *[5]QuintilesIMS, Solna, Sweden*; *[6]Novartis Sweden AB, Stockholm, Sweden*

Background and purpose: To implement cost-effective management programmes, it is important to understand the costs associated with heart failure (HF) with preserved (HFpEF) versus reduced (HFrEF) ejection fraction. We aimed to estimate direct costs associated with HFpEF and HFrEF using population data from two Swedish counties.
Methods: Patients with HF were identified via electronic medical records (EMRs) from primary and/or secondary care in Västerbotten, linked via unique identifiers to data from the National Patient Register and Swedish Prescribed Drug Register. Local echocardiography data were used to identify HFpEF (defined as ejection fraction ≥50%) and HFrEF (defined as <50%). Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. Patients were followed from date of first diagnosis (index date) to end of study period or EMR collection, date of death or loss to follow-up for other reasons, whichever came first. Unadjusted all-cause and cardiovascular disease (CVD)-related (defined by ICD-10 codes) costs associated with secondary care were estimated based on diagnosis-related group codes and price lists. Costs of drug use and comorbidities were available in Uppsala only; impact of the latter on total costs was assessed using a multiple Gamma regression model.
Results: In total, 8702 patients with HF were identified. HF phenotype was known in 3167 patients: 35.4% had HFpEF and 64.6% had HFrEF. Patients with HFpEF were older (mean ± SD: 74.2 ± 12.6 vs 69.9 ± 13.7 years) and had a higher Charlson comorbidity index (1.83 vs 1.65) than those with HFrEF. Total all-cause costs dropped substantially after 1 year after diagnosis. CVD-related costs followed the same pattern, and comprised 85.9% and 89.6% of total costs over 4 years after diagnosis for patients with HFpEF and HFrEF, respectively. Inpatient costs, which accounted for ~90% of total costs, generally decreased over time, whereas outpatient all-cause and CVD-related costs (accounting for ~10%) tended to increase over time, especially for patients with HFpEF (Figure). In Uppsala, drug use in the

year after diagnosis cost SEK 18171.0 and 11109.7 per patient with HFpEF and HFrEF, respectively. Furthermore, anaemia, cancer, chronic kidney disease, chronic obstructive pulmonary disease, diabetes, hypotension and aortic insufficiency were significant drivers of all-cause costs in the year after diagnosis (all $p < 0.05$) in the Uppsala cohort.
Conclusions: This analysis highlights the substantial economic burden of HFpEF and HFrEF. Costs were highest in the first year after diagnosis, and were driven by inpatient costs due to CVD and other comorbidities.

All-cause and cardiovascular disease (CVD)-related inpatient and outpatient costs after diagnosis of heart failure with preserved (HFpEF) versus reduced (HFrEF) ejection fraction in Sweden



1384

Significance of ischemic heart disease in patients with heart failure with preserved, mid-range and reduced ejection fraction - A nationwide cohort study

O Ola Vedin[1]; CSP Lam[2]; AS Koh[2]; L Benson[3]; THK Teng[2]; WT Tay[2]; OÖ Braun[4]; G Savarese[5]; U Dahlstrom[6]; LH Lund[5]
[1]Uppsala University Hospital, Department of Medical Sciences, Cardiology, Uppsala, Sweden; *[2]National Heart Centre Singapore, Singapore, Singapore*; *[3]Karolinska Institute, Stockholm, Sweden*; *[4]Skane University Hospital, Cardiology, Lund, Sweden*; *[5]Karolinska Institute, Department of Medicine, Stockholm, Sweden*; *[6]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*

Funding Acknowledgements: Swedish reseatch council, Swedish Heart-Lung foundation, Stockholm County Council, Swedish Society of Medicine

Background: The importance of ischemic heart disease (IHD) is well established in heart failure with reduced ejection fraction (HFrEF, [EF $<40\%$]). However, its epidemiological and prognostic significance in heart failure with preserved and mid-range ejection fraction (HFpEF [EF $\geq 50\%$] and HFmrEF [EF 40-49%], respectively) is much less certain.
Purpose: We explored the relationship between ischemic heart disease (IHD), all three HF types and outcomes in the nationwide Swedish Heart Failure Registry (SwedeHF).
Methods: A total of 42,987 patients from SwedeHF were characterized according to EF and IHD status at baseline and followed for new IHD events, other outcomes and EF changes. Associations between baseline IHD and HF type and HF type, baseline IHD and outcomes were assessed using multivariable Generalized Estimating Equations and multivariable Cox regression, respectively.
Results: Overall, 23% of patients had HFpEF (52% IHD, 29% prior myocardial infarction [MI]), 21% had HFmrEF (61% IHD, 41% prior MI) and 55% had HFrEF (60% IHD, 43% prior MI). The association with prevalent IHD was similar for HFmrEF and HFrEF (risk ratio [RR] 1.00, 95% CI 0.98-1.01), and lower in HFpEF (RR 0.91 [0.89-0.93] vs. HFmrEF; RR 0.90 [0.88-0.92] vs. HFrEF). During a median follow-up of 2.2 years, there were 9,629 new IHD events; 16,005 HF events; 26,734 cardiovascular events; and 16,866 all-cause death events. Adjusting for prevalent IHD and clinical risk factors, the independent risk of new IHD events was relatively similar for HFmrEF vs. HFrEF (hazard ratio [HR] 0.95, 95% CI 0.90-1.00), and lower in HFpEF (HR 0.89 [0.84-0.95] vs. HFmrEF; HR 0.84 [0.80-0.90] vs. HFrEF). Prevalent IHD was independently associated with increased risk of new IHD events in all EF categories, although more pronounced in HFrEF (HR for IHD vs. no IHD 3.13, 2.87-3.40) than in HFmrEF (HR 2.43, 2.14-2.75) and HFpEF (HR 2.34, 2.10-2.62). Prevalent IHD was also associated with an increased risk of all other events except all-cause mortality in HFpEF. Patients with IHD, particularly those with new IHD events, were more likely to change to a lower EF category and less likely to change to a higher EF category over time.
Conclusion: HFmrEF resembled HFrEF rather than HFpEF with regard to both a higher prevalence of IHD and a greater risk of new IHD events. Prevalent IHD was an important determinant of prognosis in all HF types suggesting that management of IHD is important in these patients and that further evaluation of management strategies is warranted.

1385

Physical activity measured with implanted devices predicts heart failure outcomes

C Linde[1]; A Tang[2]; MR Cowie[3]; T Bergemann[4]; WT Abraham[5]
[1]Karolinska University Hospital, Stockholm, Sweden; *[2]University of Ottawa, Ontario, Canada*; *[3]Royal Brompton Hospital, London, United Kingdom*; *[4]Medtronic, Mounds View, United States of America*; *[5]The Ohio State University, Columbus, United States of America*

Background: There is increasing evidence that physical activity (PA) levels have prognostic value in patients with chronic heart failure (HF). Purpose—The aim of this research is to assess PA as a surrogate endpoint for HF clinical outcomes in patients indicated for cardiac resynchronization therapy (CRT).
Methods: Data from 2,408 randomized patients with implantable cardioverter defibrillator (ICD) with or without CRT enrolled in the RAFT and REVERSE studies were pooled. The devices continuously measured and stored total daily active time (single-axis accelerometer). Average activity measured in minutes per day over a 30-day period at 1 and 6 months post-implant were examined. Statistical analyses were adjusted for age, LBBB, diabetes mellitus, ischemia, NYHA class, and diastolic blood pressure in a multivariable model. The main effect of PA and the interaction between PA and assignment to CRT was tested.
Results: Device data available from 2,249 patients were analyzed (65 ± 10 years; 82% men; left ventricular ejection fraction, $23 \pm 6\%$; 4% NYHA I, 81% NYHA II, 15% NYHA III). Of these patients, 404 died and 445 experienced a HF hospitalization (35 ± 20months of follow-up). For the analysis of 1 month PA, 359 patients were removed due to death prior to 1 month ($n = 25$) or insufficient device data ($n = 334$) and for 6 month data, 350 patients were removed due to death prior to 6 months ($n = 70$) or insufficient device data ($n = 280$). Results are shown in the table. The 1 month PA, 6 month PA and the change in PA were statistically significant predictors of time to death and improvement in NYHA. Both the 1 month PA and 6 month PA were statistically significant predictors of time to death or HF hospitalization. The interaction between PA and assignment to CRT was not statistically significant in any of the models. PA at 6 months was 5 minutes higher per day in patients randomized to CRT, after adjustment for 1 month PA levels (P=0.36).
Conclusions: Physical activity measured at either 1 or 6 months after ICD +/- CRT implantation predicted death or HF hospitalization as well as mortality and improvement in NYHA class in patients with chronic HF.

		Death or HF hospitalization	Death	Improvement in NYHA class at 12 months
Activity variable*	n	HR (95% CI); P-value	HR (95% CI); P-value	OR (95% CI); P-value
One month PA	1890	0.96 (0.94-0.98); $P < 0.0001$	0.94 (0.92-0.95); $P < 0.0001$	1.02 (1.01-1.04); P=0.004
Six month PA	1899	0.96 (0.94-0.98); $P < 0.0001$	0.93 (0.91-0.95); $P < 0.0001$	1.03 (1.02-1.05); $P < 0.0001$
Change in PA from 1 to 6 months	1880	0.98 (0.96-1.01); P=0.24	0.97 (0.94-1.00); P=0.04	1.03 (1.00-1.06); P=0.03

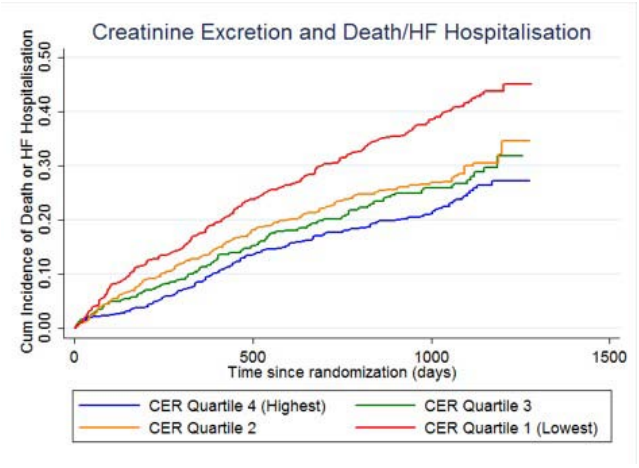
*Adjusted for baseline variables

1386

Clinical and prognostic value of spot urinary creatinine in chronic heart failure

J M Jozine Ter Maaten[1]; A P Maggioni[2]; R Latini[3]; S Masson[3]; G Tognoni[3]; L Tavazzi[4]; A P Voors[1]; K Damman[1]
[1]University Medical Center Groningen, Groningen, Netherlands; *[2]ANMCO Foundation For Your Heart, Florence, Italy*; *[3]IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy*; *[4]Maria Cecilia Hospital, Cotignola, Italy*

Background: Twenty-four-hour urinary creatinine excretion is an established marker of muscle mass in heart failure and other populations. Spot urine creatinine might be an easy obtainable, cheap marker of muscle wasting and prognosis in heart failure (HF) patients.
Purpose: This study aimed to identify patient characteristics associated with low urinary creatinine in morning spot urine and investigate its association with clinical outcome.
Methods: Spot urinary creatinine concentration was measured in 2130 patients included in the GISSI-HF trial. We evaluated the prognostic value of urinary creatinine and its relation with clinical variables.
Results: Median spot urinary creatinine was 0.80 (IQR 0.50 to 1.10) g/L. Lower spot urinary creatinine was associated with older age, smaller height and weight, higher NYHA class, worse renal function and more frequent spironolactone and diuretic use (all $P < 0.02$). During a median follow-up of 2.8 years, 655 patients (31%) experienced the combined endpoint of all-cause mortality or HF hospitalization. Lower urinary creatinine was independently associated with an increased risk of all-cause mortality or HF hospitalization (Hazard ratio (HR): 1.59 [1.21-2.08] per log decrease, P=0.001), and all-cause mortality (HR: 1.75 [1.25-2.45] per log decrease, P=0.001).
Conclusion: Lower urinary creatinine, measured in morning spot urine in patients with chronic HF, is associated with worse renal function, smaller body size, more severe HF and is independently associated with an increased risk of all-cause death and HF hospitalization. Urinary creatinine might therefore be a valuable marker to assess muscle wasting and heart failure severity.



Creatinine excretion and outcome

1387

Heart failure with mid-range ejection fraction in patients admitted to internal medicine departments: findings the RICA registry.

P Salamanca-Bautista[1]; ME Guisado-Espartero[2]; O Aramburu-Bodas[1]; A Conde-Martel[3]; JL Arias-Jimenez[1]; P Llacer-Iborra[4]; JC Arevalo-Lorido[5]; JM Cerqueiro-Gonzalez[6]; MF Davila-Ramos[7]; F Epelde-Gonzalo[8]; J Perez-Silvestre[9]; JA Satue-Bartolome[10]; A Martin-Ezquerro[11]; L Manzano[12]; M Montero-Perez-Barquero[13]
[1]University hospital Virgen Macarena, Internal Medicine, Seville, Spain; *[2]Infanta Margarita Hospital , Internal Medicine , Cabra (Córdoba), Spain*; *[3]University Hospital Dr. Negrin, Internal Medicine , Las Palmas, Spain*; *[4]Hospital of Manises, Internal Medicine , Manises (Valencia), Spain*; *[5]Hospital of Zafra, Internal Medicine , Zafra (Badajoz), Spain*; *[6]University Hospital Lucus Augusti, Internal Medicine , Lugo, Spain*; *[7]University Hospital Nuestra Señora de la Candelaria, Internal Medicine , Santa Cruz de Tenerife, Spain*; *[8]Parc Tauli Hospital, Internal Medicine , Sabadell (Barcelona), Spain*; *[9]University General Hospital of Valencia , Internal Medicine , Valencia, Spain*; *[10]University Hospital of Fuenlabrada, Internal Medicine , Fuenlabrada, Spain*; *[11]University Hospital of Burgos, Internal Medicine , Burgos, Spain*; *[12]University Hospital Ramon y Cajal, Internal Medicine , Madrid, Spain*; *[13]University Hospital Reina Sofia, Internal Medicine., Cordoba, Spain*

On behalf of: RICA investigators group

Introduction: In the recently published European guidelines, a new term has been defined for patients with heart failure (HF) and ejection fraction (EF) between 40-49%: HF with mid-range EF (HFmrEF). Limited data exist on the epidemiology, treatment and short or long-term prognosis of these patients.
Purpose: To describe clinical characteristics, treatment and prognosis in patients with heart failure and mid-range ejection fraction (HFmrEF) discharged after admission for decompensation.
Method: We prospectively included and followed 2753 patients admitted with acute heart failure to Internal Medicine units. They were classified according to ejection fraction into three strata: reduced, EF $<40\%$ (HFrEF); mid-range EF 40-49% (HFmrEF); and preserved EF $\geq 50\%$ (HFpEF). Clinical, echocardiographic and laboratory data, and treatment at discharge were collected, and the three groups were compared. A multivariable analysis was performed to assess the relationship between EF and outcomes at 30 days and one year.
Results: A total of 10.2% of patients had HFmrEF. They were more likely to be men and to have a history of chronic kidney disease and higher levels of NT-proBNP than those with HFpEF. Compared to patients with HFrEF, they had less ischaemic aetiology and chronic obstructive pulmonary disease, and a higher proportion of atrial fibrillation and hypertension. In HFmrEF, the use of beta-blockers, aldosterone antagonists and antiplatelet drugs was lower than in HFrEF, but the use of calcium channel blockers and anticoagulants was higher. There were no differences between groups in 30-day and 1-year readmission rates. However, patients with HFrEF had significantly higher 1-year mortality (28%) than patients with HFmrEF and HFpEF (20% and 22%, respectively, $p < 0.001$, Figure 1).
Conclusion: Clinical characteristics and treatment among patients with heart failure admitted to Internal Medicine departments differ depending on EF. Prognosis of patients with HFmrEF is closer to that of HFpEF, and survival is better than in HFrEF.

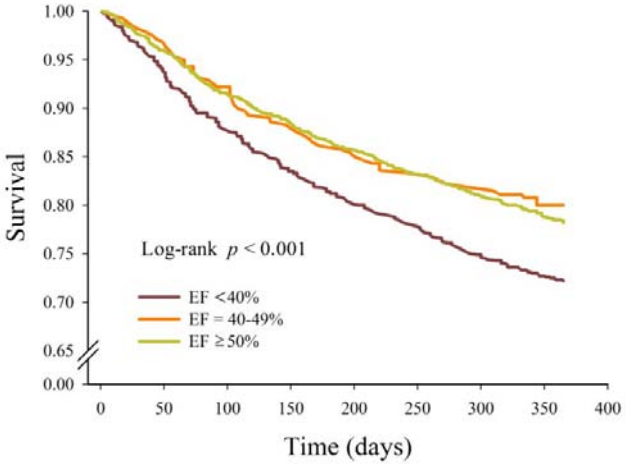


Figure 1

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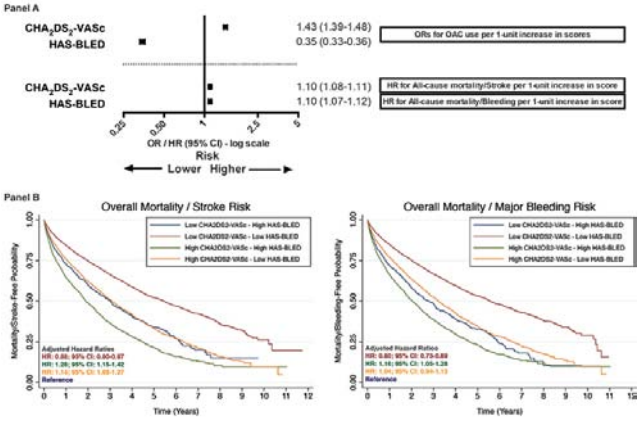
Impact of CHA2DS2-VASc and HAS-BLED on oral anticoagulant use and outcomes in patients with atrial fibrillation and concomitant heart failure: an analysis of 22,055 patients from the SwedeHF

G Savarese[1]; L Friberg[2]; M Rosenqvist[2]; U Dahlstrom[3]; LH Lund[1]
[1]Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden; *[2]Danderyd University Hospital, Department of Clinical Sciences, Stockholm, Sweden*; *[3]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*

Background. Atrial fibrillation (AF) is common in patients with heart failure (HF). HF is a risk factor for both thromboembolic and bleeding events in patients with AF.
Purpose: To assess the impact of CHA2DS2-VASc and HAS-BLED scores on oral anticoagulant (OAC) use and outcomes in AF patients with concomitant HF.
Methods: We included patients with AF, HF and no previous valve replacement enrolled in the Swedish Heart Failure Registry. High and low CHA2DS2-VASc and HAS-BLED scores were defined as above/below median. Multivariable logistic regression analysis was performed to assess the association between CHA2DS2-VASc and HAS-BLED scores and OAC use. Kaplan Meier curves and adjusted Cox regression models including 28 baseline variables including OAC use were fitted to evaluate the association between CHA2DS2-VASc (adjusted also for

HAS-BLED) and HAS-BLED (adjusted also for CHA2DS2-VASc) scores and two composite outcomes: all-cause death and stroke; and all-cause death and major bleeding.
Results: Of 22,055 included patients, 37% were female, 48% had ejection fraction (EF) ≤40%, 26% EF 40-49% and 26% EF≥50%. Mean age was 76 + 10 years. In total, 12,756 (58%) patients were receiving OACs. The use of OACs was significantly predicted by CHA2DS2-VASc and HAS-BLED scores. In particular, the likelihood of OAC use was 1.43-fold increased for each 1-unit increase in CHA2DS2-VASc and 2.4-fold decreased (odds ratio 0.35) for each 1-unit increased in HAS-BLED (Fig Panel A). The risk of death/stroke increased progressively from low CHA2DS2-VASc / low HAS-BLED, to low/high, high/low and high/high. The risk of death/major bleeding increased progressively from low/low, to high/low, low/high and high/high. Additionally, 1-unit increase in HAS-BLED and CHA2DS2-VASc determined the same increase in risk of death/major bleeding and death/stroke, respectively (Fig Panel A,B).
Conclusions. In this nation-wide HF registry, only 58% of patients with AF received OAC. Thrombotic and bleeding risk affected both OAC use and outcomes in the expected directions. However, bleeding risk inappropriately affected decision making more than stroke risk.



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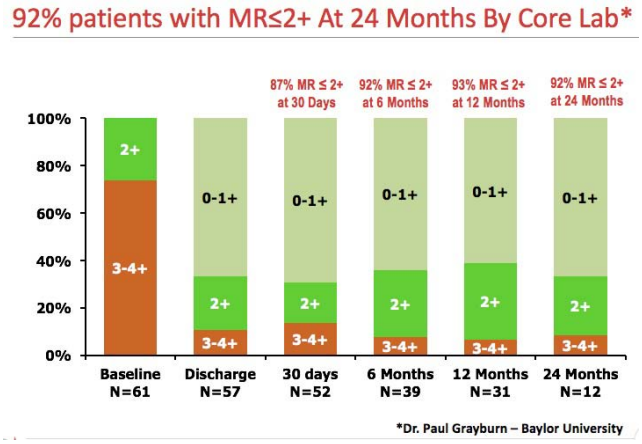
Multicentre trial of a transfemoral mitral valve reconstruction system

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

Background/Objective: The Cardioband system enables percutaneous implantation of an adjustable "surgical-like" mitral annuloplasty ring using a transseptal approach. The aim of this multicentre study was to evaluate the feasibility, safety and outcomes up to 24 months of Cardioband implantation in patients with secondary mitral regurgitation (MR).
Methods: Between February 2013 and June 2016, 61 high-risk patients with significant secondary MR were enrolled at 11 European sites. All patients were screened by a heart team using echocardiography and cardiac CT.
Results: Mean patient age was 72 ± 7 years, 44 were males (72%). Mean EuroSCORE II was 7.1%. At baseline, 53 patients (86%) were in NYHA functional class III-IV, with a mean left ventricular ejection fraction of 33 ± 11%. Device implantation was achieved in all patients but one. At discharge, 51 patients (90%) had MR ≤2+. After device cinching, an average 30% reduction in septolateral mitral annular diameter was observed (from 37 ± 4 mm to 26 ± 4 mm; p < 0.01). Thirty-day mortality was 3.3% (2 patients; death adjudicated as unrelated to the device). MR ≤2+ was measured in 29/31 (93%) and 11/12 (92%) patients at 12 and 24 months of follow-up, respectively (Figure). NYHA functional class I-II was present in 26/33 (79%) and 11/15 (77%) at 12 and 24 months, respectively. A significant improvement was observed at 12 months in the mean quality of life score (Minnesota Living with Heart Failure Questionnaire) from 41 to 23 (p < 0.01); and mean six-minute walk distance improved from 299 m to 372 m (p < 0.01).
Conclusions: Transseptal mitral repair with the Cardioband device resulted in significant MR reduction by reconstruction of the mitral annulus. Thirty-day mortality is comparable to other transcatheter mitral procedures. MR severity reduction and clinical benefit remain stable up to 24 months.



Distribution of MR severity over time

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Hypoxic-hyperoxic preconditioning: a novel technique for myocardial protection against ischemia-reperfusion injury

I A Mandel[1]; Y K Podoksenov[2]; S L Mikheev[3]; Y S Svirko[3]; N O Kamenschikov[3]; I V Sukhodolo[4]; V M Shipulin[3]
[1]Federal Scientific Clinical center of specialized methods medical care and medical technology, Anesthesiology and intensive care, Moscow, Russian Federation; *[2]Cardiology Research Institute, Anesthesiology and intensive care, Tomsk, Russian Federation*; *[3]Cardiology Research Institute, Cardiovascular surgery, Tomsk, Russian Federation*; *[4]Siberian State Medical University, Morphology and general pathology, Tomsk, Russian Federation*

Introduction: Preconditioning by moderate hypoxia, as well as hyperoxia, constitute an effective drug-free method to amplify adaptive response to various negative influences of cardiopulmonary bypass (CPB) during cardiac surgery.
Purpose: The study aimed to assess the mechanisms and impact of hypoxic-hyperoxic preconditioning (HHP) on functional state of myocardium in patients with coronary artery disease (CAD) undergoing cardiac surgery with CPB.
Methods: The study included 120 patients randomly assigned to two groups: 61 patients received hypoxic-hyperoxic preconditioning before the CPB (HHP group) and 59 patients were not preconditioned (control group). Coronary artery bypass grafting with CPB for multivessel coronary artery disease was performed in all cases (2014-2016). Safety control of the preconditioning procedure included ECG monitoring, invasive blood pressure control, cardiac output, pulse oximetry, capnography, cerebral oximetry, measurement of anaerobic threshold. To monitor acid-base status and metabolic state we measured saturation of arterial and mixed venous blood, lactate and glucose level, plasma pH every 10 min during the HHP procedure; calculated oxygen consumption and delivery indices, ratio between venous-to-arterial carbon dioxide difference to arteriovenous oxygen content difference (ΔPCO2/C(a-v)O2).
Results and Conclusion: Spontaneous sinus rhythm recovery after CPB was registered more often in HHP group - 34 (55.7%) comparing to controls - 19 (32.2 %), X^2=8.38, p = 0.015. The length of inotropic support in early postoperative period was significantly lower in HHP group comparing to control group (12 [9; 15] vs 28 [24; 32] hours, U=98.1, p = 0.001). Mechanical ventilation time in HHP group was 10 [7.25; 15] hours comparing to 16 [10; 24] hours in control group, (U=34.2, p=0.023). Thus, hypoxic-hyperoxic preconditioning with individual parameters selection based on anaerobic threshold in patients with CAD before the main stage of cardiac surgery enhances adaptive response to the surgical stress, facilitates sinus rhythm recovery and provides a faster recovery after surgery.

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Effect of ivabradine in patients with heart failure with preserved ejection fraction: the EDIFY randomised placebo-controlled trial

M Michel Komajda[1]; R Isnard[1]; A Cohen-Solal[2]; M Metra[3]; B Pieske[4]; P Ponikowski[5]; AA Voors[6]; F Dominjon[7]; C Henon-Goburdhun[7]; M Pannaux[7]; M Bohm[8]

[1]AP-HP - Hospital Pitie-Salpetriere, University Pierre & Marie Curie Paris VI, Dept of Cardiology, Paris, France; *[2]UMR-S942, Paris Diderot University, Sorbonne Paris Centre, Lariboisiere Hospital, Department of Cardiology, Paris, France*; *[3]University of Brescia, Department of Cardiology, Brescia, Italy*; *[4]Campus Virchow, Charite University, Department of Cardiology, Berlin, Germany*; *[5]Medical University and Centre for Heart Diseases, Military Hospital, Department of Heart Diseases, Wroclaw, Poland*; *[6]University of Groningen, Groningen, Netherlands*; *[7]Institut de Recherches Internationales Servier (IRIS), Suresnes, France*; *[8]Universitatskliniken des Saarlandes, Klinikum fur Innere Medizin III, Homburg, Germany*

On behalf of: for the prEserveD left ventricular ejection fraction chronic heart Failure with ivabradine studY (EDIFY) Investigators.

Funding Acknowledgements: It is funded wia grants from SERVIER France

Background. Heart failure with preserved ejection fraction (HFpEF) is prevalent, but no treatment has yet shown to reduce morbidity or mortality in these patients. Elevated heart rate is a predictive factor of worse outcomes and increased mortality in patients with heart failure, including in HFpEF.

Purpose: In this proof of concept, randomised, double-blind placebo-controlled trial, we assessed whether heart rate (HR) reduction with ivabradine improves diastolic function, exercise capacity and reduces NT-proBNP in patients with HFpEF.

Methods: EDIFY (prEserveD left ventricular ejectIon fraction chronic heart Failure with ivabradine study) included chronic HFpEF patients in NYHA class II-III, in sinus rhythm, with a HR $\geq$ 70 bpm, plasma NT-proBNP $\geq$ 220 pg/mL (BNP $\geq$ 80 pg/mL), LVEF $\geq$ 45% and echocardiographic evidence of diastolic dysfunction. Ivabradine (or matching placebo) was titrated to a target dose of 7.5 mg twice daily. Patients were followed for 8 months on the change in three co-primary endpoints: E/e' on Doppler echocardiography, 6 minutes walking distance and plasma level of NT-proBNP.

Results: A total of 179 patients were randomised to ivabradine (n = 95) or placebo (n = 84). One hundred and seventy one patients (87 versus 84) were evaluated for the three co-primary endpoints. Ivabradine reduced HR (-12.1 bpm, SD 8.9) more than placebo (-4.3 bpm, SD 9.8) with a mean between group difference at 7.7 bpm (90% CI -10 to -5.4, $p < 0.0001$). No statistically significant changes were observed in any of the co-primary endpoints. Mean E/e' increased from 13.1 (SD 4.7) to 14.0 (SD 4.9) with ivabradine and decreased from 13.9 (SD 6.9) to 13.0 (SD 5.4) with placebo (mean between group difference 1.4, 90% CI 0.3 to 2.5, p = 0.135); the mean distance on 6MWT (m) changed with ivabradine vs placebo from 305.4 (SD 92.2) to 309.7 (SD 102.8) and from 308.7 (SD 83.3) to 316.6 (SD 100.8), respectively (mean between group difference -3.8, 90% CI -19.1 to 11.6, p = 0.882) and geometric mean plasma NT-proBNP (pg/mL) increased marginally in both groups (from 447.7 to 483.4 with ivabradine and from 390.1 to 420.9 with placebo (geometric mean ratio 1.0 90% CI 0.9 to 1.2, p = 0.882). Ivabradine was well tolerated with no significant safety concern

Conclusion: In patients with HFpEF, HR reduction with ivabradine did not improve E/e', exercise capacity and did not reduce NT-proBNP plasma levels. These findings do not support the use of ivabradine in HFpEF.

Moderated Poster session 4 - Basic Science

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stem cells improve kidney function and remodelling in CRS type II

C Castellani[1]; G Vescovo[2]; P Cortiana[1]; M Pozzobon[3]; G Thiene[1]; R Tavano[4]; M Fedrigo[1]; A Angelini[1]
[1]*University of Padua, Dept. of Cardiac,Thoracic and Vascular Sciences, Padua, Italy*; [2]*Hospital S.Antonio, Padua, Italy*; [3]*University of Padua, Padua, Italy*; [4]*University of Padova, Dip. of Biomedical Sciences, Padua, Italy*

Background: we investigate the effects of human amniotic fluid stem cells (hAFS) and rat adipose tissue stromal vascular fraction GFP-positive cell (rSVC-GFP) therapy in a monocrotaline rat model of cardio-renal syndrome type II (CRSII).
Methods: RHF was induced by monocrotaline (MCT) in Sprague-Dawley rats.Three weeks later, four million of hAFS or rSVC-GFP were injected via tail vein. BNP, sCreatinine, kidney and heart NGAL and MMP9, sCytokines, kidney and heart apoptosis (TUNEL technique) were studied. Stem Cells (SC) engraftment was detected with immunofluorescence.Results: SC treated rats showed a significant reduction of serum NGAL and Creatinine (NGAL 335.6 ± 92.60 ng/mL sCrea 0.36 ± 0.05 pg/mL,p = 0.01) compared to CHF rats. In both hAFS and rSVC-GFP group, kidney protein expression of NGAL was significantly lower than in CHF group (SC 2.6*106 ± 1.2*106 vs CHF 5.1*106 ± 1.5*106 A.U., p = 0.0008) and similar to that to controls. In both hAFS and rSVC-GFP treated rats, we observed a substantial number of SC engrafted in the medulla and differentiated in tubular cells. Apoptosis was significantly decreased (hAFS 10.29 ± 10.81 and rSVC-GFP 24.82 ± 25.19 cells/mm2, p = 0.05 vs CHF) and similar to controls (9.85 ± 7.2 cell/mm2). TUNEL-positive cells were mainly located in the kidney medulla. Pro-inflammatory cytokines were down regulated in SC-treated groups (p = 0.05 vs CHF) and similar to controls. In SC treated rats, kidney and heart tissue NGAL was not complexed with MMP9 as showed in CHF groups, suggesting inhibition of MMPs activity.Conclusion: SC treatment produced improvement in kidney function in rats with CRSII. This may be the results of tubular regeneration due to SC engraftment, decrease tubular cells apoptosis and mitigation of pro-inflammatory milieu. Reduction of NGLA-MMP9 complexion mainly to decrease MMPs activity with prevention of further negative heart remodelling

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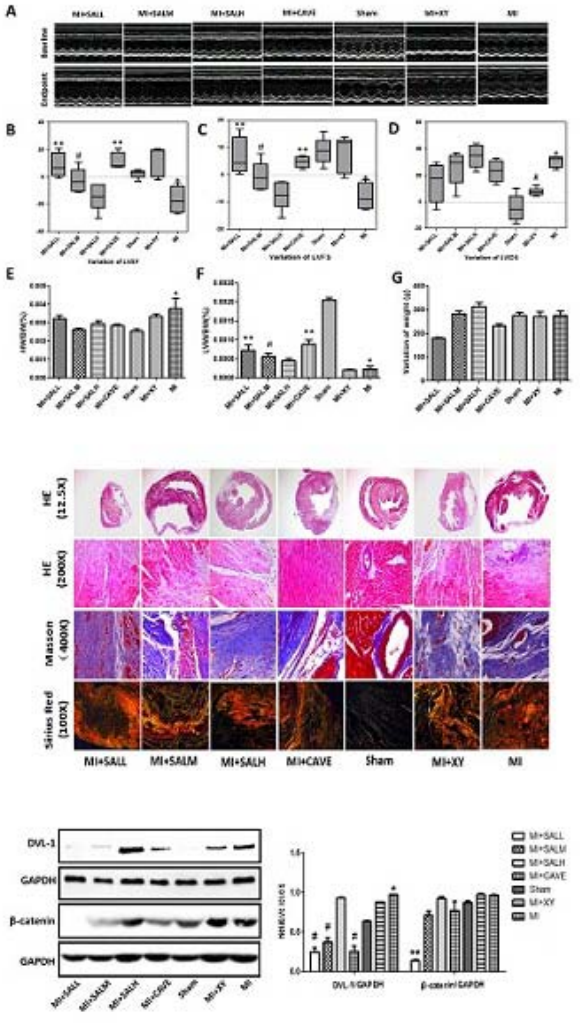
The cross-talk of Salidroside on TGF-beta / Smads and Wnt /beta-catenin signaling pathway in the myocardial fibrosis after AMI in rats and its correlation with Galectin3

J Jie Ma[1]; LH Ma[1]
[1]*Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China People's Republic of*

On behalf of: Departament of TCM,Fuwai Hospital
Funding Acknowledgements: Beijing Administration of Traditional Chinese Medicine "3 + 3" Fundation

Background: TGF-β /Smads pathway is currently recognized as the most important myocardial fibrosis signaling pathway. As another signaling pathway, Wnt/β-catenin also involves the proliferation and fibrosis. Recent experimental studies reported the role of salidroside on the angiogenesis and apoptosis in liver fibrosis, while there was no evidence of salidroside on preventing or reversing myocardial fibrosis, and the underlying mechanism remain unclear.
Methods: The myocardial infarction model of male Sprague-Dawley rats were made by ligation of the left anterior descending coronary artery. Rats were randomly divided into Salidroside low dose (12mg·kg-1)28 days or 56 days group, salidroside high dose (36mg·kg-1)28 days or 56 days group, Carvedilol group, the sham group and the control group. The cardiac function was evaluated by M-mode Doppler echocardiography. HE staining, Masson staining and Sirius red staining analysis were performed and observed for myocardial pathophysiological changes. Expression of TGF-β/Smads and Wnt/β-catenin signaling pathway was detected by Immunohistochemistry and Western blot. The level of Galectin-3 (a novel biomarker of myocardial fibrosis) in peripheral blood was detected by ELISA.
Results: The degree of myocardial fibrosis of the experimental group was attenuated significantly (P < 0.05). Sirius red staining showed that the ratio of collagen I/III in experimental group was significantly lower than that in model group, while it was a slight higher in carvedilol group (P>0.05). Western blot and RT-PCR analysis showed that the expression levels of P-Smad3 and Smad2/Smad3 were down-regulated (P < 0.05) as well as DVL-1 and β-catenin in Wnt/β-catenin Pathway, but the protein/mRNA level of Smad7 did not change significantly in the experimental group, especially in salidrosidehigh dose group (28 days). Compared with the control group, the expression of Smad3 and β-catenin in the non-infarcted myocardium of the group [(17.90 ± 1.36) vs (37.66 ± 2.21), (8.14 ± 1.23) vs (12.39 ± 1.37)μm2] were significantly lower (P < 0.05) with positively correlation. In addition, the number of the experimental group had a lower level of Gal-3 in the peripheral blood both on the 28th day and the 56th day (P < 0.05).
Conclusions: These results show for the first time that Salidroside can improve myocardial fibrosis in ventricular remodeling in experimental AMI rats. It functions through the mechanism of regulation of TGF-β / Smads and Wnt / β-catenin signaling pathway simultaneously. The positive regulation of TGF-B by the crosstalk pathway of Smad3 and β-catenin may serve as a potential target for anti-fibrosis.



COMBINED

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Identification and isolation of cycling cardiomyocytes for single cell analysis

M Marion Baniol[1]; J Panula[1]; EL Graham[1]; E Lazar[1]; O Bergmann[2]
[1]Karolinska Institute, CMB, Stockholm, Sweden; *[2]Dresden University of Technology, Dresden, Germany*

Funding Acknowledgements: Karolinska Institutet, the Swedish Research Council, the Ragnar Söderberg Foundation, Åke Wiberg Foundation, and Jeanssons Foundations

Purpose: One of the major goals in cardiac regeneration research is to replace lost ventricular tissue with new cardiomyocytes. However, the rate of cycling cardiomyocytes in adult hearts is too low to efficiently compensate for the loss of functional myocardium in heart disease. We hypothesize that cardiomyocyte proliferation is tightly controlled by regulatory mechanisms that can be reactivated to promote endogenous repair after heart injuries. Unequivocal identification of cycling cardiomyocytes is a fundamental requirement for the investigation of these mechanisms.
Methods: We used preexisting as well as novel transgenic mouse models based on the FUCCI (Fluorescent Ubiquitination-based Cell Cycle Indicator) system to discriminate cycling cardiomyocytes (S/G2/M phases, green fluorescent nuclei) from non-cycling ones (G0/G1 phases, red fluorescent nuclei). In mice ubiquitously expressing FUCCI constructs, we used the myocyte-specific perinuclear marker Pericentriolar Material 1 (PCM-1) to distinguish cardiomyocyte from non-myocyte cells in the heart tissue.
Results: The presented transgenic strategy proved to be efficient for the identification of cycling cardiomyocytes in neonate, juvenile and adult mouse hearts in vitro and in vivo. The validity of transgenes expression was verified in both systems with immunohistochemistry by co-localization of cardiomyocytes and cell cycle markers with FUCCI fluorescence. The FUCCI system allowed us to confirm previous observations of a gradual decrease in the number of cycling CM during the neonatal period. By combining CM isolation from FUCCI mice neonatal hearts and FACS sorting, we were able to separate cycling from non-cycling CM populations, while preserving total RNA integrity, therefore providing a suitable source for downstream analysis such as bulk RNA-seq and single cell RNA-seq.
Conclusion: Strategies that allow to unambiguously identify cycling cardiomyocytes in vitro and in vivo provide important tools to study the regulation of cardiomyocyte proliferation. With the FUCCI system we seek to identify novel molecular targets that could promote cardiomyocyte proliferation, by using transcriptome profiling (RNA-seq) of isolated cycling cardiomyocytes.

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Gemfibrozil, a potential preconditioning agent to reduce ischemia/reperfusion injury after heart transplantation

K Kalman Benke[1]; CS Matyas[1]; AA Sayour[1]; A Olah[1]; BT Nemeth[1]; M Ruppert[1]; G Szabo[2]; I Hartyanszky[1]; Z Szabolcs[1]; B Merkely[1]; T Radovits[1]
[1]Semmelweis University, Heart and Vascular Center, Budapest, Hungary; *[2]University of Heidelberg, Department Of Cardiac Surgery, Heidelberg, Germany*

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Background: The incidence of terminal heart failure is continuously growing, thereby increasing the clinical importance of its definitive treatment, heart transplantation (HTX). Pharmacological activation of soluble guanylate cyclase (sGC) and increased cGMP-signalling have been reported to have cardioprotective effects, however, potent sGC activator compounds are still under development. Gemfibrozil, a widely used lipid-lowering fibrate has recently been shown to exert sGC activator properties in vitro.
Purpose: The aim of the present study was to investigate whether pharmacological preconditioning of donor hearts with gemfibrozil could protect against ischemia/reperfusion injury and preserve myocardial function in a heterotopic rat heart transplantation model.
Methods: Donor Lewis rats received p.o. gemfibrozil (150mg/kg BW) or vehicle for 2 days. The hearts were explanted, stored for 1h in cold preservation solution, and heterotopically transplanted. 1h after starting reperfusion, left ventricular (LV) pressure-volume relations and coronary blood flow were assessed to evaluate early post-transplant graft function. Additional histological and molecular biological measurements were performed.
Results: After 1h reperfusion, LV contractility (at 140µl LV volume: LV systolic pressure: 125 ± 14 vs. 77 ± 8mmHg, $p < 0.05$; dP/dtmax: 3260 ± 398 vs. 2116 ± 240mmHg, $p < 0.05$; active relaxation (dP/dtmin: -2233 ± 263 vs. -1184 ± 151mmHg, $p < 0.05$) and coronary blood flow (2.7 ± 0.2 vs. 2.1 ± 0.2ml/min/g, $p = 0.03$) were significantly improved in the gemfibrozil pretreated hearts when compared to controls. Additionally, gemfibrozil treatment effectively reduced nitro-oxidative stress and apoptosis and improved the cGMP-signalling (increased plasma/cardiac cGMP levels) in HTX.
Conclusion: Pharmacological preconditioning with gemfibrozil reduces ischemia/reperfusion injury and preserves graft function in a rat HTX model, which could be the consequence of enhanced myocardial cGMP-signalling. Gemfibrozil might represent a useful tool for cardioprotection in the clinical setting of HTX surgery in the future.

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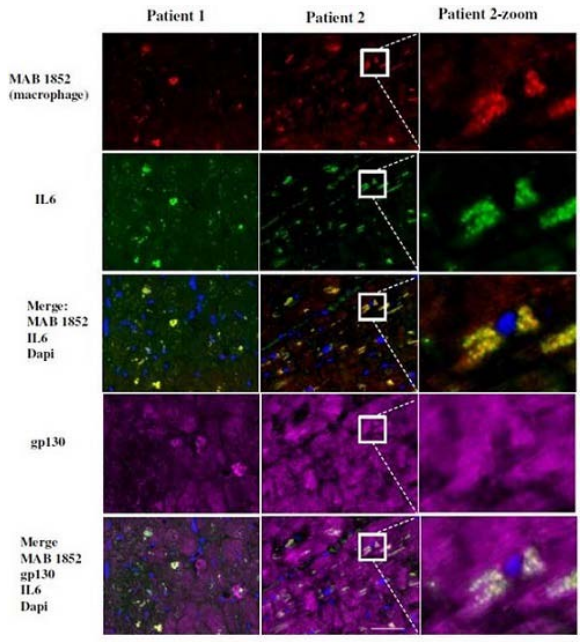
Role of global and local inflammation in cardiac fibrosis induced by aortic stenosis and its impact on LV function in patients referred for surgical aortic valve replacement

A Arnault Galat[1]; AG Guellich[1]; DB Bodez[1]; SG Guendouz[1]; SM Moutereau[2]; EB Bergoend[2]; JPC Couetil[2]; NB Benhaiem[2]; SH Hue[2]; LH Hittinger[2]; JLDR Dubois-Rande[2]; DM Mothy[3]; LL Lipskaia[2]; CR Radu[2]; TD Damy[2]
[1]University Hospital Henri Mondor, Cardiology, Creteil, France; *[2]University Hospital Henri Mondor, Creteil, France*; *[3]University Hospital of Poitiers, Poitiers, France*

Background: Cardiac fibrosis is associated with LV remodeling and dysfunction in aortic stenosis (AS). The pathological process is still unclear.
Objectives: To determine the fibrosis load in patients with AS and to explore its correlation with regional contractile dysfunction, serum and local cardiac inflammation.
Methods: Patients with AS referred for surgical valve replacement were prospectively and onsecutively included. They all had an echocardiography including 2D-strain. Blood samples were collected to measure cytokines and biomarkers using Luminex bead-based assays. Persurgical myocardial biopsy of the antero-septo-basal segment (S1) was performed on which serial sections were stained with Sirius red to quantify collagen. Immunostaignings using specific antibodies against macrophage, glycoprotein (gp) 130 and IL-6 were also performed. Patients were divided into tertiles according to fibrosis (TF1 to 3).
Results: Fifty-eight patients were included. Mean age was 73 ± 11 years. Mean aortic stenosis peak-velocity and mean gradient were respectively 4.5 ± 0.8 m/s and 54 ± 15 mmHg. Mean global strain was -15 ± 4% and mean S1 strain was -10 ± 6 % which was strongly correlated to fibrosis load ($R=0.83$, $p < 0.0001$). TF3 was associated with higher mortality ($p = 0.009$), higher serum CRP and IL-6 and lower gp130 compared to the other tertiles ($p < 0.05$). IL-6 and gp130 were expressed in the heart respectively in the plasma membrane of macrophages and in the cytoplasm of cardiomyocyte.
Conclusion: Cardiac fibrosis is associated with LV dysfunction, poor outcome and inflammation in AS. Strategies aiming at preventing inflammation might be considered to decrease or limit the progression of cardiac fibrosis in patients followed for AS.



Macrophage, IL-6 and gp130 staining

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Cardiosphere-derived cells exert anti-inflammatory effects and confer structural and functional benefits in rat hearts with autoimmune myocarditis

E Leventaki[1]; M Nana[1]; N Poulianitis[1]; C Chris Kapelios[1]; S Vakrou[1]; D Rontogianni[1]; AS Manolis[1]; D Perrea[1]; JN Nanas[1]; K Malliaras[1]
[1]*Laiko University General Hospital, Athens, Greece*

Background: Cardiosphere-derived cells (CDCs) exert cardioprotective, regenerative, immunomodulatory and anti-fibrotic effects in hearts with ischemic and non-ischemic cardiomyopathy. The effect of CDC therapy in the setting of myocarditis (a potentially lethal inflammatory cardiomyopathy without effective treatment options) is unknown.
Purpose: To investigate the effects of global intracoronary infusion of CDCs in rats with autoimmune myocarditis.
Methods: CDCs were grown from hearts explanted from healthy Lewis rats using established protocols. 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 underwent lateral thoracotomy and were subsequently randomized to undergo global intracoronary infusion of 500,000 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 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 and interstitial fibrosis were assessed by whole-field microscopy. Myocardial T cell infiltration was assessed by immunohistochemistry.
Results: Histologically-confirmed autoimmune myocarditis was induced in 14/14 rats. Left ventricular ejection fraction was comparable on day 1 ($83\pm2\%$ vs $83\pm4\%$, $p=0.95$) and on day 10 ($81\pm6\%$ vs $79\pm6\%$, $p=0.57$) between the 2 groups. Intracoronary CDC infusion prevented myocarditis-induced functional depression and resulted in significantly higher left ventricular ejection fraction at 3 weeks post-infusion compared to controls ($85\%\pm1\%$ vs $61\pm8\%$, $p=0.02$). Infusion of CDCs resulted in dramatic attenuation of lymphomononuclear infiltration ($8\%\pm7\%$ vs $22\pm4\%$ of the myocardium, $p=0.03$), profound reduction of interstitial fibrosis ($17\%\pm13\%$ vs $38\pm2\%$, of the myocardium, $p=0.01$) and significant reduction of T cell infiltration (30.4 ± 29 vs 125.8 ± 49 per high power field, $p<0.01$) at 3 weeks post-infusion compared to controls.
Conclusions: Global intracoronary infusion of CDCs dramatically attenuates myocardial inflammation, fibrosis and T cell infiltration, while preserving systolic function in rats with autoimmune myocarditis.

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ERK1/2 autophosphorylation at threonine 188 in cardiac fibroblasts contributes to the maladaptive remodelling of the heart in response to chronic pressure-overload

OW Wiens[1]; E Nenad[2]; K Lorenz[1]
[1]*Leibniz Institute for Analytical Sciences -ISAS- e.V., Dortmund, Germany*;
[2]*University of Wuerzburg, Pharmacology, Wuerzburg, Germany*

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Introduction. The phosphorylation of the extracellular signal-regulated kinases 1 and 2 (ERK1/2) at threonine 188 (pERKT188) was identified as a trigger for pathological cardiac hypertrophy. Upon activation, ERK1/2 can dimerize and autophosphorylate at threonine 188, which leads to nuclear translocation and activation of nuclear ERK1/2 targets known to cause cardiac hypertrophy. The "gain-of-function" ERKT188D mutant, mimics autophosphorylation and has been shown to induce pathological cardiac growth.
Purpose: So far, the effect of ERK1/2 was analysed in cardiomyocytes. However, a human heart is mostly composed by non-cardiomyocytes, in particular cardiac fibroblasts, which are known to contribute to cardiac remodelling. For this reason, the impact of cardiomyocyte-specific expression of ERKT188D in an α-MHC promoter driven mouse model (αMHC-ERKT188D-tg) and ubiquitous expression through the CAG promoter (CAG-ERKT188D-tg) was analysed in vivo.
Methods: Transverse aortic constriction (TAC) was used as a model for pressure overload-induced cardiac hypertrophy and heart failure, which was analysed by echocardiography. The mRNA levels of heart failure markers as e.g. atrial natriuretic factor (ANF) and brain natriuretic peptide (BNP) were quantified by real-time PCR. Hematoxylin and eosin (H&E) and Sirius Red staining were used to analyse cell size and fibrosis. Cell proliferation was measured using the 3H-thymidine incorporation assay.
Results: In account of the reduced viability of CAG-ERKT188D-tg after TAC, mice were analysed after ten days already. Despite the short exposure to pressure overload, a non-significant but trend-setting increase in lung and heart weights was detected in CAG-ERKT188D-tg compared to αMHC-ERKT188D-tg or wild-type mice. In addition, echocardiographic analyses revealed a reduced ejection fraction and impaired fractional shortening, increased mRNA expression levels of ANF and BNP as well as an increase in cardiomyocyte size and fibrosis after TAC in CAG-ERKT188D-tg in comparison to the control mice. As these experiments suggest that pERKT188 impacts on cardiac integrity in fibroblasts, we analysed its effect on the proliferation of isolated neonatal rat cardiac fibroblasts by overexpressing ERK2T188D: indeed, by measuring 3H-thymidine incorporation, an increase of proliferation in ERK2T188D transduced cells was detected compared to controls. This result suggests that pERK2T188 is a trigger for fibroblast proliferation. We could confirm the involvement of pERK2T188 in fibroblast proliferation by the use of a peptide that interferes with pERKT188 by preventing ERK dimerization.
Conclusion: These preliminary results show that pERKT188 has – also via non-cardiomyocyte cells – an important impact on cardiac hypertrophy and heart function. Further experiments are needed to elucidate the exact role of pERKT188 in fibroblasts and cardiac remodelling.

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Remote ischemic conditioning improves post-ischemic cardiac function: the role of Neuregulin-1

O Hamza[1]; A Kiss[1]; P Pilz[1]; IF Goncalves[1]; M Inci[1]; D Santer[1]; F Nagel[1]; B Podesser[1]
[1]*Ludwig Boltzmann Cluster for Cardiovascular Research, Center for Biomedical Reasearch, Vienna, Austria*

Background: There is substantial evidence that remote ischemic conditioning (RIC) induced by short repeated episodes of ischemia and reperfusion (IR) on the arm is a clinically applicable method to protect the myocardium against acute IR injury. Neuregulin-1 (NRG-1), an endogenously produced polypeptide, is the ligand of cardiomyocyte ErbB receptors, with cardiovascular protective effects. Aims: The present study was aimed to investigate the effect of RIC on post-ischemic cardiac function in association/correlation with the plasma levels of NRG-1.
Methods: Adult male anaesthetized OFA-1 rats were subjected to 30 min left coronary artery occlusion followed by 21 days reperfusion and allocated to (1) sham operated (SOP, without occlusion; n=4); (2) IR ($n=6$) and (3) IR + RIC (3 cycles of 5 minutes of hindlimb ischemia, 5 minutes of reperfusion, started at 5th min of index ischemia; n=7). Functional parameters on the heart such as cardiac output (CO) and external heart work (EHW) were evaluated on an isolated erythrocyte-perfused working heart model. Cardiac pump function was evaluated by rise afterload from 30 to 170 mm Hg in 10 mm Hg steps while CO was recorded. Plasma level of NRG-1 was measured by ELISA. Results: Myocardial IR resulted in significant increase of left ventricle/body weight ratio compared to SOP group ($P<0.05$). This was in line with the reduction in CO (29.6 ± 1.6 ml/min/g heart vs. 43.7 ± 1 ml/min/g heart, $P<0.01$) and EHW (12.8 ± 0.3 ml mm Hg/g heart vs. 21.1 ± 0.7 ml mm Hg/g heart). The concentration of NRG-1 was significantly dropped following IR (2.1 ± 0.5 vs. 6.1 ± 0.6 ng/µl in SOP, $P<0.05$) as well as NRG-1 and CO positively correlated ($r2=0.51$, $P<0.001$, slope 2.6 ± 0.76). RIC markedly improved post-infarcted cardiac function compared to IR group (CO: 39.5 ± 1.6 ml/min/g heart and EHW: 17.8 ± 0.9 ml mm Hg/g heart, $P<0.05$, respectively) in association with enhanced NRG-1 levels (4.3 ± 0.5 ng/µl). Cardiac pump function was significantly impaired following IR (80 mm Hg: 24.4 ± 1.6 vs. 37.9 ± 1.4 in SOP, $P<0.01$) which was reversed by RIC (32.4 ± 2.0, $P<0.05$). Conclusions: We demonstrated for the first time that the improvement of post-infarcted cardiac function initiated by RIC is associated with the plasma levels of NRG-1. This findings might represent a novel cardioprotective mechanism of RIC mediates via the upregulation of NRG-1.

1400

Circulating miRNAs and BAG3-related Dilated Cardiomyopathy

R Toro[1]; M Saura[2]; D De Gonzalo-Calvo[3]; V Llorente-Cortes[3]; F Rosa-Longobardo[1]; C Rodriguez-Leal[4]; MD Mesa-Rubio[5]; A Mangas[4]; JL Zamorano[6]; C Zaragoza[7]
[1]*University of Cadiz, Medicine Department, Cadiz, Spain*; [2]*University of Alcalá, School of Medicine (IRYCIS), Department of Systems Biology (Physiology),, Madrid, Spain*; [3]*Cardiovascular Research Center (CSIC-ICCC), Research Institute Of The Sant Pau Hospital, Barcelona, Spain*; [4]*Hospital Puerta del Mar, Cadiz, Spain*; [5]*University Hospital Reina Sofia, Cardiology, Cordoba, Spain*; [6]*University Hospital Ramon y Cajal de Madrid, Cardiology, Madrid, Spain*; [7]*University Francisco de Vitoria/Hospital Ramón y Cajal Research Unit (IRYCIS), , Cardiology, Madrid, Spain*

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BACKGROUND: A new familial dilated cardiomyopathy (DCM) was recently found related to mutations in the antiapoptotic BAG3 gene. MicroRNAs (miRNAs) are

short non-coding RNAs playing significant roles in cardiac disease, including DCM, thus representing new potential targets of treatment. Circulating miRNAs have been proposed as potential biomarkers of cardiovascular disease. However, no previous study has evaluated the clinical association between BAG3-related DCM and circulating miRNAs.

Purpose: We aimed to evaluate whether the clinical association between BAG3-related familial DCM and the circulating miRNA profile may represent a new tool for the diagnosis and progression assessment of the disease.

Methods: Detailed clinical and echocardiographic information was obtained from 21 patients with familial DCM carrying the BAG3 mutation and 21 age-matched healthy subjects. RNA was isolated from peripheral blood and analysed using ultrasequencing. Bioinformatic analysis was performed to explore the potential molecular pathways related to the miRNA profile.

Results: To determine the miRNA profile in BAG3-associated DCM, the analysis of 1759 circulating miRNA was performed in symptomatic and asymptomatic patients with BAG3 mutation, and compared to healthy age-matched subjects. The expression profiles showed significant differences between controls and BAG3 mutation carriers: miRNAs 3191-3p, 6769b-3p, 1249-ep, 154-5p, 6855-5p, and 182-5p were at least 2-fold downregulated in patients compared to healthy subjects. Endogenous gene targets of these miRNAs are now under investigation, highlighting miR-182-5p,and its target Ankyrin G. No differences were observed in the circulating miRNA profile between symptomatic and non-symptomatic patients containing the BAG3 mutation.

Conclusions: miRNAs emerge as a novel tool to differentiate healthy subjects and patients with BAG3-related DCM. Of particular interest is the downstream analysis of endogenous miRNA targets, the Ankyrin G gene. Inhibition of Ankyrin G is related to sinus node dysfunction, atrial fibrillation, conductional abnormalities, and ventricular arrhythmias. Further investigation regarding the contribution of Ankyrin G and other target genes of the miRNA profile described in BAG3-related DCM will be a key step to deeply understand the contribution of miRNAs in the pathophysiology of familial DCM.

1401

Heart rate reduction opposes acute decompensation of chronic heart failure

N Peschanski[1]; M Lachaux[1]; N Harouki[1]; N Nicol[1]; JP Henry[1]; J Salzmann[2]; F Fougerousse[2]; V Richard[1]; C Thuillez[1]; P Mulder[1]
[1]Inserm U1096, Rouen University Medical School, Rouen, France; *[2]Institut de Recherche International SERVIER, Department of Cardiovascular Translational and Clinical Research, Suresnes, France*

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Background: Exacerbation of heart failure (HF), better known as acute decompensated HF, is associated with a rapid increase in heart rate (HR) and a further decrease in an already HF-related impaired cardiac function, which only partially recovers over time. However, whether HR reduction (HRR) limits the acute impairment and improves the cardiac recovery is unknown. Objective. We evaluated the effects of HRR induced by S38844 on cardiovascular dysfunction due to acute decompensation in rats chronic HF model.

Methods: Three months after coronary artery ligation, HF rats received water (control) or 1.8 g/kg NaCl (dissolved in 2.5 ml tap water PO) provoking acute decompensation. Left ventricular (LV) end-systolic pressure-volume (LVESPVR) and LV end-diastolic pressure-volume relation (LVEDPVR; Millar), cardiac output (CO, echocardiography), LV tissue perfusion (MBF; MRI) and coronary endothelial function (Ach induced relaxation; Mulvany) were assessed at 1 and 13 days after salt-loading (D1 and D13, resp.) and after S 3844 administration (starting 12 hours after salt-loading for 2.5 days; 12 mg/kg twice a day).

Results: In rats with HF, salt-loading provokes acute decompensation. Indeed, the HF related reductions of CO, MBF as well as LVESPVR were further reduced at D1, while LVEDPVR, was increased. Moreover, the HF-related impaired coronary relaxation was aggravated. Thirteen days after salt-loading, only CO partially recovered, but MBF, LVESPVR, LVEDPVR and coronary relaxation remained aggravated. As soon as 12 hours after administration, S38844 improved CO and MBF, increased LVESPVR and decreased LVEDPVR, while coronary relaxation was increased. Moreover, 11.5 days after interruption of S38844, CO, MBF, LVESPVR, LVEDPVR and coronary relaxation remained improved.

Conclusion: In chronic HF rats, salt-loading provokes immediately a further aggravation of cardiac and coronary dysfunctions, but only the aggravation of cardiac dysfunction only partially recovers over-time. S38844, starting 12 hours after salt-loading immediately re-establishes cardiac and vascular functions which all persist beyond the administration of S38844 and probably results from indirect effects provoked by the increase in MBF.

Left ventricular hemodynamics

Group	HF Control	HF + Salt (D1)	HF + Salt (D13)	HF + Salt + S38 (D1)	HF + Salt + S38 (D13)
CO (ml/min)	123±3	105±3*	117±5	125±3†	130±6
MBF (ml/min/g)	6.01±0.19	4.41±0.23*	4.51±0.23*	7.00±0.31†	6.46±0.42†
LVESPVR (mm/RVU)	15.4±0.4	11.3±0.9*	12.5±0.7*	16.7±1.3†	17.0±0.4†
LVEDPVR (mmHg/RVU)	1.76±0.12	3.19±0.18*	2.77±0.23*	1.99±0.34†	1.70±0.15†
Coronary Relax. (%)	55±1	27±5*	28±1*	79±2†	71±4†

*:$p < 0.05$ vs HF control: †: $p < 0.05$ vs HF + Salt (D1)

CLINICAL CASE CORNER 4 - CAD AND HEART FAILURE: A LIAISON DANGEREUSE

1402

Acute heart failure and cardiogenic shock induced by ruptured coronary arteriovenous fistula

J-H Ju-Hee Lee[1]; DH Bae[1]; KK Hwang[1]; MC Cho[1]
[1]*Chungbuk National University Hospital, Cardiology, Cheongju, Korea Republic of*

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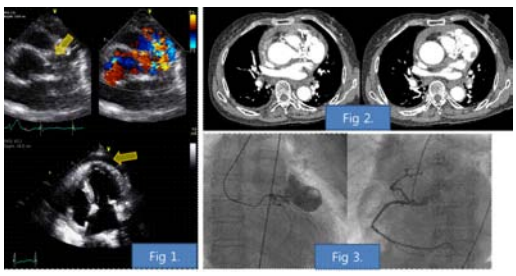
Case Summary: A 72-year-old woman was referred to emergency department from outside hospital with a diagnosis of septic shock. Her chief complaint was right upper quadrant abdominal pain for a day. Her BP was 84/64 mmHg and HR was 100/minute. Physical examination revealed hepatomegaly and tenderness at right upper quadrant abdomen. Laboratory tests were as follows: leukocytes 18390/μL; high sensitivity C-reactive protein 0.14 mg/dL; AST/ALT 483/212 IU/L; total bilirubin 0.34 mg/dL. Abdomen CT revealed diffuse wall thickening of gallbladder and perivascular low attenuation in liver. She had admitted infection department with IV meropenem and norepinephrine support under the diagnosis of cholecystitis. At 3rd hospital day, the patient was consulted cardiology department because she complained progressive dyspnea and chest X-ray revealed worsening pulmonary congestion. At that time, ECG showed T wave inversion on anterior leads and cardiac enzymes were slightly elevated: CPK 334 IU/L, CK-MB 18.0 ng/mL, troponin T 0.110 ng/mL. Echocardiography (Fig. 1) showed normal LV systolic function and no regional wall motion abnormality. But we can detect dilated abnormal vasculatures with continuous Doppler flow which is suggesting coronary arteriovenous fistula (CAVF). There was a small amount of pericardial effusion (PE) without hemodynamic significance, and it was reckoned decreased amount compared with previous abdomen CT. Chest CT revealed tortuous vasculature in intrapericardial space and aneurysmal dilatation of the abnormal vessels with thrombus (Fig. 2).
Questions: 1. What is your next plan? 2. What was the cause of elevated cardiac enzyme and changes on ECG and chest X-ray? 3. What caused her abdominal pain and shock? Was there real bacterial infection?
Clinical Course: Our impressions were as follows; 1) High cardiac output heart failure (HF) d/t CAVF, 2) Liver congestion d/t HF, 3) Incidentally detected PE, and we started medical therapy for HF. The patient's dyspnea was improved after the medical treatment and the vital signs were also stabilized. Coronary angiography revealed huge, dilated CAVF originated from both coronary arteries with internal filling defect (Fig 3). We continued conservative management for HF because of stable vital sign and decreased amount of pericardial effusion on the follow up echocardiogram. At 9th hospital day, the patient experienced sudden collapse and refractory hypotension despite full-dose of inotropics. The patient received CPCR and transferred to ICU. On bedside echocardiography, LV systolic function was normal and the amount of pericardial effusion was similar compared with previous day. At that time, we obtained 7cc of bloody pericardial effusion by echo-guided pericardiocentesis. Her vital signs were stabilized immediately, and 250cc of bloody fluid was drained during 24 hours. Our final diagnoses were; 1) Pericardial tamponade d/t ruptured CAVF, 2) High cardiac output HF d/t CAVF, 3) Liver congestion d/t HF. The patient underwent surgical closure of CAVF, and we detected ruptured aneurysmal vessel wall with blood clot.
Discussion: Although most of the patients who have small communications may be asymptomatic, myocardial ischemia or heart failure can be occurred depends on the amount of shunt flow. Although rupture of aneurysmal vessel is very rare complication of CAVF, it should be remembered that shock or cardiac arrest can be caused by small amount of blood.



1403

A life-saving plug: spontaneous closure of ventricular rupture by a coincident thrombus after stemi

VD Dornberger[1]; RB Buelow[2]; AH Hummel[3]
[1]*German Centre for Cardiovascular Research (DZHK), Greifswald, Germany*; [2]*University of Greifswald, Radiology, Greifswald, Germany*; [3]*University of Greifswald, Cardiology, Greifswald, Germany*

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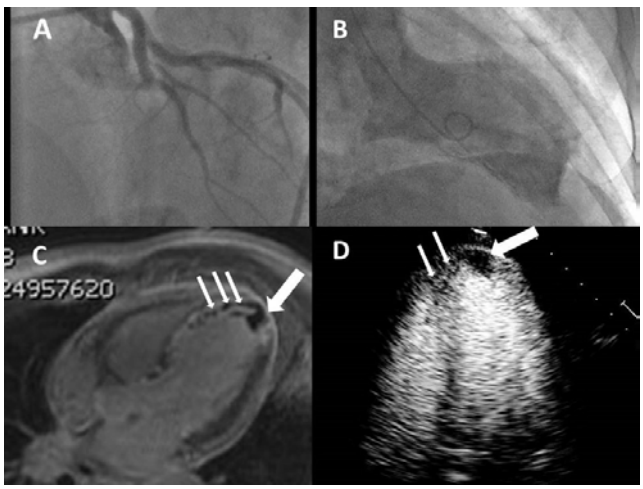
A 47 year old previously healthy male complained of pain in the left shoulder after physical strain. Four days later, the consulted general practitioner referred him to cathlab because of anterolateral ST segment elevation. Subsequently a verified proximal thrombotic occlusion of the LAD (panel 1A) was dilated and treated by bare metal stent implantation. Ventriculography showed a moderately reduced ejection fraction with all apical segments being hypokinetic. Images were characteristic for an apical left ventricular thrombus (panel 1B). A few hours after this angiography, the patient rapidly developed cardiogenic shock. Echocardiography revealed a hemodynamically relevant pericardiac tamponade. The patient was immediately transferred back to cathlab to perform a pericardiocentesis evacuating 500 ml of blood. The subsequent coronary angiography revealed no leakage of contrast agent. After the initial pericardiocentesis no further pericardial effusion occurred and the patient stabilized quickly. Myocardial contrast echocardiography suggested the ventricular thrombus to be plugged in a free wall rupture of the apex (arrow in panel 1C) and septal microvascular occlusions (MVO, small arrows). Contrast enhanced cardiac magnetic resonance imaging confirmed this perception (panel 1D). For further therapeutic purposes the patient was immediately sent to cardiac surgery where the thrombus was being removed and an epicardial patch plastic of the LV apex was successfully performed. The patient was able to return back to working life with only a mildly reduced ejection fraction.



1404

First series of ST-elevation myocardial infarction with acute coronary occlusion and coexisting Takotsubo Syndrome

L C Lars Christian Napp[1]; VL Cammann[2]; M Jaguszewski[2]; J Bauersachs[1]; T Luescher[2]; JR Ghadri[2]; C Templin[2]
[1]*Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany*; [2]*University Hospital Zurich, University Heart Center, Zurich, Switzerland*

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Takotsubo Syndrome (TS) accounts for an estimated 2% of acute coronary syndromes, and diagnosis was historically believed to require a "clean" angiogram without coronary artery disease (CAD). In contrast, we and others have shown that CAD is indeed present in a significant proportion of TS patients, however in

most cases in coronary arteries not supplying the myocardial segments affected by TS, and the majority of stenoses did not require immediate intervention. Here, we present 3 cases with the rare combination of ST-segment-elevation myocardial infarction (STEMI) with acute coronary artery occlusion and coexisting TS. Case 1: A 52-year-old woman was admitted after out-of-hospital resuscitation for ventricular fibrillation for 35 minutes. After 9 electrical shocks and amiodarone spontaneous circulation returned. ECG showed ST-segment elevation in leads II, III and aVF. Coronary angiography demonstrated thrombotic occlusion of the distal RCA with coexisting apical TS. RCA was treated with angioplasty without stenting. An IABP was inserted and neuroprotective hypothermia was started. The patient was extubated after 2 days, and after 5 days LV function had returned to normal. Case 2: A 62-year-old woman was admitted with acute chest pain and suspected STEMI. Before arrival at the hospital defibrillation for ventricular fibrillation and very short cardiopulmonary resuscitation (< 1 minute) had been necessary. ECG showed ST-segment elevation in leads II, III and aVF. Coronary angiography demonstrated thrombotic occlusion of the proximal RCA with coexisting apical TS. LVEF was 25%. RCA was successfully treated with angioplasty with a drug-coated balloon. CKmax was 1030 U/l. 3 days after PCI acute decompensation developed, which was treated with diuresis and non-invasive ventilation. The patient gradually recovered, and LVEF after 10 days was 51% without regional wall motion abnormalities. Case 3: A 75-year-old woman was admitted with acute chest pain and suspected STEMI. ECG showed ST-segment elevation in leads V5 and V6. Coronary angiography demonstrated thrombotic occlusion of a posterolateral branch of the RCX and coexisting midventricular TS. LVEF was 43%. RCX was treated with angioplasty. 7 days later LVEF had returned to normal, with residual hypokinesia of the posterolateral wall. In summary, as CAD may be present in TS cases as in other causes of acute heart failure, ST-segment-elevation myocardial infarction with coronary artery occlusion is a potential finding in TS patients. This finding is essential to consider for diagnosis and treatment of STEMI as well as of TS patients, who have ST-segment elevation in 50% of cases. In patients with suspected TS coronary angiography is mandatory in most cases, to uncover coexisting coronary lesions. In patients with STEMI, ventriculography is highly recommended to match the angiogram with wall motion abnormalities, in order to make the correct diagnosis.

1405

Coronary vasospasm; a silent enemy in orthotopic heart transplant.

A Arthur Omondi[1]; PV Spinett[1]; J Shin[1]
[1]*Montefiore Medical Center (Bronx), New York, United States of America*

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Introduction: The etiology of coronary vasospasm (CV) in orthotopic heart transplant (OHT) recipients is unknown. It has been reported in small series of patients, most of them associated with coronary vasculopathy (CAV) or allograft rejection in the setting of an acute coronary syndrome, malignant arrhythmia or cardiac arrest. We report a case of asymptomatic CV in a cardiac transplant recipient.
Case Report: A 37 year-old female with non-ischemic cardiomyopathy presented with transient dizziness 8 years post OHT. Her transplant was complicated by early rejection International Society for Heart and Lung Transplant (ISHLT) 2R/3A treated with steroids. 3 years post transplant she had antibody-mediated rejection with ISHLT 3R/3B treated with steroids, thymoglobulin and plasmapheresis. Left heart catheterization (LHC) 6 years post transplant revealed non-obstructive coronary artery disease (CAD). Biopsy 11 months prior was ISHLT 0. The disequilibrium was transient. Her home medications were tacrolimus, aspirin, atorvastatin, carvedilol and nifedipine. Electrocardiogram revealed normal sinus rhythm with old T wave inversions in leads V1 to V3. Laboratory work-up revealed hemoglobin 8.8 g/dL, white blood cell count 3.6k/uL, Troponin T < 0.01 ng/ml,pro B natriuretic peptide 482 pg/mL - within normal range. LHC revealed severe spasm in the mid to distal left anterior descending artery that was relieved with nitroglycerin.There was no evidence of CAV. Her nifedipine dose was increased to 120mg a day. At one-year follow-up she remained asymptomatic.
Discussion: Coronary vasospasm is rarely described as a cause of acute ischemic syndromes in patients following cardiac transplantation. CAV is a diffuse, accelerated form of CAD characterized by circumferential neointimal proliferation and luminal obstruction along the length of the epicardial coronary arteries of the transplanted heart. CAV is the main cause of late death following cardiac transplantation, due to accelerated atherosclerosis and coronary events. CV is often related to late atherosclerosis in the transplanted heart. Reported cases of CV were symptomatic with patients having angina, myocardial infarction, malignant arrhythmia and cardiac arrest. Our patient presented with transient dizziness and was asymptomatic at the time of catheterization. Autonomic nervous system and cardiac innervation are not essential mechanisms in patients with CV. Circulating catecholamines and/or other metabolic and hormonal products may play an important role in patients with CV. Conclusion. This is the first report of asymptomatic CV in a patient with OHT without CAV, as such, adds to the literature on both the presentation and pathophysiology, demonstrating that the etiology of CV can be related to other factors besides CAV or acute rejection. Clinicians should have a high index suspicion even in asymptomatic patients.

1406

Non-compact cardiomyopathy in elderly patient with acute primary anterior STEMI

M Maria Kercheva[1]; V Ryabov[1]; T Ryabova[1]; M Gulya[1]
[1]*State Research Institute of Cardiology of Tomsk, Tomsk, Russian Federation*

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A 70-year-old man was hospitalized with primary anterior STEMI 1h 40 min from the onset pain. Fibrinolysis was held through 2h 20min from the symptoms onset, but ECG did not reveal features of the reperfusion. Rescue PCI (through 4h 20min after the symptoms onset) revealed the occlusion in proximal third of left anterior descending artery and the drug-eluting stent was implanted. Then on the 6-th day of STEMI the recurrent acute pulmonary embolism was occurred. It was confirmed by the increasing of D-dimer to 426 ng/ml, appearance of orthopnea and the hemoptysis, bilateral hydrothorax, subfebrile condition. Simultaneously, the disease was complicated by the following arrhythmias ventricular and subventricular extrasystoles, paroxysms of ventricular tachycardia and atrial fibrillation. Implantable cardioverter-defibrillator was recommended and it was implanted. Transthoracic echocardiography revealed hypokinetic basal inferolateral segment and apex, EF was about 51%. It was not extended the left ventricular thrombus. The patient was discharged on dual antiplatelet therapy, β-blockers, statins, angiotensin-converting enzyme, rivaroxaban and amiodarone. Through 6 months echocardiography was repeated. Two-layered myocardial structure with a thin compacted epicardial layer and non-compacted endomyocardial layer with deep myocardial trabeculae were revealed, EF decreased to 45%, akinetic of apex, septal and anterior wall. The ratio between the trabeculated and normal myocardium was more in 2 times. The data of multi-spiral computed tomography confirmed of non-compacted myocardium. Decrease of global systolic function and bilayer structure of the left ventricular wall with a presence of lots of trabeculae was recorded. This form of cardiomyopathy is rare and usually associated with the failure of the myocardial compaction process at the embryogenesis, which leads to the persistence of numerous trabeculae at the left ventricular cavity. The main clinical manifestations are heart failure, arrhythmias and thromboembolism. The differential diagnosis included other cardiomyopathies (hypertrophic, dilatation), acute myocarditis, fibroelastosis, pericarditis, thrombosis of LV, hypertrophy of LV, tumor, pulmonary atresia, Bland-White-Garland syndrome, additional trabeculae. The case is unique, because this heart pathology has been detected in the elderly man. It is known, that non-compacted myocardium associated with the high frequency of sudden cardiac death at the youth. The specialty of this case was acute the single-vessel coronary artery lesion with probably thromboembolic genesis. It is important, that multi-spiral computed tomography was used in this case to confirm and demonstrate non-compacted myocardium, as long as MRI could not performed due to implanted cardioverter-defibrillator. Thus, non-compacted myocardium could be diagnosed in elderly patients, differential diagnosis of non-compacted myocardium included using of imaging technologies. In cases with contraindication to MRI, the multi-spiral computed tomography would be useful for confirmed echo findings

1407

Post-infarction mechanical complications: a successful case

AC Ana Catarina Gomes[1]; I Rangel[1]; A Marques[1]; S Alegria[1]; G Morgado[1]; I Joao[1]; I Cruz[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

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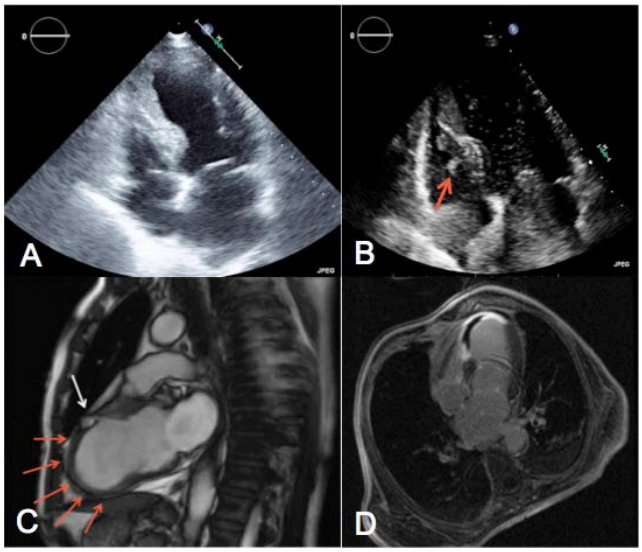
Introduction: Post-infarction mechanical complications are rare in the era of coronary revascularization but they should be suspected in the appropriate clinical context. Case Report: 62 year-old man with previous history of hypertension and smoking. He came to attention in June of 2016 due to progressive heart failure symptoms (at admission in NYHA class III). The previous history was unremarkable except for a sudden and prolonged episode of severe epigastric pain in the previous month. At admission he presented hypertensive profile, a IV/VI systolic murmur audible in all auscultatory areas and bilateral basal crackles. He was admitted for further study. The analysis were normal besides the T Troponin elevation: 129 ng/L in the first analysis and 136 ng/L in the next evaluation. The electrocardiogram showed sinus rhythm,100 bpm, slow R wave progression, ST-segment elevation and T-wave inversion in precordial leads. The thorax x-ray revealed bilateral interstitial infiltrate and mild bilateral pleural effusion. The thransthoracic echocardiogram showed mildly dilated left ventricle, thin ventricular septum, dyskinesia of all apical segments, medium segments of septum, anterior and inferior walls, hypokinesia of the basal segments of the same walls, severe systolic left ventricular dysfunction (LVEF of 23%), a huge sessile thrombus adjacent to the ventricular septum and anterior wall and a restrictive apical ventricular septum defect with a left-to-right shunt (Figures A and B). The patient was submitted to cardiac magnetic resonance which confirmed the echocardiographic findings described: wall motion abnormalities, a ventricular septal defect (VSD) surrounded by thrombus, lying

the septum and reaching the right ventricle hinge points (confirmed in the early gadolinium enhancement study) and also a small pseudoaneurysm in the anterior wall previously unnoticed (Figures C and D). The late gadolinium enhancement study showed transmural necrosis in the dyskinetic segments. The pre-surgery coronarography revealed an occluded median left anterior descending artery. During hospitalization he remained clinically stable, without electrical complications or need of hemodynamic support. He was submitted to successful surgical repair of the VSD and a single left mammary artery to left anterior descending artery bypass. He was discharged on the 4th post-surgery day and has remained in NYHA class II, under medical therapy. Discussion: Imaging techniques are essential for diagnosis of mechanical complications. Cardiac magnetic resonance is particularly helpful in anatomic diagnosis and functional evaluation, adding prognostic information and guiding patient's management. Conclusion: Although rare, multiple post-infarction complications can occur. Late surgical approach is beneficial in clinical stable patients.



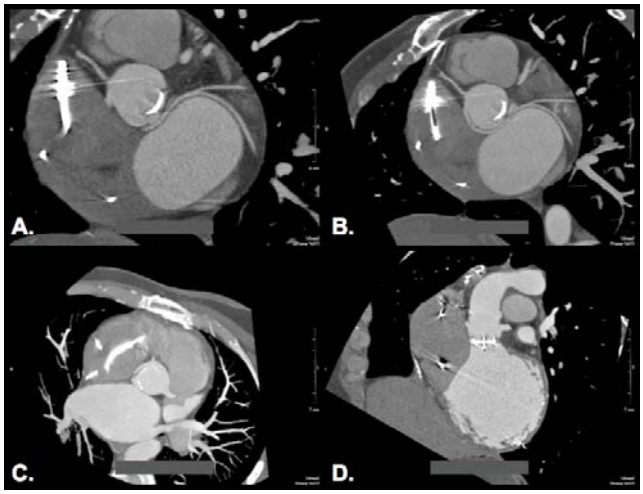
1408

Abnormal origin of the left circumflex artery a GUCH patient mystery solved after 15 years.

M Rozanska[1]; O Olga Mozenska[1]; K Jaworski[2]; DA Kosior[1]
[1]Clinical Hospital of the Ministry of Internal Affairs, Cardiology and Hypertension, Warsaw, Poland; *[2]Institute of Cardiology, The Second Department of Coronary Artery Disease, Warsaw, Poland*

Funding Acknowledgements: SERVIER

Introduction and case description. In recent years, the remarkable improvement in survival of patients with congenital heart disease (CHD) has led to a continuously growing number of grown-up patients with CHD (GUCH). We present a case of a GUCH patient in whom omission of the coronary arteries (CAs) imaging before cardiac surgery for patent ductus arteriosus (PDA) and severe aortic regurgitation (AR) led to catastrophic consequences. Description of the problem. In 1999, a 23-year-old male patient with history of PDA and severe AR underwent cardiothoracic surgery for his CHD. During the procedure, there was a sudden aortic annulus rupture what resulted in extension of cardiopulmonary bypass duration and need to eventually replace the aortic valve (AV). Intraoperative TEE showed signs of massive infero-lateral myocardial infarction (MI). Left circumflex artery (LCx) ligation during the rescue AV replacement was therefore suspected. After 3 months of hospitalization the patient left the hospital with new AV and iatrogenic heart failure (HF) with reduced left ventricular ejection fraction (LVEF) of 20%. Questions. 1.Was LCx ligation the only possible cause of the massive infero-lateral MI? 2.Should coronary artery assessment be obligatory for GUCH patients prior to interventions? Answers and discussion. 1)Our patient in the following years slowly deteriorated and in January 2014, the Heart Team met to discuss possible options for further treatment. Cardiac computed tomography (CT) was performed as a part of pre-procedural planning. It revealed a surprising finding of LCx being fully patent and originating from the proximal part of the right coronary artery (RCA). Apparently, in 1999 LCx was not ligated, but the lack of knowledge about its anomalous origin resulted in improperly given selective cardioplegia. The ectopic origin of the LCx is a well-recognized variant and considered the second most common coronary anomaly. It can be found in approximately 0.37-0.7% of all patients. The anomalous LCx most commonly arises from a separate ostium within the right sinus or, as it was in our case, directly from the proximal portion of the RCA. 2)Based on the currently available data, ESC practice guidelines recommend routine CAs assessment in valvular heart disease only to diagnose coronary artery disease (CAD) if any of the following is present: history of CAD, suspected myocardial ischemia, LV systolic dysfunction or if patients are men aged over 40 years or postmenopausal women or if they have at least one cardiovascular risk factor. At the time of surgery, none of the above-mentioned situations were present in our case. According to the ESC guidelines in patients with PDA cardiac CT is indicated when additional quantification of LV volumes or evaluation of pulmonary artery anatomy are required. Cardiac catheterization is indicated when PAP is high on echo for estimation of pulmonary vascular resistance. At the time of surgery, also none of the above-mentioned situations were present in our case. So, even though back in 1999 neither of the cited ESC guidelines were available, today going step by step with the guidelines, one can easily imagine such clinical scenario. Conclusions and implications for clinical practice. Our case shows that even in the era of big data, large clinical trials and great guidelines to follow, some GUCH patients remain very challenging. They keep the requirement for individualization of medical therapy, since behind every GUCH patient there is an individualized clinical history and unique coexistence of congenital cardiac defects.



Cardiac CT

1409

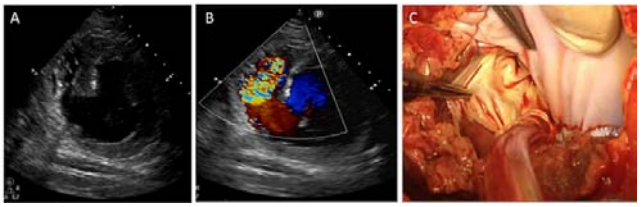
ECMO as bridge to surgery in post-infart ventricular septal defect

A Pardo Sanz[1]; S Del Prado Diaz[1]; J Lopez Menendez[2]; C Lozano[1]; M Plaza[1]; JM Monteagudo[1]; M Jimenez Mena[1]; M Sanmartin[1]; J Roda Stuart[2]; JL Zamorano[1]
[1]University Hospital Ramon y Cajal de Madrid, Department of Cardiology, Madrid, Spain; *[2]University Hospital Ramon y Cajal de Madrid, Cardiac Surgery Department, Madrid, Spain*

Funding Acknowledgements: SERVIER

A 72 year-old patient arrived to the emergency department in cardiogenic shock with a three-days history of chest pain and dyspnoea. On physical examination blood pressure of 55/34 mmHg, sinus tachycardia, hypoperfusion and a V/VI pansystolic murmur panfocal were remarkable. EKG showed established an inferior myocardial infarction. Echocardiogram revealed a large ventricular septal defect (2,2 cm) in the basal inferior septum (Image 1, Panel A and B) with bidirectional shunt, moderately depressed left ventricular function and very dilated and dysfunctional right ventricle. Cardiac catheterization showed triple vessel disease, severe distal left coronary artery stenosis, occluded left anterior descending artery from the ostium, severe circumflex stenosis and dominant right coronary artery with subtotal distal lesion with diffuse disease of posterior descending artery. Despite of increasing doses of inotropes and vasopressors and circulatory support with intra-aortic balloon pump patient remained in refractory cardiogenic shock. Therefore peripheral veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was implanted without complications achieving hemodynamic stability. Hypoxemia was corrected and hepatic and renal function improved. After ten days under ECMO support surgical repair was planned. Double coronary artery bypass (saphenous vein graft to left anterior descending artery, and saphenous vein graft to ramus intermedius artery) without

extracorporeal circulation was performed. Afterwards, the patient was cannulated for cardiopulmonary bypass, and the aorta was cross-clamped. Myocardial protection was achieved with intermittent cold blood cardioplegia. Through a posterior left ventriculotomy, ventricular septal rupture was completely closed with a large bovine pericardium patch (Image 1, Panel C). ECMO could be removed and thansesophageal echocardiogram confirmed no residual defect. Post-infarct ventricular septal defect after primary angioplasty development is an infrequent (0,2-0,3%) but usually lethal complication whose mortality reaches up to 90%. Timing of the surgical approach remains controversial due to the difficult balance between maintaining hemodynamic stability and waiting for infarcted necrotic tissue to organised. Usually rapid hemodynamic deterioration limits surgical delay and leads to early repair, frequently unsuccessful, and directly related to mortality rate. VA-ECMO offers circulatory support as bridge to ensure appropriate maturation and fibrosis of infracted tissue, allowing the deferral of surgery. When compared to other assist device, ECMO could be quickly and easily implanted in a crash and burn patient and additionally contribute to improve oxygenation in cardiogenic shock and allows to renal and hepatic recover.



Post-infart ventricular septal defect

THE VERY BEST FROM CLINICAL CASES - 2

1449

Familial left ventricular non compaction with LV apical thrombus and concominant paroxysmal atrial fibrillation antiocoagulated with NOAC, with thrombus resolution on follow-up

A Alexander Valerievitch Nossikoff[1]; G Lazarova[1]; A Atanasova[1]; T Donova[1]
[1]*University Hospital "Lozenets", Cardiology, Sofia, Bulgaria*

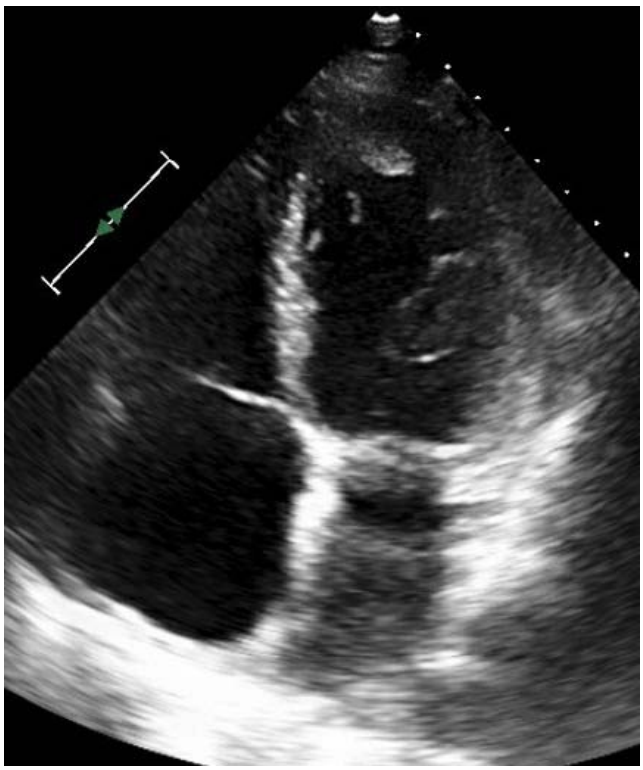
Funding Acknowledgements: SERVIER

Introduction. 58-year old female was referred to our department due to shortness of breath and paroxysmal nocturnal dyspnoea in the last 2 weeks. Her history was remarkable of total right mastectomy followed by chemo- and radiotherapy 2 years ago. She was considered to be cancer-free at present and recently treated for pneumonia. Her 38-year old son was diagnosed with dilatative cardiomyopathy with left ventricle (LV) apical thrombus few years back.

Diagnosis and treatment: Physical examination was unremarkable except for bilateral basal crackles and lower limb pitting oedema. EKG showed normal sinus rhythm and precordial T-wave inversion. Echocardiography revealed severely depressed LV systolic function with ejection fraction of 28% and global longitudinal strain of -7,8. The LV showed typical morphological features of left ventricular non-compaction (LVNC) with multiple trabeculations and deep intrabecular recesses and prominent apical thrombus. We commenced guideline based treatment with iv heparin, ACE, beta-blocker and iv furosemide with rapid improvement. She was offered long term treatment with Vitamin K antagonist (VKA), which she refused, despite all the risks explained, as she did not want to be INR monitored. EKG telemetry revealed paroxismal atrial fibrillation with 3 episodes of about 30 second duration. Her CHADSVASC2 was 3 and her HASBLED score was 1. We offered novel oral anticoagulant (NOAC) treatment as alternative and explained that although appropriate for her atrial fibrillation, NOACs have not been studied in LV thrombosis setting and are off-label. She decided to go for NOAC despite the lack of clinical data explained. Her creatinine clearance was 83ml/min estimated by Cockroft-Gault. She was discharged on bisoprolol 5mg, perindopril 2.5mg, furosemide 40mg and rivaroxaban 20mg all once daily. The LV thrombus was in place and unchanged at the time of discharge of follow up transthoracic echocardiogram. On follow up at 3, 6, 12 months she was clinically stable and her LV thrombus was fully resolved and there were no signs of systemic embolism. The echocardiography of her son was reviewed and was showing same typical features of LVNC, so this was now considered a case of familial LVNC and we offered echocardiography screening to other family members. Her 30-year old daughter was screened, but showed no features of LVNC.

Discussion: NOACs have not been studied in LV thrombosis and remain off-label and not recommended by guidelines in this setting. However, there have been several case reports published, describing patients with LV thrombus treated with NOACs (mainly rivaroxaban), most of them after anterior myocardial infarction, showing thrombus resolution at follow up.

Conclusions and implications for clinical practice: In patients with LV thrombus and LVNC, who refuse VKA or when it is not possible to monitor INR, NOACs may prove as valuable alternative. Off-label NOAC therapy could and probably should be considered in cases of LV thrombosis when there is no possibility of VKA treatment and indications for long term anticoagulation. Of note, we suggest that echocardiographic screening in LVNC may identify other affected family members.



A4 view - prominent thrombus in LV apex

1450

Dilated cardiomyopathy as a result of powerlifting and anabolic agents use

A Galyavich[1]; Z Galeeva[1]; L Baleeva[1]; E Safina[2]; M Browne[1]
[1]*Kazan State Medical Univ, Kazan, Russian Federation*; [2]*Interregional Clinico-Diagnostic Center, Kazan, Russian Federation*

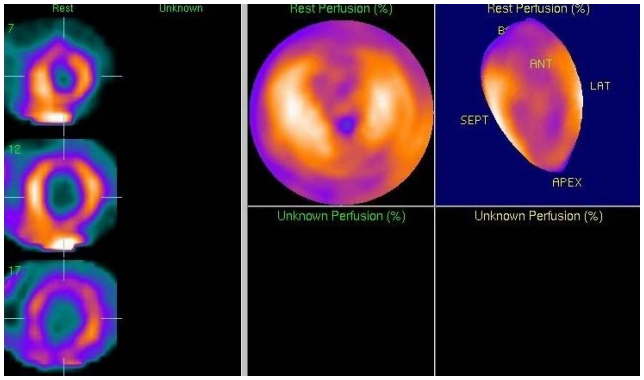
Funding Acknowledgements: SERVIER

Introduction. Dilated cardiomyopathy (DCM) may be caused by an array of external factors including heavy physical exercise (sports, such as powerlifting) coupled with taking supplements, particularly anabolic agents. Case report description. Patient Kh., a 42 years old male was admitted to inpatient care on 12.08.2016 with chief complain of periodic increase in blood pressure (BP) (systolic BP up to 180-200 mmHg), followed by dizziness, nausea, palpitations, and shortness of breath which were associated with significant physical exertion. He has been a body builder for more than 20 years with a history of taking supplements (anabolic agents) for 10 years. High blood pressure and shortness of breath during intense physical activity were noticed within the last year. Physical Assessment: Height 186 cm, weight 145 kg, body mass index 41.9. The patient is in a stable condition, with blood pressure (BP) of 170/110 mmHg, heart rate (HR) 98/min, heart sounds rhythmic with no murmurs. EKG: see PDF file. Echocardiography: Diffuse left ventricular hypokinesis with ejection fraction (EF) by Simpson's method of 33%. Left atrial volume 135 ml. The thickness of the posterior wall of the left ventricle was 14 mm, the thickness of the interventricular septum was 14 mm, moderate mitral and mild tricuspid regurgitation. Systolic pulmonary artery pressure of 39 mmHg. Computer Tomography (CT): coronary arteries calcium score 138; left coronary artery 138, right coronary artery 0. Myocardial perfusion imaging (at rest) with Technetium-99m: diffuse left ventricular hypokinesis, left ventricular end-diastolic volume 380 ml (N 81-121 ml), left ventricular ejection fraction 25% (N 50%-64%), moderately disseminated areas of hypoperfused regions in the myocardium of left ventricle. Laboratory values: Hemoglobin 195 gr/l; Red blood cells (RBC) 6.1 x 1012/l; Hematocrit (Ht) 59.3%,

Erythrocyte sedimentation rate (ESR) 0.5 mm/h; Total serum cholesterol 4.6 mmol/L (N < 5.2 mmol/L); Creatinine 133 umol/dL (N < 115 umol/dL); GFR (MDRD) 51 ml/min/1,73 m2; level of NT-proBNP not measured. After six weeks of therapy with Ramipril, Bisoprolol, Spironolactone and cessation of powerlifting and anabolic agents use his BP normalized to 125/80 mmHg. Echocardiography: EF was 38%, systolic pulmonary artery pressure was 32 mmHg, moderate mitral regurgitation, mild tricuspid regurgitation. Laboratory values: NT-proBNP 262 pg/mL (N < 125 pg/mL); Creatinine 100 umol/dL, GFR (MDRD) 71 ml/min/1,73 m2.

Problems or possible differential diagnosis: Hypertension in this patient was most likely associated with heavy weights lifting combined with anabolic agents use for a long period of time. These factors, together with the lack of proper hypertension management apparently led to the development of DCM and congestive heart failure. The ban on heavy lifting and cessation of anabolics use together with adequate therapy lowered patient's blood pressure, improved cardiac contractility, and substantially increased blood flow through the kidney and thus improved creatinine clearance rate. The peculiarity of this case report is the inadequately low level of NT-proBNP in response to substantially reduced left ventricular ejection fraction. The above discrepancy is suggesting irreversible changes in the heart muscle; therefore it is unlikely that contractile cardiac function will ever recover fully.

Conclusions and implications for clinical practice: DCM developed as a result of powerlifting combined with anabolic agents use. Elimination of both factors and adequate therapy stabilized the patient's medical condition. However, the relatively low level of NT-proBNP in response to reduced cardiac contractility is the most probable evidence of myocardial fibrosis.



Kh., 42 perfusion imaging

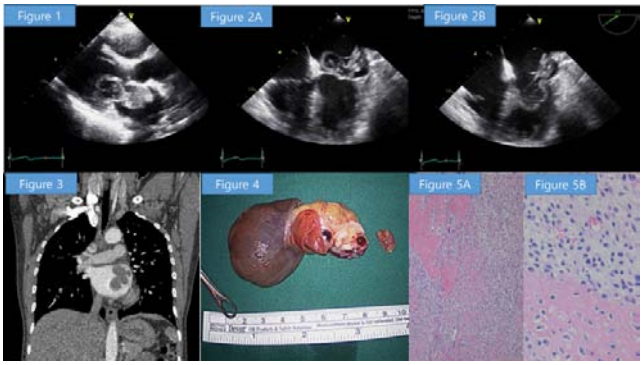
1451

Primary cardiac osteosarcoma

J-H Ju-Hee Lee[1]; DH Bae[1]; KK Hwang[1]; MC Cho[1]
[1]*Chungbuk National University Hospital, Cardiology, Cheongju, Korea Republic of*

Funding Acknowledgements: SERVIER

Case Summary: A 44-year-old women presented in June, 2013 with a 2-week history of chest tightness and shortness of breath to our cardiology outpatient clinic. She denied having hypertension, diabetes mellitus, dyslipidemia, tobacco use, or any family history of atherosclerotic disease. Her vital signs were as follows: blood pressure 124/80 mmHg, heart rate 64/minute, respiratory rate 24/minute, and body temperature 36.5. Physical examination revealed diastolic murmurs at the cardiac apex with grade 2/6. An electrocardiogram was normal and chest radiography showed no active lesion in lung. Transthoracic echocardiography (Fig. 1) showed a broad based mass filling the left atrium, which was attached to the posterior wall of left atrium nearby Q tip. The mass was composed of three different parts; thin-walled cystic portion (2.3 x 2.1 cm), solid portion with lobulating contours and heterogenic echogenicity (2.8 x 2.4 cm), and thick-walled mixed portion (3.7 x 2.9 cm). The mixed portion of the mass was protruding into the LV cavity during diastole and causing severe functional mitral stenosis. Trans-mitral mean diastolic pressure gradient was 5 mmHg and right ventricular systolic pressure was 38 mmHg. Transesophageal echocardiography (Fig. 2A and 2B) showed the heterogeneous feature of the mass more clearly. There was no evidence of invasion to pulmonary vein on transesophageal echocardiography. Thoracoabdominal computed tomography (Fig. 3) revealed an intracardiac mass occupying the left atrium without local invasion and there was no evidence of distant metastasis. X-ray studies did not identify any lesions in the skeletal system. The presumptive diagnosis was a benign cardiac tumor, such as an unusual type of left atrial myxoma and she was referred to cardiac surgeon for surgical removal of the mass. During the operation, we found a 7 x 5 x 4 cm sized huge mass, which have a hard part originated from nearby left atrial appendage and two cystic parts (Fig. 4). Complete excision of the mass and partial endocardiectomy was performed. In pathologic examination, the tumor consisted of proliferating pleomorphic spindle shaped cells suggested sarcoma and there were massive osteoid and chondroid materials produced by tumor cells (Fig. 5A and 5B). High mitotic activity and moderate cytologic atypia were detected and there were scattered hemorrhagic and necrotic foci. The tumor cells invades resection margin. Finally, the tumor was diagnosed as primary cardiac osteosarcoma, chondroblastic type. She received six cycles of systemic chemotherapy with doxorubicin and cisplatin. During 9 months of follow up, the patient remains healthy with no evidence of tumor recurrence.



1452

A successful multidisciplinary approach to pregnancy and delivery in pulmonary artery hypertension.

A Marocco[1]; G Giardina[1]; M Corda[1]; G Chessa[2]; P Spanu[3]; E Massidda[4]; L Pibiri[5]; D Zwicke[6]; M Porcu[1]
[1]*G. Brotzu Hospital, Cardiology, Cagliari, Italy*; [2]*G.Brotzu Hospital, Obstetrics and Gynaecology, Cagliari, Italy*; [3]*G.Brotzu Hospital, Anesthesiology, Cagliari, Italy*; [4]*G.Brotzu Hospital, Post-Surgical ICU, Cagliari, Italy*; [5]*G.Brotzu Hospital, Neonatology, Cagliari, Italy*; [6]*School of Medicine and Public Health-MCC, Pulmonary Hypertension Clinic, Wisconsin, United States of America*

Funding Acknowledgements: SERVIER

Pulmonary artery hypertension (PH) frequently affects women of childbearing age. Due to the very high maternal mortality risk, with most of the deaths occurring in the 3rd trimester and within the first 10 post-delivery days, pregnancy should generally be avoided in PH. We describe the case of a 39-year-old woman who was transferred to our department at the 25th week of pregnancy with a severe right heart failure. Since the 14th week she experienced increasing dyspnea, palpitations and generalized edema. She declined termination of the pregnancy after thorough counselling. The echocardiogram showed a dilated, hypertrophic and hypokinetic right ventricle, with a pulmonary artery (PA) systolic pressure 85 mmHg. The clinical status improved with diuretics. A team including cardiologists, obstetricians, anaesthesiologists, neonatologists and staff coordinators was made up. A complete diagnostic work-up for PH was performed: CT scan excluded pulmonary thromboembolism, no evidence of an intracardiac shunt, and blood tests were negative for vasculitis, thyroid disorder, connective tissue disease and thrombophilia. A right heart catheterization demonstrated a PA pressure of 60/42 mmHg, PCW pressure 11 mmHg, a severely elevated PVR at 16.9 WU, and significant reduction of the cardiac output, without any fall in the PA pressure or PVR after inhaled nitric oxide. A complete obstetrical and fetal evaluation excluded other relevant diagnoses. LMW heparin was prescribed. In the following days a step treatment with continuous infusion Epoprostenol and oral Sildenafil was initiated. The PDE-inhibitor was not tolerated after few weeks for flushing and hypotension. An elective caesarean section was successfully performed at the 31st week, under epidural anaesthesia. The baby demonstrated normal growth, development, and birth apgar scores. The patient was discharged from the ICU on day four. The postdelivery course was uneventful and the mother was discharged on day 30. At 6-month follow up, she was a WHO FC-II. This patient was diagnosed with severe PH in an advanced stage of pregnancy. Critical decisions, rapid escalation of the prostacyclin therapy, and the use of an experienced multidisciplinary team led to a successful delivery, with no complications for the mother or baby. The management of these infrequent, but critical situations, should be strictly handled by experienced tertiary referral centers.

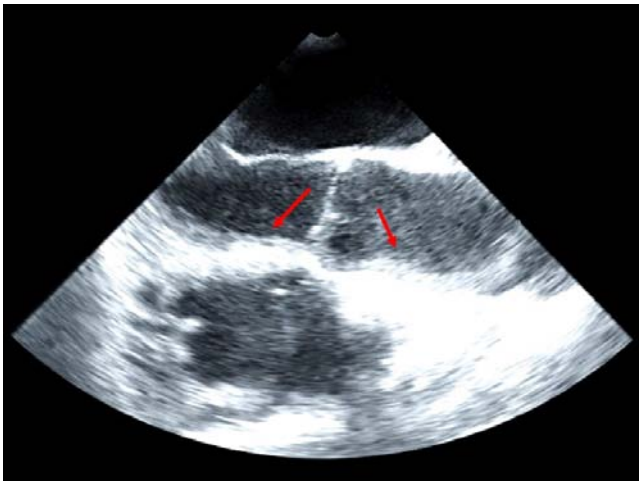
1453

Rapidly progressive, undifferentiated ventricular failure requiring urgent extra-corporeal membrane oxygenation

I Shiekh[1]; J Teng[2]; K Lam[1]; L Dembo[1]; RF Alcock[2]
[1]Fiona Stanley Hospital, Advanced Heart Failure and Cardiac Transplant Service, Perth, Australia; *[2]Royal Perth Hospital, Department of Cardiology, Perth, Australia*

Funding Acknowledgements: SERVIER

A normally healthy 57 year-old male presented with increasing headache, abdominal pain, chest pain and rapidly worsening dyspnoea. His background included long-standing systemic hypertension, well controlled with an angiotensin II receptor antagonist. On arrival he was tachycardic, hypertensive, tachypneic and hypoxic requiring oxygen supplementation. Physical examination was consistent with acute pulmonary oedema, with chest X-ray demonstrating bilateral, diffuse airspace changes. The ECG showed sinus tachycardia with 2mm up-sloping ST depression in the anterior leads. An urgent CT aortogram showed no aortic dissection and bedside transthoracic echocardiography revealed severe global left ventricular impairment with no valvular or pericardial abnormalities. Coronary angiography showed an anomalous right coronary artery origin arising from the left coronary cusp. Left coronary system did not show any significant disease. He was initially managed with intravenous diuretic, glyceryl trinitrate infusion and non-invasive ventilation. Within an hour of presentation he developed respiratory failure requiring intubation for ventilatory support. Progressive haemodynamic collapse followed despite escalating vasopressor support and intra-aortic balloon pump insertion. Veno-arterial extra-corporeal membranous oxygenation (VA-ECMO) was commenced, maintaining adequate perfusion and oxygenation. Transoesophageal echocardiogram showed persisting left ventricular impairment with substantial spontaneous echo contrast and early thrombus formation in the left ventricle and aortic root (Figure). Differential diagnoses at this point included fulminant myocarditis, hypertensive crisis, illicit drug use or stress-induced cardiomyopathy. Over the next 24-hours the patient remained haemodynamically stable, left ventricular function normalised on repeat echocardiography and VA-ECMO and inotropes were weaned. Within 48 hours the patient was extubated with no neurological deficit. A subsequent cardiac MRI showed no myocardial abnormality, normal perfusion and a left ventricular ejection fraction of 66%. The initial CT aortogram was reviewed in further detail, demonstrating a 23 x 20mm left-sided adrenal lesion, intensely active on Iodine-123 meta-iodobenzylguanidine (MIBG) scan. Plasma and urine catecholamine levels were consistent with a phaeochromocytoma. The patient was started on phenoxybenzamine prior to an uncomplicated adrenalectomy with histo-pathology showing no signs of malignancy. At 6-month review he was normotensive and remained well. Phaeochromocytoma classically presents with paroxysmal headaches, sweating, and tachycardia with intermittent or sustained hypertension. On rare occasions, presentation can be acute cardiogenic shock and pulmonary oedema. The precipitating episode can be life-threatening however ventricular dysfunction in catecholamine induced cardiomyopathy is typically resolves upon resection of the tumour. The exact mechanism is unknown; proposed causes include direct catecholamine myocardial toxicity, catecholamine-induced oxygen-derived free radical production or myocardial ischaemia from coronary arterial spasm. This case demonstrates the abrupt deterioration and rapid improvement in catecholamine induced cardiomyopathy secondary to phaeochromocytoma and highlights the importance of prompt escalation of resuscitation measures, including VA-ECMO, for patients with undifferentiated cardiogenic shock.



Transoesophageal Echocardiogram

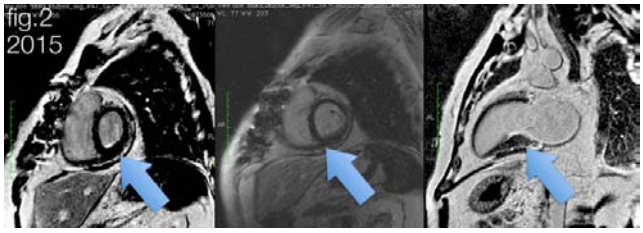
1454

Constrictive pericarditis due to rheumatoid arthritis 6 years follow up

M Dudek[1]; M Kaluzna-Oleksy[1]; J Migaj[1]; E Straburzynska-Migaj[1]
[1]Poznan University of Medical Sciences, 1st Cardiology Department, Poznan, Poland

Funding Acknowledgements: SERVIER

Pericarditis is one of the most common cardiac complications of rheumatoid arthritis(RA), it's present in 30-50% patients on post-mortem examination. However, in most cases it remains without hemodynamic consequences. Pericarditis occurs more often in male patients with active, seropositive RA. The constriction is thought to be chronic process persisting for years. A 59-year-old man with a 14-years history of seropositive RA was admitted to the cardiology department for evaluation of clinical status in stable state with well-controlled symptoms. RA was diagnosed in 2001. His past medical history include interstitial pulmonary fibrosis (2001), neoplastic process and tuberculosis were excluded. Additionally cholelithiasis, gastritis with H. pylori infection, osteoporosis with pathological, multi-level compression fracture and hip osteoarthritis, depressive syndrome, impaired fasting glucose and permanent AF. In Nov-2009, patient with decompensated congestive HF was admitted to the cardiology clinic. He was referred because of fatigue, increasing shortness of breath (NYHA IV) and chest pain. Examination revealed ascites and pitting oedema of lower extremities, elevated pressure in jugular veins, the irregular heart rate about 80-bpm, BP-120/70mmHg. The electrocardiogram (ECG) showed atrial fibrillation (AF), chest x-ray - compaction at the base of the lungs and enlarged heart. Echocardiography revealed enlarged left atrium (LA), elevated right ventricular systolic pressure (RVSP) and thickness of the pericardium. Patient underwent coronary angiography, which showed no severe stenosis in coronary arteries and calcification in the pericardium. To confirm constrictive pericarditis magnetic resonance imaging (MRI) was taken (Figure 1). Hemodynamic instability lead to partial pericardiotomy thru the median sternotomy in urgent. Pericardial effusion and diastolic restriction of LV were noted in the control echocardiography. After 55-days patient was discharged. In Apr-2013 increasing signs of respiratory failure occurred. Patients was qualified for home oxygen therapy. Three months later (08.2013) reduced global contractility and contraction asynchrony have been noticed in echocardiography, with 45%-LVEF. To evaluate the clinical condition patient was admitted in March-2015. He was stable, with no hospitalization because of worsening HF since 2years. The examination revealed with dry crepitation at the bases of lung bilaterally and irregular heart rate. Laboratory parameters were in norm, expect a small elevation of NT-proBNP-305,0 pg/mL. ECG showed AF, BP-110/90mmHg. MRI revealed thickness of pericardium behind posterior and inferior LV-wall with the features of fibrosis and calcification, enlargement of LA-50mm, flattening of the interventricular septum (IVS) in diastole with shift into the left site during breathing and apical akinesia (Figure 2). Clinical relevant pericarditis is a rare but serious complication of RA. It might be life-threatening condition. This kind of extra-articular disease manifestation should be considered in patients with unexpected cardiac insufficiency. Timely diagnosis and adequate intervention, as highlighted in presented case, can lead to favorable clinical outcomes. Development of MRI technology dramatically improved the visualization of the pericardium, the diagnosis of constrictive pericarditis remains a challenge in many cases.



Picture 1

RAPID FIRE 5 - DIAGNOSIS - PATHOPHYSIOLOGY - PROGNOSIS

1518

Predictors of left ventricular hypertrophy in hypertensive patients. Data from SEPHAR III study.

R O Darabont[1]; OF Tautu[2]; D Dimulescu[3]; C Sinescu[4]; D Pitic[2]; G Tamasescu[2]; M Stoian[2]; S Onciul[2]; D Cadil[2]; A Vijiiac[2]; C Angelescu[2]; M Dorobantu[2]
[1]UNIVERSITY EMERGENCY HOSPITAL BUCHAREST, BUCHAREST, Romania; *[2]Emergency Clinic Hospital "Floreasca", Bucharest, Romania*; *[3]Elias Emergency Universitary Hospital, Bucharest, Romania*; *[4]Bagdasar-Arseni Emergency Hospital, Bucharest, Romania*

On behalf of: SEPHAR III study team
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Introduction: Left ventricular hypertrophy (LVH) is considered as a main feature of heart failure with preserved ejection fraction (EF), largerly attributable to arterial hypertension. However, the heart response to increased blood pressure is highly variabile and depends on associated factors that still need to be defined.
Purpose. We aimed to evaluate the predictors of left ventricular hypertrophy (LVH) in hypertensive subjects with preserved ejection fraction identified in SEPHAR III study which was conducted on a representative sample of the Romanian population.
Methods: Subjects selected on the base of stratified proportional sampling and consented to participate in the study were evaluated during the two study visits. Hypertension was diagnosed according to current ESH-ESC guidelines (≥140/90 mmHg). Visit-to-visit blood pressure variability was assessed as the s.d. of the mean systolic blood pressure (SBP). Pulse wave velocity in the aorta (PWVao) was recorded with an oscillometric device. LVH was defined as indexed left ventricular mass (ILVM) > 95g/m2 in females and > 115 g/m2 in males on standard echocardiography. Hypervolemic state was evaluated by transthoracic bioimpedance and 24h sodium excretion was estimated from spot urine with Kawasaki formula.
Results. From a total of 1970 enrolled subjects we have identified 650 hypertensives with preserved EF (mean age 55.78 ± 15.61, 51.1% females). Mean ILVM values was 90.30 – 27.31 g/m2. LVH was found in 25.8% of the sample. Binary logistic regression adjusted for age and mean arterial pressure validated as predictors for LVH: active smoking (OR 1.45; 95% CI for OR: 1.34-1.57), body mass index (OR 1.03; 95% CI for OR: 1.02-1.03), visceral obesity (OR 1.59; 95% CI for OR: 1.44-1.75), HbA1c (OR 1.04; 95% CI for OR: 1.01-1.08), total serum cholesterol (OR 1.01; 95% CI for OR: 1.01-1.02), LDL-cholesterol (OR 1.08; 95% CI for OR: 1.03-1.09), triglycerides (OR 1.08; 95% CI for OR: 1.07-1.09), s.d. SBP >8.49 mmHg (OR 1.91; 95% CI for OR: 1.86-1.95), PWVao >10m/sec (OR 1.92; 95% CI for OR: 1.87-1.98), aortic pulse pressure (OR 1.02; 95% CI for OR: 1.01-1.02), estimated 24h sodium urinary excretion (OR 1.01; 95% CI for OR: 1.00-1.02), hypervolemia (OR 1.02; 95% CI for OR: 1.10-1.30). Blood pressure control, treatment with ACEIs/ARBs, diuretic treatment with mineralocorticoid receptor antagonists and beta-blockers have been found as protective factors for LVH.
>**Conclusions:** The results of our study indicate that, alongside with conventional risk factors, PWVao, central pulse pressure, increased visit-to-visit SBP variability, hypervolemia and estimated urinary sodium excretion are independent predictors for LVH in hypertensives with preserved ejection fraction. Moreover, these correlations reveals a possible pathophysiologic link between sodium metabolism and arterial stiffness parameters that might be addressed with specific therapeutic strategies in patients with hypertensive cardiomyopathy.

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A description of characteristics of very elderly patients newly diagnosed with heart failure: a retrospective population-based cohort study in Sweden

M Olofsson[1]; K Boman[1]; K Lindmark[2]; G Wikstrom[3]; G J Bergman[4]; M Tornblom[4]; C C Proenca[5]; B Balas[6]; F Calado[6]; J Stalhammar[7]
[1]Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden; *[2]Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[3]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*; *[4]QuintilesIMS, Solna, Sweden*; *[5]Wellmera AG, Basel, Switzerland*; *[6]Novartis Pharma AG, Basel, Switzerland*; *[7]Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*

Background and purpose: Over a quarter of patients with heart failure (HF) in Sweden are very elderly (defined as aged ≥85 years). Evidence on the demographic and clinical characteristics of these patients, and on the diagnostic procedures they receive in clinical practice, is scarce.

Methods: Patients with HF were identified via electronic medical records from primary and/or secondary care in Västerbotten, linked via unique identifiers to data from the National Patient Register and Swedish Prescribed Drug Register. Local echocardiography data were used to identify patients with HF with preserved (HFpEF, ≥50%) and reduced (HFrEF, <50%) ejection fraction. Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/2010 and 31/03/2015 and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. The date of the first diagnosis was the index date. ICD-10 codes were also used to identify comorbidities. A 10-year look-back period was used to exclude prevalent HF cases. Patient characteristics were assessed at index, except comorbidities (in the 5 years before index) and pre-diagnosis comedications (in the first year before index).
Results: In total, 8702 patients with HF were identified; 27.7% were aged ≥85 years. Compared with patients <85 years, more patients ≥85 years were female (60.2% vs 40.6%) and fewer were overweight (BMI >25 kg/m^2, 42.3% vs 63.5%). In both groups, HF was more commonly diagnosed in secondary than in primary care, but patients ≥85 years were more often diagnosed in primary care than those <85 years (31.2% vs 20.9%). Fewer patients ≥85 years than those <85 years received an echocardiogram at diagnosis (19.3% vs 42.9%); of those who did, more patients ≥85 years than <85 years had HFpEF (46.8% vs 33.4%). Patients ≥85 years had a comorbidity burden similar to those <85 years (mean number of comorbidities/patient, 2.4 vs 2.3); prevalence of atrial fibrillation (32.0% vs 30.4%), hypertension (53.2% vs 53.0%) and ischaemic heart disease (20.5% vs 22.5%) were also similar in both age groups. N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and systolic blood pressure (BP) increased with age, and diastolic BP and estimated glomerular filtration rate decreased. Potassium and sodium levels did not differ between age groups (Table). The most common pre-diagnosis comedications were β-blockers, antithrombotic agents and diuretics; β-blockers were less frequently prescribed in patients ≥85 years (59.6% vs 64.4%), and antithrombotic agents and diuretics were more frequently prescribed in those ≥85 years (antithrombotic agents, 57.0% vs 54.3%; diuretics, 50.1% vs 43.1%).
Conclusions: Very elderly patients with HF in Sweden are clinically different from younger patients, with a higher prevalence of HFpEF and higher NT-proBNP levels (as expected). Most importantly, very elderly patients seldom receive an echocardiogram at diagnosis.

Laboratory measures at the index date, by age.

Parameter	Age group (years)				
	18–54	55–64	65–74	75–84	≥85
NT-proBNP (pg/mL)	4133.5 (9187.6)	3750.4 (6433.5)	4681.0 (8788.2)	4953.5 (7927.7)	5942.8 (8415.5)
Systolic BP (mmHg)	132.2 (30.1)	134.6 (25.7)	136.9 (23.6)	139.0 (24.6)	141.8 (25.8)
Diastolic BP (mmHg)	82.2 (19.1)	81.0 (15.1)	79.4 (14.8)	78.0 (14.7)	77.0 (14.3)
eGFR (mL/min/1.73 m^2)	74.9 (29.5)	68.5 (27.9)	59.0 (26.4)	48.0 (22.3)	42.2 (20.2)
Potassium (mmol/L)	4.1 (0.5)	4.1 (0.5)	4.1 (0.5)	4.2 (0.6)	4.2 (0.6)
Sodium (mmol/L)	139.4 (3.3)	139.0 (4.2)	139.4 (3.8)	139.5 (4.1)	139.2 (4.2)

Data are presented as mean (standard deviation).
BP, blood pressure; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

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Elamipretide, a cardiolipin-targeting peptide, decreases mitochondrial oxidant stress in the failing human heart

GC Sparagna[1]; KC Chatfield[2]; S Chau[1]; DA Brown[3]; E Phillips[1]; N Stafford[1]; A Ambardekar[1]; A Korst[1]; SD Miyamoto[2]; CC Sucharov[1]; B Stauffer[1]
[1]University of Colorado, Medicine/Cardiology, Aurora, United States of America; *[2]University of Colorado, Pediatrics/Cardiology, Aurora, United States of America*; *[3]Virginia Tech, Human Nutrition, Foods, and Exercise, Blacksburg, United States of America*

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Background: Mitochondrial dysfunction contributes to myocellular abnormalities through the generation of reactive oxygen species (ROS) in the failing human heart. We have previously shown significant abnormalities in human heart cardiolipin (CL) content that are thought to play a mechanistic role in mitochondrial abnormalities. Elamipretide is a cardiolipin-targeting peptide currently being investigated in several

Phase 2 clinical trials for heart failure. In vitro and animal studies demonstrate improvements in mitochondrial ROS with elamipretide treatment independent of improvements in CL content.
Purpose: To determine whether acute elamipretide treatment of the human failing heart improves supercomplex function and lowers reactive oxygen species.
Methods: Human ventricular tissue was rapidly harvested in the operating room at the time of cardiac transplantation for end-stage heart failure with left ventricular dysfunction (F), or from age-matched donor hearts (NF) not implanted for technical reasons. Tissue was rapidly divided for elamipretide treatment or vehicle control. Immediately following treatment high-resolution respirometry was performed with simultaneous measurement of mitochondrial ROS. Tissue from each treatment arm was rapidly frozen at -80°C for MS/MS analysis of CL content.
Results: In vehicle treated samples the supercomplex coupling factor (SC CCF), a measure of the integrity of the mitochondrial supercomplex, was 35% lower in the F ventricles than NF tissue (1.11 ± 0.14 vs 1.75 ± 0.25, $p < 0.03$). Treatment with elamipretide improved SC CCF in the F human heart (1.58 ± 0.12, P=0.007) with no significant change in the NF heart (1.96 ± 0.19). Total mitochondrial ROS generation in the oligomycin-induced leak state was 44% higher in the F than NF heart (3.42 ± 0.62 vs 2.38 ± 1.34 mM H2O2) and was substantially lower following elamipretide treatment (2.51 ± 0.35 mM H2O2, P=0.06) and similar to elamipretide treated NF tissue (2.44 ± 0.34 mM H2O2). Importantly, acute elamipretide treatment did not change total, tetralinoleoyl- or monolyso-CL content in the F or NF human heart.
Conclusion: Elamipretide treatment improves supercomplex integrity and reduces mitochondrial ROS in the failing human heart in the absence of changes in total CL or expression of critical CL isoforms. These findings suggest that stabilizing the mitochondrial supercomplex, in the absence of changes in CL content, can reduce oxidative stress and represents a novel treatment for improving mitochondrial function in human heart failure.

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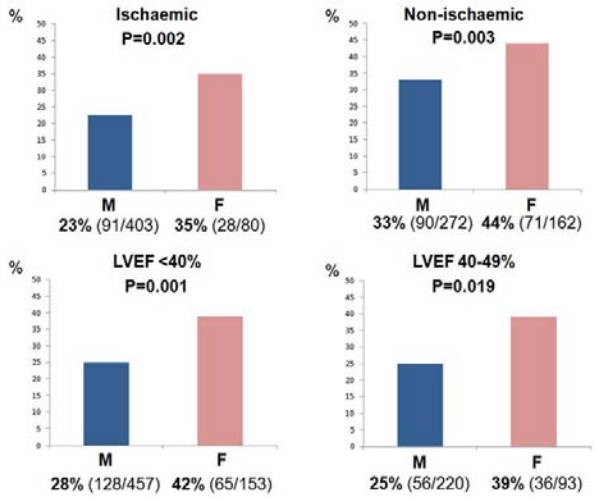
Sex, reverse remodeling and prognosis in chronic systolic heart failure

A Alberto Aimo[1]; G Vergaro[2]; V Castiglione[1]; A Barison[2]; A Giannoni[2]; R Poletti[2]; V Chubuchny[2]; L Zyw[2]; S Maffei[2]; C Passino[1]; M Emdin[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*

Background: Both female sex and reverse remodeling (RR, i.e. the reversal of ventricular dilation and dysfunction in response to treatment) are associated with better prognosis in heart failure (HF).
Purpose: To determine the relationship between sex and RR and to evaluate the prognostic impact of RR.
Methods: Data from stable systolic HF patients (left ventricular ejection fraction - LVEF $< 50\%$), undergoing two transthoracic echocardiograms (TTE) within 12 ± 2 months, were analyzed. RR was defined as indexed LV end-systolic volume reduction $\geq 15\%$. The follow-up started with the second TTE. The primary endpoint was a composite of all-cause death or heart transplantation (HT), and the secondary endpoint was a composite of cardiovascular death or HT.
Results: Out of 927 patients (age 68 ± 12 years, LVEF $34 \pm 9\%$), 250 were females (27%). Ischaemic aaetiology was less represented among females (33% vs. 60%; $P < 0.001$), while most other baseline clinical and pharmacological characteristics did not differ significantly. Across the two TTE examinations, females had a higher incidence of RR in the whole population (41% vs. 27%; $P < 0.001$), among patients with either ischaemic or non-ischaemic aetiology, and in the subgroups with either LVEF $< 40\%$ or $\geq 40\%$ (Figure). In the whole population, female sex was an independent predictor of RR (odds ratio - OR 1.542 [95% confidence interval - CI 1.114-2.135], P=0.011) in a model including the univariate predictors of RR (non-ischaemic HF aetiology, lower disease duration, no left bundle branch block - LBBB). Over a 33-month [IQR 15-59] follow-up, females showed a better prognosis for both endpoints (P=0.002 and 0.005, respectively), achieved in 188 (20%) and 126 (14%) patients, respectively. In a model including age, HF aetiology and duration, LBBB, LVEF, and N-terminal fraction of pro-brain natriuretic peptide, female sex and RR were both independent predictors of all-cause death or HT (OR 0.580 [95% CI 0.356-0.944]; P=0.028 and OR 0.649 [95% CI 0.415-0.992]; P=0.048). Only RR independently predicted cardiac death or HT (OR 0.573 [95% CI 0.333-0.987]; P=0.045).
Conclusions: In systolic HF, RR is more frequent among female patients. Female sex is an independent predictor of RR and all-cause death or HT.



Sex and reverse remodeling

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The clinical meaning of selected single nucleotide polymorphisms in patients with hypertension and heart failure with preserved and mid-range ejection fraction

A Bielecka-Dabrowa[1]; A Sakowicz[2]; M Misztal[3]; T Pietrucha[2]; J Rysz[4]; M Banach[1]
[1]Department of Hypertension, Chair of Nephrology and Hypertension, Medical University of Lodz, Lodz, Poland; *[2]Medical University of Lodz, Department of Medical Biotechnology, Lodz, Poland*; *[3]University of Lodz, Chair of Statistical Methods, Faculty of Economics and Sociology, Lodz, Poland*; *[4]Medical University of Lodz, Department of Nephrology, Hypertension and Family Medicine, Lodz, Poland*

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Aim: This study aimed to assess the clinical meaning of the single nucleotide polymorphisms (SNPs) reflecting different pathophysiological pathways in hypertensive patients with diastolic heart failure: inflammation (-174 G/C IL-6 rs1800795, TNF-608 G/A rs1800629), fibrosis (Arg25Pro TGFβ rs1800471), endothelial function (-786 T/C NOS rs2070744), glucose and lipid metabolism (Pro12Ala PPARγ rs1801282), vitamin D metabolism (CYP27B1 C-1260A).
Methods: 110 patients (mean age 63 years, 69% males) with heart failure (HF) with preserved and mid-range heart failure (HFpEF and HFmrEF) were recruited. Functional polymorphisms were selected from six candidate genes: IL-6, TNF alpha, TGF beta, NOS3, PPAR gamma, CYP27B1. We also assessed the levels of selected HF biomarkers and performed echocardiographic examinations.
Results: Homozygotes GG in 174 G/C of IL6 polymorphism are characterized by higher values of GFR MDRD and systolic mitral annuar velocity ($p = 0{,}01; p = 0{,}03$). HF patients with A allelle in TNF-308 G/A rs1800629 polymorphism had lower systolic blood pressure and higher incidence of paroxysmal atrial fibrillatio ($p = 0{,}006; p = 0{,}005$). Patients with HF and CC profile of TGF beta polymorphism had higher LV mass and higher level of TNF alpha in plasma ($p = 0{,}04; p = 0{,}04$). Patients with C allelle in NOS polymorphism had higher class according NYHA classification, lower blood pressure, higher level of cystatin C and lower GFR, lower LVEF compared to patients without C allele ($p = 0{,}04; p = 0{,}03; p = 0{,}02; p = 0{,}02; p = 0{,}02; p = 0{,}008$). Patients with AA profile in C-1260A of CYP27B1 polymorphism had lower values of eGFR (MDRD) and higher levels of uric acid compared to CA and CC profile ($p = 0{,}03; p = 0{,}02$). In multivariate analysis CG genotype for 174 G/C of IL-6 (odds ratio OR=7,5; 95% CI:1.1-50; $p = 0.03$), A allele in C-1260A of CYP27B1 (OR=4,3; 95%CI: 1,3-13,8; $p = 0.01$), higher GFR (MDRD) (OR=0,96; 95%CI:0,92-1,0; $p = 0{,}05$), lower level of cystatin C (OR=6.6; 95%CI: 1,2-35,2; $p = 0.02$) and higher level of TGF beta 1(OR=0,96; 95%CI: 0,57-0,84; $p = 0.001$) were independent risk factors of worse course of heart failure.
Conclusions: These data confirm the importance of the selected SNPs in aggravation and complications of hypertension. The CG genotype for 174 G/C of IL-6 and A allele in C-1260A of CYP27B1 are SNPs independently associated with worse course of HFpEF and HFmrEF.

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Association between troponin I and left ventricular global longitudinal strain in outpatients with heart failure

J Jensen[1]; H Bosselmann[2]; J Rasmussen[3]; ML Johansen[3]; F Gaborit[1]; M Jurgens[3]; K Iversen[1]; F Gustafsson[4]; G Soletormos[5]; C Kistorp[3]; M Schou[1]
[1]Herlev-Gentofte Hospital, Department of Cardiology, University of Copenhagen, Herlev, Denmark; *[2]North Zealand Hospital, Department of Cardio-, Nephro- and Endocrinology, University of Copenhagen, Hillerod, Denmark*; *[3]Herlev-Gentofte Hospital, Department of Endocrinology and Internal Medicine, University of Copenhagen, Herlev, Denmark*; *[4]Rigshospitalet, Department of Cardiology, University of Copenhagen, Copenhagen, Denmark*; *[5]North Zealand Hospital, Department of Research, University of Copenhagen, Hillerod, Denmark*

Background: Troponin I (TnI) is an established prognostic marker in heart failure (HF). However, the pathophysiological mechanisms of TnI elevations in compensated HF are poorly understood. Hence, it is unknown whether TnI elevations are associated with an impaired left ventricular function evaluated by echocardiography or only reflect frequently present comorbidities.
Purpose: To test the hypotheses that TnI is associated with an impaired left ventricular function estimated by left ventricular (LV) global longitudinal strain (GLS) in outpatients with compensated HF.
Methods: We prospectively enrolled 112 patients with reduced left ventricular ejection fraction (LVEF) referred to an outpatient HF clinic. LV GLS was assessed by two-dimensional speckle tracking, plasma concentrations of TnI were analyzed on frozen plasma with a standard contemporary TnI assay. The cut-off value at the 99th percentile of concentrations obtained among healthy individuals is 45 ng/L. Baseline data were collected. The association between plasma concentrations of TnI and LV GLS was evaluated in logistic regression models before and after adjustment for important confounders (age, sex, renal function, anemia, atrial fibrillation, NT-proBNP, diabetes and ischemic heart disease).
Results: The patients had a median age of 70 years (interquartile range: 64-75), 26.5% were female, median LVEF was 33% (27-39%) and 29% were in New York Heart Association (NYHA) class III-IV. TnI was detectable in 36%. Of the patients with detectable plasma concentrations of TnI, 63% had a markedly impaired LV GLS (>/= -11%) and this was only the case for 31% of the patients with undetectable TnI ($P < 0.001$). In univariate analyses, LV GLS and TnI were closely associated (Odds ratio (OR): 3.86 (95% Confidence Interval (CI): 1.71-8.68, $P < 0.001$), and the association remained significant in a multivariate adjusted analysis (OR: 3.45 (95% CI: 1.24-9.62, $P < 0.018$). Detectable TNI was not associated with any comorbidity (renal function, anemia, atrial fibrillation, diabetes and ischemic heart disease) in an adjusted statistical model ($P>0.05$ for all).
Conclusions: Detectable TnI is independently associated with impaired LV GLS and may, therefore, reflect impaired left ventricular function rather than comorbidities. Future trials should use TnI to identify high risk patients since detectable TnI is both associated with a poor outcome and impaired left ventricular function in compensated HF.

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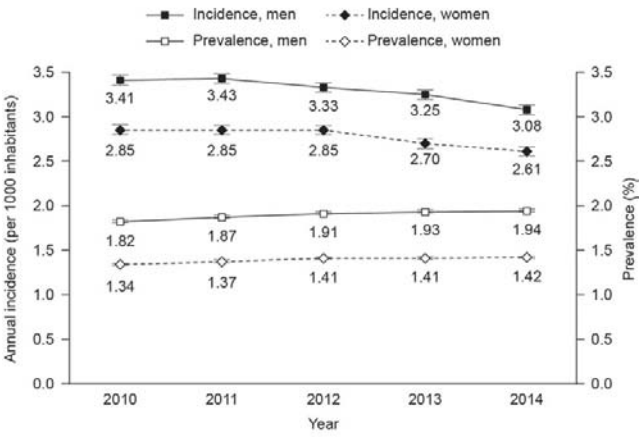
Epidemiology of heart failure in Sweden: a retrospective population-based cohort study

K Lindmark[1]; K Boman[2]; M Olofsson[2]; G Wikstrom[3]; G J Bergman[4]; M Tornblom[4]; E Gullberg[5]; D Johansson[5]; R Schlienger[6]; J Stalhammar[7]
[1]Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden; *[2]Umea University, Research Unit, Medicine, Skellefteå, Department of Public Health and Clinical Medicine, Umea, Sweden*; *[3]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden*; *[4]QuintilesIMS, Solna, Sweden*; *[5]Novartis Sweden AB, Stockholm, Sweden*; *[6]Novartis Pharma AG, Basel, Switzerland*; *[7]Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden*

Background and purpose: Considering the limited and conflicting data on temporal trends in the incidence, prevalence and mortality of heart failure (HF) in Sweden, we aimed to provide an update on the epidemiology of HF in Sweden.
Methods: Patients with HF were identified using data from secondary care from the National Patient Register (NPR, primary care was not covered), linked via unique identifiers to primary and secondary care data from the Cause of Death Register. Patients aged ≥18 years with ≥2 diagnoses of HF between 01/01/1997 and 31/12/2014 (for incidence and prevalence) or between 01/01/2005 and 31/12/2013 (for mortality) and an ICD-10 diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I110, I130 or I132 in any position were included. The date of the second HF diagnosis was the index date for incidence and prevalence; the date of the first HF diagnosis was the index date for mortality. ICD-10 codes also identified comorbidities occurring in the 5 years prior to index. Annual incidence and prevalence estimates were assessed for the years 2010–2014 using a look-back period from 2000 onwards. Estimates were age-standardized to the Swedish population in 2015. Age-adjusted hazard ratios (HRs) for all-cause and cardiovascular disease (CVD)-related mortality was estimated using a Cox proportional hazards model.
Results: Data from 845 276 patients with HF were extracted from the NPR. Of these, 174 537 patients (20.6%) did not have a diagnosis of HF in the look-back period and were considered to be newly diagnosed (median age: 79.9 years; 46.9% women). The most common comorbidities were hypertension (36.3%), atrial fibrillation (26.1%) and ischaemic heart disease (22.9%). Overall annual incidence (95% confidence interval [CI]) of HF decreased over the 5 years from 3.20 (3.16–3.24) to 2.91 (2.87–2.95) per 1000 inhabitants, and prevalence increased over the 5 years from 1.61 (1.60–1.62)% to 1.72 (1.71–1.72)%. Incidence and prevalence estimates were higher in men than in women (Figure). All-cause mortality over 1 and 3 years (95% CI) was 19.7 (19.5–19.9)% and 40.5 (40.2–40.7)%, respectively; 1- and 3-year CVD-related mortality was 11.8 (11.6–11.9)% and 25.9 (25.7–26.1)%, respectively. All-cause mortality was higher in women than in men (1-year mortality, 21.1 [20.8–21.4]% vs 18.4 [18.2–18.7]%; 3-year mortality, 43.3 [42.9–43.6]% vs 38.0 [37.6–38.3]%), as was CVD-related mortality (1-year mortality, 12.9 [12.6–13.1]% vs 10.8 [10.5–11.0]%; 3-year mortality, 28.3 [27.9–28.6]% vs 23.8 [23.5–24.1]%). However, age-adjusted HRs (95% CI) suggested mortality was higher in men than women (all-cause, 1.12 [1.10–1.13]; CVD-related, 1.11 [1.10–1.13].
Conclusions: Increasing prevalence of HF with decreasing incidence indicates improved survival. Incidence, prevalence and age-adjusted mortality of HF were higher in men than in women.

Annual incidence and prevalence of HF in men and women in Sweden from 2010 to 2014



Error bars indicate 95% CIs.

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Clinical characteristics and outcomes of patients with chronic heart failure and 'mid-range' ejection fraction: data from the IN-HF Outcome Italian Registry

F Orso[1]; A P Aldo Pietro Maggioni[2]; G Fabbri[2]; M Gorini[2]; O De Donno[3]; G Guazzotti[4]; S Luca'[5]; L Scelsi[6]; L Tavazzi[7]
[1]AOU Careggi, Department of Geriatrics, Section of Geriatric Medicine and Cardiology, Florence, Italy; *[2]ANMCO Research Center, Florence, Italy*; *[3]Ignazio Veris Delli Ponti Hospital, Cardiology-ICU Dept., Scorrano, Italy*; *[4]ICS Maugeri Spa Società Benefit, Cardiological Rehabilitation Dept., Montescano, Italy*; *[5]Incurabili Hospital, Medicine Department, Naples, Italy*; *[6]Policlinic Foundation San Matteo IRCCS, Cardiology Department, Pavia, Italy*; *[7]Maria Cecilia Hospital, GVM Care&Research - E.S. Health Science Foundation, Cotignola, Italy*

On behalf of: IN-HF Outcome Investigators
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Background. ESC guidelines identify patients (pts) with heart failure (HF) and ejection fraction (EF) between 40 and 49%, defined HF 'mid-range' (HFmrEF), confirming the values for HF with preserved EF (≥50% HFpEF) and HF with reduced EF (<40% HFrEF).
Aims: To compare in outpts with chronic heart failure (CHF) clinical characteristics and outcomes of HFmrEF pts with those of HFpEF or HFrEF.
Methods: Data derived from the Italian Network on Heart Failure (IN-HF) Outcome Registry which collected data of pts with HF and any level of EF.
Results: 2135 HF outpts had EF data: pts with HFmrEF were 23.9%, 59.7% had HFrEF and 16.4% HFpEF. Mean age was 69 ± 12 years, 68 ± 12 years and 72 ± 12 respectively ($p < 0.0001$), prevalence of females in HFmrEF was 26.1% compared to 18.5% and 39.9% in HFrEF and HFpEF respectively ($p < 0.0001$). Ischemic aetiology was more frequent in HFrEF (49.8%) and HFmrEF pts (46.1%) than in HFpEF pts (26.8%), $p < 0.0001$, which had a higher rate of hypertensive etiology. Pts with

HFpEF also had a higher prevalence of history of atrial fibrillation (39.1% vs 26.5% of HFmrEF and 26.4 of HFrEF, p < 0.001). There were no differences in the rates of HF hospitalisations in the previous year among the three groups. NYHA III and IV were less frequent in HFmrEF (9.4%) compared to HFrEF (23.6%) and HFpEF 21.9%, p < 0.0001. Drug treatments are reported in the table. Pts with HFmrEF were treated similarly to those with HFrEF with respect to ACE-I/ARBs or BBs while they were less treated with diuretics and digoxin compared to the other two groups of HF pts. MRAs were more frequently prescribed in HFrEF while in HFmrEF the prescription is similar to HFpEF pts. At 12 months follow-up, HFrEF pts were more frequently hospitalized (25.9%) compared to HFmrEF (14.5%) and HFpEF (19.7%), p < 0.0001. All-cause mortality was reported in 6.7% in HFrEF pts versus 3.3% of HFmrEF versus 3.7% of HFpEF (3.7%), p = 0.006.

Conclusions: Pts with HFmrEF represent a significant portion of HF outpts, they are currently treated similarly to those with HFrEF. One year mortality of HFmrEF pts seems to be better than that of HFpEF and particularly HFrEF pts.

Drug	Total n=2135	HFrEF n=1274	HFmrEF n=510	HFpEF n=351	p value
ACE-I/ARBs, %	90.3	91.2	91.2	85.8	0.007
BBs, %	80.9	84.8	80.0	68.1	< 0.0001
MRAs, %	43.5	50.8	34.9	29.3	< 0.0001
Diuretics, %	86.0	91.2	77.3	80.1	< 0.0001
Digoxin, %	18.9	20.8	13.7	19.4	0.003
ACE-I/ARBs + BBs + MRAs, %	33.1	40.7	26.5	15.4	< 0.0001

Treatment in the three CHF groups

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Prognostic value of calculated plasma volume status in patients with heart failure and reduced ejection fraction insights from the PARADIGM-HF trial

SL Kristensen[1]; R Roerth[1]; PS Jhund[1]; J Rouleau[2]; M Zile[3]; SD Solomon[4]; K Swedberg[5]; M Packer[6]; JJV Mcmurray[1]
[1]*Cardiovascular Research Centre of Glasgow, Glasgow, United Kingdom*; [2]*University of Montreal, Montreal, Canada*; [3]*Medical University of South Carolina, Charleston, United States of America*; [4]*Brigham and Women's Hospital, Boston, United States of America*; [5]*University of Gothenburg, Gothenburg, Sweden*; [6]*Baylor University Medical Center, Dallas, United States of America*

On behalf of: PARADIGM-HF investigators
Funding Acknowledgements: The PARADIGM-HF study was funded by Novartis

Background: Estimated plasma volume (ePV) derived from haematocrit and body weight correlates well with PV measured using 125Iodine labelled human serum albumin. We calculated ePV and relative PV (rPV), which is ePV as a fraction of ideal PV (iPV), in patients with HFrEF enrolled in PARADIGM-HF and examined the association between rPV and outcomes, as well as the effect of randomized treatment on rPV.

Methods: iPV was calculated as: iPV = c × weight (kg) where c=39 in males and c=40 in females. ePV was calculated using subjects' haematocrit and weight as follows: ePV = (1 − haematocrit) × [a + (b × weight in kg)], where haematocrit is a fraction, a=1530 in males and a=864 in females, and b=41 in males and b=47.9 in females. rPV was the relative deviation of EPV from iPV where 0% means ePV and iPV are the same, a negative value indicates an ePV less than iPV and a positive value an ePV greater than iPV. The relationship between rPV quartile and the primary composite outcome of CV death or HF hospitalization was examined in a multivariable Cox regression model (including age, sex, race, region, HF duration, NYHA class, LVEF, HR, BMI, ischaemic aetiology, history of MI, AF, stroke, KCCQ Score, ICD, eGFR, NTproBNP). We also examined absolute change in rPV at 12 months of follow-up.

Results: PV indices were available for 8071 of the enrolled patients (96%). The median ePV at screening was 2717 (IQR 2416, 3039) ml compared with an iPV of 3081 (IQR 2640, 3588) ml; the median rPV was -11.6% (IQR -17.7, -4.7) and 87% of patients had a rPV < 0%. The primary composite outcome occurred in 480 (24%), 451 (22%), 489 (24%), and 534 (27%) of patients in quartiles 1-4 of rPV, respectively (where Q4 had the highest rPV). Using quartile 1 as reference, adjusted hazard ratios (HR) for the composite outcome were HR 1.00 (95% CI 0.87-1.15) for Q2, HR 1.18 (1.02-1.37) for Q3 and HR 1.27 (1.08-1.49) for Q4 (Figure). There was no interaction between rPV quartile at screening the benefit of sacubitril/valsartan over placebo (p = 0.56). Change in median rPV from screening to 1 year in the enalapril group was from -11.8% to -11.3%, an increase of 0.5%; in the sacubitril/valsartan group rPV changed from -11.8% at screening to -12.2%, a decrease of 0.4% (P < 0.001).

Conclusion: Estimating PV using a simple calculation based on haematocrit, sex and bodyweight provided incremental predictive information on morbidity/mortality in patients with HFrEF. Compared with enalapril, sacubitril/valsartan led to a reduction in rPV.

1528

Plasma adrenomedullin and risk of heart failure in people with type 2 diabetes: the Surdiagene and Diabhycar prospective studies

B Gellen[1]; M Fraty[2]; G Velho[3]; E Gand[4]; F Fumeron[3]; S Ragot[2]; P Sosner[5]; PJ Saulnier[2]; JM Halimi[6]; D Montaigne[7]; G Ducrocq[8]; M Rehman[9]; M Marre[10]; R Roussel[3]; S Hadjadj[2]
[1]*ELSAN, Polyclinique de Poitiers, Cardiology, Poitiers, France*; [2]*University Hospital of Poitiers, Centre d'Investigation Clinique and Endocrinology Department, Poitiers, France*; [3]*INSERM, UMR_S 1138, Centre de Recherche des Cordeliers, Paris, France*; [4]*University Hospital of Poitiers, Pole DUNE, Poitiers, France*; [5]*Centre médico-sportif MON STADE, 5 Rue Elsa Morante, Paris, France*; [6]*University Hospital of Tours, Service Néphrologie, Dialyse et Transplantation, Tours, France*; [7]*CHRU Lille, Clinique de Physiologie et département d'échocardiographie, Lille, France*; [8]*Hospital Bichat-Claude Bernard, Cardiology, Paris, France*; [9]*CHU de Poitiers, Cardiology, Poitiers, France*; [10]*Hopital Bichat - Claude Bernard, Service de Diabétologie, Endocrinologie et Nutrition, Paris, France*

Aims/hypothesis: – Adrenomedullin (ADM) is a vasoactive peptide with vasodilator and natriuretic properties. Plasma concentration of ADM is increased in the acute phase of heart failure and is a predictor of the risk of short-term mortality. Here, we evaluated the prognostic value of plasma midregion-pro-ADM, MR-proADM (a surrogate for ADM) for the occurrence of severe congestive heart failure (CHF) necessitating hospitalization, in people with type 2 diabetes.

Methods: Plasma MR-proADM concentration was measured in baseline samples of two cohorts of type 2 diabetes patients recruited in France: SURDIAGENE (n = 1438, median follow-up 5.3 years) and DIABHYCAR (n = 2962, median follow-up 4.7 years).

Results: – The incidence rate of CHF was 2.5 (95% CI 2.2-2.9) for SURDIAGENE and 1.0 (95% CI 0.8-1.1) per 100 person-year for DIABHYCAR, respectively, corresponding to 206 and 127 events, respectively. The highest tertile of plasma MR-proADM concentration at baseline was associated with the risk of CHF during follow-up in both cohorts (log-rank test: p < 0.0001 and p = 0.01, respectively). The associations of MR-proADM with CHF remained significant in Cox regression analyses when adjusted for other risk factors for CHF, such as a history of coronary heart disease, proteinuria and decline of renal function (HR in pooled cohorts: 1.99 (1.58-2.50); p < 0.0001). MR-proADM also contributed significant supplementary information to the prediction of CHF, when we considered the clinical risk factors of CHF identified in the UKPDS study (IDI: 0.013 ± 0.006, p = 0.02).

Conclusions/interpretation: – MR-proADM is a predictive biomarker for occurrence of severe heart failure in people with type 2 diabetes.

1529

Prognostic value of malnutrition screening tools in patients with chronic heart failure

S Shirley Sze[1]; P Pellicori[1]; AS Rigby[1]; S Kazmi[1]; AL Clark[1]
[1]*Castle Hill Hospital, Hull, United Kingdom*

Background: Cachexia in heart failure (HF) is associated with adverse outcomes. Malnutrition is common in HF patients and contributes to cachexia but it is not part of the routine assessment of patients. There is no consensus on how best to screen for malnutrition in patients with HF.

Purpose: To evaluate the prevalence, clinical associations and prognosis of malnutrition using three common multi-dimensional malnutrition indices in a large cohort of well-characterised patients with chronic heart failure (CHF).

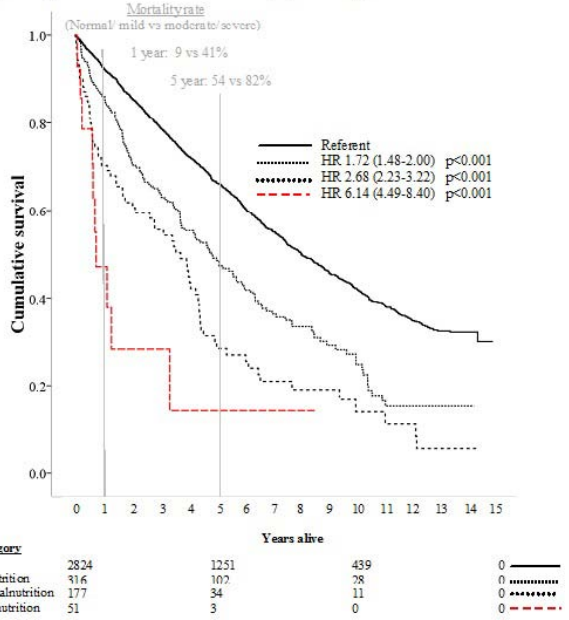
Methods: Consecutive referrals to a community HF clinic between 2000 and 2016 were analysed. HF was defined as signs or symptoms and evidence of cardiac dysfunction, either a reduced left ventricular ejection fraction at echocardiography (LVEF, < 50%) or raised NTproBNP (>125 ng/L). Patients were screened for malnutrition using the geriatric nutritional risk index (GNRI), the controlling nutritional status (CONUT) score and the prognostic nutritional index (PNI).

Results: 3386 patients had CHF (61% males, median age 75 (interquartile range (IQR): 67-81) years, median NTproBNP 1573 (IQR: 702-2799) ng/L). Of these, 1198 (35%) and 1458 (43%) patients had HF with reduced (HeFREF, LVEF < 40%) and normal (HeFNEF, LVEF≥50%) ejection fraction, respectively. According to the GNRI (≤91), CONUT score (>4) and PNI (≤38), 6.7%, 10.0% and 7.5% patients were moderately to severely malnourished, respectively. Patients with HeFREF were at higher risk of malnutrition than those with HeFNEF. (8-12% vs 5-8%, respectively) Compared to normal patients, malnourished patients were older, had lower body

mass index (BMI), worse symptoms and renal function; more likely to have atrial fibrillation, anaemia and reduced mobility. Worsening malnutrition correlated with increasing NTProBNP levels regardless of HF phenotypes.(R2 = 0.36-0.45(CONUT), 0.28-0.43(GNRI), 0.37-0.43(PNI), all p < 0.001) During a median follow-up of 1573 days (IQR: 702-2799 days), 1723 (50.9%) patients died. We created 25 prognostic Cox regression models using K-fold cross validation (k=25). CONUT and GNRI category (worse outcome with worsening malnutrition categories) were independently associated with outcome in 100% of the models while PNI category was an independent predictor in 19 models (76%). A base model for predicting mortality including variables with an inclusion frequency > 18 of 25 (>70%) models: age, sex, diastolic BP, heart rate, NYHA class III& IV vs I&II, urea, logNTProBNP, stroke and peripheral vascular disease had a C statistics of 0.72. Amongst the malnutrition indices, GNRI improved model performance most compared with base model. Patients who were severely malnourished according to GNRI had over 6 times greater mortality risk than normal patients. (Figure)

Conclusion: Malnutrition is common amongst patients with CHF and is strongly related to mortality. Screening for malnutrition using GNRI should be routine adopted during assessment of HF patients to guide management.

Figure. Kaplan-Meier curve for all-cause mortality by GNRI categories.



GNRI category and all-cause mortality

1530

One-year change in ejection fraction and long-term outcomes in patients with heart failure with mid-range ejection fraction

N Farre[1]; J Lupon[2]; E Sole-Gonzalez[3]; J Gonzalez-Costello[4]; J Vila[5]; S Perez[5]; S Ruiz[6]; M Domingo[2]; A Mendez-Fernandez[3]; C Sanchez-Enrique[4]; C Enjuanes[1]; E Roig[3]; E Zamora[2]; A Bayes-Genis[2]; J Comin-Colet[1]

[1]Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; *[2]Germans Trias i Pujol University Hospital, Department of Cardiology, Badalona, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Department of Cardiology, Barcelona, Spain*; *[4]University Hospital of Bellvitge, Barcelona, Spain*; *[5]Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain*; *[6]Hospital del Mar, Department of Cardiology, Barcelona, Spain*

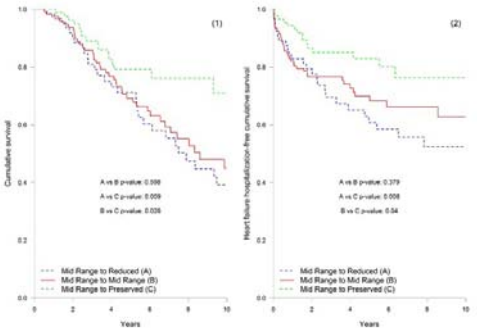
Background: In patients with heart failure (HF) and reduced ejection fraction (HFrEF) an improvement in ejection fraction (EF) has been associated with better outcomes. Whether this is true in patients with mid-range EF (HFmrEF) is unknown.

Purpose: To analyze the effect of 1-year change in EF in outcome of patients with HFmrEF (defined as EF 40-49%).

Methods: Prospective observational study of HF patients followed up at 4 university hospitals with a dedicated Heart Failure Unit. Baseline characteristics, 1-year EF and outcomes were collected.

Results: Fourteen percent (n = 504) of the 3580 patients included in the study had HFmrEF. Mean age was 68 ± 13 years (compared with 66 ± 13 in HFrEF (defined as EF < 40%) and 74 ± 11 in HFpEF, defined as EF>50%), 40% were female (30% in HFrEF and 57% in HRpEF), both p < 0.001. As expected, among 1-year survivors only 40% of patients with HFpEF had EF measured at 1 year follow-up, and the majority (85%) had EF>50%. The majority of patients with HFrEF (62%) still had EF < 40% at 1-year follow-up. Interestingly, EF of patients with HFmrEF had the greatest variation: 24% had reduced EF, 43% maintained EF 40-49% and 33% had EF >50%. Figure 1 shows Kaplan-Meier curves for long-term outcome. Of the 2409 patients with EF < 50% that survived 1 year, 1561 (65%) had an echocardiogram performed. In this group, after adjustment for age, sex and baseline EF, hazard ratios for survival for change in EF was 0.97 (95% CI 0.96-0.98, p < 0.001).

Conclusions: At 1-year follow-up patients with HFmrEF had the greatest variability (up and down) in EF and this change was associated with survival.



1531

HLM as a new staging system for heart failure. Comparison with NYHA

P Paolo Severino[1]; M Alfarano[1]; M Pucci[1]; I Ferrari[1]; S Peroni[1]; S Calcagno[1]; A Fusto[1]; D Alunni Fegatelli[2]; A Vestri[2]; S Sciomer[1]; M Mancone[1]; F Fedele[1]

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

Background. Although NYHA is the most used classification for heart failure (HF), it does not include patients clinical features and other organs involvement. We proposed a new staging system for HF, named HLM (JACC 2014;20;63(19):1959-60), analogous to the TNM classification used in Oncology. HLM refers to heart damage (H), lung involvement (L), and malfunction of peripheral organs, such as kidney, liver, brain and hematopoiesis.

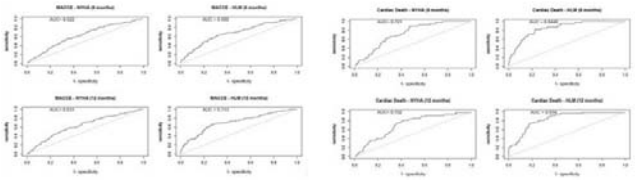
Purpose: The aim was a preliminary comparison between HLM and NYHA to achieve the most accurate prognosis of HF patients in terms of rehospitalization and mortality.

Methods: We performed an observational registry of consecutive 780 patients with diagnosis of heart failure or at risk for it. All parameters for cardiac heart (systolic and diastolic left ventricular function and volumes, structural damage, left ventricular remodeling, biventricular dysfunction), lungs (hemodynamic or clinical pulmonary congestion, cardiac lung) and peripheral organs (i.e. kidney, liver, central nervous system, and hematopoietic system) function have been examined. Each patient has been classified according to NYHA and HLM. The MACCE (major adverse cardiovascular and cerebrovascular events) and cardiac death rates were calculated at 6 months and 12 months follow up.

Results: Among 780 enrolled patients, the etiology for heart failure was: 52% coronary artery disease, 17% hypertensive cardiomyopathy, 13% dilated cardiomyopathy, 11% valvular heart disease and 7% other. At 6 months follow-up, comparing to NYHA, HLM showed a greater area under the ROC curve (AUC) for rehospitalization (HLM AUC= 0.680 vs NYHA AUC= 0.622) as well as for cardiac death (HLM AUC= 0.844 vs NYHA AUC= 0.721), with significant differences regarding L (p = 0.03, OR= 7.103) and M (p = 0.02, OR= 12.439) and NYHA IV (p = 0.016, OR= 12.801); similar findings have been observed at 12 months follow-up (for rehospitalization HLM AUC= 0.713 vs NYHA AUC= 0.631; for cardiac death HLM AUC= 0.834 vs NYHA AUC= 0.702) (Fig. 1). Cardiac death has been assessed separately for each parameter (H, L and M): L and M showed the most accurate prognostic power; at 1 year-follow-up, L1 was significantly correlated (p = 0.027, OR=0.3.554) with cardiovascular mortality as well as L2 (p = 0.001, OR= 6.358), L3 (p = 0.000, OR= 11.231), M2 (p = 0.008, OR= 7.736) and M3 (p = 0.005, OR= 9.972).

CONCLUSIONS. Basing on the preliminary results, compared to NYHA classification, HLM nosology appears as more accurate to stratify risk of rehospitalization for MACCE and of cardiac death for HF patients. Interestingly, only NYHA IV presented significant results. Regarding HLM, any lung involvement (L1-3) and two or more

organs dysfunction (M2-3) presented the most accurate prognostic power. This means that a wider and systemic approach should be used in HF patients, giving up the "cardiocentric" methodology of NYHA. Those preliminary data need to be confirmed in a greater population with a longer follow up.



ROC curves at 6 and 12 months follow up.

1532

Prevalence and clinical consequences of dysglycaemia in nondiabetic patients with chronic heart failure

M Mohan[1]; FATIMA Baig[1]; U Bhalraam[1]; CHIM Lang[1]
[1]*University of Dundee, Division of Cardiovascular & Diabetes Medicine, Ninewells Hospital, Dundee, United Kingdom*

On behalf of: BIOSTAT-CHF Investigators
Funding Acknowledgements: European commission Seventh Framework Programme (FP-7)

Background & Aim: Chronic heart failure (CHF) and diabetes mellitus (DM) frequently co-exist and its clinical consequences has been undoubtedly established in the past. CHF is a state of insulin resistance and it is believed that glucose abnormalities are very common in CHF patients even in the absence of DM, exposing them to a higher risk of developing DM. This study sought to establish the prevalence and risk related to prediabetes among nondiabetic CHF patients.
Methods: 1805 CHF patients (age 74 ± 11, 34% females, 64% IHD aetiology; 57% in NYHA III/IV; BMI 29 ± 6 kg/m^2, 42% all-cause deaths) were evaluated prospectively from the BIOSTAT-CHF Scotland study. Pre-diabetes was defined using the new glycosylated haemoglobin A1C (HbA1c) criteria (6.0-6.4%) proposed by the International Diabetes Expert Committee (IEC). Patients with a diagnosis of DM (33%) or undiagnosed DM (5%, baseline HbA1c≥ 6.5 %) and patients with no baseline HbA1c (14%) were excluded from the study. Cox regression models were used to assess all-cause mortality rates, adjusting for significant covariates.
Results: After exclusion, prevalence of prediabetes was 33% by IEC criteria in our cohort of CHF patients (n = 876). During a median follow-up period of 4.7 years (IQR 4.5, 4.9), there were 39% all-cause deaths. A Kaplan- Meier analysis showed that mortality rates were significantly higher (46% vs 35%; p = 0.006) in prediabetic CHF patients as compared to normoglycemic (NG) CHF patients. Prediabetic CHF patients had more symptomatic CHF (% of patients in NYHA III-IV, 62% vs 52%, p = 0.009) as compared with NG-CHF patients. A Cox regression model, adjusted for significant covariates showed that prediabetic CHF patients were at higher risk of deaths (HR 1.3 [1.02 – 1.7]; p < 0.05) compared to NG-CHF patients.
Conclusion: In patients with CHF, high-normal baseline HbA1c levels in the absence of DM have a significantly increased risk of all-cause mortality. Targeted therapeutic strategies to prevent or delay the onset of DM is urgently needed in these CHF patients identified to have pre-diabetes.

MODERATED POSTER SESSION 5 - TIPS AND TRICKS TO PREVENT READMISSIONS

1533

Interleukin-1 blockade in recently decompensated systolic heart failure: the recently decompensated heart failure anakinra response trial (REDHART)

B Van Tassell[1]; J Canada[1]; S Carbone[1]; C Trankle[1]; LF Buckley[1]; C Oddi Erdle[1]; N Abouzaki[1]; DL Dixon[1]; D Kadariya[1]; S Christopher[1]; H Billingsley[1]; J Regan[1]; A Bhatnagar[1]; E Lesnefsky[1]; A Abbate[1]
[1]*Virginia Commonwealth University, Richmond, United States of America*

Funding Acknowledgements: National Institutes of Health - National Heart, Lung, and Blood Institute

Background. An enhanced systemic inflammatory response (i.e. elevated plasma levels of C reactive protein [CRP]) in patients with decompensated heart failure (HF) predicts worse outcomes. We hypothesized that inhibiting Interleukin-1 (IL-1) activity using recombinant human IL-1 receptor antagonist (anakinra) would improve aerobic exercise capacity in patients with recently decompensated systolic HF and systemic inflammation.
Methods: We randomly assigned 60 patients with recently hospitalized HF who had been discharged in the prior 14 days, had reduced left ventricular ejection fraction (LVEF $<50\%$), and elevated CRP levels (>2 mg/l) to daily subcutaneous injections with anakinra 100 mg for 12 weeks, anakinra for 2 weeks followed by placebo for 10 weeks, or placebo for 12 weeks. Patients underwent clinical assessment, transthoracic echocardiography, non-invasive hemodynamic testing, and cardiopulmonary exercise testing (CPX) at 2, 4, 12, and 24 weeks.
Results: Fifty-two patients (87%) completed the first 14 days of treatment and repeated CPX allowing to measure the interval change in peak oxygen consumption (pVO2 [mL/kg/min]) and ventilator efficiency (VE/VCO2 slope, co-primary endpoints). Treatment with anakinra significantly reduced CRP by>80% ($P<0.01$) but did not affect pVO2 or VE/VCO2 (P>0.20) at 2 weeks. At 12 weeks, a significant improvement in pVO2 (from 14.5 [10.5-16.6] to 16.1 [13.2-18.6], P=0.008) and VE/VCO2 slope [from 34.9 [29.4-41.4] to 31.7 [27.3-34.2, P=0.035), and not in the placebo nor in the anakinra in 2-week groups (all P>0.15). The incidence of death or HF admission was 30% (placebo), 31% (anakinra 2-week), and 6% (anakinra 12-week, Log-Rank test P=0.104). An analysis measuring events while on-treatment showed lower events while on anakinra [combined] versus on placebo (1 [3%] vs 7 [21%], P=0.024). Anakinra treatment was also associated with improvements in E/E' ratio, LVEF, and quality of life measures at 12 weeks. Non-invasive hemodynamic testing revealed significant improvements with anakinra in ventriculo-arterial coupling and stroke work efficiency at 12 weeks.
Conclusion: IL-1 blockade with anakinra in patients with recently decompensated HF failed to improve peak aerobic capacity measured at 2 weeks. Treatment with anakinra for 12 weeks was associated with a clinical improvement at 12 weeks and a signal for reduced hospital readmission for HF. Further studies are needed to confirm these findings and explore the therapeutic value of IL-1 blockade on clinical outcomes.

1534

Correlation between degree of pulmonary congestion and rate of heart failure hospitalization in heart failure patients with reduced left ventricle ejection fraction: results from extended impedance-

M Michael Kleiner Shochat[1]; A Shotan[1]; M Kazatsker[1]; I Kleiner[2]; JM Weinstein[2]; D Blondheim[1]; A Asif[1]; I Dahan[1]; S Meisel[1]
[1]*Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel*; [2]*Saroka Medical Center, Cardiology, Beer Sheva, Israel*

Results of the IMPEDANCE-HF trial have shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The main trial was extended for an additional year to accrue more data on predictors of hospitalizations due to HF. The main aim of the study was to prove that HF patients with higher degree of long-standing pulmonary congestion are hospitalized more often.
Methods: Study population included 266 patients, with HF and LVEF$\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. Patients were examined and LI measured monthly in our outpatient clinics. Noninvasive LI measurements were performed with the high-sensitive device. Assessment of the degree of pulmonary congestion was by the new index LIR, measured at each visit and calculated as LIR = [currently measured LI/ normal baseline (calculated for each patient) -1] $\times$ 100 expressed as percentage. The annual average LIR for each patient was calculated as the mean of all LIR measurements at each consecutive year of follow-up (FU).
Results: The cumulative FU period was 634 patient×years in the monitored group and 483 patient×years in the control group ($p=0.001$). Groups were similar with respect to baseline characteristics. There were 228 HF hospitalizations in the monitored group (mean 0.54 per year) and 431 HF hospitalizations in the control group (1.29 per year, $p<0.001$). Rate of HF hospitalization was divided into 5 categories as follows: Q0: no HF hospitalizations during FU period, Q1: 0.01-0.3; Q2: 0.31-0.8; Q3: 0.81-1.7, and Q4 >1.7 HF hospitalizations/ per year of FU. Number of patients in Q0:Q1:Q2:Q3:Q4 were 53 (40%), 29 (22%), 25 (19%), 16 (12%) and 10 (8%) in the monitored group and 41 (31%), 17 (13%), 21 (16%), 21 (16%) and 33 (25%) in the control group, respectively ($p<0.01$, Figure 1). Results show that the level of congestion according to LIR during FU period was low in subgroup Q0 while increasing progressively from Q1 to Q4 in both groups ($p<0.001$). On the other hand, no difference in the level of congestion between the same quartile groups was measured. Conclusions (1) LI-guided treatment of HF patients significantly reduces the incidence of HF hospitalizations. (2) Preemptive LI-guided treatment cases a shift of patients from Q3-4 to Q0-1-2 in the monitored group in comparison with the control group. (3) There were no significant differences in the degree of pulmonary congestion between monitored and control patients of the same quartile. (4) As a result of the above, the main predictor for HF hospitalizations is the degree of pulmonary congestion during the FU period.

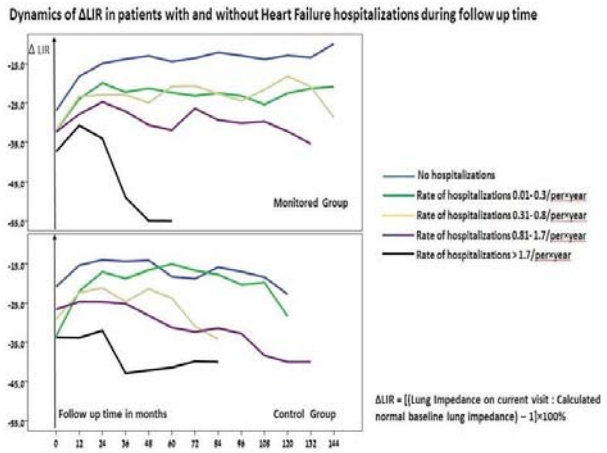


Figure 1

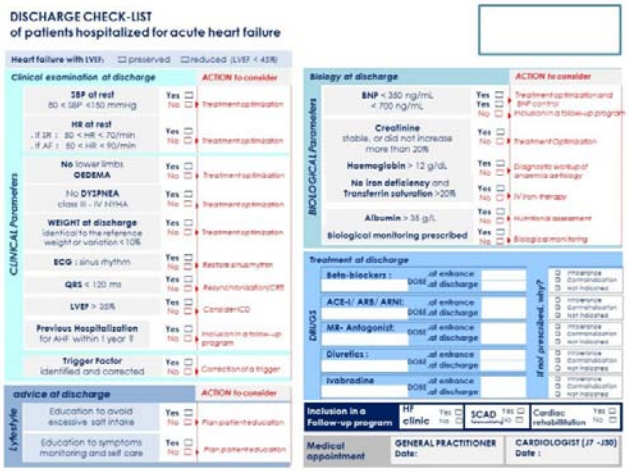
1535

Usefullness of a discharge check-list in acute heart failure

L Chaufourier[1]; K Blanchart[1]; D Legallois[1]; JJ Parienti[2]; A Belin[1]; P Milliez[1]; R Sabatier[1]
[1]*University Hospital of Caen, Cardiology, Caen, France*; [2]*University Hospital of Caen, Department of biostatistics and clinical research, Caen, France*

Background: Besides significant in-hospital mortality reduction in acute heart failure (AHF), rehospitalization rate remains a powerful predictor of mortality. AHF ESC guidelines recommend pre-discharge and long-term management to prevent early readmissions.
Purpose: We hypothesized that the systematic use of a discharge checklist (CL) after an AHF could have an impact on cardiovascular mortality and readmission rates.

Methods: Our checklist was designed according to ESC recommendations in order to promote treatment optimization and the development of a careplan after discharge (Fig 1). We included 240 patients hospitalized for AHF in our center: 137 patients from June to December 2014 before introduction of the CL, and 103 patients from July 2015 to January 2016 after introduction of the CL. The primary endpoint was cardiovascular death at 6-month. Propensity score matching was performed using a logistic regression model.
Results: Mean age was 77 ± 12 years, 56% were male, and 57% were HFrEF patients. There was a significant reduction in cardiovascular death at 6 months in the CL group (OR 2.1, IC 95 [1.1 to 3.98], p = 0.02). There was a non-significant decrease in the 6-month AHF re-admissions rate in the CL group (29.1 vs. 32.1%, p = 0.57), but the increased death rate in the control group may have reduced this impact. Disease management program was more often used in the CL group (36,3% vs 15,4%, p = 0.0002). At discharge, 82% of patients among CL group had a medical appointment within a month, compared to 33% of patients in the control group (p < 0,0001). Therapeutic optimization was better in the CL group, especially for patients with HFrEF: ARB/ACE-I and beta-blockers were more often prescribed or up-titrated according to ESC guidelines (p = 0,016 and p = 0,03).
Conclusion: In unselected patients hospitalized for AHF, the use of a standardized checklist reduced cardiovascular mortality at 6 months. It also improved therapeutic optimization at discharge and increased systematic follow-up plan utilization. Larger studies are needed to demonstrate a significant reduction in re-admission rates.



Check-List

1536

Comparison of ultrafiltration versus diuretic treatment in patients with acute decompensated heart failure - A meta-analysis

B Bastian Wobbe[1]; L Czopf[1]; K Farkas[2]
[1]*University of Pécs, 1st Department of Medicine, Division of Angiology and Cardiology, Pécs, Hungary*; [2]*University of Pécs, Institute of Bioanalysis, Pécs, Hungary*

Background: Diuretics are the number one treatment choice for patients hospitalized with acute decompensated heart failure (ADHF) presenting with signs and symptoms of volume overload. Inconsistent responsiveness to diuretic treatment and treatment-related side-effects have led to the development of new and potentially safer treatment options. Several studies investigated the effectiveness and safety of the use of ultrafiltration (UF) on decongestion in patients with ADHF so far. But, due to the heterogenic study outcomes, uncertainty remains, whether UF is a safe and valid alternative to the standard diuretic treatment.
Purpose: We conducted a systematic meta-analysis with the primary goal of assessing the impact of extracorporeal UF compared to the standard diuretic treatment using diuretic agents.
Methods: We searched EMBASE, the Cochrane Registry and PubMed to identify studies comparing UF with the usual care therapy using diuretic agents in patients hospitalized for ADHF. We used the search terms "acute heart failure", "ultrafiltration", "diuretic agent" (for EMBASE and Cochrane) or "diuretics" (for PubMed) and filtered for "randomized controlled trials". The date of the search was the 17.10.2016.
Results: We identified 9 randomized controlled trials enrolling 820 participants, of whom 402 (49%) were randomized to UF and 418 (51%) to control. Overall, UF treatment lead to significantly larger amount of fluid removal (Difference in means: 1325 ml, 95% CI: 817 to 1833 ml, p = < 0.001) and weight loss (Difference in means: 1.52 kg, 95% CI: 0.27 to 0.99 kg, p = < 0.001). Furthermore, we found significant lower incidences of worsening heart failure in patients treated with UF (OR: 0.63, 95% CI: 0.43 to 0.94, p = 0.022). However, further analysis of adverse events showed no difference between groups concerning incidences of renal impairment (OR: 1.44, 95% CI: 0.91 to 2.28, p = 0.117), cardiovascular disorders except heart failure (OR: 1.57, 95% CI: 0.92 to 2.68, p = 0.097) and potentially treatment-related adverse events (including hypotension, syncope and electrolyte disorders) (OR: 1.17, 95% CI: 0.64 to 2.14, p = 0.614). No differences were observed in the analysis of all-cause mortality (OR: 1.13, 95% CI: 0.75 to 1.71, p = 0.546). The treatment with UF was associated with a significant reduction in heart failure related re-hospitalizations compared to diuretic treatment (OR: 0.543, 95% CI: 0.362 to 0.815, p = 0.003).
Conclusion: Compared to diuretic therapy, UF induces larger weight loss and fluid removal, reduces the number of heart-failure related re-hospitalizations and the risk of worsening heart failure in congestive patients. The available evidence suggests that ultrafiltration is a safe and effective treatment option for volume overloaded heart failure patients.

1537

Serum chloride and sodium interplay in patients with acute myocardial infarction and heart failure with reduced ejection fraction: an analysis from the high-risk myocardial infarction database initiat

JP Ferreira[1]; N Girerd[1]; K Duarte[1]; S Coiro[1]; JJV Mcmurray[2]; H Dargie[2]; B Pitt[3]; K Dickstein[4]; JM Testani[5]; F Zannad[1]; P Rossignol[1]
[1]*Clinical Investigation Centre Pierre Drouin (CIC-P), Nancy, France*; [2]*Cardiovascular Research Centre of Glasgow, Glasgow, United Kingdom*; [3]*Northwestern University, Chicago, United States of America*; [4]*Bergen University College, Bergen, Norway*; [5]*Yale University, New Haven, United States of America*

On behalf of: High Risk MI initiative

Background: Serum chloride levels were recently found to be independently associated with mortality in heart failure (HF).
Methods: and Results: We investigated the relationship between serum chloride and clinical outcomes in 7195 subjects with acute myocardial infarction (MI) complicated by reduced left ventricular function and heart failure (HF). The studied outcomes were all-cause mortality (ACM), cardiovascular mortality (CVM), and hospitalization for HF (HHF). Both chloride and sodium had a non-linear association with the studied outcomes (p < 0.05 for linearity). Patients in the lowest chloride tercile (chloride ≤100) were older, had more comorbidities, and lower sodium levels (p < 0.05 for all). Serum chloride showed a significant interaction with sodium with regard to all studied outcomes (p for interaction < 0.05 for all). The lowest chloride tercile (≤100 mmol/L) was associated with increased mortality rates in the context of lower sodium (≤138 mmol/L) [adjusted HR (95%CI) for ACM = 1.42 (1.14-1.77), p = 0.002], whereas in the context of higher sodium levels (>141 mmol/L), the association with mortality was lost. Spline-transformed chloride and its interaction with sodium did not add significant prognostic information on top of other well established prognostic variables (p >0.05 for all outcomes).
Conclusions: In post-MI with systolic dysfunction and/or HF, low serum chloride was associated with mortality (but not HHF) in the setting of lower sodium. Overall, chloride and its interaction with sodium did not add clinically relevant prognostic information on top of other well established prognostic variables. Taken together, these data support an integrated and critical consideration of chloride and sodium interplay.

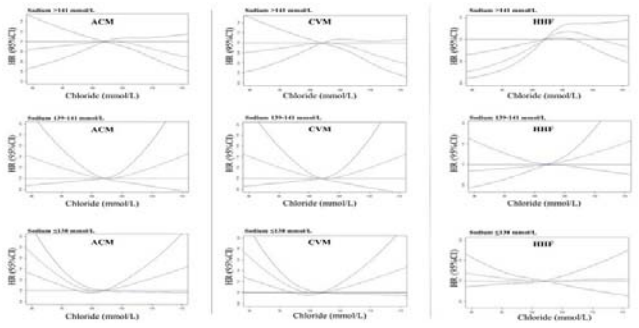


Figure 1

1538

Prognostic impact of glucose in acute myocardial infarction complicated by cardiogenic shock - A substudy of the IABP-SHOCK II-trial

A Abdin[1]; J Poess[1]; G Fuernau[1]; S Desch[1]; T Ouarrak[1]; S De Waha[1]; I Eitel[1]; U Zeymer[2]; M Boehm[3]; H Thiele[1]
[1]University Hospital of Schleswig-Holstein , Heart Center Lubeck, Lubeck, Germany; *[2]Hear Center Ludwigshafen, Ludwigshafen, Germany*; *[3]Saarland University Hospital, Homburg, Germany*

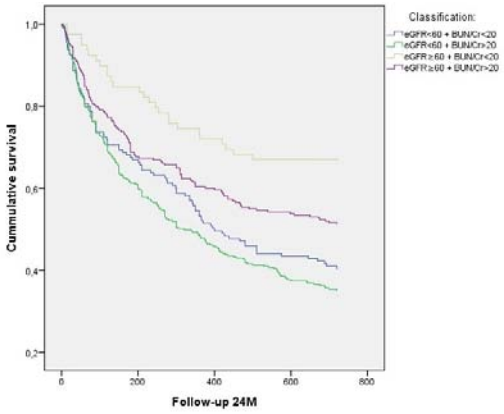
Background: In the setting of acute illness and as a stress response, glucose levels have been shown to be significantly increased. Data from observational studies suggest an association between glucose levels and prognosis of patients with cardiogenic shock (CS). Aim of the present study was to investigate the prognostic role of glucose at admission with respect to 30-day mortality in patients with CS complicating acute myocardial infarction (AMI) included in the large, randomized Intraaortic Balloon Pump in Cardiogenic Shock (IABP-SHOCK II) trial.
Methods: In IABP-SHOCK II, 600 patients with CS complicating AMI undergoing early revascularization were randomized to therapy with either IABP or no IABP. There were no differences between the groups with respect to the primary and secondary endpoints. Glucose levels at admission were available in 513 patients. The investigated endpoint was 30-day mortality.
Results: Out of the 513 patients, 213 (41.6%) died. Compared to survivors, non-survivors had higher glucose levels at admission (median [interquartile range (IQR)]: 13.0mmol/L [9.2; 18.2] vs. 10.5mmol/L [7.8; 15.5]; p = 0.0004). Patients with glucose concentrations above the median (11.5 mmol/L) had higher 30-day mortality compared to those below the median (47.7% vs. 36.5%; p = 0.005). This negative prognostic impact of increased glucose remained significant in a multivariate analysis adjusted for several factors which were associated with mortality in univariate analysis, such as age, renal function, Thrombolysis In acute Myocardial Infarction (TIMI) flow after percutaneous coronary intervention (PCI), and arterial lactate concentrations (Hazard ratio for each 10mmol/L increase of glucose 1.2; 95% confidence interval; 1.01-1.46, p = 0.039). In total, 33.7% of the patients had diabetes. Patients with diabetes had higher glucose levels compared to those without diabetes (median [IQR]: 13.1 [9.5-18.3] vs. 10.8 [7.8-15.4], p = 0.0003). Notably, the adjusted prognostic impact of increased glucose levels at admission was not influenced by presence or absence of a diabetes mellitus (p for interaction=0.41).
Conclusions: In patients with CS complicating AMI included in IABP-SHOCK II, increased glucose concentrations at admission were independent predictors for 30-day mortality, independently of the diabetic state.

1539

The application of ratios urea/ creatinine and BUN/ creatinine in acute heart failure

M L Goncalves[1]; JULIO Gil[1]; LUIS Abreu[1]; HUGO Antunes[1]; BRUNO Marmelo[1]; M I Pires[1]; ISABEL Cunha[1]; DAVIDE Moreira[1]; INÊS Almeida[1]; COSTA Cabral[1]
[1]Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal

Introduction: Worsening renal function (WRF) is an important comorbidity that is often seen in acute heart failure (AHF). The pathological mechanism is multifactorial, not completely understood, and is defined by an increase in creatinine>0.3mg/dL or a fall in eGFR>20%. WRF is not always clinically dangerous. Urea (U), creatinine (Cr) and BUN have been classically used as proxies for RF assessment with low specificity, limited by external factors. In acute kidney injury, BUN/Cr ratio>20 is indicative of pre-renal injury. The objective of this study is to investigate the usefulness and prognostic implications of U/Cr and BUN/Cr ratios in P with AHF.
Methods: Included 1006P hospitalized for AHF in a Cardiology ward between 2009-2015. Excluded P undergoing renal replacement therapy or eGFR by CKD-EPI < 15mL/min/1.73m2. The values of BUN, eGFR and ratios were calculated. Ratio BUN/Cr was considered elevated when >20, and U/Cr when >100. Division into groups accordingly with ratios (increased vs. normal) and eGFR (≥60 vs < 60). Follow-up of 24 months. The groups were compared in relation to in-hospital death (IHD) and long-term survival.
Results: Sample of 983D. 51.7% male, mean age 76.5 ± 9.8 years, mean U 69.0 ± 35.5mg/dL, mean Cr 1.3 ± 0.5mg/dL, mean BUN 32.2 ± 16.6mg/dL, mean BUN/Cr 25.8 ± 9.4, mean U/Cr 55.2 ± 20.1, eGFR 55.3 ± 22.7mL/min/1.73m2. WRF in 17%, 6.4% IHD, 16.2% death at 24 months. There was no statistically association between the elevated U/Cr and BUN/Cr ratios and the development of WRF throughout hospitalization. The BUN/Cr and U/Cr ratios alone were not shown to be associated with IHD. There was no difference between P-eGFR < 60 and ≥60 in relation to IHD, although there was a trend in favor of the higher number of IHD in P-eGFR < 60 (X2=2.7, p = 0.09). However, when subgroup analysis was performed, P-eGFR < 60 and elevated BUN/Cr ratio had a statistically significant association with IHD (X2=4.3 p = 0.04) when compared with P-eGFR < 60 and normal ratio. For the same population the high U/Cr ratio also had a statistically significant association with IHD (X2=4.07, p = 0.04). In the survival analysis, it was found that: high BUN/Cr ratio was associated with lower survival at 24 months (Kaplan-Meier X2=6.8, p < 0.09), whereas high U/Cr ratio was not. When eGFRr was stratified (graphic), P-eGFRr < 60 and increased BUN/Cr had lower survival than P-eGFRr < 60 without increased BUN/Cr ratio, and these had a lower survival rate than P-eGFR≥60 and increased BUN/Cr, and that P-eGFR≥60 and normal BUN/Cr ratio had the best survival rate at 24 months (Kaplan-Meier X2=36.9, p < 0.001). In relation to the U/Cr ratio, there was no difference in survival in subgroup analysis.
Conclusion: It has been shown that high BUN/Cr and U/Cr ratios are associated with IHD. In the long term, the BUN/Cr, but not the U/Cr, has an additive value to the isolated eGFR evaluation and can be used to improve the prognostic stratification in AHF.



Kaplan-Meier survival 24Months

1540

A new model to predict readmission for heart failure

M Michael Kleiner Shochat[1]; A Shochat[1]; M Kazatsker[1]; I Kleiner[2]; JM Weinstein[2]; A Asif[1]; D Blondheim[1]; I Dahan[1]; S Meisel[1]
[1]Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel; *[2]Saroka Medical Center, Cardiology, Beer Sheva, Israel*

Background Readmission of Heart Failure (HF) patients comprises a medical burden. Aim To assess the hypothesis that the extent of improvement of pulmonary congestion during hospitalization for HF as evaluated by lung impedance (LI) can predict readmission rate.
Methods: This was a randomized, single blinded 2-center study. Study population included 256 patients with HF and LVEF ≤35% in NYHA class II-IV randomized to conventional or LI-guided therapy.
Results: Baseline LI was calculated and used to derive LIR reflecting the degree of pulmonary congestion. The difference between LIR at admission and at discharge was used to assess improvement in the pulmonary congestion. The improvement in LIR was graded by quartiles (Q1 < 4.9%; Q2: 4.9-10.2%; Q3: 10.3-15.7%; Q4>15.7%). Improvement in NYHA class at discharge was graded as 1 or 2, in weight as < 3 or >3 kg, leg edema as 1-3 and level of lung rales as 1 or 2. Patients of group 1 (n = 128) were treated according to LI and group 2 (n = 128) by clinical assessment only. Mean follow-up was 56 ± 31 and 46 ± 28 months in group 1 and 2 (p < .001), accounting for 225 vs. 411 HF hospitalizations, respectively (p < .001). There were 29 and 52 HF-related and all-cause deaths in the group 1 and 50 and 71 deaths in the group 2, respectively (p < .01). Rate of readmissions according to Q1-4 was 97, 36, 2, 0% and 96, 43, 4, 0% within 1 month (p < .0001 within groups and p < .02 between groups), 100, 91, 61, 22% and 100, 99, 86, 35% (p < .0001 within groups and p < .001 between groups) within 12 months in group 1 and 2, respectively. Average times from discharge to readmission at Q1-4 were 14, 65, 244, 706 days and 11, 60, 189, 589 days for group 1 and 2 (p < .0001 within and between groups). Hazard ratios (HR) for HF hospitalizations at the level of improvement Q2, Q3, Q4 compared to Q1 were 0.21, 0.001, 0.0001 (within 1 months), 0.3, 0.1, 0.02 (within 12 months) in group 1 and 0.19, 0.01, 0.0001 (within 1 months), 0.35, 0.2, 0.04 (within 12 months) in group 2, p < .001 within and between groups, respectively. Improvement in NYHA classes, weight reduction, lung rales and leg edema improvement during HF hospitalization also reduced the probability of HF readmissions within 1 and 12 months (p < .01, within and between groups), but predictive power was weaker (HR = 0.3-0.7).
Conclusion: The extent of improvement in pulmonary congestion during HF admission assessed by LI is a strong and accurate measure for readmissions within 1and 12 months for both groups. LI-guided treatment significantly reduced HF readmissions but only if moderate or significant improvement in pulmonary congestion was achieved (Q3-4). Discharge of patients of both groups at the Q1 level of pulmonary congestion improvement resulted in an unacceptable readmission rate of 98% within one month. Prognostic power of changes in such clinical parameters as NYHA class, lung rales, weigh and leg edema is significantly lower than LI.

CLINICAL CASE CORNER 5 - CANCER AND CANCER THERAPY: A DOUBLE EDGED SWORD

1541

Exercise cardiac MRI with pulmonary artery catheter monitoring in early manifestation of carcinoid heart disease: a first in men case report

PH Timmermans[1]; T Petit[2]; J Bogaert[3]; E Van Cutsem[4]; J Van Cleemput[1]; F Rega[5]
[1]University Hospitals (UZ) Leuven, Cardiology; heart failure and transplantation, Leuven, Belgium; *[2]University Hospitals (UZ) Leuven, Cardiology, Leuven, Belgium*; *[3]University Hospitals (UZ) Leuven, Radiology, Leuven, Belgium*; *[4]University Hospitals (UZ) Leuven, Digestive oncology, Leuven, Belgium*; *[5]University Hospitals (UZ) Leuven, Cardiac surgery, Leuven, Belgium*

INTRODUCTION A first report about the use of an exercise cardiac MRI with pulmonary artery catheter measurements to investigate carcinoid heart disease. CASE REPORT A 58 years old woman was referred from the oncology department to the heart failure clinic because of progressive dsypnea on exertion. She was diagnosed with a neuro-endocrine tumor and liver metastases 4 years earlier. After several treatment cycli, she had a stable disease at the time of presentation. The dyspnea was present since a few weeks. There were no signs of heart failure on clinical examination. ECG showed only minor alterations. Echocardiography revealed a structurally normal left heart, but severe tricuspid regurgitation (TR) with retraction of the leaflets. RV function was normal, there was no RV dilatation but a clear diastolic D-shaping of the interventricular septum – indicative of volume overload. CPET showed a VO2 max of 27.3 ml/min/kg (86% of pred max). Invasive investigations were started to evaluate the patient for valve surgery. Coronary angiography did not show any significant stenoses, and right heart pressures were within normal range. However, we were still convinced that the severe tricuspid insufficiency should have an hemodynamic impact on the heart, given the complaints of the patient. Moreover, we recently analysed the results of carcinoid valve surgery executed in our centre the last 16 years (cfr separate abstract submitted to Heart Failure 2017) and concluded that late referral for valve surgery could lead to high perioperative mortality. We organized an exercise test in the cardiac MRI with measurements of the intracavitary pressures using a MRI-compatible pulmonary artery catheter. Results are shown in figure 1. Apparently, early manifestation of severe isolated TR without RV dysfunction leads to a decrease in RVESV but an increaese in RVEDV during excercise, resulting in an absence of stroke volume increase – cleary an abnormal finding - without left or right sided systolic dysfunction or congestion. Left sided volumes and pressures hardly changed during excercise; this is likely caused by a lack of LV preload increase. Based on the symptoms of our patients and the results of the CMR, our patient was referred for surgery. She underwent a tricuspid valve replacement with an bioprothesis size 29. The postoperative period was uneventfull, with extubation on day 1 and discharge from the ICU on day 3 after surgery. Further hospital stay was without complications. Symptoms of dyspnea on exertion improved after cardiac rehabilitation. She is currently in ambulatory FU more than 2 years after surgery. There are no signs of prostetic valve dysfunction on TTE. Her exercise capacity on CPET has recently dropped (VO2 max 23.6 ml/min/kg, 75% of pred max) because of both chronotropic incompetence (she is now on a low dose of b-blocker) and, unfortunately, a progressive malignancy for wich SIRS (selective intrahepatic radiation with spheres) is planned. Conclusion: Early detection of carcinoid heart disease is important for a timely referral for valve surgery. After onset of valvular manifestation, these patients may have a limited time frame in which they have a stable oncological process, a still preserved RV function and general acceptable and non-cachectic clinical condition to survive cardiac surgery and still benefit from the intervention. Multidisciplinary disease programs and exercise cardiac MRI, possibly without invasive pressure measurement, can identify the patients best suitable for valve surgery.

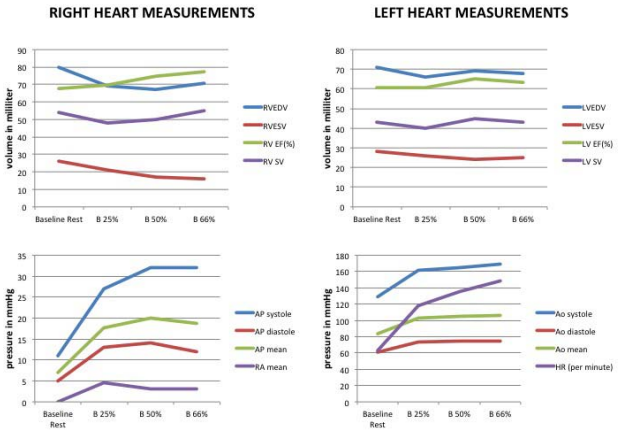


figure 1

1542

Toxic influence of cancer chemotherapy on heart function and hemodynamic parametres

I Igor Katsytadze[1]; K Filonenko[2]; I Prudkyi[1]; O Vasylenko[1]; YU Sychenko[3]; L Samoylenko[3]
[1]O. Bogomolet's National Medical University, Kyiv, Ukraine; *[2]National Institute of Cancer, Kiev, Ukraine*; *[3]Kiev Alexander Clinical Hospital, Kiev, Ukraine*

Case report description. Toxic influence of chemotherapy (ChT) in cancer patients is very common and has a wide range of manifistations. Toxic damage of cardivascular and neuro systems is one of the most serious and prognostic unfavorable complications. We represent a clinical case of a man of 46 years old with Hodgkin's Lymphoma verified with CT (conglomerates of mediastinal lymp nodes) and biopsy of lymph node (Hodgkin's cells, CD20-, CD30+, Ki-67 20%, Pax5+) (pic.1). The patient was terated according BEACOPP-esc ChT sceme which includes ethopozide, doxorubicine, cyclophosphamide, etc during 6 courses for 14 days each one. After the start of 4th course of ChT, the patient began to complain of a violation of sensitivity in hands and stumbling while walking, palpitations, difficulty breathing, weakness, aching pain in the heart.
Neuro Status: Peripheral signs of distal symmetric sense-motoric polyneuropathy Neurotoxicity II type. HR -124, arrhythmic, BP - 100/60, SpO2 - 91%
ECG: AFib, low voltage ECG. Echo: ESV- 72ml, EDV - 124ml, EF -42%, LA - 3,6, RV - 32mm, Ao - 26mm, PA - 32 mmHg, IVS - 10,5mm, PW - 10mm. Hypokinesia of all walls. Troponin I - 3,12 ng/ml ("grey zone"). NTproBNP - 2456 pg/ml (high positive). Questions, problems. The problem of this case is a wide area of backside effects of chemotherapy in the middle of course of cancer treatment. The main questions: should we continue chemotherapy or change doses? how can we improve cardiac function and stop AF? how can we reduce neuro symptomatic? As a consilium decission we've stoppet 4th course of chemotherapy, delayed 5th course of 2 weeks, changed BEACOPP-esc sceme to ABVD (low dose of doxorubicine, bleomicine, vinblastin, dacarbazine). Amiodaron iv infusion (600mg) was started to restore synus rhythm. Enoxaparine 40mg bd was added as well as Furosemide 40mg iv, Eplerenone 25mg. After 24 hours, synus rhythm was restored with HR 86' BP 105/64mmHg. Amiodarone was changed to bisoprolol (2,5mg od) and was added ivabradine 2.5mg twice a day. On 3rd day of treatment coronary angiography was performed (no serious stenosis). For the improvement of systolic function infusion of levosimendan (Lv) was started. In 3 days after Lv infusion and concominent treatment , HR 70, BP 125/75mmHg, SpO2 96% Perindopril was added 5mg od.

Neurogical treatment included vitamine B, phosphates, α lipoic acid, anticholinergic drugs, anticonvulsants.

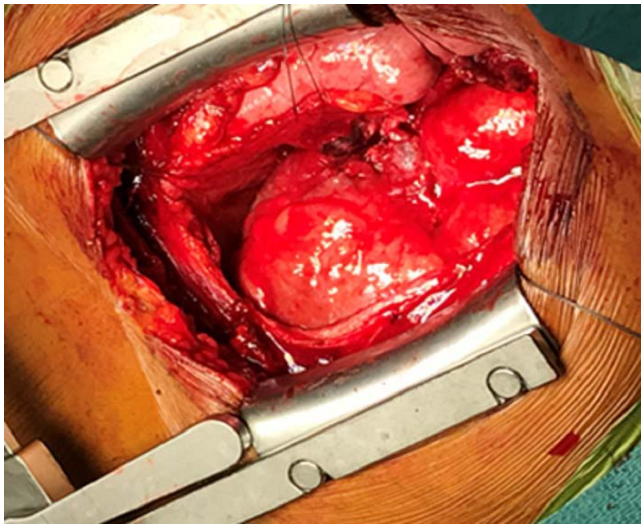
Answers: In 8 days, the patient was discharged and directed to the oncologist. with regression of neurological and cardiac sympoms, improvement of systolic function and synus rhythm.

Conclusions: Only close cooperation of different specialists may leads to success story Unfortunately, database of this patients is not significant and all the concominent treatment should be studied. Moreover, toxic effects of ChT may be observed for a long time after finishing the cancer treatrment and needs for follow up monitoring. Post hoc examination of the patient (1,5 year later) showed an stable remission of Lymphoma, no signs of heart failure, regress of neurogical symptoms.

Echo and labs data

	D0	D1	D5	Discharge	M18
EF, %	58	42	43	50	51
Serum creatinine, mmol/l	78	133	118	86	80
NTproBNP, pg/ml	n/a	2456	1846	768	456
Troponin I, ng/ml	n/a	3,12	2.76	1,19	0,12

D0 - before chemotherapy course, D1 - first day in cardiac ICU, D5 - before Lv infusion, M18 -post hoc visit in 18 mo



Picture 1.

1543

Cardiac hemorrhagic tamponade in a young adult male

A M Neagoe[1]; K Wustmann[1]; S Bloechlinger[1]; D Reineke[1]; T Suter[1]
[1]*Bern University Hospital, Cardiology, Bern, Switzerland*

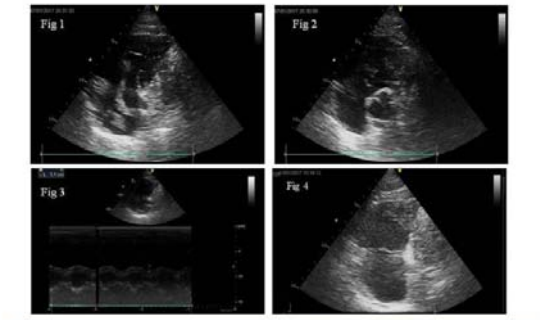
A 26-year old male, with no medical history, was admitted by ambulance after he suffered a syncope. He had been complaining about chest pain and dyspnea over the previous 6 days. During transport to the hospital the patient showed signs of bradycardia and lost his consciousness for 5 sec. Diagnostic : Transthoracic echocardiography (TTE) performed in the shock room showed tamponade. By emergency pericardiocentesis hemorrhagic fluid was removed and a drain inserted. By thoracic computed tomography (CT) an aortic dissection was ruled out, but a heterogeneous mass within the right atrium (RA) was apparent in an otherwise unremarkable scan. Cardiac magnetic resonance (CMR) revealed a 23x25x39mm sized tumor of inhomogeneous appearance with oedema in the native sequences, remarkable perfusion in the first-pass and inhomogeneous late enhancement with central necrosis, suspicious of an highly vascularized malign tumor. No other evidence of malignancy was found in a whole-body PET-CT. Work-up of the pericardial effusion revealed activated mesothelial but no malignant cells. Therapy: The tumor was removed in toto (Picture 1), the right atrium reconstructed with a pericardial patch and local pericardectomy was performed. Histopathology determined a high grade angiosarcoma of the RA with clear margins of resection. After 18 days of hospitalization, the patient was discharged in good conditions for rehabilitation. Further development: Adjuvant chemotherapy is planned. Conclusion: Pericardial effusion is a common clinical finding in young patients, frequently due to pericarditis. However, tamponade and in particularly hemorrhagic pericardial effusion is uncommon and warrants further work-up. In our patient the echocardiogram and CT scan revealed a tumor in the right atrium. Cardiac MRI was critical for further differentiation of the findings. Based on morphology and perfusion characteristics we suspected a malignant tumor, possibly an angio- or fibrosarcoma. A myxoma, lipo- or myosarcoma appeared less likely. Primary tumors of the heart are rare, and only 25% of cardiac tumors are malignant and occur mostly in adulthood. The most common malignant tumor of the RA is an angiosarcoma. There is only limited data on optimal treatment and prognosis of this disease. However, complete resection and an adjuvant, anthracycline-containing chemotherapy is currently standard of care.

1544

Acute right ventricular failure in an oncological pacient

A Andreea Rachieru[1]; B Zamfirescu[1]; R Aflorii[1]; D Rednic[1]; A Linte[1]; D Dimulescu[1]; A C Popescu[1]
[1]*Elias Emergency Universitary Hospital, Cardiology, Bucharest, Romania*

We present the case of a 63 year old woman, hypertensive, diabetic, with radical hysterectomy, admitted for shortness of breath and extreme fatigue, also dry cough and fever, denying chest pain or syncope. The patient was on chemotherapy for clear cell endometrial cancer, a rare and aggressive type of neoplasm. She was in a severe state, hypoxic (oxygen saturation of 86%), diminished breath sounds bilaterally, low BP (85/50 mmHg), tachycardia (100 bpm), oliguric and without valvular murmurs or signs of deep vein thrombosis (DVT). ECG showed sinus tachycardia, incomplete RBBB, Q wave in DIII and T wave inversion in the precordial and inferior leads. At that moment (based on findings and also 7 points on Wells score), pulmonary embolism (PE) was taken into consideration. Transthoracic echocardiography showed dilated right heart cavities, indirect signs of pulmonary hypertension, normal LVEF but severe dysfunction of the right ventricle (hypokinesia, TAPSE = 11 mm), and also a mobile structure (4.5/1 cm) extending from the RA to the RV through the tricuspid valve. CT angiogram confirmed bilateral massive pulmonary embolism with right heart trombus, thrombosis of portal and superior mesenteric veins and also hepatic secondary tumors. Biologically – there is moderate iron deficiency anemia, high ESR, positive I troponin, high NT pro-BNP, mild renal dysfunction and dyslipidemia. Even though the diagnostic was bilateral massive pulmonary embolism with high risk, due to patient's comorbidities (active cancer, moderate anemia), the management was anticoagulant therapy with unfractioned heparin, dobutamine and dopamine for acute right heart failure, oxygenotherapy, red blood cell transfusion in order to correct anemia. Ultrasonography of the lower limb veins showed no signs of DVT. Despite all of the mentioned predictors of poor prognosis, the evolution was good, with improvement of dyspnea and progressively decreased doses of inotropic agents. Follow-up showed better RV function and the disappearance of intracardiac thrombus, possibly by embolisation of the fragmented thrombus into the pulmonary circulation without additional clinical impact. After 2 weeks, a whole-body CT scan was made, confirming regression of endoluminal thrombi, but with infarction in the left superior pulmonary lobe, and also advanced peritoneal carcinomatosis. The patient was transferred to the Oncology Department for palliative care with the recommendation for indefinite anticoagulation with LMWH. The particularity of this case is that even though mortality rate is high in patients with PE and right heart thrombi-in-transit, this patient survived and improved clinically under anticoagulant therapy.



Transtoracic echocardiography performed during evolution shows in fig 1-3 – mobile structure from RA to RV; dilated right cavities and RV severe disfunction (reduced TAPSE); in fig 4 the mobile structure mentioned is no longer seen.

Echocardiography - evolution

1545

Primary pericardial mesothelioma presenting as infective pericarditis

A Krivickiene[1]; A Mikalauskas[1]; J Justina Motiejunaite[1]; A Kavoliuniene[1]
[1]*Hospital of Lithuanian University of Health Sciences, Cardiology, Kaunas, Lithuania*

Introduction: Primary pericardial mesothelioma (PPM) is a rare disease (the prevalence 0.0022%), with only 350 patients reported in the literature to date. We describe a case of a woman who presented with infective pericarditis and was diagnosed with PPM.

Case report description: 37 year old woman was referred to emergency department because of nausea, epigastric pain and fever up to 39.5°C. These symptoms started suddenly and had been lasting for 4 days. She denied any previous diseases. The laboratory tests showed inflammation (C-reactive protein 248 mg/l). Echocardiography exam revealed a large accumulation of pericardial fluid - up to 3.4 cm at left ventricle (LV) with echocardiographic signs of cardiac tamponade (Fig.1). Additional investigations were performed in order to determine the source of infection. The chest computed tomography (CT) revealed left pleural effusion up to 3.5 cm and pericardial effusion up to 1.6 cm at LV and up to 0.5 cm at right ventricle (RV) (Fig.1). Diagnostic pleural puncture with biochemical, microbiological and cytological analyses showed non-specific characteristic of exudate without atypic cells or microorganisms. While differentiating from other pericardial diseases, additional tests showed no findings for autoimmune, haematological and genitourinary diseases, viral infection or thyroid dysfunction. Diagnosis of acute infectious effusive pericarditis, complicated by asymptomatic cardiac tamponade was confirmed. Antibiotics, non-steroidal anti-inflammatory drugs and diuretics were prescribed. During the initial pharmacotherapy the clinical condition of the patient improved significantly. Inflammatory markers decreased and pericardial effusion diminished from 3.4 cm to 1.3 cm. Nevertheless, episodes of fever up to 38°C were still observed. Left thoracotomy was performed due to suspicion of purulent pleuritis and pericarditis, but the purulent process was not proven. Biopsy of both 2 pleural layers and pericardium was performed. Histological examination confirmed the diagnosis of pericardial mesothelioma. Chemotherapy with cisplatin and pemetrexed was initiated, in total 6 courses have been administered. Follow-up for additional 6 months didn't show any spread of PPM. The young woman is in a stable medical condition and continues follow-up.

Conclusions: This case highlights the diagnostic challenges of PPM and a rare case of successful treatment. Diagnosis of PPM is challenging primarily because of its rarity. While CT and MRI are useful tools for diagnosis of PPM, histological examination is required to obtain a definitive diagnosis. No standard treatment guidelines for PPM have been established yet. Novel chemotherapeutic agents have demonstrated sufficient efficacy. PPM carries a poor prognosis due to its late presentation and limited treatment options. Most patients die within 1 year of presentation. Our patient is has been stable for 21 months since the diagnosis of PPM.

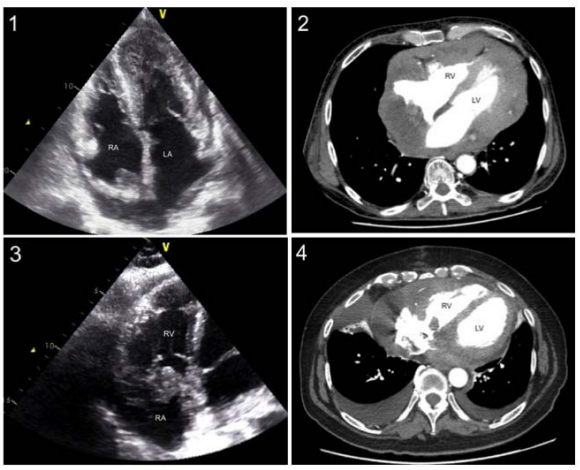
1546

Burkitt lymphoma presenting as an intracardiac mass: two cases

I Ilaria Battistoni[1]; D Contadini[1]; M Marini[1]; M Francioni[1]; L Angelini[1]; S Moretti[1]; A Gili[1]; M Dottori[1]; GP Perna[1]
[1]*University Hospital Riuniti, G.M.Lancisi Hospital, Department of Cardiology, Ancona, Italy*

Introduction: the intracardiac masses represent a rare clinical disease. They are usually due to infectious, thrombi or tumour metastasis and less frequently to primary tumours. A correct differential diagnosis is crucial to establish the appropriate therapy. We report two cases of intracardiac masses recently presented to our attention. Case 1: 57-year-old man, infected with human immunodeficiency virus (HIV) from 8 years. His previous history revealed two episodes of pericarditis in the last two months. On admission, he referred worsening dyspnoea on exertion in the last week and presented signs and symptoms of superior vena cava syndrome. ECG revealed no specific alterations. Transthoracic echocardiography (TTE) showed a slight pericardial effusion and an abundant solid tissue in the pericardial space with "ab-estrinsic" infiltration of heart wall chambers, origin of aorta and both vena cava. Moreover a pseudonodular mass with irregular margins and size of 2x2.8 cm was inside the right atrium (Figure 1). The right ventricle was hypokinetic (TAPSE 12 mm, Fractional Area Change (FAC) 30%). The left ventricle ejection fraction (LVEF) was 48%. Mild tricuspid regurgitation was noted with systolic pulmonary arterial pressure (PAPs) of 38 mmHg. Transesophageal echocardiography (TEE), computed tomography (CT) scan (Figure 2) and magnetic resonance imaging (MRI) confirmed our findings. Case 2: 55-year-old man with diabetes mellitus. He was admitted in our intensive care unit with signs of cardiac tamponade. The patient underwent urgent pericardiocentesis. On admission, ECG revealed a sinus tachycardia and low voltage QRS complex. TTE revealed a solid extra- and intracardiac mass (4.5x3.2 cm) on the atrioventricular groove near the lateral portion of the tricuspid annulus (Figure 3). A slightly dilated and hypokinetic right ventricle was also observed (TAPSE 6 mm, FAC 28%). The LVEF was 40%. Mild tricuspid valve regurgitation with PAPs of 45 mmHg was also present. The findings were confirmed by a TEE. A positron emission tomography (PET-CT) scan revealed in the mass an intense hypercaptation extended to the mediastinum (Figure 4). Both patients underwent an uncomplicated ultrasound-guided endovascular biopsy. Pathology report revealed a diffuse tumour proliferation of large lymphatic B cells. Intense mitotic activity was noted with areas of apoptosis. The diagnosis in both cases was Burkitt lymphoma with primary cardiac localization. The immunohistochemical essays confirmed the diagnosis too. Chemotherapy was immediately started next to the support cardiological therapy (fluids, diuretic, dopamine and norepinephrine in the first case) and fluids, diuretic, dopamine and dobutamine in the second one).

Discussion: Burkitt lymphoma is infrequent accounting for less than 1% of all non-Hodgkin lymphomas and 25-30% of the lymphomas in HIV-affected population. Primary cardiac lymphoma localization is extremely rare with non-specific signs and symptoms and can often be overlooked or underappreciated. Due to the very rapid growth of Burkitt lymphoma, a prompt diagnosis and treatment are crucial to get good prognostic outcomes. A multidisciplinary involvement (cardiologist, oncologist and radiologist) is essential to achieve optimal outcomes.



TTE and CT scan of the two cases

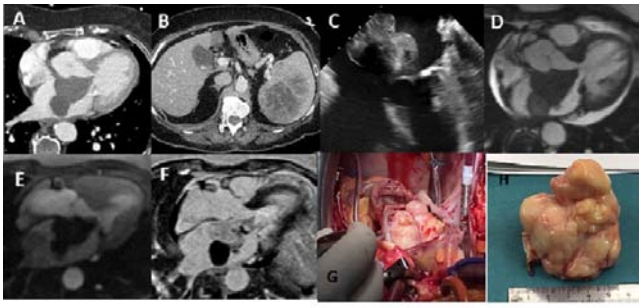
1547

Two times cancer: is a third time a relapse or a primarius?

A M Alexandra Maria Neagoe[1]; L Hunziker[1]; D Reineke[1]; S Bloechlinger[1]; V Eigenmann[1]; T Suter[1]; K Wustmann[1]
[1]*Bern University Hospital, Cardiology, Bern, Switzerland*

Case: A 75yo female with history of rectal and uterus carcinoma (1999 and 2008) presented with progressive dyspnea, palpitations and newly diagnosed anemia. Diagnosis: By thoracic computed tomography (CT) pulmonary embolism was ruled

out, but showed a large left atrial (LA) mass and calcified posterior mitral valve (MV) leaflet. Abdominal CT slices revealed an heterogeneous splenic mass without evidences of metastases. Transthoracic echocardiography depicted a severe "mitral" stenosis (mean grad. 16mmHg) caused by the hypo-echogenic LA mass. In suspicion of a thrombus, anticoagulation was started and the patient referred to our hospital. Transoesophageal echo demonstrated adherence of the LA mass to the atrial septum and anterior MV leaflet. A cardiac magnetic resonance (CMR) was performed which showed that the LA mass contained 2 parts: one 50mm sized with attachment to the LA septum and anterior MV leaflet, and a smaller one pinned to the main part, mild pericardial effusion. By native and contrast enhanced CMR, the tumor appeared inhomogeneous, moderately vascularized and presented areas of inhomogeneous late enhancement expecting a myxoma or metastasis or sarcoma with adherent thrombus. Splenic fine-needle biopsy was inconclusive. Interdisciplinary, LA tumor resection (Picture 1) because of hemodynamic reasons firstly and splenectomy secondly was decided. Therapy: Surgical treatment was attempted. Histopathology confirmed an undifferentiated sarcoma and R1-resection. Further development: After splenectomy, angiomadoid nodular transformation without malignant transformation was diagnosed. Further investigations showed liver dysplasia without evidence for hepatocellular carcinoma. New resection of the remaining cardiac tumor would be surgically impossible. Interdisciplinary, it was discussed that chemotherapy is contraindicated because of high toxicity. Radiotherapy is recommended for the expected high relapse risk, although related to high cardiotoxicity. Conclusion: Most LA masses in elderly patients represent either a thrombus or myxoma. Our patient had an high suspicion for a LA thrombus or metastasis. Against our first thoughts, a new primary cardiac tumor was diagnosed by histopathology. Interdisciplinary work-up and integrative cardiac imaging is highly recommended in cases with large cardiac masses – and also when something seems obviously.



CT scan of the heart (A) and splenic lesion (B), transoesophageal echocardiography (C), CMR – native SSFP cine still frame (D), perfusion (E), late enhancement (F), intra-operative (G) and removed tumor (H).

1548

A rare case of cardiac malignant fibrous histiocytoma

A Andreea Ravasel[1]; E Stoica[1]; C Voica[1]; L Parascan[1]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*

Introduction: Primary cardiac tumors are rare entities with a reported incidence of 0.4% to 0.7% of all cardiac tumors. 25% of primary cardiac tumors are malignant, and, of these, 75% are sarcomas and have a poor prognosis. Malignant fibrous histiocytoma is a sarcoma that constitutes less than 3% of primary cardiac tumors.
Case report description: A 37-year-old female presented with increasing dyspnea on exertion, cough and fever for 1 month. She received treatment with antibiotics and nonsteroidal anti-inflammatory drugs for the suspicion of pneumonia, without improvement of symptoms. Additionally, she was diagnosed with paroxysmal atrial fibrillation, and was referred to our institution for cardiologic evaluation. On clinical examination, the patient had a blood pressure of 100/60 mmHg, heart rate of 100 beats per minute, irregular, with a grade II/IV diastolic murmur in the mitral valve area, decreased respiratory sounds of the lower lungs, jugular vein distension, mild peripheral edema, temperature 37.7°C. A chest radiography showed bilateral pleural effusion with a normal cardiac area. The electrocardiogram demonstrated atrial fibrillation, without repolarization abnormalities. NT proBNP was 1612 pg/ml. Transthoracic and transesophageal echocardiogram (TEE) showed a large tumor mass (5 cm) attached to the posterior wall of the left atrium with prolapse through the mitral valve (Figure 1). Mean and peak gradients across the mitral valve inflow were 22 mmHg and 12 mmHg, respectively (Figure 2). Small pericardial effusion was found without signs of pericardial tamponade. Cardiac CT (Figure 3) confirmed TEE findings. No other tumor was found in the chest. She was operated with presumptive diagnosis of atrial myxoma. At surgery a large polylobulated tumor was found with a large base of implantation at the level of the postero-lateral left atrial wall, without contact with interatrial septum. The differential diagnosis was between atrial myxoma and a malignant tumor which was more probable because of the macroscopic characteristics suggesting sarcoma. The tumor was resected as completely as possible. Postoperatively she had an uneventful recovery. Echocardiography after surgery was normal. She was discharged after a week. Biopsy revealed that the tumor consisted of malignant cells with marked atypia. The histopathologic diagnosis was malignant fibrous histiocytoma (Figure 4). Following cardiac surgery, the patient began adjuvant chemotherapy.
Discussion: Among malignant cardiac tumors, malignant fibrous histiocytoma of the heart is rare and occurs almost exclusively within the left atrium. Signs and symptoms of left sided heart failure (HF) are the most common manifestation. This tumor can be clinically and histologically confused with atrial myxomas, the most common primary cardiac tumor. It is attached more commonly along the posterior atrial wall in comparison to the interatrial septum. Surgical resection is the mainstay of diagnosis and treatment, but in the most cases the resection is incomplete. Chemotherapy can prolong survival, especially when only an incomplete resection is possible. Patients with unresectable primary malignant cardiac tumors who are free of metastases may be considered for heart transplantation. Comprehensive imaging protocols made in emergency settings may be crucial for understanding the rare etiologies of acute HF.

1549

Right heart failure due to large left atrial myxoma

BP Dhakal[1]; CM Bianco[1]; B Sareyyupoglu[1]; BD Hoit[1]; GH Oliveira[1]; CA Elamm[1];
[1]*University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, United States of America*

Introduction: Cardiac myxomas is a neoplasm arising from multipotent mesenchymal cell and account for about 30-50% of primary cardiac tumors and affects mostly females (65%). Myxomas are most often single, arising from the fossa ovalis of the interatrial septum and protruding into the left atrium (LA). The clinical presentation can vary depending upon the location of the tumour. Here we present a case of large LA myxoma presenting as presyncope and right heart failure (HF) symptoms.
Case presentation: A 59 year old female with no prior medical history presented as a transfer from outside hospital for a LA mass detected on echocardiogram. She had a 3-month history of worsening shortness of breath, dyspnoea on exertion, orthopnoea and bilateral lower extremity oedema. She reported being completely healthy and without symptoms until two years ago when she found herself getting progressively dyspnoeic with ambulation and with minimal exertion. She reported a long history of presyncopal episodes which she presumed to be related to her poor eating habits but developed one episode of syncope two weeks prior. She was admitted with HF symptoms and work up revealed NT proBNP of 12369 pg/ml, BNP of 716 pg/ml, EKG with signs of RV strain and chest x ray showed cardiomegaly. Transthoracic echocardiogram revealed preserved left ventricular (LV) systolic function with LV ejection fraction of 64% but right ventricle (RV) was severely dilated and had severely reduced function (RV mid 3.9 cm, RV base 4.5 cm, RVs' 0.12 m/sec). LA was also moderately dilated with 4x4 cm mass protruding through mitral valve into the LV, the appearance of which was consistent with myxoma. There was severe tricuspid regurgitation (velocity 4.19 m/sec) and severe pulmonary hypertension. Patient was started on intravenous diuresis with furosemide and was planned to undergo resection of the LA mass due to symptoms of syncope and RV failure. Coronary angiogram revealed no stenosis. Resection of the LA mass was done under cardiopulmonary bypass. Pathology revealed irregular lobulated soft mass with a glistening tan-pink outer surface measuring 6.5x5x3.8 cm and weighing 57 grams. Postoperative course was uneventful and during 2 months follow up, she had no HF symptoms and did not require any diuretics. Follow up echocardiogram did not show any regrowth of myxoma.
Answers and Discussion: Cardiac myxomas can occur in all age groups, but present most frequently between the third and sixth decades of life. Myxoma usually occur the LA and less commonly in the right atrium, LV and RV or multiple sites. The clinical features depend upon the location of myxoma, size, and mobility. Patients may have only constitutional symptoms such as fever, weight loss, fatigue, myalgia, arthralgia and muscle weakness. They may present with signs of tumour embolism or intracardiac obstruction causing dyspoea, palpitations, chest pain, pulmonary oedema, syncope or even sudden death. Our patients had near syncopal episodes for many years which could be due to progressively enlargement of the myxoma causing obstruction of the mitral valve during diastole. Severe pulmonary hypertension and RV enlargement suggested prolonged subclinical stage in our patient which necessited urgent surgery. This case suggests that RV failure and syncope can be the complication of LA myxoma. Follow up echocardiogram is necessary to document complete resection and to rule out any recurrence particularly in suspected familial form and those with multiple myxomas. We are planning to get another follow up echo in our patient to see if RV failure improved after surgery.

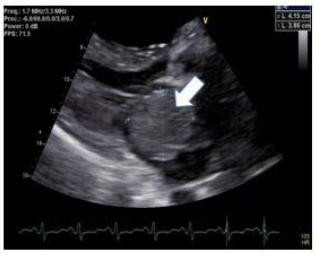


Figure 1: Parasternal long axis view of echo showing large left atrial myxoma (white arrow)

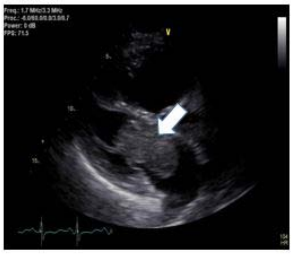


Figure 2: Left atrial myxoma traversing through mitral valve during diastole

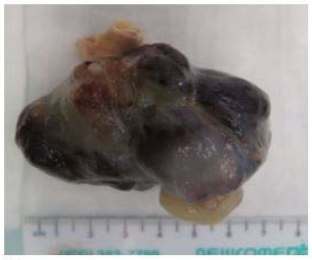


Figure 3: Gross picture of myxoma after surgical removal (6.5 cm x 5 cm x 3.8 cm, 57 grams)

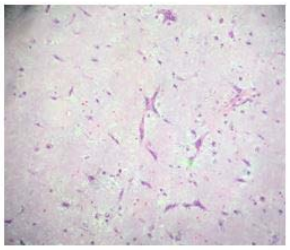


Figure 4: Microscopic picture of myxoma showing myxematous background with stellate shaped cells

Left Atrial Myxoma

1550

Progressive heart failure and accelerated myocardial ischemia with repeated in-stent restenosis in a case of multiple myeloma

M Valcovici[1]; S Dragan[1]; R Christodorescu[1]

[1]*University of Medicine and Pharmacy Victor Babes Timisoara, Timisoara, Romania*

A 70 year-old man with IgG kappa stage IIIB multiple myeloma, diagnosed after onset of acute renal failure, presented with dyspnea and severe chest pain, two days after concluding the second cycle of triple association: bortezomib 1,3 mg/m2 + melphalan 9mg/m2/d + prednisone 60mg/m2/d. His ECG demonstrated sinus tachycardia, left atrial enlargement and ST-T elevation in V2-V4. Troponine I hs was 29,5 ng/ml. Acute anterior STEMI was diagnosed. Coronary angiography revealed 85% occlusion of proximal LAD, followed by PTCA with BM Integrity stent 3.0/18mm. His echocardiogram revealed diastolic dysfunction type I, moderate left atrial enlargement, anterior wall and septal motion abnormality, no valvular abnormalities, a moderately enlarged LV (VTD=149ml) with a borderline low ejection fraction (EF) of 42%. A prior echocardiogram at initiation of MM treatment revealed normal LV volume and EF. The patient was put on betablocker, ACE inhibitor, statin and double antiplatelet therapy and after one month the treatment of MM was resumed. During the 5th cycle the patient again presented chest pain with extensive subendocardial ischemia. Troponine I hs was 0.019 ng/ml and unstable angina IIIB2 was diagnosed. Coronary angiography revealed early in-stent 90% restenosis in the proximal LAD and multiple non-significant 30-50% stenoses in the RCA and in the CXA. PTCA in the proximal LAD was performed with an Xience stent. His echocardiogram at this stage revealed further increase of LV volume and decrease of EF (170ml and 40% respectively), while renal function and platelet count continued to deteriorate. A skeletal survey performed after discharge revealed multiple lytic lesions in the pelvis and skull. It was decided to add biphosphonate 4mg/cure to his therapy. However, the condition of the patient allowed only three more cycles, due to the severe side-effects, including two upper digestive tract hemorrhages, anemia and low platelet count. During the 8th cycle the patient again presented severe anginal pain with subsequent subendocardial ischemia. Coronary angiography revealed late in-stent 85% restenosis in the proximal LAD and PTCA was performed again with an Xience stent. At echocardiography LV volume was 180 ml and EF continued to decrease to 38%. The markers of bone turnover osteoprotegerin (OPG) and receptor activator of nuclear factor-kappa B ligand (RANKL) were increased to 3,9 pg/ml, respectively decreased to 0,67 pg/ml. One week after discharge the patient developed massive anterior myocardial infarction followed by cardiac arrest and death.

Discussion: The natural history of multiple myeloma (MM) is one of progressive bone destruction, refractory cytopenias, and renal end-organ damage. This patient had disease-, treatment- and age-related increased risk for cardiac events. His disease was refractory to treatment and presented frequent relapses with intense bone destruction. The increase of biomarker of bone turnover OPG has been linked to increased cardiovascular risk in several studies. It may contribute to increased vascular rigidity and accelerate the atherosclerotic process. Collagen fragments released from the bone matrix during extensive resorption may also explain early and late in-stent restenosis. Proteasome inhibitors increase risk of ischemic heart disease and congestive heart failure and alkylating agents increase the risk of cardiomyopathy and reduce left ventricular EF. In this patient, acute anterior STEMI occurred early after initiation of treatment for MM and EF was decreased at onset of myocardial ischemia and continued to deteriorate throughout the progression of disease. OPG is a marker of both bone turnover and vascular rigidity and may be useful as predictor of ischemic events in patients with MM.

RAPID FIRE 6 - ADVANCED HEART FAILURE

1587

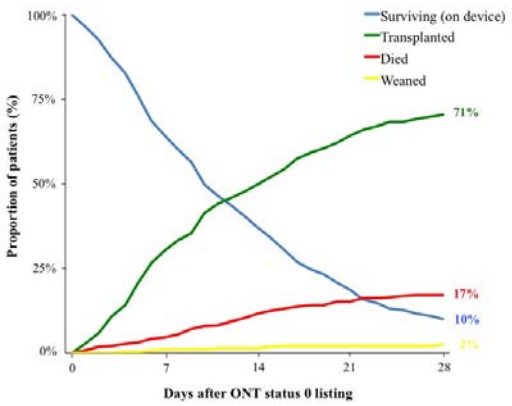
Clinical outcomes of temporary mechanical circulatory support as a bridge to heart transplantation in Spain: a nationwide registry.

E Eduardo Barge Caballero[1]; L Almenar-Bonet[2]; F Gonzalez-Vilchez[3]; JL Lambert-Rodriguez[4]; J Gonzalez-Costello[5]; J Segovia-Cubero[6]; MA Castel-Lavilla[7]; J Delgado-Jimenez[8]; IP Garrido-Bravo[9]; D Rangel-Sousa[10]; MA Martinez-Selles[11]; L De La Fuente-Galan[12]; G Rabago-Juan-Aracil[13]; M Sanz-Julve[14]; S Mirabet-Perez[15]

[1]Hospital Universitario A Coruña, A Coruña, Spain; [2]Hospital La Fe, Valencia, Spain; [3]University Hospital Marques de Valdecilla, Santander, Spain; [4]University Hospital Central de Asturias, Oviedo, Spain; [5]Hospital de Bellvitge, Hospitalet de Llobregat, Spain; [6]Hospital Puerta de Hierro, Majadahonda, Spain; [7]Hospital Clinic de Barcelona, Barcelona, Spain; [8]Hospital 12 de Octubre, Madrid, Spain; [9]Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain; [10]Hospital Virgen del Rocío, Sevilla, Spain; [11]University General Hospital Gregorio Maranon, Madrid, Spain; [12]University Hospital Clinic of Valladolid, Valladolid, Spain; [13]Hospital Clínica Universidad, Pamplona, Spain; [14]University Hospital Miguel Servet, Zaragoza, Spain; [15]Hospital Santa Creu i Sant Pau, Barcelona, Spain

On behalf of: ASIS-TC STUDY INVESTIGATORS
Funding Acknowledgements: FUNDACIÓN MUTUA MADRILEÑA

Background: In Spain, high-urgency listing for heart transplantation (HT), the so-called ONT status 0 protocol, is allowed for candidates dependent on temporary mechanical circulatory support (T-MCS). We sought to analyze the clinical outcomes of this strategy.
Methods: We conducted a nationwide, retrospective, case-by-case review of clinical records of 291 patients listed for first, single-organ high-urgent HT while on T-MCS during the period 2010–2015 in 16 Spanish institutions. Pre- and post-transplant survival was analyzed.
Results: At the time of listing, 169 (58%) patients were supported on veno-arterial ECMO, 70 (24%) on temporary left ventricular assist devices (T-LVADs) and 52 (18%) on temporary biventricular assist devices (T-BIVADs). Seven patients transitioned from ECMO to T-VADs while on the waiting list. Mean time on T-MCS was 13.1 ± 12.6 days. Mean time from listing to HT was 7.6 ± 8.5 days. Overall, 230 (79%) patients were transplanted, 54 (18.5%) died during MCS and 7(2.4%) were weaned. Competing outcomes over 28-day follow-up are shown in the Figure. In-hospital postoperative mortality after HT was 33%, 12% and 26% for patients bridged on ECMO, T-LVADs and T-BIVADs, respectively (p = 0.008). Overall survival from listing to hospital discharge was 54%, 79%, and 56%, respectively (p = 0.022). By means of backward stepwise Cox´s regression analysis, T-LVAD support at the time of listing was identified as an independent predictor of 1-year survival after listing (HR 0.52, 95% CI 0.30–0.92).
Conclusions: In a setting of short waiting list times, the use of T-MCS as a direct bridge to high-urgent HT is a feasible strategy. In our experience, listing under T-LVADs is associated with better outcomes than listing under T-BIVADs or VA-ECMO.



Competing outcomes after listing

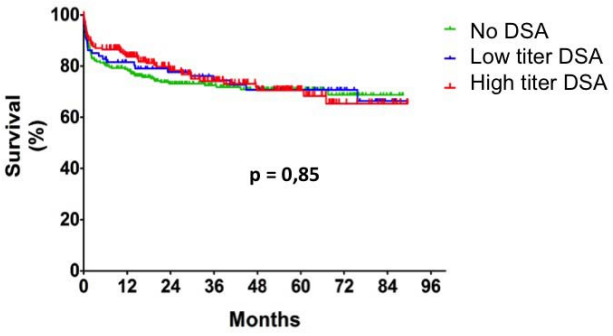
1588

Heart transplantation in patients with high immunological risk is safe when performed with a specific desensitization program.

G Coutance[1]; V D'orio[1]; S Ouldamar[1]; S Saheb[2]; P Rouvier[3]; C Vidal[4]; N Brechot[5]; G Lebreton[1]; C Gautreau[6]; J Amour[4]; A Combes[5]; P Leprince[7]; S Varnous[7]

[1]Hospital Pitie-Salpetriere, Cardiovascular and Thoracic surgery, Paris, France; [2]Hospital Pitie-Salpetriere, Hemobiotherapies, Paris, France; [3]Hospital Pitie-Salpetriere, Pathology, Paris, France; [4]Hospital Pitie-Salpetriere, Anesthesiology and cardiovascular reanimation, Paris, France; [5]Hospital Pitie-Salpetriere, Medical reanimation, Paris, France; [6]Hopital Saint-Louis, Laboratory of Immunology and histocompatibility , Paris, France; [7]Hôpital de la côte fleurie, Department of caridology and cardiac rehabilitation, Cricqueboeuf, France

Background: In France, emergency access to heart transplantation is limited to 4 days ("high emergency 1"). To limit waiting time on list and increase the chances of transplantation, we accept grafts with high immunological risk (pre-formed donor antiHLA specific antibodies - DSA). Our purpose is to analyze the efficiency of a prospective desensitization program in patients transplanted with DSA.
Methods: Patients transplanted with low titer DSA (mean fluorescence intensity – MFI – 500 to 1000) received intravenous immunoglobulins (IVIg, 2 g/kg) and patients transplanted with high titer DSA (MFI > 1000) were treated with plasmapheresis (1 before transplantation, 4 after) and IVIg (2 g/kg) on top of standard immunosuppression regimen. We included all patients with a first isolated heart transplantation from 01/01/2009 to 31/12/2015. The primary endpoint was survival after heart transplantation.
Results: From 2009 to 2015, 523 first isolated heart transplantations were performed at our centre. Patients were mostly males (n = 404, 77%). Mean age was 50 +/- 12 years. 241 patients (46 %) were transplanted without DSA, 88 patients (17 %) with low titer DSA and 194 patients (37 %) with high titer DSA. Compared to other groups, patients transplanted with high titer DSA were younger, female sex and long term assist devices were more common. Mean follow-up was 3.7 +/- 2.1 years. Survival was similar between groups even after adjustment on age, sex and assist device before transplantation (survival at one year and at the end of follow-up respectively for no DSA group: 79 and 73 %, DSA score 4 group: 80 and 72 %, DSA score 6/8 group: 84 and 76%, p = 0.85).
Conclusion: Heart transplantation in patients with low or high titer pre-formed DSA is safe when performed with a specific desensitization program. Such a protocol might increase the chances of transplantation during the short period of high emergency 1.



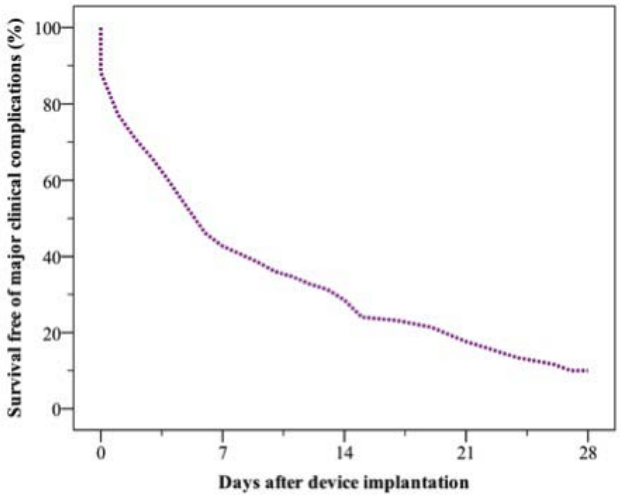
1589

Incidence and prognostic impact of adverse clinical events associated to mechanical circulatory support in patients bridged to transplantation on temporary devices: a nationwide Spanish registry.

E Eduardo Barge Caballero[1]; L Almenar-Bonet[2]; F Gonzalez-Vilchez[3]; JL Lambert-Rodriguez[4]; JL Gonzalez-Costello[5]; J Segovia-Cubero[6]; MA Castell-Lavilla[7]; J Delgado-Jimenez[8]; IP Garrido-Bravo[9]; D Rangel-Sousa[10]; M Martinez-Selles[11]; L De La Fuente-Galan[12]; G Rabago-Juan-Aracil[13]; M Sanz-Julve[14]; D Hervas-Sotomayor[15]
[1]Hospital Universitario A Coruña, A Coruña, Spain; [2]Hospital La Fe, Valencia, Spain; [3]University Hospital Marques de Valdecilla, Santander, Spain; [4]University Hospital Central de Asturias, Oviedo, Spain; [5]Hospital de Bellvitge, Hospitalet de Llobregat, Spain; [6]Hospital Puerta de Hierro, Majadahonda, Spain; [7]Hospital Clinic de Barcelona, Barcelona, Spain; [8]Hospital 12 de Octubre, Madrid, Spain; [9]Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain; [10]Hospital Virgen del Rocio, Sevilla, Spain; [11]University General Hospital Gregorio Maranon, Madrid, Spain; [12]University Hospital Clinic of Valladolid, Valladolid, Spain; [13]Hospital Clinica Universidad, Pamplona, Spain; [14]University Hospital Miguel Servet, Zaragoza, Spain; [15]University Hospital Reina Sofia, Cordoba, Spain

On behalf of: ASIS-TC Study Investigators
Funding Acknowledgements: FUNDACIÓN MUTUA MADRILEÑA

Background: In Spain, high-urgency listing for heart transplantation (HT) is allowed for candidates dependent on temporary mechanical circulatory support (T-MCS). We sought to analyze the incidence and prognostic impact of adverse clinical events (ACE) associated to T-MCS in this setting.
Methods: We conducted a nationwide, retrospective, case-by-case review of clinical records of 291 patients listed for first, single-organ high-urgent HT while on T-MCS during the period 2010–2015 in 16 Spanish institutions. The incidence and survival repercussion of T-MCS associated ACE were studied.
Results: At the time of listing, 169 (58%) patients were supported on veno-arterial ECMO, 70 (24%) on temporary left ventricular assist devices (T-LVADs) and 52 (18%) on temporary biventricular assist devices (T-BIVADs). Seven patients transitioned from ECMO to T-VADs while on the waiting list. Mean time on T-MCS was 13.1 ± 12.6 days. The overall incidence rate of T-MCS associated ACE was 59 (95% CI 42–67) per 1000 devices-day, being significantly higher among VA-ECMO supported candidates than among T-LVAD ones (71 vs. 47 events per 1000 devices-day, p = 0.008); but not significantly different than among T-BIVAD ones (71 vs. 57 events per 1000 devices-day, p = 0.199). The incidence rate of T-MCS associated major ACE –device dysfunction, stroke, bleeding or infection– was 50 (95% CI 43–58) per 1000 devices-day. Patients who experienced major ACE showed lower rates of transplantation (71.7% vs. 92.3%, p < 0.001), higher rates of death during T-MCS (25.2% vs. 6.7%, p < 0.001), lower survival from listing to hospital discharge (55.1% vs. 70.2%, p = 0.012) and lower 1-year survival after listing (52.5% vs. 66.5%, log rank p = 0.007). Survival free of major ACE after T-MCS initiation is represented in the Figure.
Conclusions: In patients bridged to high-urgent HT on T-MCS, associated ACE events are frequent, impacting the chance of getting and organ and survival.



Major ACE associated to T-MCS

1590

Hypochloremia in advanced heart failure: association with hemodynamics and prognosis

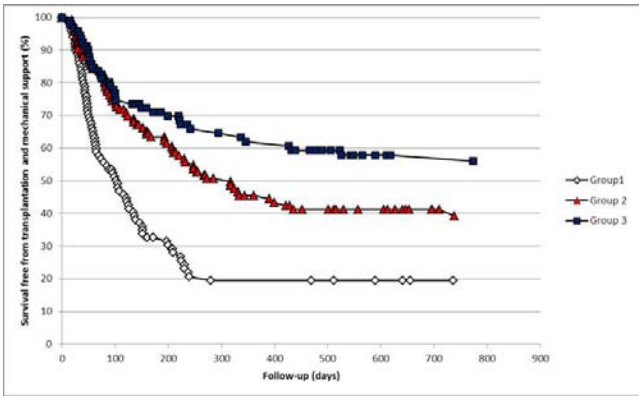
H S Hoong Sern Lim[1]; T Musa[1]; M Mukadam[1]
[1]Queen Elizabeth Hospital, Birmingham, United Kingdom

Background: Low chloride (Cl) levels are associated with poor outcomes in heart failure (HF). We hypothesized that low Cl is associated with greater hemodynamic abnormalities, which may explain the prognostic implication of low Cl in advanced HF.
Methods: 306 consecutive patients with advanced HF were included. Cl levels were measured at the time of catheter study. Cardiac power output index (CPOi)= (mean blood pressure x cardiac index/451. Primary outcome was survival free from transplantation/ mechanical support (MCS).
Results: The patients were divided into 3 groups based on Cl tertiles: T1: < 94.3 (80.1-94.2), T2: 94.3-98.6 and T3: >98.6 (98.7-105) mmol/l [TABLE]. T1 patients had lower ejection fraction, lower use of medical therapy, higher furosemide dose, lower CPOi and higher right atrial pressure (RAP). Cl level is associated with the primary outcome but only CPOi (HR 0.025, 95%CI 0.004-0.172) and RAP (HR 1.054, 95%CI 1.025-1.085) were significant on multivariable proportional hazards model. By ROC analysis, a CPOi < 0.341 and RAP≥15 were associated with survival (C-statistic about 0.6). Patients with both CPOi < 0.341 and RAP≥15 had the worst survival (Group 1), Survival was intermediate when 1 of 2 criteria was present (Group 2) and best in patients with both CPOi≥0.341 and RAP < 15 (Group 3) [FIGURE]. Cl < 94mmol/l identified patients with CPOi < 0.341 and RAP≥15 (C-statistic 0.8).
Conclusion: Low Cl is associated with worse survival free from transplantation/ MCS in advanced HF due to the association with low CPOi and high RAP.

Patient characteristics

	Tertile 1 (n = 101)	Tertile 2(n = 102)	Tertile 3(n = 103)	P
Age (years)	40±3	51±2	50±2	0.535
Males (n,%)	82 (81)	81 (79)	78 (76)	0.858
Ischemic (n,%)	29 (29)	31 (31)	34 (34)	0.949
ACEi/ARB (n,%)	76 (78)	90 (91)	88 (90)	0.048
Betablocker (n,%)	61 (63)	84 (85)	87 (88)	< 0.001
Furosemide (mg/day)	186±16	128±14	93±10	< 0.001
LVEF (%)	14.2±1.4	15.3±1.5	19.6±1.8	< 0.001
RAP (mmHg)	19.6±1.2	13.9±1.1	9.5±1.0	< 0.001
PVR (WU)	3.6±0.4	3.1±0.3	2.8±0.4	0.032
Cardiac index (L/min/m2)	1.62±0.09	1.81±0.10	2.04±0.09	< 0.001
MAP (mmHg)	80±2.2	81±2.7	85±2.6	0.159
CPOi (W)	0.291±0.018	0.326±0.019	0.382±0.021	< 0.001

RAP: right atrial pressure; PVR: pulmonary vascular resistance; MAP: mean arterial pressure; CPOi: cardiac power output index



Survival based on CPOi and RAP.

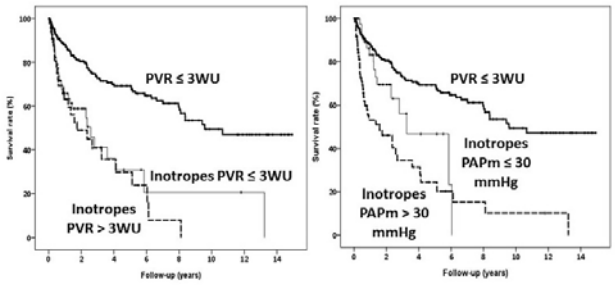
1591

What is the best hemodynamic predictor of survival in patients with advanced systolic heart failure ?

E Hebbar[1]; T Mercier[1]; A Duva Pentiah[1]; M Fertin[1]; C Goeminne[1]; A Vincentelli[1]; N Lamblin[1]; P De Groote[1]
[1]*Lille University Hospital, Institut Coeur-Poumon, Lille, France*

Background: In patients with advanced systolic heart failure (SHF), right heart catheterization (RHC) is mandatory before possible listing for cardiac transplantation. It is admitted that a reactivity test must be performed (either with inotropes or vasodilators) in patients with elevated pulmonary vascular resistance (PVR) > 3 Wood units (WU). An increase in PVR is a predictor of mortality in SHF but also in the post-operative period after heart transplantation. Few studies have analyzed the prognostic impact of hemodynamic parameters including both patients on the waiting list for heart transplantation and patients in the post-operative period of heart transplantation.
Methods: We included all the consecutive stable patients with optimal medical therapy admitted for RHC before possible either cardiac transplantation or ventricular assist device (VAD) implantation. An inotropic challenge was performed (dobutamine +/- milrinone) in patients with a baseline PVR > 3 WU.
Results: We included 425 patients with a mean age of 53 ± 11 years old, 43% had ischemic cardiopathy and LVEF was 29.4 ± 12.2%. 120 patients had an inotropic challenge because baseline PVR was > 3 WU, of whom 75 had a decrease of PVR ≤ 3 WU. During a follow-up period of 1.58 years [0.49 -4.41], there were 107 cardio-vascular deaths, 122 cardiac transplantations and 11 VAD implantation. Major events were the combination of cardio-vascular deaths (n = 107) or deaths during the hospitalization for VAD implantation (n = 3) or for cardiac transplantation (n = 24). Patients with a baseline PVR > 3WU had a worse prognosis whatever the results of the inotropic challenge on PVR (Figure). At baseline, independent predictors of survival were right atrial pressure (with a cut-off value of 9 mmHg) and PVR. After inotropic challenge, the best hemodynamic predictor of survival was mean pulmonary artery pressure (PAPm), with a cut-off value of 30 mmHg (Figure). Independent predictors are presented in the Table. In conclusion, for the selection of the most severe patients with stable advanced systolic heart failure, we propose to use a two steps hemodynamic algorithm using PVR at baseline (≤ or > 3 WU) and PAPm after inotropic challenge (≤ or > 30 mmHg). This algorithm must be prospectively validated in an independent population.

Independent predictors of survival		
HR [95%CI]	HR [95%CI]	p
Baseline right atrial pressure (9 mmHg)	2.44 [1.64 - 3.62]	< 0.0001
BaselinePVR≤ 3 WU (reference)	1	< 0.0001
InotropesPVR > 3 WU and PAPm≤ 30 mmHg	2.14 [1.21 - 3.77]	0.009
InotropesPVR > 3 WU and PAPm> 30 mmHg	2.44 [1.61 - 3.71]	< 0.0001



Survival curves

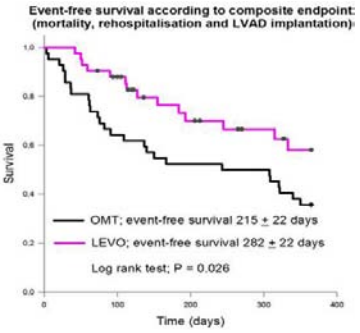
1592

Intermittent scheduled low-dose levosimendan infusions improves event-free survival in advanced chronic heart failure: a propensity score matching analysis.

N Barras[1]; K Sotiropoulos[1]; J Regamey[1]; P Vogt[1]; R Hullin[1]; PO Patrick Yerly[1]
[1]*University Hospital (CHUV), Department of cardiology, Lausanne, Switzerland*

Introduction: Advanced chronic heart failure (ACHF) is characterized by poor quality of life (QOL) and high mortality. Improved QOL can be obtained with usual inotropes like Dobutamine, but at the price of increased myocardial O2 demand and finally lower survival. By contrast, Levosimendan (Levo) doesn't increase myocardial O2 consumption. Nevertheless, neither single 24-hours nor short intervals (2 weeks) repeated 6-hours infusions of high dose Levo (0.1-0.2 μ/kg/min) showed any survival benefit in randomized-controlled trials (RCT), possibly because of dose-related side effects.
Purpose: In this study, we sought to assess the efficacy of long intervals repeated 24h low dose Levo (0.05 μg/kg/min) infusions on 1 year event-free survival.
Methods: we conducted a retrospective case control study based on our institutional HF database. Cases (n = 42) were eligible if they had their 1st Levo infusion at the time of decompensated HF in addition to standard of care (SOC) with at least 1 further infusion scheduled, and if they had ACHF, defined as LVEF < 40% not responding to > 3 months optimal therapy. They received 4.37 (range 2-12) Levo infusions at 4 weeks intervals after initial hospitalization. They were compared 1 to 1 in a propensity score matching analysis with ACHF controls matched for age, sex, ischemic heart disease, LVEF, sinus rhythm and creatinine but who received only SOC without levo. A composite endpoint of mortality, unscheduled HF-related hospitalization and LVAD implantation 1 year after 1st Levo infusion was defined for outcome.
Results: demographic and biological variables were not different between the 42 SOC + levo cases and the matched 42 SOC controls (Table). The composite endpoint was reached by 14 SOC + levo patients (33.3%) as compared to 27 SOC controls (64.3%) (HR=0.49; 95% CI 0.26-0.93) (Figure).
Conclusion: low dose 24-hours Levo (0.05 μg/kg/min) during hospitalisation for decompensated HF and regularly repeated on a scheduled basis thereafter may improve outcome as compared to SOC in ACHF patients. These data must be confirmed by larger RCTs.

	Standard of Care N = 42	SOC + Levo N = 42	P value
Age	63,8 years	60,8 years	0,19
Male sex	32/38 (84%)	34/38 (89%)	0,37
Ischemic heart disease	22/38 (58%)	20/38 (53%)	0,19
LVEF	22,50%	21,40%	0,51
Sinus rythm	26/38 (68%)	28/38 (74%)	0,13



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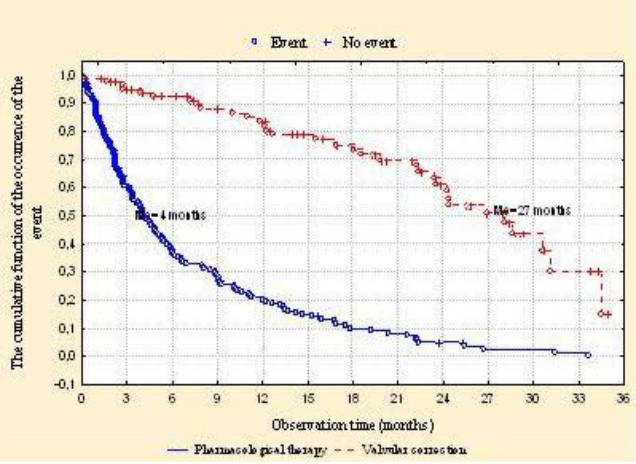
Differentiated approach to the treatment of patients with end-stage heart failure

O Olesya Shatova[1]; A Kurlianskaya[1]; L Rachok[1]; Y Ostrovsky[1]
[1]*Republican Scientific and Practical Centre of Cardiology, heart failure, Minsk, Belarus*

Background: The life expectancy of patients with end-stage heart failure is determined by the possibility of using different bridges to heart transplantation (HT). Pharmaceutical and mechanical bridges to HT are widely used nowadays. Surgical valve repair as the bridge to transplantation is still not good investigated.
Purpose: to access the efficiency of surgical valve repair as the bridge to HT.
Methods: Our study includes 159 patients with end-stage heart failure in the clinical status UNOS 2 during the period 2009-2015 years with the mean data end diastolic volume = 251 ± 15,8 ml, end systolic volume=188 ± 10,2ml, ejection fraction=25,6 ± 3,1%, proBNP level=1307 ± 112pg/ml, VO2peak=12,8 ± 3,1l/min. All patients were included in the waiting list and had medical unnecessary in surgical revascularization. Patients were randomized into 2 groups: 77 patients from the 1 group underwent surgical valve repair, 82 patients were on optimal medical treatment (2 group). In the 1 group surgical valve correction was used as the bridge

to the HT. The patients' death and the HT are two endpoints of our study. The results are presented as absolute and relative frequencies, standard error of the proportion (p ± Sp). Quantitative data are presented as median and interquartile range (Me (LQ-UQ)). the comparative analysis indicates that the median function of survival after surgical valve correction (without HT) is 27 months (17,6-34,8) and is significantly higher than in patients who receive an optimal medical therapy (4 months of 1.9 to 10.1) ($p < 0.001$). (Picture 1) The surgical valve correction in patients with end-stage heart failure allows in 50% cases to delay the HT up to 2 years.

Conclusions: The data analysis of the results shows that the successful applications of the surgical valve repair in patients with end-stage heart failure with unnecessary of revascularization could be used as a bridge to HT and in 50% cases allows to delay the HT up to 2 years.



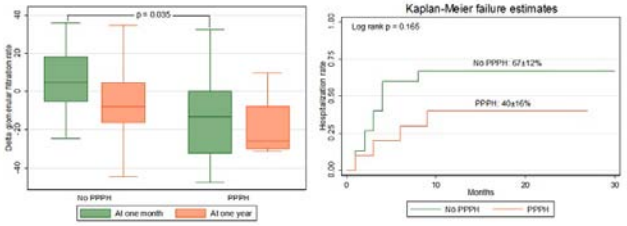
The occurrence event function

1594

Clinical outcomes and right ventricular function in patients with persistent pulmonary hypertension after heart transplantation

JB Ivey-Miranda[1]; EJ Flores-Umanzor[1]; M Farrero-Torres[1]; M Hernandez-Enriquez[1]; P Sanchez-Somonte[1]; A Garcia-Alvarez[1]; MA Castel-Lavilla[1]
F Perez-Villa[1]; [1]*Hospital Clinic de Barcelona, Barcelona, Spain*

Background: Pulmonary hypertension in heart transplant recipients is associated with worse prognosis after transplant. This study evaluated clinical outcomes and right ventricular function in patients who remained with pulmonary hypertension after heart transplantation (HT).
Purpose: To describe clinical outcomes in patients with persistent pulmonary hypertension (PPH) after HT.
Methods: We included patients with severe pulmonary hypertension that were treated with oral pulmonary vasodilators (sildenafil and/or bosentan) before heart transplant. For the aim of this study, invasive pulmonary hemodynamics were recorded at two time points: the most recent pre-transplant right heart catheterization and invasive monitoring parameters 24h post-transplant. Post-transplant persistent pulmonary hypertension (PPPH) was defined as sustained high PVR, requiring pulmonary vasodilator treatment after a month post-transplant. Post-transplant echocardiographic right ventricular failure and clinical outcomes were compared between patients with and without PPH.
Results: Twenty-five patients were included. Although 20 patients (80%) required post-transplant pulmonary vasodilator for five days post-transplant, only 10 patients (40%) showed PPPH and required therapy after a month post-transplant. The remaining 15 patients were considered as a no-PPPH control group.
Baseline pulmonary vascular resistances (PVR) were not different in patients with and without PPPH (4.0 ± 1.6 vs. 3.7 ± 1.1 Wood units, respectively, $p = 0.553$). After HT, right ventricular dysfunction prevalence was not different between patients with PPPH or without PPPH at one month and one year (50% vs. 40%, $p = 0.622$ and 30% vs. 27%, $p = 0.856$, respectively).
Although glomerular filtration rate (difference between baseline and at the time of end-point glomerular filtration rate) at one month was significantly different between groups (-13 ± 24 ml/min in PPPH vs. + 5 ± 19 ml/min in no PPPH, $p = 0.035$), there was not a significant difference after one year follow-up (-18 ± 14 ml/min in PPPH vs. -8 ± 20 ml/min in no PPPH, $p = 0.162$).
At a median follow up of 29 months, survival was 100% in both groups. In Kaplan-Meier analysis, the PPPH group showed a trend towards less hospitalization rate than the no-PPPH group (40 ± 16% vs. 67 ± 12%, $p = 0.165$).
Conclusions: In this study, patients with PPPH showed similar post-transplant outcomes compared to patients with no PPPH. Careful assessment and treatment of PPPH with pulmonary vasodilators may account for good outcomes in this high-risk population.



1595

Levosimendan improves exercise performance in patients with advanced chronic heart failure

M Mapelli[1]; E Spadafora[1]; S Paolillo[1]; S Mushtaq[1]; S Farina[1]; E Salvioni[1]; C Vignati[1]; A Del Torto[1]; N Corrieri[1]; C Fiorentini[1]; P Agostoni[1]
[1]*Cardiology Center Monzino IRCCS, Milan, Italy*

Background: Cardiopulmonary exercise test (CPET) provides several functional variables such as peak VO2 and ventilation/CO2 production (VE/VCO2) slope, which are strong prognostic parameters for patients with stable advanced chronic heart failure (ACHF). The inodilator levosimendan combines positive inotropic, vasodilatory and cardioprotective effects, without significant changes in myocardial oxygen requirements and it has been shown to improve symptoms and haemodynamics in patients with acute HF. Levosimendan might also be used for patients with ACHF.
Purpose: In the present study we analyzed the effects of levosimendan treatment on exercise capacity, alveolar capillary gas diffusion (DLCO) and B-type natriuretic peptide (BNP) in a population of patients with ACHF in stabilized clinical condition.
Methods: We enrolled consecutive patients with ACHF (peakVO2 < 12 mL/min/kg). Every patient received i.v. infusion levosimendan 12.5 mg (in 500 mL 5% glucose). The patient NYHA class, BNP, haemoglobin, creatinine, and blood urea nitrose levels were determined at baseline and after treatment. The patients underwent CPET, standard spirometry and DLCO, before and 24h after the end of the infusion. DLCO values were corrected for haemoglobin levels.
Results: We enrolled a total of 65 patients (medium age 70.45 ± 8.99 years; male 86%). Haemoglobin, BUN and creatinine showed no changes before and after the treatment. BNP levels showed a significant decrease (1277.06 ± 994.02 to 578.03 ± 591.01 pg/ml; $p < 0.01$). Minor improvement was observed for spirometry measurements, but not for DLCO. PeakVO2 showed a significant increase while VE/VCO2 slope showed a significant decrease.
Conclusions: Levosimendan treatment significantly improve peakVO2 and reduces VE/VCO2 slope and BNP in patients with ACHF without significant impact on alveolar capillary gas diffusion.

Variables changes after infusion

n=65	Pre-infusion	Post-Infusion	p.value
Haemoglobin (g/dl)	12.91±1,93	12.44±1.77	ns
Creatinine (mg/dl)	1.55±0.55	1.51±0.56	ns
BNP (pg/ml)	1277.06±994.02	578.03±591.01	≤0.01
VO2 (ml/Kg/min)	10.07±2.36	11.50±2.30	≤0.01
Watts (W)	44.45±18.29	51.15±18.34	≤0.01
VO2/Work slope	8.99±1.87	9.64±1.51	≤0.01
VE/VCO2 slope	41.96±9.86	36.36±7.13	≤0.01
FEV1 (L)	2.09±0.56	2.26±0.63	≤0.01
DLCO (ml/mmHg/min)	18.00±4.51	17.74±4.06	ns

1596

Adjusting preoperative risk models of post heart transplant survival to a european cohort in the age of a new cardiac allocation score in europe

F Felix Schoenrath[1]; J Stein[1]; TA Sargut[1]
[1]*Deutsches Herzzentrum Berlin, Cardiothoracic and Vascular Surgery, Berlin, Germany*

Purpose: Organ allocation for heart transplantation is one of the most difficult procedures in modern cardiology. Several risk models target this issue to predict post transplant survival, but none of these scoring systems have been validated in a large homogenous European cohort in a long-term approach. This aspect seems of utmost importance in a time of planned switch of the Eurotransplant allocation system from a binary system (high urgent versus transplantable status) to a scoring system similar to the Lung Allocation Score (LAS) for lung transplantation.
Methods: Our institutional transplant registry provided the patient data. Analysis included data of 761 heart transplant recipients aged 18 years or older during the time period 01/1996 to 02/2015. The primary outcome was graft failure, which was defined as death or retransplantation. In a first step we assessed 30-day, 1-year, 5-year and 10-year survival and compared different risk models including the Index for Mortality Prediction After Cardiac Transplantation (IMPACT) and Columbia Risk Stratification Score (RSS). In a second step we adjusted the risk models with different variables using a multivariable logistic regression model to achieve a better predictive value.
Results: Thirty-day, 1-year, 5-year and 10-year survival rates were 78.3 ± 1.5%, 67.7 ± 1.71%, 59.1 ± 1.8% and 44.1 ± 1.9, respectively. The 1-year incidence of graft failure in accordance with the five Columbia score risk strata was 14.1%, 25.2%, 37.4%, 28.3% and 50%. The 1-year survival stratified by three-point increments of the IMPACT score showed incidence rates varying from 22.9% (0-2 points) to 57.1% (>15 points). Area under the curve for the IMPACT was 0.59 (95% CI 0.54-0.64) and 0.62 (95% CI 0.57-0.66) for the RSS. Our adjusted risk score showed an AUC of 0.69 (95% CI 0.64-0.72) with the following variables: coronary artery disease, use of BVAD, diabetes mellitus, eGFR, sex, donor age.
Conclusion: IMPACT and Columbia risk score were suitable to predict post transplant survival but ROC curve showed only intermediate prediction accuracy. Use of the above risk factors showed improved accuracy in predicting graft failure in our cohort.

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Prognostic accuracy comparison of the IMPACT risk score, MELD XI score and INTERMACS profiles in candidates for heart transplantation: argentinian single centre analysis

M Peradejordi Lastras[1]; L E Favaloro[1]; P Morejon Barragan[1]; D Absi[1]; MF Renedo[1]; AL Guazzone[1]; RD Ratto[1]; M Lopez Rosetti[1]; J Abud[1]; RR Favaloro[1]; AM Bertolotti[1]
[1]*University Hospital Favaloro Foundation, Intrathoracic Transplantation and Heart Failure Division, Ciudad Autónoma de Buenos Aires, Argentina*

Introduction: In the last decade there has been an increased risk in the clinical profile of orthotopic heart transplant (HTx) recipients. Risk Predictors scores can be a useful tool to optimize the timing in waiting list registration and a strategy in allocation due the disparity between available heart donors and recipients.
Purpose: We aimed to evaluate the prognostic accuracy of the Index for Mortality Prediction after Transplantation (IMPACT), Model for End-stage Liver Disease excluding international normalized ratio (MELD XI) and Interagency Registry for Mechanical Circulatory Support (INTERMACS profiles) in the estimation of mortality risk after HTx at 1 year. Secondary outcome included 30-day mortality.
Methods: We retrospectively analysed HTx adult recipients, between December, 2005 and December, 2015. The risk scores were calculated for each patient with advanced heart failure according to different clinical variables. Patients were stratified into categories: IMPACT <5; 5-10 y 10; MELD XI in interquartile range and INTERMACS profiles 1, 2-3 y 4. Logistic regression was performed to assess the predictive accuracy of these scores. Afterwards we compared the scores using a receiver operating characteristic (ROC) curve thus obtaining the area under the curve (AUC) and the respective 95%CI. The AUC of risk models were compared using the non-parametric test of DeLong et.al.
Results: In our cohort of 227 HTx adult recipients, mean age (±SD) was 50 ± 13 years, 73% were men. The cumulative mortality rate was 19% at 1-year and 8% at 30-days. The overall cohort had a mean IMPACT risk score of 6.4 ± 4.5 and mean MELD XI score of 12.5 ± 3.4 (Interquartile range 9.44 to 14.21).
The models had in predicting mortality similar outcomes at 1-year, the AUC obtained from the ROC curves of IMPACT, INTERMACS and MELD XI were 0.63 (95% CI: 0.57-0.70); 0.61 (95% CI: 0.54-0.67) and 0.61 (95% CI: 0.54-0.67), respectively (p = NS). The area under the ROC curve demonstrated that IMPACT, INTERMACS and MELD were no significantly different in predicting 30-day mortality; 0.68 (95% CI: 0.62-0.74); 0.67 (95% CI: 0.60-0.72) and 0.58 (95% CI: 0.51-0.64), respectively.
In the logistic regression analysis mechanical ventilation pre-transplant was significantly associated with 30-day and 1-year mortality after HTx (OR: 5.35; 95%CI: 1.86-.15.35; p = 0.02) (OR: 2.87; 95%CI: 1.04-.7.93; p = 0.04).
Conclusion: In our analysis, IMPACT risk score, INTERMACS profiles and MELD XI score, were similar in predicting 30-day and 1-year mortality risk after HTx. There is scarse data comparing the prognostic accuracy of these models.

1598

Toxoplasma gondii serostatus is not an independent predictor of survival in heart transplant recipients: analysis of the Spanish Heart Transplant Registry

E Eduardo Barge Caballero[1]; L Almenar-Bonet[2]; S Mirabet-Perez[3]; D Rangel-Sousa[4]; J Segovia-Cubero[5]; F Gonzalez-Vilchez[6]; MA Castel-Lavilla[7]; B Diaz-Molina[8]; J Delgado-Jimenez[9]; I Sousa-Casasnovas[10]; A Lopez-Granados[11]; L De La Fuente-Galan[12]; J Gonzalez-Costello[13]; IP Garrido-Bravo[14]; T Blasco-Peiro[15]
[1]*Hospital Universitario A Coruña, A Coruña, Spain*; [2]*Hospital La Fe, Valencia, Spain*; [3]*Hospital Sant Pau, Barcelona, Spain*; [4]*Hospital Virgen del Rocio, Sevilla, Spain*; [5]*Hospital Puerta de Hierro, Majadahonda, Spain*; [6]*University Hospital Marques de Valdecilla, Santander, Spain*; [7]*Hospital Clinic de Barcelona, Barcelona, Spain*; [8]*University Hospital Central de Asturias, Oviedo, Spain*; [9]*University Hospital 12 de Octubre, Madrid, Spain*; [10]*University General Hospital Gregorio Maranon, Madrid, Spain*; [11]*University Hospital Reina Sofia, Cordoba, Spain*; [12]*University Hospital Clinic of Valladolid, Valladolid, Spain*; [13]*Hospital de Bellvitge, Hospitalet de Llobregat, Spain*; [14]*Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain*; [15]*University Hospital Miguel Servet, Zaragoza, Spain*

On behalf of: Spanish Heart Transplant Registry Investigators
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Background: A long-standing controversy exists about a potential negative impact of pre-transplant Toxoplasma Gondii (TG) seropositivity on long-term survival of patients undergoing heart transplantation (HT). We sought to test this hypothesis in a large, multi-institutional registry.
Methods: Post-transplant outcomes of 4048 patients aged > 16 years who underwent first, single-organ HT in 17 Spanish institutions from 1984 to 2014 were analyzed. Long-term post-transplant survival and long-term survival free of cardiac death or cardiac retransplantation of 2434 (60%) TG seropositive recipients and 1614 (40%) TG seronegative recipients were compared by means of univariable and multivariable Cox´s regression.
Results: Before HT, TG seropositive recipients were older, had higher body mass index, and presented higher prevalence of hypertension, hypercholesterolemia, COPD and CMV seropositivity. In univariable analysis, pre-transplant TG seropositivity was associated with increased post-transplant all-cause mortality (non-adjusted HR 1.15; 95% CI 1.04–1.26; p = 0.004). Kaplan-Meier non-adjusted survival curves of TG seropositive (blue line) and TG seronegative (red line) recipients are represented in the Figure. However, this effect was not statistically significant after multivariable adjustment by age and sex (adjusted HR 1.01, 95% CI 0.92–1.11, p = 0.842). Extended multivariable adjustment by other potential confounders did not change significantly the result (adjusted HR 0.99, 95% CI 0.89–1.11, p = 0.925). Neither a statistically significant effect of TG seropositivity on the composite outcome cardiac death or retransplantation was observed (non-adjusted HR 1.08, 95% CI 0.95–1.24, p = 0.235; sex and age-adjusted HR 1.08, 95% CI 0.95–1.24, p = 0.231). The distribution of the causes of death was comparable in TG seropositive and TG seronegative recipients.
Conclusions: This analysis of a large, multi-institutional registry did not show an independent effect of pre-transplant TG serostatus on long-term post-cardiac transplant survival.

Non-adjusted post-transplant survival

1599

How does functional mitral regurgitation affect pulmonary hemodynamic parameters in heart transplantation candidates?

Z Zubeyde Bayram[1]; C Dogan[1]; C Dogan[1]; RD Acar[1]; RD Acar[1]; C Onal[1]; C Onal[1]; B Guvendi[1]; B Guvendi[1]; A Karaduman[1]; A Karaduman[1]; OY Akbal[1]; OY Akbal[1]; F Yilmaz[1]; F Yilmaz[1]; C Kaymaz[1]; C Kaymaz[1]; K Kirali[1]; K Kirali[1]; N Ozdemir[1]; N Ozdemir[1]
[1]Kartal Kosuyolu Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

Background: It remains unknown whether there is an association between pulmonary hypertension (PHT) and functional mitral regurgitation (FMR) The aim of the present study is to determine the association between significant functional MR (FMR) and PHT, and to evaluate the effect of FMR on other right heart catheterization (RHC) findings in patients with end-stage heart failure. Methods and Results: A total of 153 patients with end-stage heart failure undergoing evaluation for heart transplantation were stratified into two groups; namely, those with and without FMR, and all of the patients underwent RHC. Fifty one patients had significant FMR and 102 patients had non-significant or no FMR. PHT was detected in 110 patients and PVR was equal to or higher than 3 in 70 patients. There was no difference in terms of left ventricular ejection fraction, NYHA and INTERMACS grades between patients with and without significant FMR (20.9 ± 5.1 vs 21.4 ± 6.7 $p = 0.286$, 3.7 ± 0.45 vs. 3.7 ± 0.44 $p = 0.74$, 4.8 ± 1.6 vs 4.7 ± 1.4 $p = 0.68$, respectively). The means of systolic, mean and diastolic pulmonary arterial pressures, pulmonary capillary wedge pressure were higher in patients with significant FMR compared to those with non-significant FMR (56.1 ± 15.2 vs. 48.9 ± 18.9 $p = 0.012$, 37 ± 11.0 vs. 31.1 ± 11.1 $p = 0.003$, 25.7 ± 9.2 vs. 21.0 ± 9.0 $p = 0.02$, 26 ± 7.7 vs 21.8 ± 7.9 $p = 0.001$). The means of PVRs, right atrial pressures, transpulmonary gradients and diastolic pulmonary gradients were similar in both groups (3.8 ± 2.4 vs 3.2 ± 2.5 $p = 0.11$, 12 ± 5.9 vs 9.8 ± 6.6 $p = 0.08$, 11 ± 6.7 vs 10.4 ± 7.7 $p = 0.125$, 5.7 ± 1.9 vs 5.5 ± 2.3 $p = 0.67$, respectively). Among the 83 patients with PVR lower than 3, 23 patients had significant FMR and among the 70 patients with PVR equal to or higher than 3, 28 patients had significant FMR, and there was no statistical difference between the two groups ($p = 0.108$). Conclusion: The presence of significant functional mitral regurgitation appears to increase pulmonary artery pressures in patients with end-stage heart failure without any effect on PVR. Therefore, the presence or absence of mitral regurgitation does not seem to be unfavorable risk factor for PVR in pre-transplantation patients.

1600

Managing critical cardiogenic shock with long term mechanical circulatory support: where is the limit?

P Piergiorgio Tozzi[1]; C Banfi[2]; K Ahmadov[1]; R Hullin[3]; PH Meyer[4]; CH Huber[2]; M Kirsch[1]
[1]University Hospital Centre Vaudois (CHUV), Cardiac Surgery, Lausanne, Switzerland; *[2]University of Geneva, CardioVascular Surgery, Geneva, Switzerland*; *[3]University Hospital Centre Vaudois (CHUV), Cardiology, Lausanne, Switzerland*; *[4]University of Geneva, Cardiology, Geneva, Switzerland*

Background: The INTERMACS registry stratifies patients in end-stage heart failure (HF) according to the severity of the clinical conditions: from profile 1 (critical cardiogenic shock) to profile 7 (ambulatory advanced HF). Patients implanted in profile 1 are at higher risk for mortality after implantation relative to less sick patient profiles. Before 2010, 29% of LVAD recipients were in profile 1, but since 2012, that proportion has diminished to 15%, reflecting the reluctance to implant a durable device in the crash-and-burn setting. However, with the appropriate strategy, it should be possible to improving clinical results even in critical cardiogenic shock patients.
Purpose: We report our management strategy in treating critical end-stage HF patients with long term mechanical circulatory support (MCS).
Methods: Prospective study to evaluate the survival to 90 days on the LVAD of critical cardiogenic shock patients (primary endpoint). Secondary endpoints were MACE related to pump activity. Patients suffered from chronic end-stage HF and met the criteria to be enrolled in the heart transplant/destination therapy programs. Device implantation criteria were persistent low output syndrome despite optimal medical treatment (LV ejection fraction $< 20\%$; cardiac index < 2.0 l/min/m2; inotrope dependent). All patients received appropriate volume and inotropic support to avoid right heart failure. Postoperative anticoagulation guidelines included starting intravenous heparin to reach a PTT of 45-55 sec (or anti-factor Xa of 0.2-0.45 U anti-Xa/ml), when bleeding was less than 50ml/h for 3 consecutive hours. The PTT was progressively increased in postoperative day 3 until it reached 65 sec. Once the patient was able to take oral medications, Aspirine (100mg daily) and anti-vitamin K were administered with a targeted INR of 2.5 to 3.0. All patients were monitored for pump flow, selected laboratory parameters, major adverse events and device malfunctions.
Results. Out of 57 patients that received LVAD, 10 were in INTERMACS profile 1 to 3 (2 were under V-A ECMO). The indication was bridge-to-transplant in 7 patients, and destination therapy in 3. All had last generation of fully magnetically suspended centrifugal LVAD implanted under CPB, on beating heart. Two patients (20%) received concomitant aortic valve surgery. Five patients (50%) required temporary right ventricle support (tRVAD) for a mean of 8 ± 1.5 days. Bleeding requiring surgical revision occurred in 5 (50%) patients, 3 during the tRVAD support. At the 90-day endpoint survival was 90%, one (10%) died due to respiratory failure. Three (30%) experienced critical illness polyneuropathy. Two (20%) had late driveline infection.
Conclusions. Morbidity rate was high. However, the 90% survival rate at 90 days endorses the assumption that, with the appropriate strategy and last generation centrifugal LAVD, even the crash-and-burn patients have excellent possibility to benefit from long term MCS.

1601

Reversibility of fried's frailty domains post-intervention among patients with advanced heart failure

S R Sunita Jha[1]; MK Hannu[1]; PJ Newton[2]; K Wilhelm[3]; CS Hayward[1]; E Kotlyar[1]; A Keogh[1]; K Dhital[1]; M Connellan[1]; E Montgomery[1]; A Smith[1]; M Harkess[1]; P Tunicliff[1]; PM Davidson[4]; PS Macdonald[1]; *[1]St Vincent's Hospital, Heart and Lung Transplant Unit, Sydney, Australia*; *[2]University of Technology, Sydney, Sydney, Australia*; *[3]St Vincent's Hospital, Psychiatry, Sydney, Australia*; *[4]Johns Hopkins University of Baltimore, Faculty of Nursing, Baltimore, United States of America*

Aim: The aim of this study was to evaluate the reversibility of frailty in AHF patients undergoing bridge-to-transplant ventricular-assist-device (BTT-VAD) implantation or heart transplantation (HTx).
Methods: Since 2013, all AHF patients referred to our centre were assessed for frailty pre- and post- BTT-VAD/HTx. Fried's five physical domains: exhaustion, grip-strength, mobility, appetite and physical inactivity (frail $\geq$ 3/5), as well as cognitive impairment (MoCA $\leq$ 26) and depression (DMI $>$ 9) were assessed.
Results: 24 frail pre-intervention patients were followed-up post intervention for reversibility: 12 VAD (124 ± 77 days post-VAD) and 12 HTx (177 ± 135 days post-HTx). Among the VAD patients there was a significant improvement in frailty score (4.2 ± 0.8 to 1.7 ± 1.1, $p < 0.003$); with significant improvements across all frailty domains except grip-strength after pump implant. Among the HTx patients, there was also a significant improvement in frailty score (3.3 ± 0.5 to 0.8 ± 0.1, $p < 0.002$); with significant improvements seen in exhaustion, appetite and physical activity after HTx. A non-significant improvement was seen in depression, and less so cognitive impairment in both the frail pre-VAD/HTx groups.
Conclusion: Frailty associated with AHF is amenable to improvement post-intervention. Improvements in appetite and physical activity were the major contributors to improved frailty score. In contrast, improvement in HGS was small and non-significant.

Reversibilty of frailty post-interventio

	Baseline	Follow-up	p-value
Frail Pre-VAD (n = 12)			
Frailty score	4.2±0.8	1.7±1.1	0.003
Exhaustion HGS*Mobility AppetitePhysical Activity	10 (83%) 9 (75%) 10 (83%) 12 (100%) 10 (83%)	4 (33%) 8 (67%) 3 (25%) 4 (33%) 1 (8%)	0.031 1.000 0.016 0.008 0.012
HGS score(kg)	22.6±11.5	26.9±10.0	0.099
MoCA score	24±5	25±3	0.306
DMI score	10±7	5±5	0.066
Frail Pre-HTx (n = 12)			
Frailty score	3.3±0.5	0.8±0.1	0.002
ExhaustionHGS* Mobility AppetitePhysical Activity	8 (67%) 7 (58%)5 (42%)11 (92%)8 (67%)	2 (17%)6 (50%)1 (8%)2 (17%)0 (0%)	0.031 1.000 0.125 0.0040.008
HGS score(kg)	26.0±8.5	28.4±8.7	0.170
MoCA score	25.4±2.4	26.4±3.2	0.280
DMI score	8±8	3±4	0.054

*categorical data

POSTER SESSION 3

ACUTE HEART FAILURE

P1602

ultrasound of the lungs for acute heart failure diagnosis in the early phase of ST-elevation myocardial infarction

M Teterina[1]; I Meray[1]; LA Babaeva[1]; AF Safarova[1]; AS Pisaryuk[1]; OI Lukina[1]; IV Shevchenko[1]; AS Milto[1]; ZHD Kobalava[1]
[1]Peoples Friendship University of Russia (PFUR), Cardiology, Moscow, Russian Federation

Introduction: Evaluation of heart failure in STEMI (ST elevation myocardial infarction) patients in real clinical practice is based primarily on subjective methods of investigation. In this respect, it is highly important to implement fast objective bedside methods of pulmonary congestion evaluation. One of them is the technique of sonographic quantification of total number of B-lines for detection of interstitial-alveolar syndrome.
Objective: To estimate frequency of detected pulmonary venous congestion by means of bedside sonographic investigation of the lungs in STEMI patients and compare the results with data received by both physical examination and well-known instrumental assessment methods.
Results: The study included 109 STEMI patients with Killip I (40%) and Killip II (60%) acute heart failure. Patients with Killip classes III and IV were excluded from the study. In addition to clinical and radiological assessment of pulmonary congestion, in the first days of myocardial infarction all patients were performed pulmonary ultrasound with the quantification of B-lines. Thus, 64% (n = 28) patients with Killip class I did not show any sonographic signs of pulmonary congestion (less than 5 B-lines), whereas 36% (n = 16) patients had congestive heart failure with total number of B-lines over 15. Of these patients, 11% (n = 5) had expressed severe congestion (B-line score≥30). Among Killip class II patients, 97% showed signs of congestion, of them 23% had severe interstitial-alveolar syndrome. In the following 2-3 days after MI onset, all patients with Killip I class and presenting with B-lines score≥6, developed signs of pulmonary congestion, confirmed by physical and/or X-ray methods of investigation.
Conclusion: Ultrasound assessment of the lungs with sonographic quantification of B-lines is an available method of early heart failure diagnosis in STEMI patients.

P1603

Changes in echocardiographic parameters and biomarkers during hospital stay in patients with acute heart failure

E Akiyama[1]; LNL Van Aelst[2]; M Arrigo[3]; J Motiejunaite[1]; E Gayat[4]; MF Seronde[5]; A Mebazaa[4]
[1]Inserm UMR-S 942, Paris, France; *[2]KU Leuven, Leuven, Belgium*; *[3]University Hospital Zurich, Zurich, Switzerland*; *[4]Hospital Lariboisiere, Paris, France*; *[5]University Hospital Jean Minjoz, Besançon, France*

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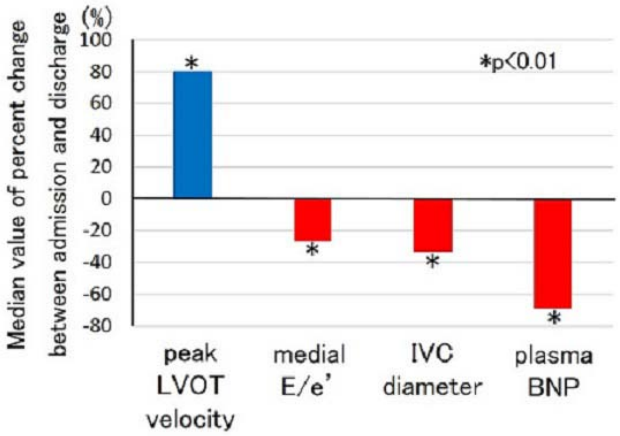
Background: Because congestion plays an important role in pathogenesis of acute heart failure (AHF), decongestion is primary treatment in patients with AHF. Echocardiographic parameters and biomarkers are useful for evaluation of congestion and diagnosis of heart failure, however, changes in these parameters according to decongestion therapy in patients with AHF are poorly defined.
Purpose: The purpose of this study was to investigate changes in echocardiographic parameters and biomarkers during hospital stay in patients with AHF.
Methods and Results: Of 101 hospitalized patients with AHF derived from MEDIA-DHF cohort, 60 had preserved left ventricular (LV) ejection fraction (EF) (HFPEF) and 41 had reduced LVEF (HFREF). Concerning echocardiography, although LVEF was unchanged during hospital stay (median: 38 [29-55] at admission, 41 [30-57] % at discharge, p = 0.37), peak LV outflow tract (LVOT) velocity and tricuspid annular plane systolic excursion (TAPSE) improved during hospitalization (median: peak LVOT velocity 0.63 [0.58-0.69] at admission, 1.13 [1.04-1.29] m/s at discharge, p = 0.005, TAPSE 16 [15-19] at admission, 19 [17-21] mm at discharge, p = 0.04). Medial E/e' decreased during hospitalization (median: 21.1 [15.8-29.6] at admission, 16.6 [11.7-24.3] at discharge, p = 0.004). Inferior vena cava (IVC) diameter at rest decreased and respiratory variability of IVC diameter improved during hospitalization (median: IVC diameter 22 [16-24] at admission, 13 [11-18] mm at discharge, p = 0.009, variability 32 [8-44] at admission, 43 [29-70] % at discharge, p = 0.04). The results were similar in HFPEF and HFREF, except that TAPSE improved in only HFREF patients (median: HFPEF 17 [13-20] at admission, 17 [16-19] at discharge, p = 0.34, HFREF 16 [15-18] at admission, 19 [18-25] mm at discharge, p = 0.06) and medial E/e' decreased in only HFPEF patients (median: HFPEF 21.3 [16.0-30.5] at admission, 14.3 [11.5-24.3] at discharge, p = 0.007, HFREF 21.0 [14.0-25.5] at admission, 19.2 [12.0-22.0] at discharge, p = 0.20). Concerning plasma biomarkers, B-type natriuretic peptide (BNP), mid-regional pro-atrial natriuretic peptide (MR-proANP), and soluble CD146 levels all significantly decreased during hospitalization (median: BNP 935 [514-2037] at admission, 308 [183-609] pg/mL at discahrge, p < 0.001, MR-proANP 449 [274-653] at admission, 366 [242-549] pmol/L at discharge, p < 0.001, soluble CD146 528.0 [405.9-653.8] at admission, 449.8 [373.9-529.2] ng/mL at discharge, p = 0.003). The results were consistent between HFPEF and HFREF.
Conclusions: Echocardiographic parameters and biomarkers which indicate the severity of congestion and cardiac function significantly improved during hospital stay in patients with AHF.



P1604

Performance of early change of cardiac output in the diagnosis of acute heart failure (AHF) in patients with acute dyspnea

EZ Ezzina[1]; EM Malek Echeikh[1]; ZW Zhani[1]; AN Azaiez[1]; SA Sekma[1]; BAA Ben Abdallah[1]; BK Beltaief[1]; MMA Msolli[1]; DZ Dridi[1]; BH Boubaker[1]; GMH Grissa[1]; BW Bouida[1]; NS Nouira[1]
[1]*university of monastir, monastir, Tunisia*

On behalf of: great network

Purpose: To evaluate the performance of cardiac output (CO) change with dynamic and pharmacological maneuvers in the diagnosis of AHF in patients admitted to emergency department (ED) with acute dyspnea.
Methods: A prospective study conducted in the emergency department (ED) including patients over 18 years admitted for acute dyspnea. We measured CO using thoracic bio impedance: at baseline, during supine position (SP), leg rising (LR), under Valsalva maneuver (VM) and after administration of sublingual nitroglycerin (NTG test). Heart failure (HF) is defined on the basis of clinical findings, serum levels of pro-BNP and echocardiographic criteria.
Results: 395 patients were included, 212 patients with HF. Cardiac output at baseline was higher in the non-AHF group ($p < 0.01$). The effects of the various maneuvers on COwere summarized in the figure.
Conclusion: Early changes of cardiac output with VM and NTG can be a simple method to recognize HF in patients who are admitted to ED for acute dyspnea

P1605

Value of systolic time intervals in the prediction of 30 day mortality after hospital discharge in Acute Heart Failure patients

I Imen Trabelsi-Bchir[1]; MS Messous[1]; BK Beltaief[1]; MMA Msolli[1]; SA Sekma[1]; BN Bziouich[1]; FN Fredj[1]; EZ Ezzina[1]; EM Echeikh[1]; GMH Grissa[1]; BH Boubaker[1]; BR Boukef[1]; BW Bouida[1]; NS Nouira[1]
[1]*university of Monastir, monastir, Tunisia*

Background: Acute heart failure (AHF) is one of the leading causes of unscheduled hospitalization and is associated with frequent readmissions and substantial mortality. Simple and noninvasive measurements of systolic time intervals (STI) could be helpful to predict these complications in patients admitted to the emergency room (ER). The present study assessed the prognosis performance of STI in AHF patients.
Patients and methods: We included all patients over 18 years old admitted to the ER for AHF. The diagnosis of AHF was determined on the basis of clinical examination, echocardiography, and brain natriuretic peptide value. Measurement of STI included the pre-ejection period (PEP), left ventricular ejection time (LVET), and systolic time ratio (STR=PEP/LVET). STI were determined by thoracic bio-impedance method, at admission in all included patients. Survival status data at 30 days was prospectively collected. The values of STI were compared between survivor and non survivors patients in order to determine their prognostic value.
Results: A total of 500 AHF patients were included, with a mean age 68,41 ± 12 years, sex ratio (M / F) 1,04. Compared to survivors, Non survivors patients had higher STR (48.7 ± 17 vs 43.2 ± 11, $p < 0.01$) values. LVET and PEP values were not significantly different between both groups.
Conclusion: Only STR value could be considered as a meaningful non invasive method to predict mortality 30 days after hospital discharge in AHF patients.

Table. Patient's characteristics at emer

	All patients (n = 500) Yes (n = 27)	30 days death No(n = 473)	
Age	68.4±12.3	73.2±11	68.5±12
Sex (H/F)	256/244	16/11	241/232
Comorbidity n(%)Arterial	314 (62.8)	16 (59.3)	297 (62.8)
hypertensionDiabetesCoronary	237 (47.4)	13 (48.1)	224 (47.4)
Artery DiseaseChronic Heart	98 (19.6)	9 (33.3)	89 (18.8)
FailureRespiratory Failure	100 (20)	5 (18.5)	95 (20.1)
	86 (17.2)	5 (18.5)	81 (17.2)
PEP (ms)LVET (ms)STR (%)	118±23	120±16	115±21
	274±52	258 ±47	275 ±45
	44.3±13	48.7 ±17	43.2±11*

*$p < 0.05$ between the two groups

P1606

Diastolic left ventricular function and relation to coronary and myocardial flow after primary coronary angioplasty

D Dawood Sharif[1]; H Abu Shqara[2]; Y Sharif[2]; A Sharif-Rasslan[3]; U Rosenschein[1]
[1]*Bnai Zion Medical Center, Haifa, Israel*; [2]*Technion, Haifa, Israel*; [3]*The Academic Arab College, Mathematics, Haifa, Israel*

Primary percutaneous coronary intervention (PPCI) in patients with acute ST-elevation myocardial infarction (STEMI), resumes coronary flow in the infarct related artery (IRA) and myocardial perfusion which both determine left ventricular (LV) function and prognosis.
Objective: Evaluate LV diastolic function, coronary velocity parameters and their inter-relationship in the infarct related and non-infarct related coronary artery.
Methods: Eighty patients with acute STEMI, 60 anterior and 20 non-anterior, treated with PPCI were studied. Complete transthoracic Doppler echocardiography and sampling of blood velocity in the left anterior descending (LAD) coronary artery were performed immediately after PPCI and 5 days later.
Results: In the control group, LAD velocity and diastolic function parameters did not change during hospitalization and were unrelated. In the study group these parameters were dynamic; LAD diastolic time velocity integral and diastolic pressure half time increased, E wave deceleration time increased before discharge while A wave peak velocity decreased. TIMI grade < 3 was associated with larger mitral E-wave velocities, $p < 0.02$, Early after PPCI, longer LAD diastolic deceleration time was associated with longer mitral E-wave deceleration time, $p < 0.04$, ST-Elevation resolution>70% was associated with longer late mitral E-wave deceleration time, $p < 0.04$. Killip Class>1 was associated with lower mitral annular E-velocities, $p < 0.04$. E/Ea>8 and PCWP>12 were related to larger late LAD systolic velocities, $p < 0.05$, and longer early pressure half time, $p < 0.02$.
Conclusions: IRA flow and LV diastolic function are dynamic and interrelated but not non-IRA.

P1607

Interest of a systematic investigation when a tako tsubo syndrome is suspected

C Clement Delmas[1]; L Marty[1]; C Biendel[1]; M Elbaz[1]; D Carrie[1]; M Galinier[1]; O Lairez[2]
[1]*Toulouse Rangueil University Hospital (CHU), Cardiology department, Toulouse, France*; [2]*Toulouse Rangueil University Hospital, Cardiac Imagery Center, Toulouse, France*

Background: Diagnostic criteria for Tako Tsubo Cardiomyopathy (TTC) exist since 2004, but there is currently no recommendation of learned societies as the minimum balance required. Exponential increase of TTC diagnoses assumes the risk of misdiagnosis and delayed appropriate management.
Aim: Determine the prevalence of differential diagnosis in a "real life" population of patient with suspected TTC.
Methods and Results: Between 10.2009 and 01.2016, 8726 patients were admitted for acute coronary syndrome (ACS) with troponin elevation in our center. Among them 144 (1.7%) patients were suspected for TTC and were included in a prospective cohort. According to the initial presentation, cardiac MRI, urinary and/or plasma catecholamines and thyroid balance were conducted. Among them, 26 (18%) diagnosis and therefore management were changed after the completed assessment. Fourteen (9.7%) patients were reclassified as ACS (2 with spastic angina), 3 (2.1%) as myocarditis, 2 pheochromocytoma (1.4%), 6 misceallenous diagnosis (4.2%) and 1 thyrotoxisis (0.7%). MRI was the most efficient exam to catch misdiagnoses in 14 cases (9.7%).
Conclusion: Differential diagnosis in patients with suspected TTC represents more than 15% of these population and need to perform a minimum check-up with MRI and catecholamines measurement.

P1608

Clinical characteristics and in-hospital outcomes among patients hospitalized for acute heart failure stratified by clinical response to initial therapy

CI Radulescu[1]; L Antohi[1]; M Chivulescu[1]; I Cosei[1]; A Covaliov[1]; R Radu[1]; A Ambrosy[2]; S Collins[3]; C Macarie[1]; O Chioncel[1]; M Gheorghiade[4]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania*; [2]*Duke University Medical Center, Cardiology, Durham, United States of America*; [3]*Vanderbilt University, Emergency Medicine, Nashville, United States of America*; [4]*Northwestern University, Cardiology, Chicago, United States of America*

Introduction: Patients hospitalized for acute heart failure (AHF) have variable in-hospital trajectories as a result of different etiologies and precipitating factors. There are limited data adressing the heterogeneity of in-hospital course by initial therapy.

Objective: To identify clinical characteristics and in-hospital outcome of patients hospitalized for AHF and stratified by clinical response to initial intravenous (IV) therapy.
Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients admitted for AHF over a 12-month period. Based upon clinical response in the first 24 hours to initial IV therapy, patients were divided into four subgroups: A. persistent improvement, B. initial improvement followed by clinical decompensation, C. continuous worsening, and D. refractory signs and symptoms. In-hospital outcomes included all cause mortality (ACM) and length of stay (LOS).
Results: Overall, the breakdown of patients included 75.1% in group A, 16.1% in group B, 3.4% in group C, and 5.4% in group D. Baseline characteristics and in-hospital management are shown in Table 1. In-hospital ACM was 6.8% in group A, 8.2% in group B, 34% in group C, and 27% in group D. Similarly, median (25th, 75th) LOS was 6 (3, 9) days in group A, 8 (4,12) days in group B, 9 (3,18) days in group C, and 12 (7, 22) days in group D.
Conclusions: Although the vast majority of AHF patients substantially improved in response to initial IV therapy, some patients experienced a persistently unfavourable or a deteriorating in-hospital trajectory. A better characterization of the pathophysiology of AHF may facilitate targeted aplication of existing therapies and development of novel interventions in patients at-risk for an unfavourable clinical course.

Table 1

	An=2421	Bn=519	Cn=110	Dn=174
Age(years)%	68.5	68.8	67.8	69.4
Gender(Male)%	52	53	57	51
Ischemic etiology(%)	55	56	71	57
Cardiogenic Shock(%)	2	4	55	19
Creatinine(mg/dl)	1.2 +/-0.6	1.3 +/-1.1	1.5 +/-1.3	1.9 +/-1.1
Na(mmol/l)	134 +/-7	133 +/-7	133 +/-11	130 +/-9
LVEF < 40%	59	61	73	79
IV Furosemide(%)	91	87	53	72
IV Vasodilators(%)	26	34	8	7
IV Inotropes(%)	8	23	58	43

P1609
Evaluation of the sST2-guided optimization of medical treatments of patients admitted for HF, to prevent readmission: the STADE-HF study

C Corentin Curinier[1]; K Solecki[1]; AM Dupuy[2]; S Cade[1]; F Cransac[1]; A Decorps[1]; S Soltani[1]; A Verchere[1]; C Belloc[1]; C Roubille[1]; P Fesler[1]; G Mercier[1]; JP Cristol[2]; Y Audurier[1]; F Roubille[1]
[1]University Hospital of Montpellier, Cardiology, Montpellier, France; [2]University Hospital of Montpellier, biochemistry, Montpellier, France

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Background: The prevalence of heart failure (HF) is about 1-2%. It is a major cause of health burden representing between 2 billions euros per year in France. 63% of these costs are due to hospitalization. The sST2 (member of Interleukine-1 receptor family) is a potent predictor for survival in HF, probably better than natriuretic peptides. In this trial we aim at evaluating the sST2-guided therapy as a help for the physician to optimize the recommended treatments in order to prevent readmissions.
Methods: The trial will be a prospective biomedical interventional randomized open-labelled trial of evaluation of the two strategies with two parallel arms: conventional (sST2 is not known from the clinician) versus sST2-guided therapy (sST2 assessed at day 4 is known from the clinician). It will be conducted in the University Hospital of Montpellier. The study will include adults hospitalized for HF. If ST2 at day 4 is > 37 ng/mL, the clinician will be encouraged to optimize the therapy as much as the patient tolerates it. If ST2 is < 37 ng/mL, no incentive to optimize the treatment will be made. Based on the hypothesis of a 50% reduction of readmissions, 300 patients will be included.
Discussion: Many tools have been proposed to decrease the burden of readmission in patients with HF but the cornerstone remains the optimization of recommended medical treatment with improvement of survival: beta-blockers, ACE-inhibitors or ARA-2 inhibitors, mineralocorticoid inhibitors, ivabradine and sacubitril-valsartan. The higher the sST2 is, more likely is the impact of drugs with antiremodeling effect. The optimal dosage of these agents in individuals is guided largely by subjective indices, namely the clinician's assessment of symptoms, bedside signs and tolerability. There is therefore an interest in a biomarker (sST2) to guide the management of patients admitted for HF, in order mainly to reduce the burden of readmissions. It is the first time that this kind of approach is evaluated in patients with HF.

P1610
Use of invasive mechanical ventilation in acute heart failure: the experience of a referral cardiological centre

G Giulio Binaghi[1]; D Congia[1]; A Muroni[2]; A Pani[1]; D Pasqualucci[1]; E Serra[1]; M Porcu[1]
[1]G. Brotzu Hospital, Department of Cardiology, Cagliari, Italy; [2]University of Cagliari, Cagliari, Italy

Acute heart failure (HF) refers to rapid onset or aggravation of symptoms and signs due to elevated intracardiac pressures and/or a reduced cardiac output. It is a life-threatening condition requiring urgent evaluation and treatment. Data from registries of HF showed that up to 16% of cases need an invasive mechanical ventilation (IMV). Our aim is to perform a retrospective evaluation of clinical and haemodynamic characteristics and outcomes of patients (pts) hospitalized in an 8-bed CCU of a referral cardiological centre from January 2014 to May 2016 for acute HF, who underwent IMV. During the study period 1437 pts have been hospitalized for any cause, of them 54 (3,8%) need an IMV because of acute HF. Mean age of pts was 68 ± 16 years, 36 (67%) were males and in 52% of cases, HF was due to acute coronary syndrome. Arrhythmia was the reason of decompensation in 26% of pts, in 2 (3,7%) cases the cause of HF was a myocarditis and in other 2 a pulmonary embolism. 35% of pts were diabetics, 57% had a history of cardiopathy, while 28% had a chronic kidney disease and 15% a COPD. Before hospitalization, 44% of pts were treated with a RAAS-blocker (ACE-I or ARB), 41% with a B-blocker, 41% took an anti-platelet drug, 46% followed a diuretic treatment and 24% an anticoagulant regimen. At the time of intubation, mean systolic blood pressure and heart rate were 114 ± 33 mmHg and 96 ± 33 bpm respectively. Lab tests showed that the mean value of serum creatinine was 1,8 ± 1 mg/dl and of hemoglobin was 12,3 ± 2 g/dl. First blood-gas-analysis performed displayed an acidosis in 23 cases (59%). In 28% of pts, ECG showed a ST-elevation and in 9,3% a presumed new left bundle branch block. During IMV, in 49 pts (91%) a sedative agent was employed and about in 2/3 also a neuromuscular blocking drug was necessary. In the hospitalization, 59,3% (n: 32) of cases need an inotrope: adrenaline was the most used (42,6%; n: 23), then noradrenaline (27,8%; n: 15) and dobutamine (25,9%; n: 14). Levosimendan and dopamine have been used much less commonly (13% and 7,4%). 24 pts (44,4%) underwent coronary angiography and 66% of those (n: 16) need a PCI. 11 (21%) pts had a renal replacement treatment and 6 (11,1%) necessitated the use of IABP. The mean time of IMV was 3,9 ± 3,3 days and the average length of hospitalization was 16,7 ± 15,3 days. The intra-hospital mortality registered was 42,6% (n: 23), but only 10% (n: 5) in pts requiring IMV due to an arrhythmic storm. Our data show that a patient hospitalized in a CCU for HF and requiring IMV is not so common. However, according to data from registries of HF, his management is very complex, not only for the treatment of HF's etiology, but also for the comorbidities, the failure interesting other organs and the different therapies, pharmacological and not, used. In order to better manage these cases, multiplies skills are required to cardiologist that necessitate a wide and correct knowledge of pathophysiology of whole organism.

P1611
Right heart failure and cardiogenic shock contribute to longer length of stay in patients with acute heart failure

B Bambang Widyantoro[1]; I Firdaus[1]; SS Danny[1]; DA Zamroni[1]; I Irmalita[1]; DPL Tobing[1]; DA Juzar[1]
[1]Dept of Cardiology and Vascular Medicine, Universitas Indonesia-NCVC Harapan Kita Hospital, Jakarta, Indonesia

Morbidity and mortality of patients admitted with acute heart failure (AHF) remains high. The aim of this study was to describe patient profiles and predictor of length of stay in patients with AHF.
We examined 1846 patients hospitalized in CVCU of our National Cardiovascular Center in 2015. Among those, 697 (37.76%) were patients with AHF, with acute coronary syndrome as the most prevalence cause (62.13%). Median age was 60 (32-89) years old, and 81.8% were male. Hemodynamic profiles showed 68.15% patient had wet and warm presentation, and 7.6% had cardiogenic shock. The most prevalence co-morbid are diabetes (44.8%), chronic kidney disease (6.31%) and pneumonia (21.52%). Median length of stay in CVCU was 3 (1-75) days, and patient with cardiogenic shock and right HF stay longer in CVCU [6.5 (1-50) days and 7 (6-21) days, respectively]. These 2 groups of patients also need more inotropes and vassopressors, and morelikely to have acute kidney injury that need continuous renal replacement therapy. In conclusion, we observed that patient with right heart failure and cardiogenic shock who need renal replacement therapy during hospitalization contributed to longer length of stay in hospital among all patients with acute heart failure.

P1612

Twenty percent of patients with acute decompensated heart failure (ADHF) do not receive appropriate treatment in the emergency department (ED)

J Mc Cambridge[1]; C Keane[1]; M Walshe[1]; P Campbell[1]; PR Kalra[2]; MR Cowie[3]; J Riley[3]; R O' Hanlon[1]; M Ledwidge[1]; J Gallagher[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland; *[2]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*; *[3]Royal Brompton Hospital, London, United Kingdom*

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Introduction: Increasing heart failure (HF) admission and ED attendance rates present a major challenge. It is generally accepted that early appropriate intervention reduces length of hospital stay and time to clinical stability.
Purpose: To evaluate the numbers being diagnosed with ADHF and numbers receiving HF-directed treatment in those presenting to ED with ADHF.
Method: This analysis is taken from one of the centres in an ongoing multicentre study evaluating clinical care pathways for patients admitted with ADHF. It focuses on the patient experience in ED. Specifically, we looked at patients' initial diagnosis (ADHF, mixed respiratory infection/ADHF, respiratory infection alone, acute coronary syndrome, other), numbers receiving diuretics/nitrates in ED and time from presentation to treatment. A p value < 0.05 was taken as significant.
Result: This analysis included 84 patients presenting to ED with ADHF, of which 47 (55.9%) had a new diagnosis of HF (de novo, DN) and 37 (44.1%) had a known history of HF (recurrent admitters, RA). Median age for this group was 75 years (71 for DN, 78 for RA). RA had a higher median number of co-morbidities (4) compared to DN (3). The time from presentation to first medical contact in ED was documented in 78.6% (66) of patients, with no significant difference between the median times for DN and RA (101 minutes and 91 mins respectively, $p = 0.381$). Only 80.95% (68) of all patients were initially diagnosed as either ADHF or mixed respiratory infection/ADHF. RA were more likely to be diagnosed as either ADHF or respiratory infection/ADHF than not when compared to DN (89.2% vs. 74.5% respectively, $p = 0.044$). Of the entire cohort, 81.7% (67) received some sort of HF-directed therapy (oral/intravenous diuretic and/or transdermal/intravenous nitrate). RA received a HF-directed therapy more often than DN (88.6% vs. 76.6% respectively, $p = 0.246$) and RA also received IV diuretics more often than DN (82.9% vs. 70.2% respectively, $p = 0.192$), though neither difference reached statistical significance. DN tended to receive HF-directed therapy earlier with a median time-to-treatment of 232 mins (IQR 301 mins) compared to 324 mins (IQR 214 mins) with RA ($p = 0.202$).
Conclusion: One fifth of patients presenting to ED with ADHF were not initially diagnosed with ADHF and did not receive HF-directed therapy as part of their initial management. RA were more likely to be diagnosed with ADHF than DN. Earlier recognition and treatment of ADHF in ED may be improved via increased clinician awareness/comfort with the features of HF, easier access to a patient's HF record (for RA) and training ED doctors in the use of rapid, focussed echocardiography.

P1613

The Beacon patient management system for outpatient heart failure monitoring

FA Frank Mcgrew[1]; SC Sandra Harlton[1]; LLR Letitia Redden[1]; HS Norman[2]
[1]Stern Cardiovascular Foundation, Germantown, United States of America; *[2]Medtronic, Little Rock, United States of America*

Background: Acute Heart Failure (HF) management often results in expensive emergency room visits and hospitalizations. Remote patient managing systems could permit outpatient management of acute worsening of CHF with significant economic savings.
Purpose: Demonstrate how the use of the Beacon Patient Management System for outpatient HF monitoring can permit heart failure management in an outpatient setting and prevent emergency room visits and hospitalizations.
Methods: The beacon outpatient monitoring system uses transtelephonic monitoring of multimodality information, which can be integrated by the patient's physician and allied health personnel managers. The ability to monitor various components of the patient's status including heart rate variability, percentage of atrial and ventricular pacing, and thoracic impedance are utilized to "trigger" communication with the health care providers to permit resolution of HF rapidly and economically.
Results: A sample case of a 65 yo female with renal insufficiency, hypertension, multiple sclerosis, and severe systolic HF requiring intermittent inotropic infusions, and limited ambulatory status was monitored using the beacon system. Serial transmissions eventually showed her ventricular pacing declined, impedance index increased, and heart rate variability indicated clinical instability. As a result of these remote monitoring transmissions the patient was brought to an outpatient facility where her ventricular lead capture was reprogrammed to 100% pacing, atrial fibrillation frequency was treated with amiodarone and anticoagulation therapy, and milrinone infusions were adjusted from intermittent to continuous. Within two weeks beacon transmissions confirmed impedance index returned to normal, atrial fibrillation frequency dropped to zero, and ventricular pacing had risen to 100%.
Conclusions: The Beacon system offers a remote monitoring system, which is rapid and provides accurate assessment of a patient's HF status. This permits prompt changes in device programming, initiation or adjustment of anticoagulation, medication adjustments, and optimum scheduling of subsequent care. This not only provides a method with extreme patient acceptance, but also a major economic advantage. In this further use of remote monitoring can greatly enhance congestive HF management. The beacon management system transmissions information made it possible to easily treat clinically unstable symptoms in an outpatient setting ($300.00) resulting in considerable financial savings to the patient as compared to the high cost of an inpatient hospitalization ($4000.00).

P1614

Management features of postoperative right ventricular failure after tetralogy of fallot repair

S Sardor Ibragimov[1]
[1]Republican Specialized Centre of Surgery , Intensive Care Unit, Tashkent, Uzbekistan

Objective: The aim of the study was to develop the diagnostic and treatment algorithm for patients with right ventricular (RV) failure (RVF) in an early postoperative period after tetralogy of Fallot repair (TFR) in an Intensive Care Unit.
Methods: We studied early postoperative period of 48 patients who underwent TFR during 2015. In 6 patients the postoperative period was complicated by the development of RVF. After surgery, all patients received on prolonged mechanical ventilation. Data of hemodynamics and echocardiography served as diagnostic criteria of postoperative RVF. Drug therapy includes the use of vasopressor and inotropic agents. Oxygen therapy was in accordance with the concepts of "safe ventilation", "safe hypoxemia", and by using different modes of ventilation.
Results: One of the most important principles in managing postoperative RVF is to be able to maintain systemic blood pressure while minimizing RV dilation. Other important principles include reducing RV afterload, minimizing blood transfusions and optimizing ventilator settings. It is also essential to tailor therapy to the specific etiology of postoperative RVF.
Norepinephrine combined with dobutamine showed good results in maintaining systemic blood pressure, increasing cardiac index and decreasing pulmonary pressure in patients with RV failure and hypotension associated with acute or chronic increased pressure in the pulmonary artery.
An inhibitor of phosphodiesterase - milrinone, at the same time having a positive inotropic action, and the ability to normalize the myocardium compliance, allowed to significantly increase the drug therapy efficiency of RVF.
Non-invasive respiratory support in CPAP mode (NiCPAP) is an effective method, which is in complex of adequate intensive and pharmacotherapy allows to quickly stabilizing the clinical condition, respiratory and hemodynamic status of patients with RVF after TFR.
Conclusions: Modern and comprehensive monitoring of cardiac hemodynamics in the early postoperative period allows to detect a RVF development after TFR, with the establishment of its causation.
Designed treatment algorithm of managing RVF after TFR allows to maximum use of the entire drugs' arsenal of hemodynamic correction and methods of respiratory support, and significantly improve a treatment outcomes of this serious complication.

P1615

The efficacy of urapidil in the treatment of acute heart failure complicated with hypertension in elderly patients

J Jing Gao[1]; QI Hua[1]; XIAO H Liu[2]
[1]Xuan Wu Hospital, Capital Medical University, department of cardiology, Beijing, China People's Republic of; *[2]Yuquan Hospital of Tsinghua University, Cadre ward, Beijing, China People's Republic of*

Objective: To assess the efficacy of urapidil in the treatment of acute heart failure complicated with hypertension in elderly patients.
Methods: 140 cases of acute heart failure complicated with hypertension in elderly patients were randomized into urapidil or nitroglycerin group. All patients were monitored for systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), situation at the time of before treatment,24h,48h,72h,7d after treatment,and contrasted to observe the changes in N-terminal pro-B-type natriuretic peptide raw (NT proBNP) and left ventricular ejection fraction LVEF in elderly patients with acute heart failure of urapidil at the time of before treatment, 48h and 7d after treatment.
Result: The level of SBP DBP and HR in urapidil group was significantly lower on hour 24,hour 48, hour 72 and day 7 after treatment than before treatment $P < 0.05$. The level of BNP in urapidil group was significantly lower on hour 48 and day 7 after treatment than before treatment $P < 0.05$. The level of LVEF in urapidil group

was significantly higher on day 7 after treatment than before treatment P < 0.05.The effect of urapidil was significantly lower than that of nitroglycerin on SBP P < 0.05).
Conclusion: The effect of urapidil is obvious on reducing and stabilizing SBPDBPHR and improving cardiac function in elderly patients with hypertension accompanying acute heart failure.

P1616

Utilization of mechanical ventilation in patients hospitalized for acute heart failure

M Monica Chivulescu[1]; L Antohi[1]; C Radulescu[1]; RI Radu[1]; C Macarie[1]; AP Ambrosy[2]; M Gheorghiade[3]; O Chioncel[3]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania; [2]Duke University Medical Center, Durham, United States of America; [3]Northwestern University, Chicago, United States of America

Background: During hospitalization for acute heart failure (AHF), in some patients hypoxemia may be too severe or may not be promptly improved by pharmacotherapies and these patients are emergently requiring invasive mechanical ventilation(IMV) via intubation. Although in this setting IMV may be a life-saving therapy, it is associated with an immediate decrease in cardiac output and later on with in-hospital complications including barotrauma and pulmonary infections.
Aim: To identify clinical variables independently associated to need of IMV during hospitalization for AHF.
Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients admitted for AHF in 5 academic and 8 community hospitals, over a 12-month period. A multivariate logistic regression model was developed to identify baseline clinical variables predictive of in-hospital utilization of IMV.
Results: IMV has been performed in 113 (3.5%) of patients during hospitalization for AHF. Patients who required IMV had higher respiratory rate(RR) (30 +/-11 vs 21 +/-7;p = 0.006) and lower systolic blood pressure(SBP)(101 +/-22mmHg vs 143 +/-27mmHg;p < 0.001) at presentation compared to patients who did not require IMV.
A proportion of 43% of patients in IMV group were in cardiogenic shock (CS) at presentation, distinct to 3.9% CS in patients without IMV.
IMV has been associated to higher in-hospital mortality (24.7% vs 7.1%;p < 0.001) and with longer median length of stay(14 vs 6 days).
Using a multivariate logistic regression model, sodium at admission (HR=1.26;95%CI= 1.12-1.41), EF < 40% (HR=1.55;95%CI= 1.33-1.82), respiratory rate (HR=1.79;95%CI= 1.63-1.85), need of inotropic agents (HR=3.94;95%CI= 2.91-6.15) were found to be independent risk factors for need of IMV during hospitalization.
Conclusions: In present study, rate of MV utilization was lower compared to other registries. Clinical variables associated to hemodynamic abnormalities were highly predictive for subsequent utilization of IMV and may be useful for disposition decision-making pathways.

P1617

Clinical characteristics and outcome of decompensated heart failure patients according to ACE-inhibitor titration

R M Christodorescu[1]; IR Lala[2]; D Darabantiu[2]; A Pop-Moldovan[2]; AM Apostolescu[3]; M Trofenciuc[2]; S Dragan[1]
[1]University of Medicine Victor Babes, Timisoara, Romania; [2]Vasile Goldis Western University, Arad, Romania; [3]Institute of Cardiovascular Diseases, Cardiac Rehabilitation Clinic, Timisoara, Romania

Background and purpose: ACE inhibitors are currently the standard therapy for HF patients. The aim of the study was to evaluate in-hospital management and outcome of patients hospitalized with chronic decompensated heart failure according to ACE-inhibitors therapy.
Methods: In this study we evaluated consecutive patients, enrolled during 2015 in a county hospital with a primary diagnosis of decompensated heart failure. Patients were divided according to ACE-inhibitor therapy during hospitalization: group 1 (no initiation, maintained or lowered doses of ACE-inhibitors), group 2 (initiation or uptitration of ACE-inhhibitors doses). Both groups were evaluated at baseline and reevaluated at 6 months follow-up (heart failure rehospitalizations, death). For statistical analysis we used independent t test for comparison of continuous values, Pearson x^2 test for comparison of categorical values, and multivariate logistic regression for predictors of in-hospital mortality.
Results: A total of 109 consecutive patients (63%males) with chronic HF hospitalized for a decompensation episode were enrolled. Mean age was 66 ± 11 years and mean ejection fraction was 33 ± 13%. 63% of patients had no ACE inhibitor therapy at admission. Patients in group 1 (n = 69) had a significantly lower glomerular filtration rate)(60 ± 22 vs 69 ± 20 ml/mim, p = 0.024) than in group 2 (n = 40). Patients in group 1 had a lower SBP (131 ± 29 vs 146 ± 28 mmHg, p = 0.037) than in group 2. By logistic regression, at 6 months of follow-up, lack of initiation or lowering of ACE-inhibitors doses did not influence mortality while initiation or uptitration of ACE-inhibitor treatment proved to be a protective factor for outcome (p = 0.049, OR=0.2).
Conclusions: ACE-inhibitor initiation or uptitration during hospitalization for decompensated heart failure is safe and improves short-term outcome while no initiation or lowering doses does not influence the short-term outcome. ACE inhibitors are still underused in HF treatment and guidelines recommendations are not routinely followed for these patients.

P1618

Clinical inertia following discharge of patients with acute heart failure

E Berthelot[1]; JC Eicher[2]; M Saval[3]; P Degroote[4]; R Isnard[5]; T Damy[6]; JN Trochu[7]; E Donal[7]; M Galinier[8]; D Damien Logeart[1]
[1]AP-HP - Hospital Lariboisiere, Department of cardiology, Paris, France; [2]Hospital Bocage, Cardiology, Dijon, France; [3]University Hospital of Grenoble, Grenoble, France; [4]Cardiology Hospital of Lille, Lille, France; [5]Hospital Pitie-Salpetriere, Paris, France; [6]University Hospital Henri Mondor, Creteil, France; [7]University Hospital of Nantes Nord Laennec, Nantes, France; [8]Toulouse Rangueil University Hospital (CHU), Toulouse, France

On behalf of: OFICA

Background: after acute heart failure (AHF), most patients are often discharged early and before treatment is optimized. Thus, following months are critical for optimization of care. Using a cohort of patients admitted for AHF, we analyzed treatments at discharge, during the next 3 months and relationships with mortality in patients with reduced left ventricular ejection fraction (LVEF)
Methods: a single-day national HF survey was conducted in a sample of 170 hospitals. Clinical characteristics including LVEF as well as treatment at discharge and at 3 months were obtained. Vital status was also obtained at one year. Data was recorded during both hospitalizations and one-year follow up.
Results: early changes in HF treatment was recorded and analyzed in 275 patients admitted with AHF and LVEF ≤ 40% (age 72 ± 14y, 66% males). At discharge, ACE-I or ARB were prescribed in 80% with daily mean dose reaching 36 ± 31% of target dose, beta blocker (BB) in 70% with daily mean dose of 27 ± 51% of target dose, aldosterone antagonists (AA) were prescribed in 23% and loop diuretics in 88% cases. At 3 months, there was relatively few changes in rates of prescriptions as well as doses as compared to discharge: loop diuretics were started/increased and stopped/decreased in 7/25% and 6/7% of patients respectively, ACE-I or ARB in 6/21% and 9/7% respectively, beta-blockers in 8/23% and 8/8% respectively, and aldosterone antagonists in 7% and 5% respectively. All cause mortality at 12 months was 19% with differences according to prescription or not of ACE-I/ARB at 3 months (15 vs 29%, p = 0.002) as well as BB (15 vs 27%, p = 0.008). After adjustment on clinical characteristics, only the lack of ACE-I or ARB was related to mortality (OR 2.50 [95%CI 1.33-4.73], p 0.005).
Conclusion: individual treatments remain poorly optimized after discharge and such inertia impacts outcome. These results suggest a large room to improve HF management in the daily practice, especially in the post-discharge period.

P1619

Predictive factors for in-hospital mortality in patients hospitalized for acute heart failure and treated with iv inotropes

CI Radulescu[1]; L Antohi[1]; M Chivulescu[1]; I Cosei[1]; A Covaliov[1]; R Radu[1]; A Ambrosy[2]; C Macarie[1]; M Gheorghiade[3]; O Chioncel[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; [2]Duke University Medical Center, Cardiology, Durham, United States of America; [3]Northwestern University, Cardiology, Chicago, United States of America

Introduction: Although, intravenous inotropes/vasopressors are used in the initial management of patients with acute heart failure (AHF), their utilization is associated to increased short-term mortality.
Aim: We sought to assess clinical predictors of in-hospital mortality in patients hospitalized for AHF and who received intravenous (iv) inotropes/vasopressors during hospitalization.
Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients admitted for AHF in 5 academic and 8 community hospitals, over a 12-month period. This is a post-hoc analysis of 571 (17.7%) patients who received inotropes and/or vasopressors during AHF hospitalization. A multivariate logistic regression model was developed to identify clinical variables predictive of in-hospital mortality.
Results: Inotropes/vasopressors administered in the registry were: Dobutamine (61%), Dopamine (45%), Noradrenaline (14%) and Levosimendan (2%). Differences in baseline characteristics based on utilization of inotropes are shown in Table 1.
In-hospital mortality in patients treated with inotropes/vasopressors was significantly higher compared to patients not requiring inotropes during hospitalization (23.8% vs 5.4%; p < 0.001).

Independent clinical predictors of in-hospital mortality among AHF patients treated with inotropes/vasopressors included: age (HR = 1.09, 95% CI 1.04-1.13), ischemic aetiology (HR = 1.42, 95% CI 1.14-1.73), QRS duration >120msec (HR = 1.78, 95% CI 1.54-1.93), non-academic clinical settings (HR = 1.91, 95% CI 1.74-2.23) administration for more than 24 hours (HR = 2.02, 95% CI 1.74-2.51).
Conclusions: Association between utilization of inotropic agents and in-hospital mortality reflects a complex relationship between cardiac electromechanical abnormalities and variation of indication in different clinical settings.

Table 1

	Inotropes/ vasopressors + (n = 571)	Inotropes/ vasopressors- (n = 2653)	P
Age(years)	71 + /-8	69 + /-9	0.02
Gender(Male)	55	53.8	0.1
Ischemic aetiology(%)	67	60	0.03
SBP(mmHg)	98 + /-22	139 + /-34	< 0.001
HR(beats/min)	104 + /-18	91 + /-22	< 0.001
QRS duration>120msec(%)	39.4	30.2	0.01
LVEF(%)	30 + /-11	39 + /-9	< 0.001
Creatinine(mg/dl)	1.9 + /-0.9	1.5 + /-0.8	0.03
Na(mmol/l)	130 + /-4	136 + /-3	< 0.001

P1620

Temporal trends in nitrate utilization for acute heart failure in elderly emergency patients: a single-centre observational study

N Najla Lemachatti[1]; B Bloom[2]; P Hausfater[1]; B Riou[1]; P Ray[3]; Y Freund[1]
[1]Hospital Pitie-Salpetriere, Emergency department, Paris, France; *[2]Queen Mary University of London, London, United Kingdom*; *[3]Hospital Tenon, Emergency department, Paris, France*

Background: We previously conted a pilot study that reported the safety of isosorbide dinitrate boluses for elderly emergency patients with acute heart failure syndrome.
Aims: To assess the temporal trend in the rate of elderly patients treated with isosorbide dinitrate, and to evaluate subsequent outcome differences.
Methods: This was a single-centre study. We compared patients aged > 75 years who attended the emergency department with a primary diagnosis of acute pulmonary oedema in the years 2007 and 2014. The primary endpoint was the rate of patients who received isosorbide dinitrate boluses in the emergency department. Secondary endpoints included in-hospital mortality, need for intensive care and length of stay.
Results: We analyzed 368 charts, 232 from patients included in 2014 (63%) and 136 in 2007 (37%). The mean age was 85 ± 6 years in both groups.There was a significant rate in the number of patients treated with isosorbide dinitrate between 2007 and 2014 : 97 patients (42%) in 2014 vs 24 patients (18%) in 2007 (p < 0,01). Comparing the two periods, we report similar in-hospital mortality rates (8% vs 11%, p = 0,5), rates of admission to the intensive care unit (13% vs 17%, p = 0,3) and lengths of stay (10 days in both groups).
Conclusion: We observed a significant rise in the rate of elderly patients treated with isosorbide dinitrate boluses for acute heart failure. However, we did not observe any significant improvement in outcomes.

P1621

Argentinean Registry of Inotropes and Vasoactives Drugs (REINA Registry)

R L Ricardo Luis Levin[1]; JA Bilbao[2]; M Seijo[1]; H Gomez Santa Maria[3]; JP Costabel[4]; I Rios[5]; CT Ruano[6]; MP Marturano[7]; J Mariani[8]; F Mando[1]; P Fabi[1]; M Rossi Pratt[5]; H Fernandez[2]
[1]Universidad Abierta Interamericana University, Buenos Aires, Argentina; *[2]Austral University Hospital, Buenos Aires, Argentina*; *[3]Finochietto Clinic, Buenos Aires, Argentina*; *[4]Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina*; *[5]Hospital Center Churruca-Visca, Buenos Aires, Argentina*; *[6]Julio Mendez Hospital, Buenos Aires, Argentina*; *[7]Hospital de Catamarca, Catamarca, Argentina*; *[8]Hospital El Cruce, Florencio Varela, Argentina*

On behalf of: Cardiovascular Emergencies and Critical Cardiology Council

Objetives: To analyze preferences of utilization of Pulmonary Artery Catheter and Echocardiography as monitoring tools in patients requering vasoactive drugs admitted to REINA registry.
Methods: Population: There were included patients over 18 years old admitted in 21 argentinean institutions due to vasoactive drugs requirements. REINA registry was a prospective, observational and multicenter evaluation with hemodynamic scenarios previously defined as: hypovolemia, cardiogenic, non septic distributive, septic distributive, mixed pattern (cardiogenic plus distributive), isolated right ventricle failure, left ventricle obstruction and hypotensive, normotensive and hypertensive hypervolemia.
Results: There were included 376 patients from 21 centers, with an average age of 66.1 years, being 77.4% of them males. The observed prevalence for each scenario and the use of pulmonary artery catheter and echocardiography were respectively: distributive non sepsis 30(7.9%)patients, 43.3% and 33.3%, distributive sepsis 16(4.2%)patients, 18.7% and 68.7%, isolated failure of right ventricle 10(2.6%) patients, 60% and 70%, hypertensive hypervolemia 39(10.3%) patients, 7.6% and 64.1%, hypotensive hypervolemia 22(5.8%)patients, 59% and 67.2%, normotensive hypervolemia 29(7.7%)patients, 13.7% and 79.3%, hypovolemia 82(21.8%)patients, 26.8% and 59.7%, left ventricle obstruction 1(0.2%)patient,100% and 100%, mixed pattern 36(9.5%)patients, 41.6% and 55.5% and cardiogenic 111(29.5%)patients, 47.7% and 71.1%.
Two hundred and eighty four cardiovascular patients presented with hypotensive states corresponding 112 of them to medical scenarios and 172to surgical ones. The pulmonary artery catheter was utilized in 56(50%) medical patients against 67 surgical (38.9%) ones (P=0.03) while echocardiography was used in 91 medical(81.2%) patients against 86 surgical (50%)patients (P < 0.0000001).
Conclusions: an elevated utilization of both methods was detected. The observed use of pulmonary artery catheter was largely over the referred numbers of the literature. In patients with hypotension it was observed a superior use of both methods in medical conditions over surgical ones.

P1622

Risk factors for in-hospital worsening heart failure in patients hospitalized with acute heart failure

CI Radulescu[1]; L Antohi[1]; M Chivulescu[1]; I Cosei[1]; A Covaliov[1]; R Radu[1]; A Ambrosy[2]; S Collins[3]; C Macarie[1]; O Chioncel[1]; M Gheorghiade[4]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; *[2]Duke University Medical Center, Cardiology, Durham, United States of America*; *[3]Vanderbilt University, Emergency Medicine, Nashville, United States of America*; *[4]Northwestern University, Cardiology, Chicago, United States of America*

Introduction: Although most patients hospitalized for acute heart failure (AHF) respond to standard therapy, a subset of patients may clinically decompensate and experience in-hospital worsening heart failure (WHF), placing them at substantial risk for in-hospital mortality.
Objective: To identify clinical variables associated with in-hospital WHF in patients hospitalized for AHF.
Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients admitted for AHFS over a 12-month period. In-hospital WHF was defined as worsening of signs or symptoms of HF necessitating intensification of intravenous (IV) diuretics and/or initiation of IV vasodilators and/or inotropes, assisted ventilation, and/or mechanical circulatory support. Clinical predictors of in-hospital WHF were identified using multivariate logistic regression analysis.
Results: The incidence of in-hospital WHF was 16.1% and the majority of episodes occurred within 3 days of hospitalization. Patients experiencing in-hospital WHF tended to be older (72 ± 9 vs. 69 ± 11 years; p = 0.04), have an ischemic etiology of HF (59% vs. 55.8%; p = 0.05) and lower ejection fraction (35 ± 9 vs. 38 ± 10%; p < 0.001), and have a previous HF hospitalization within the last year (69% vs. 51%; p = 0.01). In-hospital all cuse mortality was higher in patients experiencing in-hospital WHF (8.8% vs. 7.1%, p = 0.03). Independent risk factors for in-hospital WHF included older age (HR = 1.02, 95% CI 1.01-1.09), an ischemic etiology of HF (HR = 1.31, 95% CI 1.12-1.54), left bundle branch block on admission ECG (HR=1.51; 95% CI 1.42-1.78), baseline serum Na + < 135mEq/l (HR = 1.68, 95% CI 1.24-2.03), and signs and symptoms of hypoperfusion at presentation (HR = 3.05, 95% CI 1.72-4.38).
Conclusions: In-hospital WHF occurred in 16.1% of patients hospitalized for AHF and was associated with higher in-hospital mortality. The ability of clinical variables readily available at initial presentation to risk stratify patients for in-hospital WHF should be studied prospectively.

P1623

Clinical outcomes of de novo and acute decompensated heart failure patients according to ejection fraction

KH Ki Hong Choi[1]; GY Lee[1]; JO Choi[1]; ES Ju[1]; YJ Lee[1]; ES Jeon[1]
[1]*Samsung Medical Center, Divison of Cardiology, Seoul, Korea Republic of*

On behalf of: KorAHF investigators

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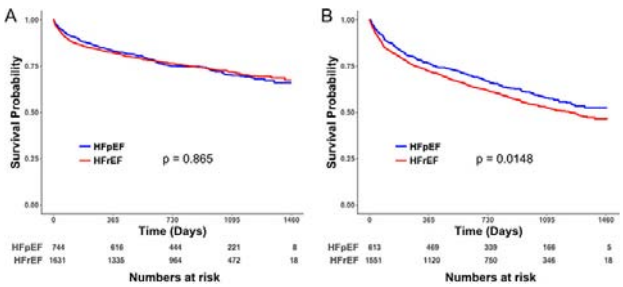
Purpose: To compare the outcomes of patients with de novo acute heart failure (AHF) or acute decompensated HF (ADHF) according to preserved ejection fraction (HFpEF, EF ≥50%), or reduced EF (HFrEF, EF <40%) and to define the prognosis of HF patients with a mid-range EF (HFmrEF, 40≤ EF <50%).
Methods: Between March 2011 and February 2014, 5,625 consecutive AHF patients were recruited from 10 university hospitals. A total of 5,414 (96.2%) patients with EF data were enrolled, which consisted of 2,867 (53.0%) patients with de novo and 2,547 (47.0%) with ADHF. Each of the enrolled group was stratified by EF (HFpEF, HFrEF, or HFmrEF).
Results: In de novo, all-cause death rates were not significantly different between HFpEF and HFrEF (adjusted hazard ratio [HR] 1.15, 95% confidence interval [CI] 0.96 to 1.38, p = 0.14). However, among ADHF patients, HFrEF had a significantly higher mortality rate compared to HFpEF (adjusted HR 1.25, 95% CI 1.06 to 1.47, p = 0.007). Also, in ADHF, HFmrEF was associated with a significantly lower mortality rate within one year compared to HFrEF (adjusted HR 0.76, 95% CI 0.60 to 0.96, p = 0.02), but a significantly higher mortality rate after one year compared with HFpEF (adjusted HR 1.42, 95% CI 1.05 to 1.93, p = 0.02).
Conclusions: HFpEF may indicate a better prognosis compared with HFrEF in ADHF, but not in de novo AHF. For ADHF patients, the prognosis associated with HFmrEF was similar to that of HFpEF within the first year following hospitalization and similar to HFrEF one year after hospitalization.

Prognosis of HFmrEF in ADHF

	HFmrEF	Comparison group	Adjusted HR(95% CI)	P value
Comparison with HFpEF (n = 996)				
All cause death	171 (44.6)	245 (40.0)	1.15 (0.94 to 1.42)	0.17
Death within 1 year	88 (23.0)	144 (23.5)	0.97 (0.73 to 1.28)	0.81
Death after 1 year (n = 764)	83 (28.1)	101 (21.5)	1.43 (1.05 to 1.94)	0.02
Comparison with HFrEF (n = 1934)				
All cause death	171 (44.6)	694 (44.7)	0.91 (0.77 to 1.09)	0.30
Death within 1 year	88 (23.0)	430 (27.7)	0.76 (0.60 to 0.96)	0.02
Death after 1 year (n = 1415)	83 (28.1)	264 (23.6)	1.14 (0.88 to 1.46)	0.33

CI = confidence interval; HFmrEF = heart failure mid-range ejection fraction; HFpEF = heart failure preserved ejection fraction; HFrEF = heart failure reduced ejection fraction; HR = hazard ratio



Survival curve in denovo(A) and ADHF(B)

P1624

Hemodynamic alterations and 90-day mortality in cardiogenic shock complicated by acute kidney injury

T Tarvasmaki[1]; A Mebazaa[2]; M Haapio[3]; A Sionis[4]; J Silva-Cardoso[5]; H Tolppanen[6]; K Pulkki[7]; J Parissis[8]; V-P Harjola[9]; J Lassus[10]
[1]*Hospital District of Helsinki and Uusimaa, Department of Emergency Medicine and Services, Helsinki, Finland*; [2]*Hospital Lariboisiere, Paris, France*; [3]*Helsinki University Central Hospital, Division of Nephrology, Helsinki, Finland*; [4]*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*; [5]*University of Porto, Center for Health Technology and Services Research, Department of Cardiology, Faculty of Medicine, Porto, Portugal*; [6]*Paijat-Hame Central Hospital, Lahti, Finland*; [7]*Eastern Finland Laboratory Centre, Kuopio, Finland*; [8]*Attikon University Hospital, Heart Failure Unit, Athens, Greece*; [9]*Helsinki University Central Hospital, Department of Emergency Medicine and Services, Helsinki, Finland*; [10]*Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland*

On behalf of: the GREAT Network

Purpose: To analyze hemodynamic alterations and 90-day mortality in cardiogenic shock (CS) complicated by acute kidney injury (AKI).
Methods: CS patients with serial plasma samples (n = 154) from the prospective CardShock study were included. AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria: >0.3 mg/L or >50% increase in creatinine from baseline value (AKI-crea) or urine output <0.5 ml/kg/h for 6 h (AKI-UO). Creatinine was analyzed from the plasma samples at baseline (0 h), 12 h, 24 h, 36 h and 48 h. Urine output was recorded in 6-h intervals until 24 h from baseline. Changes in mean arterial pressure (MAP), central venous pressure (CVP), and cardiac index (CI) over time until 96 h from baseline were compared between patients with and without AKI by linear mixed modeling. Poisson regression with robust variance was used to estimate relative risk (RR) of 90-day mortality in AKI adjusting for gender, systolic blood pressure and CardShock risk score.
Results: The mean age was 66 (12) years, 74% were men, and 81% had acute coronary syndrome as CS etiology. Median baseline creatinine was 1.11 (0.87-1.54) mg/dl. Overall, the 90-day mortality was 38%. The incidence of AKI-crea was 31% and of AKI-UO 50%. Differences in patient characteristics between AKI and non-AKI were few: AKI patients were older and they had worse renal function, higher lactate levels and lower arterial pH at baseline. Patients with AKI had higher 90-day mortality than those without AKI: 70% for AKI-crea vs 24% for non-AKI-crea (p < 0.001), and 46% for AKI-UO vs 29% for non-AKI-UO (p = 0.034). The association of 90-day mortality with AKI-crea, but not AKI-UO, remained after multivariable adjustment: RR 2.8, 95% CI 1.6-3.3 (p < 0.001). Figure 1 shows average values of MAP, CI and CVP within time intervals, and their evolution over time in patients with and without either AKI-crea (upper row) or AKI-UO (lower row). Overall, MAP and CI levels were constantly lower while CVP levels higher in patients with than without AKI (p < 0.05 for all pooled between-group comparisons).
Conclusions: AKI is frequent in CS and AKI-crea predicts a very poor outcome. Development of AKI is associated with persistent hemodynamic alterations reflecting venous congestion and hypoperfusion.

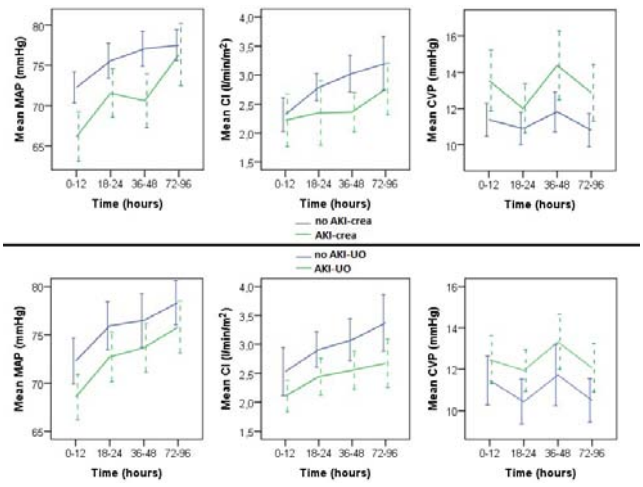


Figure 1

P1625

Impact of atrial fibrillation in hospital evolution of decompensated heart failure patients: Insights from CONAREC XVIII registry.

E J Zaidel[1]; GE Perez[1]; IM Cigalini[1]; M Galli[1]; M Altamirano[1]; LR Corradi[1]; M Bernal[1]; JC Jauregui[1]; DG Cornejo[1]; RMA Colque[1]
[1]*CONAREC. Argentine Council of Cardiology Residents., Buenos Aires, Argentina*

Introduction: Altough atrial fibrillation (AF) is a frequent arrhythmia in patients hospitalized for decompensated heart failure (HF), the information about its impact in prognosis is conflicting, and there is lack of information in this regard in Latin America.
Objective: The main objective was to analyze if chronic AF modifies hospital evolution (mortality, lenght of stay) of HF patients in a contemporary population from Argentina. A key secondary objective was to find clinical predictors of death in AF – HF patients.
Methods: An analysis of the database of the prospective registry CONAREC XVIII, developed by residents of cardiology from 64 centers from Argentina was performed. The baseline characteristics and hospital evolution were analized. The AF diagnosis and treatment before hospital admission was coded as "chronic AF", and first episodes of AF were excluded from the analysis. In a second time the factors related to hospital mortality in AF-HF patients were evaluated. The statistical analysis was conventional for descriptive and comparative analysis, and a multivariable model was developed to search for predictors of death. A p value of ≤ 0.05 was considered significative.
Results: Of 1160 consecutive HF patients recluted at 64 cardiology residency centers in two consecutive months, 415 (35 %) had chronic AF (AF group) and 745 did not (non-AF group).
The median age was 78 years in the AF group vs 70 in the non-AF group ($p\leq 0.01$). 43% in the AF group were female (vs 38 %, $p\leq 0.01$). The AF group had higher rate of HF with preserved ejection fraction (53 vs 38 %, $p\leq 0.01$), and the rates of all the comorbidities analyzed (renal failure, COPD, thyroid diseases) were higher in AF patients. No differences in the length of hospitalization (median 6 days in both groups) or in mortality (10.4% vs 11.8 % p = NS) were found: In the multivariable analysis, shock, renal failure, and prior use of digoxin were independent predictors of death in AF patients (OR= 6.59, 2.05, and 2.07, respectively, all $p\leq 0.05$).
Conclusion: Prior AF does not modify hospital evolution of decompensated heart failure patients. Patients with AF and HF represent a high-risk population, with higher rates of comorbidities, and among them, digoxin use was independently associated with hospital mortality.

P1626

Hyponatremia and long-term outcomes in heart failure

K Kaoutar Kharbouche[1]; I Elhaddad[1]; K Kharbouche[1]; R Habbal[1]; L Azouzi[1]
[1]*chu ibn rochd, cardiology, casablanca, Morocco*

Background: Hyponatremia (serum sodium [Na]≤135mmol/L) is a predictor of morbidity and mortality in patients with heart failure (HF), but the long term outcomes associated with hyponatremia are less clear. We aimed to evaluate the long-term outcomes of hyponatremic patients in a large HF cohort.
Methods: a descriptive study was carried from May 2008 to November 2014. 1600 patients presenting clinical and echocardiographic signs of heart failure and followed at the heart failure unit were included. Serum sodium measurement at the time of catheterization was used to assess sodium status. Baseline characteristics and outcomes for patients with hyponatremia were compared to those without hyponatremia. Kaplan-Meier survival estimates were generated out to 6 years, with a median follow-up time of 3.8 years in the study population.
Results: 1600 patients were enrolled. For the entire cohort median age was 61; 70% were male; median EF was 27%. 16% of the patients had hyponatremia. The hyponatremic group had significantly worse survival at 6 years (p = .0001).
Conclusion: Hyponatremia was associated with worse survival for HF patients in our cohort. Hyponatremia is an important risk factor for poor outcomes and a potential target for the development of new therapies

P1627

Survival in heart failure according to ejection fraction: the mid-range gains its place - seven years follow up.

L Lucas Celia Petersen[1]; B Donay[2]; E Magedanz[2]; VE Closs[3]; AV Azevedo[1]; NMB Kreuz[4]; LC Bodanese[1]; MH Miglioranza[5]; LC Danzmann[6]
[1]*Hospital Sao Lucas, Cardiology, Porto Alegre, Brazil*; [2]*Hospital Sao Lucas, Nursing, Porto Alegre, Brazil*; [3]*Hospital Sao Lucas, Nutricion, Porto Alegre, Brazil*; [4]*Lutheran University of Brazil, Cardiology, Canoas, Brazil*; [5]*Institute of Cardiology of Rio Grande do Sul, Cardiology / Echocardiography, Porto Alegre, Brazil*; [6]*Lutheran University of Brazil, Hospital Sao Lucas, Cardiology, Canoas, Brazil*

Introduction: Although ejection fraction may not be ideal to stratify heart failure (HF) patients, it has a historical importance to guide therapy and prognosis in clinical practice. Recently, the European Society of Cardiology defined a new HF category – the mid-range ejection fraction (EF). However, there may be few studies evaluating the long-term survival in this new category.
Purpose: To analyze characteristics and long-term survival in HF patients with mid-range (40-49%) EF in comparison with reduced (<40%) and preserved (>50%) EF categories.
Methods: A historical cohort from a registry of consecutive patients admitted with acute heart failure in a tertiary hospital from January 2009 to December 2011. The follow up time was 7 years. Categorical variables were compared with Pearson chi-square and continuous with ANOVA tests. A Kaplan-Meier survival curve was analyzed according to ejection fraction.
Results: Mid-range EF was present in 17%, reduced in 33% and preserved in 50% of the 381 patients analyzed. There was no statistical difference on comorbidities, presence of atrial fibrillation and causes of decompensation. Patients with preserved EF were older, mostly females, with non-ischaemic aetiology, admitted with higher blood pressure and had a smaller diastolic diameter. Patients with reduced EF were younger, mostly males, admitted with lower blood pressure and had a higher diastolic diameter. Ischaemic aetiology was similar between patients with reduced and mid-range EF (table). Survival was worse in patients with mid-range EF (mean 0,8 years with 95% CI 0,5 – 1,0) when compared with patients with reduced EF (mean 1,3 years with 95% CI 1,0 – 1,6)(P=0,027)(figure).
Conclusion: Patients with mid-range ejection fraction had worse survival when compared with patients with reduced EF in our preliminary analysis.

Table: Population chacarteristics.

VARIABLES	TOTAL SAMPLEN (%)	EJECTION FRACTION (%)	P		
	40 - 50	≥50			
<40					
Age in years (mean±SD)	68,1±13,8	64,0±12,6*	66,6±15,3	71,3±13,4*	<0,001
Gender					
Male	180 (47,2)	82 (64,6)*	29 (45,3)	69 (36,3)	<0,001
Female	201 (52,8)	45 (35,4)	35 (54,7)*	121 (63,7)	
Aetiology					
Non-ischaemic	241 (63,4)	76 (60,3)	31 (48,4)	134 (70,5)*	0,004
Ischaemic	139 (36,6)	50 (39,7)	33 (51,6)*	56 (29,5)	
LV Diameter (mean±SD)	5,6±1,1	6,1±1,1*	5,7±1,1*	4,8±0,8*	<0,001

LV = left ventricle. * Statistical difference.

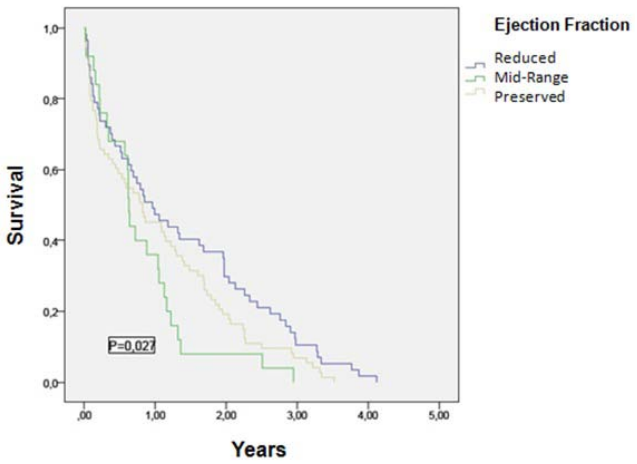


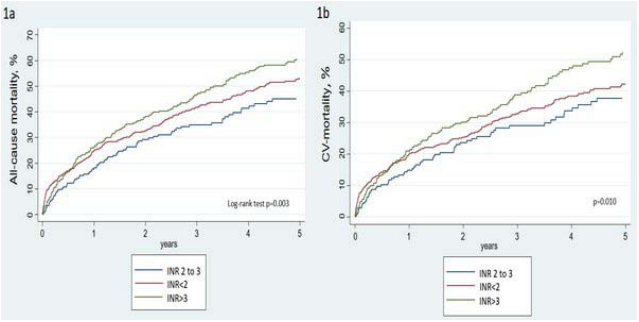
Figure: Kaplan-Meier survival curve.

P1628

International normalized ratio at admission and mortality risk in patients with acute heart failure

E Enrique Santas Olmeda[1]; A Paya[1]; R Heredia[1]; J Gummel[1]; R Farcasan[1]; I Cardells[1]; E Valero[1]; D Escribano[1]; G Minana[1]; A Bayes-Genis[2]; J Lupon[2]; J Sanchis[1]; J Nunez[1]
[1]*Hospital Clinic Universitari. Universitat de València, Valencia, Spain*; [2]*Germans Trias i Pujol Hospital, Badalona (Barcelona), Spain*

Introduction: Anticoagulation control in heart failure (HF) patients on treatment with vitamin K antagonist (VKA) is often suboptimal, especially in the setting of acute HF (AHF). However, evidence regarding the prognostic value of international normalized ratio (INR) at admission in patients with AHF is scarce. In this work, we aimed to evaluate the association between INR and the risk of long-term mortality in patients with AHF treated with AVK.
Methods: In this observational study, we retrospectively assessed INR on admission in 1137 consecutive patients with AHF on treatment with acenocoumarol. INR was categorized according to the degree of anticoagulation quality: a) low-INR:<2, b) normal-INR: 2-3 and, c) high-INR:>3. Cox regression and Cox regression adapted for competing events were used for evaluating the association among INR categories and the risk of all-cause and cardiovascular mortality, respectively.
Results: Mean age was 74 ± 10 years, 51.1% were females, 62.4% showed left ventricular ejection fraction>50% and 50.2% were previously admitted for AHF. Median NT-proBNP was 4174 pg/ml (2450-7813). Normal, low and high-INRs were found in 660 (58%), 210 (18.5%) and 267 (23.5) patients, respectively. During a median (interquartile range) follow-up of 2.3 years (0.8-4.3), 568 (49.9%) patients died (74.8% of them of CV-etiology). Compared to patients with normal-INR, cumulative risk of all-cause and CV-mortality were higher for those patients belonging to low and high-INRs categories (Figure 1a and 1b, respectively). In multivariate analysis, both patients with infra and supratherapeutic INR showed an independent increase of risk of all-cause mortality (HR= 1.56, CI 95%:1.23-1.98, p = <0.001, and HR=1.52, CI 95%: 1.17-1.96, p = 0.002, respectively), and CV-mortality (HR= 1.40, CI 95%: 1.06-1.82, p = 0.016 and HR=1.30, CI 95%: 1.01-1.73, p = 0.045, respectively).
Conclusion: In AHF patients on treatment with AVK, INR<2 and >3 at admission are associated with higher risk of all-cause and CV-death. Further studies are warranted to clarify the pathophysiological mechanisms behind these findings.

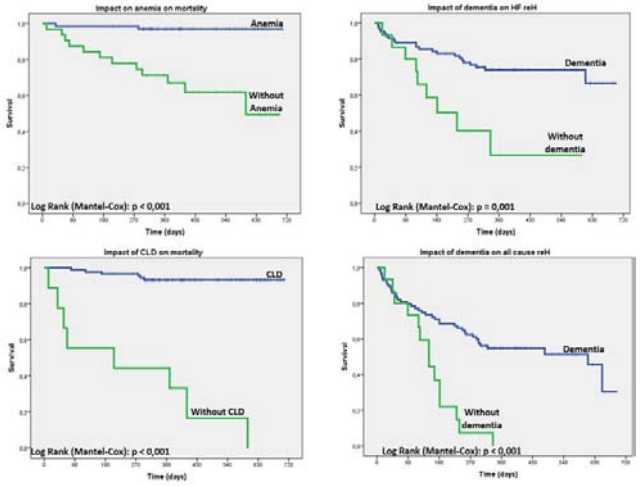


P1629

Comorbidities in heart failure patients: the impact on re-hospitalization and long-term mortality

J Agostinho[1]; P Alves[1]; J Rigueira[1]; I Ricardo[1]; T Guimaraes[1]; I Goncalves[1]; N Andre[1]; R Santos[1]; F Veiga[1]; M Pedro[1]; FJ Pinto[1]; D Brito[1]
[1]*Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

Introduction: Hospitalization for heart failure (HF) is associated with high in-hospital and post-discharge mortality rates, regardless the documentation of a reduced or preserved left ventricular ejection fraction (EF). Comorbidities, particularly non-cardiovascular, have a major role in the post-discharge event rates of HF patients (pts), especially regarding readmissions (reH) and mortality, although these outcomes may not be necessary related.
Purpose: To evaluate the burden of comorbidities in long-term mortality and reH in pts discharged from hospital after an episode of acute/chronic decompensated HF (AHF).
Methods: Demographic, clinical, laboratorial and echocardiographic data of 100 pts consecutively admitted for AHF (cardiology ward, tertiary hospital center) and discharged alive, were retrospectively analyzed. The influence of comorbidities on post-discharge events occurring during the follow up was determined (Cox regression, Kaplan-Meier survival analysis and Mann-Whitney test, were applied).
Results: The included population (55% men, 68.3 ± 13.1 years) was followed during a period of 14.2 ± 5.5 months after hospital discharge. The post-discharge mortality rate (MR), HF reH, and all cause reH was 14%, 31% and 54%, respectively. The median number of comorbidities was 4 (2-6) per pt.
Anemia (HR= 12.7, CI= 1.99-81.5, p = 0.007) and chronic liver disease (CLD) (HR= 25.9, CI= 5.1-130.4; p < 0.001) were independent predictors of long-term mortality. Dementia was the only independent predictor of HF reH (HR= 2.9, CI= 1.3-6.8, p = 0.013), or all cause reH (HR= 2.5, CI= 1.2-4,9; p = 0.01).
In particular, in the subgroup of patients with preserved EF (n = 35), CLD was an independent predictor of long-term mortality (HR = 7.6; CI: 1.3-45.8; p = 0.027), and dementia was an independent predictor of HF reH (HR= 5.5, CI= 1.2-24.4, p = 0.025).
No independent predictors of mortality were found in pts with reduced EF or mid-range EF.
Anemia (p = 0.027), history of cancer (p = 0.023), CLD (p < 0.001), dementia (p = 0.002), previous stroke (p = 0.003), and the presence of more than 4 comorbidities (p = 0.026), correlated with the number of all cause reH.
Conclusion: The presence of multiple comorbidities correlate significantly with post-discharge adverse events in pts admitted to hospital with AHF. In this series, anemia and CLD were associated with increased mortality, and dementia with increased rate of reH. Noncardiovascular morbidities are related to the clinical course of pts with HF, some may be preventable, and need to be timely diagnosed and managed.



P1630

One month prognosis after decompensated heart failure through the assembly of artificial neural networks

J John Sprockel[1]; A Fandino[1]; W Chaves[1]; J Diaztagle[1]
[1]*Hospital San Jose, Medicina Interna, Bogota, Colombia*

Introduction: Heart failure is the main reason for hospitalizations in people aged 65+. Physicians usually overestimate the risk of death in these patients. The individual determinants of risk are not sufficient to determine an accurate global prognosis. Artificial intelligence has gained a position as an alternative to statistical tools, promising a better performance.
Objective Train and validate a system based on the assembly of a set of artificial neural networks for the prognosis of mortality one month after decompensated heart failure.
Methodology: Prognostic evaluation study based on a prospective cohort of patients that were admitted into the emergency service between 2010 and 2013 diagnosed with decompensated heart failure, aged 18+, who met the Framingham criterion. The population was divided into 70% (323 patients) for training and tests for the different neural networks and 30% (139 patients) for the validation of the assembly mechanism. The neural networks were trained using a genetic algorithm, its architecture consisted of 15 input variables, a hidden layer, and an output neuron. The 11 networks exhibiting the best performance in the tests were selected for assembly through three systems: simple voting, weighted voting by predictive values, and likelihood ratio. The operational characteristics were calculated for the

prognosis of death after 30 days and were compared with two clinical prediction rules and a logistic regression applied on the same population.
Results: The average age was 72.4, 51.9% were females, 80% had hypertension, 23.3% diabetes, and 87 coronary disease. 30 days mortality was 13,8%. The different methods of assembly exhibited better results in the prognosis than the individual networks that were part of them. Weighted voting by predictive values had the best global performance (See table).
Conclusion: The assembly of neural networks through weighted voting by predictive values showed satisfactory performance for the prognosis of death after 30 days in acute heart failure, improving the results obtained by two clinical prediction rules and a logistic regression.

TABLE 1.

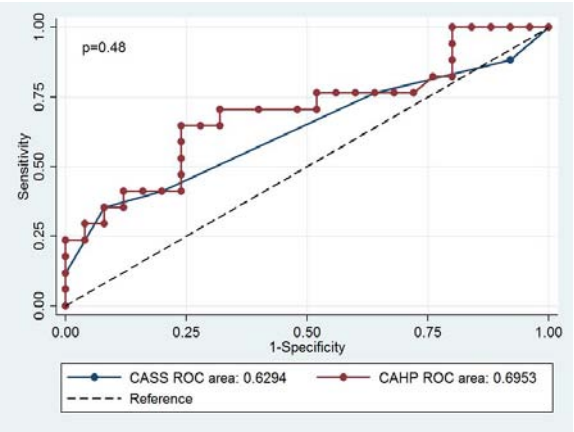
	GWTG-HF	OPTIMIZE-HF	LR	BEST ANN	SV	WV PV	WV LR
SENSIBILITY	94	81	15	25	31	26	42
ESPECIFICITY	16	38	98	90	94	99	99
PPV	-	-	-	25	46	83	53
NPV	-	-	-	87	89	89	90
ACCURACY	22	41	89	81	85	88	86

Operational characteristics of the tools assessed. ANN: artificial neural networks, SV: simple voting, WV: weighted voting

P1631
Risk stratification post cardiac arrest: comparison of CASS (cardiac arrest survival score) and CAHP (cardiac arrest hospital prognosis) score.

M Manoj Thangam[1]; BH Hsi[1]; A Dasilva-Deabreu[1]; B Alhafez[1]; V Gacad[1]; A Dhoble[2]; Y Zhao[2]; S Arain[2]; K Charitakis[2]; HV Anderson[2]; R Smalling[2]; P Doshi[2]; P Balan[2]
[1]The University of Texas Medical School, Internal Medicine, Houston, United States of America; *[2]The University of Texas Medical School, Cardiovascular Medicine, Houston, United States of America*

Background: Mortality post cardiac arrest (CA) remains alarmingly high. Few prognostic tools have evaluated patients with return of spontaneous circulation (ROSC) post CA. Although the CAHP score has been utilized in this population, its cumbersome calculations have impaired wide spread adoption.
Methods: CASS- a novel prognostic score- was developed based on established CA risk factors and implemented via an easy to use web-application available on smart phones. This score was prospectively compared to the CAHP score in 43 patients who suffered CA with ROSC. The primary end point was in-hospital mortality. We evaluated the discrimination between both scores using the area under the receiver-operating characteristic (ROC) curve. Additionally, Hosmer-Lemeshow goodness-of-fit was used to determine calibration between CASS and CAHP score.
Results: The AUC were similar between CASS (AUC=0.63, 95% CI (0.45-0,81)) and CAHP (AUC=0.70, 95% (0.52-0.87)). Additionally, the calibration of CASS (p-.47) was better then CAHP ($p = 0.08$).
Conclusion: Both CASS and CAHP perform similarly in prognostication of mortality in patients post CA with ROSC. However, CASS offered additional benefits including ease of use, automated calculation, and inter-specialty communication via a downloadable web application.



CASS vs CAHP ROC Curve

P1632
Blood pressure variation and mortality from acute decompensated heart failure in case of first and second hospitalization

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

Introduction: For patients with damaged target organs can be J or U dependence between blood pressure (BP) level and cardiovascular death (OPTIMIZE-HF register).
Purpose: evaluate systolic BP (SBP) and diastolic BP (DBP) and their changes between hospitalizations on patients prognosis with acute decompensated heart failure (ADHF)
Methods: Between July/2014 and July/2015, we studied a total of 852 hospital cases with ADHF. Patients cases were divided on quartiles (Q) depending from BP level: Q1 SBP≤120 and DBP≤75 mmHg; Q2 121≤SBP≤140 and 76≤DBP≤80mmHg; Q3 141≤SBP≤160 and 81≤DBP≤90mmHg; Q4 SBP≥160 and DBP≥90mmHg.
Results: The risk of hospital mortality had a negative correlation with Q SBP and Q DBP. The maximum risk level was in Q1. Median of time interval between hospitalizations was 104.5 days. At readmission to hospital, Q SBP decreased in 43.6% of patients and Q DBP decreased in 51.3% of patients. Q SBP and Q DBP remain without change in 34.6% and 25.6% of patients respectively. Q SBP and Q DBP increased in 21.8% and 23.1% of patients respectively. Hospital mortality was associated with decreased or not changing Q SBP and Q DBP. Were analyzed etiologies of chronic HF among different Q patients. We found that patients having lower Q SBP and Q DBP had much prevalence of target organs damage (myocardial infarction, dilated cardiomyopathy, chronic atrial fibrillation, valvulopathy, chronic obstructive pulmonary disease and asthma). Moving to higher Q SBP and Q DBP, the prevalence of hypertension, diabetes mellitus and non-complicated coronary artery disease had increased.
Conclusion: Patients with low Q SBP and Q DBP had a serious damage of target organs. Hospital mortality among patients with ADHF was significantly associated with the lowest Q SBP and Q DBP. At readmission, almost 50% of patients had a tendency to move at lower Q SBP and Q DBP, what increased the hospital mortality rate.

Quartiles (Q)	H. mortality for QSBP %	Increase of risk	H. mortality for Q DBP %	Increase of risk
Q1	15.4	-	16.8	-
Q2	3.3	5,3(95% CI:2,3-12,4; p < 0,001)	4.1	4,7(95% CI:2,0- 10,6; p < 0,001)
Q3	3.2	5,5(95% CI: 2,1- 14,7; p < 0,001)	3.0	6,6(95% CI:2,5- 17,7; p < 0,001)
Q4	2.2	8,2(95% CI:2,5- 27,7; p < 0,001)	2.3	8,5(95% CI:2,9- 24,9; p < 0,001)

H. mortality: Hospital mortality

P1633
Biomarkers in the prognosis of acute heart failure

M Manuel Lobo Gonzalez[1]
[1]University Hospital of Virgen Macarena, Cardiology, Seville, Spain

Recurrent heart failure (RHF) is a main problem in the heart failure specter, and every new event worsens the vital prognosis and the subsequent functional class. Develop strategies to early detentions of those patients at risk for RHF is critical. Biomarkers such as B-type natriuretic peptide precursor (pro-BNP), high-sensitivity troponin T (Tn-T), and C-reactive protein (CRP) assessed at discharge may be useful.
114 patients with heart congestive heart failure admitted to our coronary care unit and with pro-BNP, Tn-T and CRP measure prior to discharge were included. Patients within acute coronary syndrome evidences were excluded.The management of patients was made according to European Clinical Practice Guidelines.The primary endpoint was HF hospitalization at 3 months from discharge.
67 of 109 patients included were men, the mean age was 70 ± 15 years. The primary endpoint was observed in 22 patients (20,18%). Patients with the event were older (79 ± 6 vs 67 ± 4 years, p < 0.001) had more risk factors (hypertension 72% vs 49% p = 0.02; and diabetes 74% vs 32% p = 0,009),

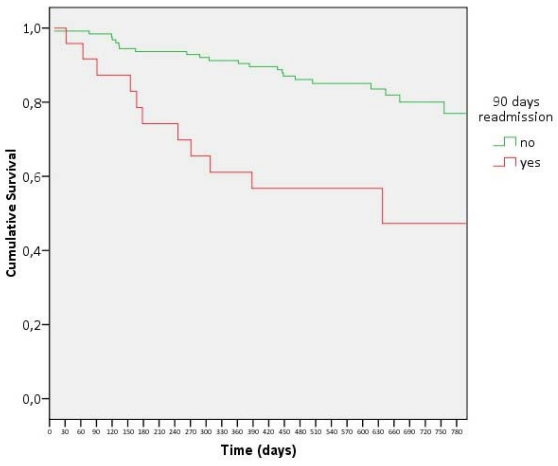
had more severe valvulopathies (78,5% vs 60,6% p = 0,02). No other significant differences in the clinical characteristics of the patients were found. Patients who presented the primary endpoint had higher levels of Tn-T (129,78[118,9-140,8]ng/L), pro-BNP(16.987,89[12.954-17.956]pg/mL), and also in CRP(89,12[78,76,09-98,01]mg/dL) compared to those patients without events (Tn-T 69,08[55,09-78,3]ng/L), pro-BNP(9.548,01[8.498-10.655]pg/mL, CRP(38[28,06-48,09]mg/dL)) p = 0.03, p < 0.001, p < 0.04 respectively).In the univariate analysis each one marker was associated with the occurrence of the primary endpoint at 3 months (odds ratio : 1.9 [1.1-2.1] , p = 0.002). This relationship remained in the multivariate analysis (OR 1.5 [1.2-2.1], p = 0.009)
Pro-BNP,Tn-T, and CRP assessed at discharge could be useful for early detection of patients at risk of recurrences and design a close follow-up after hospitalization. These suggestions should be validated in large studies.

P1634

Early readmission and poor prognosis in acute decompensated heart failure patients.

A Alfonso Varela Roman[1]; R Agra Bermejo[1]; I Gomez Otero[1]; R Gonzalez Ferreiro[1]; N Lopez Canoa[1]; C Abou-Jhok Casas[1]; M Moure Garcia[1]; A Blanco Seoane[1]; JR Gonzalez-Juanatey[1]
[1]*Clinical University Hospital. Service of Cardiology, Santiago de Compostela, Spain*

Background: despite the advances in management and improved prognosis of chronic heart failure (HF) in the past decades, patients with acute decompensated HF continue to have a high mortality and readmission rate, at 90 days post-discharge.
Purpose: the aim of this study is to evaluate the readmission rate at 90 days, the characteristics and the outcome of this group of patients.
Material and methods: we analyzed 150 consecutive patients (mean age 69,9 years, 61% men) admitted to a cardiology service for acute decompensated HF, 54 with previous HF hospitalization (36%), 116 with hypertension (HTA) (77%); 69 diabetic (DM) (46%); 140 class III or IV NYHA (93%), and 42 ischemic etiology (28%), with mean left ventricular ejection fraction (LVEF) 42,9%.
Results: at 90 days 24 patients (16%) were readmitted. This group of patients were more frequently men (79,2% vs 57,1%, p = 0,05); diabetic (66,7% vs 42%, p 0,027); with ischemic etiology (45,8% vs 24,6%, p = 0,034), previous cardiovascular disease (54,2% vs 27,0%, p = 0,009), and HF hospitalization (58,3% vs 31,7%, p = 0,013), compared with those without readmission. Also glomerular filtration rate (MDRD) (55,2 vs 72,2 ml/min/1,72m2, p = 0,007), plasmatic sodium levels (138,6 vs 141,0 mMol/l, p = 0,019), and NT-proBNP levels (10.269,7 vs 4.291,8 pg/ml, p < 0,001) were statistically different. Age, history of hypertension, NYHA III-IV class, heart rhythm, haemoglobin levels, LVEF were no statistically different.
After a mean follow-up of 18,3 ± 6,9 months, 34 patients died (22,7%), 11 (45,8%) in the readmitted group and 23 (18,3%) in the not readmitted group. The analysis by Kaplan-Meier curves, and log rank test, showed that these differences were statistically significant (p < 0,001) (Figure 1). Multivariate cox regression analyses showed that 90 days readmission (hazard ratio (HR): 3,82, CI 95% (1,78-8,24), p = 0,01); age (HR: 1,05, CI 95% (1,01-1,09), p = 0,024); and history of previous HF hospitalization (HR: 2,10, CI 95% (1,04-4,21), p = 0,037) were independent predictors of mortality.
Conclusions: early readmission is associated with poor prognosis in acute decompensated HF patients. This results underscored the need of reducing readmission with the aim of improving HF prognosis.



Kaplan-Meier curves (mortalitty)

P1635

Is there any difference between the new three groups of heart failure? A single center experience.

SM Pereiro Gonzalez[1]; SM Mettini[1]; DA Fernandez[1]; L Lapadula[1]; IL Ramella[1]; MG Masuelli[1]; G Sumay[1]; P Diaz Uberti[1]; C Cejas[1]; L Secco[1]
[1]*Hospital Center Churruca-Visca, Buenos Aires, Argentina*

Background: In 2016, the new European guidelines differentiate 3 groups in heart failure, those with ejection fraction (EF) over 50%, those between 40 and 49% and those with less than 40%. We analyzed if the middle group has any special difference between the others in our particular population.
Method: It is a prospective analysis of 474 patients admitted for decompensated heart failure, consecutively, in our Cardiology Department, from June 2012 to November 2016, with a median follow up of 26 months (Q1 13 - Q3 33). We divided 3 groups (G) according to their EF: G1 ≤39% (206 p), G2 40-49% (61 p) and G3 ≥50% (122 p). Quantitative variables with normal distribution were expressed with medium and with standard deviation (analyzed by test Fisher's Test); those with not normal distribution, were expressed with median (m) and quartiles (analyzed by Mann Whitney's Test). Dichotomous variables were analyzed by Chi^2.
Results: We observed the same median age between G1 and G2, but differences statistically significant (DSS) between G2 and G3 (p = 0.0059), with same amount of elders (>75 years old) in G1 and G2, but bigger with G3, and no DSS in gender. The main data found was there were no DSS between G in hospital follow up, but there were DSS between G2 and G1 in rehospitalization (p = 0.035, G1 25,5% vs G2 12,3%), but not with G3. The intermediate group appears to be similar to G1 in cardiovascular risk factors, previous infarction, clinical presentation, treatments and etiology of myocardiopathy. On the other hand, G2 is similar to G3 on hematocrit, renal function, the presence of LBBB, RBBB and treatment. The differences observed between G2 and G1 were the cause of decompensation (progression, p = 0.01 -G1 18,4% vs G2 5%-, and arrhythmias, p = 0.0482 -G1 10.2% vs G2 20%), the presence of hiper bilirubin (p = 0.01, G1 60,3% vs G2 41,7%), hyperthyroidism (p = 0.0000, G1 13,3% vs G2 22,2%) and LBBB (p = 0.0042, G1 36,3% vs G2 16,7%). The ones between G2 and G3, were age (p = 0.0059, G2 70 years old vs G3 77 years old), diabetes (p = 0.028, G2 39,3% vs G3 23,8%), history of infarction (p = 0.0092, G2 31,1% vs G3 14,8%), etiology (different to ischemic or valvular, p = 0.043, G2 13,1% vs G3 26,2%) and presence of sinus rhythm (p = 0.048, G2 64,4% vs G3 48,8%). None of the G had DSS in presence of previous devices, renal clearance, use of mechanical ventilation or non-invasive one and renal evolution.
Conclusions: We observed that in our population, patients with intermediate EF, 40-49%, are similar to both G in some characteristics, but on the evolution, they behave like those with normal EF.
We think we should compare both extremes into G2 (those near EF41% and those near 49%), but our sample is still too small.

P1636

Prognostic significance of B-type natriuretic peptide and pulmonary arterial pressure in patients with acute heart failure

D Petrovic[1]; M Deljanin Ilic[1]; S Ilic[1]; S Stojanovic[1]; D Marinkovic[1]; D Simonovic[1]
[1]*Institute for treatment and rehabilitation Niska Banja, Clinic for cardiology, Nis, Serbia*

Background: Natriuretic peptide has become the gold standard for diagnosis in patients with acute heart failure due to antifibrotic and antiproliferative actions. There are few studies that have investigated the significance of the parameters of the right ventricle in predicting the mortality of patients with ahf.
Purpose: To investigate association B-type natriuretic peptide (BNP) level with pulmonary arterial pressure (PAP) and to estimate their prognostic significance on one-year mortality in patients with acute heart failure (AHF).
Methods: The prospective study evaluated 225 patients (pts) (70.29 ± 9.74 years) who were admitted to Intensive care unit due to signs and symptoms of AHF during three years. The values of BNP were determined during the first 24 hours after admission in all subjects. Two-dimensional and doppler echocardiography was performed in all patients. Post-discharge mortality was observed one year. All medical therapy was documented, and for this analysis, we focused on the impact BNP, the right ventricular diameter, PAP on one-year mortality.
Results: Out of 225 pts, those with PAP < 40 mmHg (n = 104) had lower value of BNP, than pts (n = 121) with PAP≥40 mmHg (P < 0.001). Pts with right ventricular diameter ≤30 mm (n = 158) had lower value of BNP than pts (n = 67) with right ventricular diameter >30 mmHg (P < 0.001). Total one-year mortality was 34.7% (78 pts). As compared with the group of survivors (n = 147) the group of non-survivors had higher values of BNP (853.10 ± 384.92 vs 1399.68 ± 464.44 pg/mL, P < 0.001), right ventricular diameter (27.02 ± 3.93 vs 31.09 ± 5.60 mm, P < 0.001) and PAP (40.09 ± 8.24 vs 49.67 ± 10.65 mmHg, P < 0.001). There was a significant positive correlation BNP and PAP (ρ=0.255, P < 0.001) and BNP and right ventricular diameter (ρ=0.304, P < 0.001). After multivariate adjustment, using age, sex, body mass

index, blood pressure, right ventricular diameter as covariates, logistic regression analysis independent predictors for one-year mortality were: BNP (OR 1.003, CI 1.002-1.004, P < 0.001), and PAP (OR 1.099, CI 1.038-1.164, p < 0.001). The cut-off value of BNP≥ 1062.04 pg/ml was associated with a higher risk of one-years mortality (AUC=0.820, P < 0.001; sensitivity 74.4%, specificity 72.8%). The cut-off value of PAP≥44.5 mmHg was also associated with a higher risk of mortality (AUC=0.776, P < 0.001).

Conclusion: Our results show that BNP levels are strongly associated with pulmonary arterial pressure in hospitalized patients with acute heart failure. The most significant and independent predictors of one-year mortality are BNP and the PAP in patients with AHF.

The simultaneous application of echocardiography (parameters of right ventricular function) and laboratory biomarkers (BNP) in the early phase of hospitalization, can help fast and accurate diagnosis od AHF.

P1637

Impact of community-acquired pneumonia on prognosis of patients with acute decompensated heart failure.

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

Introduction: Community-acquired pneumonia (CAP) is a factor that has to be taken into consideration when evaluating the prognosis of patients with acute decompensated heart failure (ADHF). NIS cohort (USA 2001-2009) showed pneumonia like most frequent comorbidity in patients with ADHF.

Purpose: evaluate CAP on prognosis of patients with ADHF

Methods: In one year period, was analyzed 852 medical records of patients hospitalized for ADHF.

Results: the prevalence of CAP among patients was 16.5% not age depending. Patients having decompensated heart failure and CAP had a longer hospitalization period (13.1 vs 11.9 days; p= 0,009), higher risk of readmission to hospital (OR 1.9; p = 0.02) and higher hospital mortality (OR 13.5; p < 0.001).The mortality at the first day of hospitalization was significantly higher when HF is associated with CAP.During one-year follow-up, the combination of ADHF and CAP makes the risk of death higher (OR 4.8; p < 0.001).

Conclusion: CAP is a factor worsening the one year prognosis and hospital prognosis of patients with acute decompensated heart failure.

Variable	CAP - %	CAP + %	P value
Male sex, %	57.3	38.7	< 0.001
Cardiogenic pulmonary edema	17.9	31.5	< 0.001
Pulmonary embolism	1.4	1.6	0.88
Chronic obstructive pulmonary disease	17.1	20.2	0.41
Bronchial astma	3.0	1.6	0.38
Pulmonary hypertension	2.2	4.0	0.24
Core pulmonale	1.6	0.8	0.50
H. mortality in group 50-59 years old	0	9.1	
H. mortality in group 60-69 years old	1.9	28.6	< 0.001
H. mortality in group 70-79 years old	1.6	27.6	< 0.001
H. mortality in group 80-89 years old	5.1	30.0	< 0.001
Hospitalization period	11.9	13.1	0.009
Readmission to hospital	30.4	45.6	0.02
Hospital mortality	2.7	27.4	< 0.001
First day hospitalization mortality	1.1	12.7	< 0.001
One year mortality	19.9	54.4	< 0.001

H.mortality-Hospital mortality

P1638

Deterioration of renal function does not condition poor prognosis in acute decompensated heart failure patients with previous renal insufficiency

A Alfonso Varela Roman[1]; R Agra Bermejo[1]; I Gomez Otero[1]; R Gonzalez Ferreiro[1]; N Lopez Canoa[1]; CH Abou-Johk Casas[1]; A Seoane Blanco[1]; M Moure Gonzalez[1]; JR Gonzalez-Juanatey[1]
[1]*Clinical University Hospital. Service of Cardiology, Santiago de Compostela, Spain*

Background: renal insufficiency is one of the main prognostic factors in heart failure (HF). However, the prognostic value of worsening renal function during episodes of HF decompensation is controversial.

Purpose: the aim of this study is to analyse the rate of renal function impairment during acute HF episodes and its impact on prognosis depending on previous renal function.

Material and Methods: we analysed 150 consecutive patients (mean age 69,9 years, 61% men) admitted to a cardiology service for acute decompensated HF, 54 with previous HF hospitalization (36%), 116 with hypertension (HTA) (77%); 69 diabetic (DM) (46%); 140 class III or IV NYHA (93%), and 42 ischemic aetiology (28%), with mean left ventricular ejection fraction (LVEF) 42,9%. We classified the patients into two groups based on the glomerular filtration rate (MDRD) ≥ 60 or < 60 mL/min/1,73m2. Worsening of renal function was defined as the occurrence of both a > 25% and a > 0.3 mg / dL increase in serum creatinine from admission.

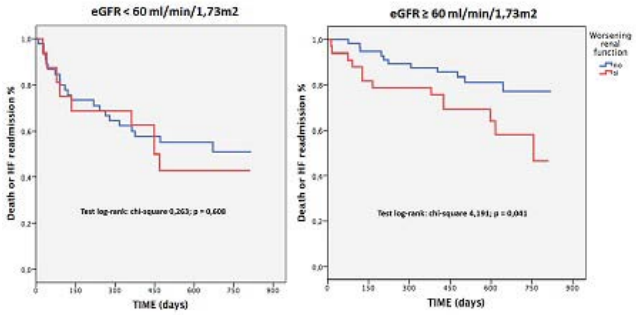
Results: 89 patients had MDRD ≥ 60 mL/min/1,73m2 and 61 patients had MDRD < 60 mL/min/1,73m2. When we compared the two groups we found that patients with MDRD < 60 mL/min/1,73m2 had more frequently previous HF hospitalization (45,9% vs 29,0%, p = 0,036), were less frequently treated with ACEIS/ARBS (82% vs 94%, p = 0,016), betablockers (70,2% vs 84,3%, p = 0,043), mineralocorticoid recpetor antagonists (78,7% vs 91%, p = 0,013), and more frequently treated with hydralazine (4,9% vs 0%, p = 0,035). Also they have lower levels of haemoglobin (12,6 ± 1,9 vs 13,5 ± 1,8 g/dL, p = 0,007) and higher levels of NT-proBNP (7822,86 ± 8448,81 vs 3474,45 ± 3966,87 pg/mL, p < 0,001).

Age, sex, history of hypertension, diabetes, NYHA III-IV class, ischemic aetiology and left ventricular ejection fraction were no statistically different between the two groups.

During the hospitalization worsening of the renal function was observed in 49 patients (32,7%): 16 (26,2%) in the group with MDRD < 60 mL/min/1,73m2, and 33 (37,1%) MDRD ≥ 60 mL/min/1,73m2 (p = 0,164).

After a mean follow-up of 18,3 ± 6,9 months, 54 (36%) patients had an event (exitus or HF readmission). In the MDRD < 60 mL/min/1,73m2 group, 30 patients (49,1%): 9 out of 16 (56,2%) who suffered worsening of renal function and 21 out of 45 (46,7%), without it, had an event. In the MDRD ≥ 60 mL/min/1,73m2 group 24 patients (27,0%): 13 out of 33 (39,4%) who worsening of renal function and 11 out of 56 (19,6%), without it, had an event. The analysis by Kaplan-Meier curves, and log rank test showed that these differences were only statistically significant in MDRD ≥ 60 mL/min/1,73m2 group (p = 0,041) (Figure 1).

Conclusions: Worsening of renal function is not associated with poor prognosis in acute decompensated heart failure patients with previous renal insufficiency.



Kaplan-Meier curves

P1639

Right ventricular longitudinal systolic dysfunction is associated with worse clinical outcomes in acute dyspnea patients

A Krivickiene[1]; J Motiejunaite[1]; D Rimkeviciute[1]; R Norvilaite[2]; G Ziubryte[2]; A Montvilaite[2]; J Bugaite[3]; D Gabartaite[3]; D Zaliaduonyte-Peksiene[1]; R Jurgaitiene[1]; G Balciunaite[4]; I Alitoit[4]; A Mebazaa[5]; A Kavoliuniene[1]; J Celutkiene[4]
[1]*Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; [2]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [3]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [4]*Vilnius University, Clinic of Cardiac and Vascular diseases, Vilnius, Lithuania*; [5]*Hospital Lariboisiere, U942 Inserm, Université Paris Diderot, Paris, France*

On behalf of: the GREAT network

Introduction: Acute right ventricular (RV) failure is a complex clinical syndrome which has been poorly studied worldwide. So far just few data have been published on the incidence and characteristic of the RV dysfunction including its association with clinical outcomes, functional parameters of left ventricle (LV) and co-morbidities.

Purpose: To evaluate the association of longitudinal RV systolic dysfunction (RVSD) with 1-year rehospitalisations and deaths in patients with acute dyspnea; to study clinical findings and co-morbidities typical for patients having RVSD.
Methods: Prospective multicentre observational cohort study enrolled consecutive patients admitted to the emergency department in two university hospitals with acute dyspnea due to decompensated heart failure, exacerbation of chronic obstructive pulmonary disease, pneumonia, pulmonary embolism and other conditions. Demographic, clinical, echocardiographic data, co-morbidities and clinical outcomes of 307 patients were included in the analysis. Echocardiography was performed during the first 48 hours after the presentation to hospital. The longitudinal RVSD was defined by reduced tricuspid annular plane systolic excursion (TAPSE) of <17 mm. Rehospitalisations and deaths were assessed after 1-year follow-up period. For statistical analysis Mann Whitney U and Pearson Chi-Square tests were used. P-value < 0.05 was considered statistically significant. Kaplan-Meier curves illustrate the survival analysis.
Results: In analysed cohort mean age was 69.1 ± 12.3 years and 189 pts (61.56%) were female. The first (I) study group consisted of 166 (54.1%) patients with longitudinal RVSD; in the second (II) group 141 (45.9 %) patients had normal RV longitudinal function (TAPSE ≥17 mm).
Rehospitalisations and deaths in 1-year follow-up period occurred significantly more often in the group with longitudinal RV dysfunction than in group II: 37 (15.0 %) vs. 14 (5.7 %), (p = 0.002) and 11 (9.4 %) vs. 3 (2.5 %) (p = 0.029), respectively (Fig. 1).
Atrial fibrillation had a tendency to be more frequent in group I (84 [27.5%] vs. 50 [16.3%], p = 0.049), meanwhile the frequency of other co-morbidities (diabetes mellitus, arterial hypertension, chronic obstructive pulmonary disease, smoking, obesity) did not differ between the both groups (p>0.05). Heart rate at presentation was significantly higher (92.7 ± 26.0 bpm vs. 86.9 ± 21.2 bpm; p = 0.01) and pulmonary rales were more frequent (81 [26.4%] vs. 54 [17.6%], p = 0.033) in group I. Left ventricular ejection fraction was significantly lower in group I than in group II (33.1 ± 15.2 % vs. 44.4 ± 12.9 %, p = 0.006).
Conclusion: Patients with acute dyspnea and longitudinal RV dysfunction demonstrated significantly worse clinical outcomes with higher rate of rehospitalisations and deaths during 1-year follow-up, more severe LV dysfunction and unfavourable clinical profile.

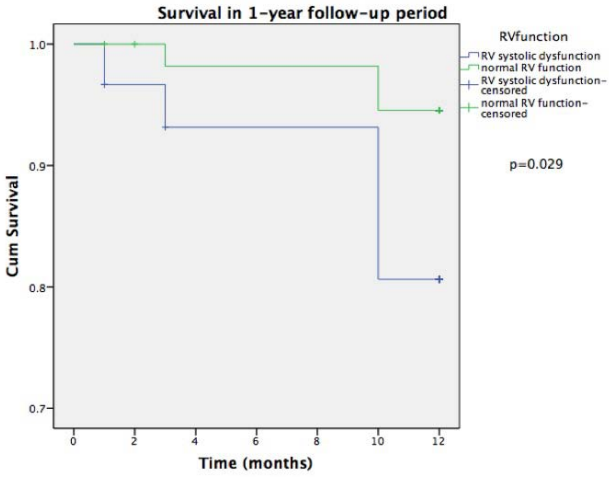


Fig.1 Survival estimate (Kaplan-Meier curves)

P1640

Utility of bio-adrenomedullin (bio-ADM) and penKidephalin (penKid) in evaluating congestion grading and acute kidney injury in patients admitted for acute heart failure

S Navarin[1]; R Marino[1]; S Santarelli[1]; G Zoccoli[1]; A Bergmann[2]; O Hartmann[2]; J Struck[2]; S Di Somma[1]
[1]Faculty of Medicine and Psychology, Sapienza University, Sant'Andrea Hospital, Rome, Italy, Department of Medical Sciences and Translational Medicine, rome, Italy; [2]Sphingotec GmbH, Neuendorfstr. 15a, 16761 Hennigsdorf, Germany, Hennigsdorf, Germany

Background: Bio-Adrenomedullin (bio-ADM) and PenKidephalin (penKid) have already proved to be good predictors of short-term mortality and worsening renal failure respectively in patients with acute heart failure (AHF). No data are available so far on the utility of the combination of the two biomarkers in detecting congestion, acute kidney injury (AKI) and in-hospital mortality.
Purpose: In patients hospitalized for AHF, objective of this study was to assess the value of bio-ADM in grading total body congestion amount and of penKid in predicting AKI, main reasons of AHF worsening.
Methods: This was a prospective, observational trial conducted in intensive care unit. We enrolled patients admitted for AHF from the emergency department (ED) of Sant'Andrea hospital in Rome. Clinical and laboratory data including Clinical Congestion Score (CCS: peripheral edema, jugular vein distension and orthopnea), diuretic treatment, BNP, bio-ADM and penKid values were collected at arrival and patients were followed until hospital discharge.
Results: 209 patients with a final diagnosis of AHF were recruited (44% male, mean age 78.4 ± 9.5). 49.7% of patients had prior history of heart failure, 58% had reduced systolic function, 17% presented with pulmonary edema. 17,5% presented AKI at ED arrival, while 20.8% developed AKI, defined as serum creatinine (sCr) increase by 0.3 mg/dl within 48 hours after hospitalization. 22.6%, 38.1%, 21.4% and 17.9% of patients presented with a CCS of 0, 1, 2 and 3, respectively. Compared to patients with a CCS between 0-2, bio-ADM resulted higher in patients with a CCS of 3 (p = 0.01) and in patients with vena cava index >1 (p = 0.05), suggesting a potential role of bio-ADM in the detection of congestion, that is considered the main cause of death and re-hospitalization for heart failure patients. Moreover, higher levels of bio-ADM were linked to increase in furosemide treatment at home and to higher rate of in-hospital mortality, probably related to congestion amount (p = 0.002 and p < 0.001, respectively). PenKid values proved to be significantly related to the presence of chronic kidney dysfunction, AKI detection at ED arrival, and furosemide use (p < 0.001). When considering patients with both Cre >1 mg/dl and penKid > 80pmol/l at ED arrival, we were able to increase the detection of AKI.
Conclusions: In patients hospitalized for AHF, bio-ADM and penKid seem to be suitable biomarkers for early detection of congestion severity and AKI occurrence, respectively, and for risk prediction of in-hospital mortality. For AHF patients, the role of the two biomarkers in predicting in-hospital death seems to be linked to the pathophysiological mechanism of congestion for bio-ADM and of renal dysfunction for penKid, respectively.

P1641

Acute myocardial infeartion of complicated with heart failure in women

SM Macin[1]; G Aristimuno[1]; M Onocko[1]; ML Coronel[1]; ER Eduardo Perna[1]; DM Burguener[1]; F Falcon[1]; N Cristaldo[1]; Y Parisi[1]; G Pozzi[1]; N Chatich[1]
[1]J.F. Cabral Cardiology Institute, Corrientes, Argentina

Objective: To evaluate clinical characteristics and hospital evolution in women with acute myocardial infarction complicated by HF
Material and method: Prospective, observational study of of 328 patients with acute myocardial infarction admitted to the ICU of the Institute of Cardiology of Corrientes, between August 1, 2012 and May 20, 2014 within 24 hours of onset of symptoms, 91 pts were female, of which 22% had HF, representing group I: women with HF, and the remaining Group II. Group 1 (women with HF, 22%) and the remaining conform Group 2. Both groups were different in age (71.2 ± 10 vs. 68.8 ± 11years, p = 0.017), diabetes (50 vs 23.9%, p = 0.024), obesity (23.1 vs 16.2%, p = 0.04), cholesterol at admission (164.5 ± 54 vs 144.7 ± 25 mg / dl, p = 0.029), previous location (50 vs 29.4%, p = 0.012) and rales (40 vs 11.3, p = 0.003).
There were no differences regarding the use of angiopraphy (90.5 vs 92.6%, p = 0.40) and primary angioplasty (39.4 vs 41.7%, p = 0.10). Group 1 had more frequent death (35 vs 2.8%, p < 0.0001), pulmonary edema (26.3 vs 1.2%, p < 0.001), BCR (10.5 vs 2%, p = 0.008), Ventricular atrial block complete (25 vs 2.8%, p = 0.01), Sustained ventricular tachycardia (15 vs 2.8%,p = 0.04), required more invasive procedures such as hemodynamic monitoring (18 vs 6.1%, p = 0.01) and mechanical ventilation (4 vs 1.4%, p = 0.009), were more need Cardio-defibrillator (4.6 vs 0%, p = 0.32). Ejection Fraction was different in both groups (45 ± 18 vs 59 ± 12, p < 0.001). At admission were predictors of development to Heart Failure: anterior location (OR=3.15, 95% 1.5-5.7, p = 0.002), and diabetes (OR=2.8, 95% CI,1. 2-7.1, p = 0.023).
Conclusions: Women with acute myocardial infarction who develop HF are older, more obesity, had more frequency of diabetes, in spite of being treated in an invasive form in a similar way had worse in-hospital evolution. Anterior location and diabetes were independently predictors was development to HF

P1642

Do the gender differences in laboratory parameters in patients with myocardial infarction with acute heart failure influence on outcomes?

A Galyavich[1]; Z Galeeva[1]; L Baleeva[1]; E Kharisova[1]
[1]State Medical University, Kazan, Russian Federation

Background: It is the question of gender differences in laboratory parameters in patients with myocardial infarction with acute heart failure and outcomes.
Methods: In our study of 135 patients with acute heart failure were included - 56 women aged 74.4 ± 8.9 years and 79 men 59.6 ± 13.1 years. 52% men and women had inferior myocardial infarction. The levels of laboratory parameters have been analyzed: blood urea, creatinine, transaminases, cholesterol, low-density lipoproteins, prothrombin by Quick, thrombin time, the acid-base balance.
Results: Women with acute heart failure had significantly higher levels of aspartate transaminase, serum creatinine, low-density lipoprotein cholesterol. Men with acute heart failure had significantly higher levels of total bilirubin, activated partial thromboplastin time, thrombin time. In the group of women with acute heart failure was 6 deaths ((10.7%), in the group of men with acute heart failure were 3 deaths (3.8%). Regression analysis showed no relationship between the studied parameters and outcomes with the exception of age.
Conclusion: In patients with myocardial infarction with acute heart failure there are some gender differences in biochemical parameters, but they do not affect the outcomes. The main factor of poor prognosis of patients with myocardial infarction with acute heart failure is age.

P1643
High-dose loop diuretics at discharge is associated with cardiovascular mortality in patients with heart failure

T Toshitaka Okabe[1]; T Kido[1]; T Yakushiji[1]; Y Oyama[1]; W Igawa[1]; M Ono[1]; S Ebara[1]; K Yamashita[1]; MH Yamamoto[1]; S Saito[1]; K Amemiya[1]; N Isomura[1]; M Ochiai[1]
[1]*Showa University Northern Yokohama Hospital, Division of cardiology and cardiac catheterization laboratories, Yokohama, Japan*

Background: Few studies have reported on the impact of high-dose loop diuretics at discharge on prognosis in Japanese patients with heart failure (HF).
Purpose: Our purpose was to assess the relationship between loop diuretic dose at discharge and cardiovascular mortality in patients with HF.
Methods: We enrolled decompensated HF patients who were admitted to our hospital between April 2010 and March 2015. High loop diuretic dose was defined as >40 mg/day of oral furosemide at discharge. We compared HF patients that were received high-dose loop diuretics at discharge (HL group) with low-dose loop diuretics at discharge (LL group) with regard to risk of cardiovascular mortality, all-cause mortality, and the rate of readmission due to HF.
Results: A total of 301 patients with HF were admitted to our hospital. We excluded 13 patients who died during hospitalization and 73 patients who did not receive loop diuretics at discharge. The median follow-up duration was 631 days. Cardiovascular mortality was significantly lower in the LL group than in the HL group (2.3% vs. 25.0%, $P < 0.001$). In addition, all-cause mortality was significantly lower in the LL group than in the HL group (10.6 % vs. 32.1%, $P < 0.001$). High-dose loop diuretics was associated with cardiovascular mortality in multivariate Cox proportional hazards model (hazard ratio, 8.905, 95% confidence interval 2.5 to 42.1; $P < 0.001$). High-dose furosemide was also associated with all-cause mortality (P=0.01) and rate of readmission (P=0.039).
Conclusion: High-dose loop diuretics at discharge was a strong predictor of long-term cardiovascular mortality in patients with HF.

P1644
Acute heart failure: who die?

L Cardoso[1]; L Reis[1]; C Lourenco[1]; R Teixeira[1]; P Dinis[1]; M Madeira[1]; J Ribeiro[1]; L Puga[1]; A Rodrigues[1]; L Goncalves[1]
[1]*University Hospitals of Coimbra, Coimbra, Portugal*

Background: Acute heart failure (AHF) is characterized by its heterogeneity and complexity, being associated with both high morbidity and mortality. Despite multiple treatment options, mortality remains high.
Purpose and methods: From a population admitted to a cardiac intensive care unit, in the setting of AHF, the cases resulting in death were studied. Clinical parameters and therapeutic strategies were evaluated.
Results: 264 consecutive patients (P) (78% male, age 69 ± 14 years) were admitted along 6 years. The in-hospital mortality was 11% and during follow up was 36% (112 P - 80% male, age 73 ± 11 years). Hospital length of stay was 14 ± 11 days.
The most frequent aetiology of HF in the deceased P was ischemic heart disease. The median evolution time of HF was 6 years and 55% of those P had been previously admitted with decompensate HF. 48% had concomitant chronic kidney disease, 77% were hypertensive and 34% diabetic. 15% had an ICD and 3,8% a CRT-D.
At admission, 33% of P were in acute pulmonary oedema and 13% in cardiogenic shock. Infection was the precipitating factor in 36% of patients. Analytically: 54% had lower haemoglobin (< 12.0 g/dL); 48% had a lower glomerular filtration rate (GFR) (< 30 ml/min/1.73m2) and 39% had a GFR 30-60 ml/min/1.73m2; 30% of P had hepatic cholestasis and 15% hypoperfusion and NTproBNP 20 855 ± 23 703 pg/nl.
Transthoracic echocardiography showed LVEF < 35% in 46% of P and a restrictive pattern of filling in 23%; moderate/severe mitral regurgitation was present in 38%, and 52% had moderate to severe pulmonary hypertension.
Regarding therapy: furosemide infusion was used in 55%, being the maximum daily dose 294 ± 203mg, despite association with other diuretic; 42% were treated with levosimendan, 35% with dobutamine and 15% required noradrenaline. Non-invasive ventilation was used in 52% and invasive in 11%; renal replacement therapy was required in 12% of patients.
Hospitalization was complicated with cardiorenal syndrome in 62% and with hospital acquired infection in 54%.
The cause of death was end stage heart failure in 69% of P and infection in 31%.
Conclusions: Our study highlights the progressive deterioration of patients with chronic heart failure, being admitted several times previously to the final admission, when they present with multi-organ dysfunction. This population deserves a special look concerning how far we should go with them in escalating therapies, and when is it time to start palliative care.

P1645
Predictors of high Killip class after ST segment elevation myocardial infarction in the era of primary reperfusion.

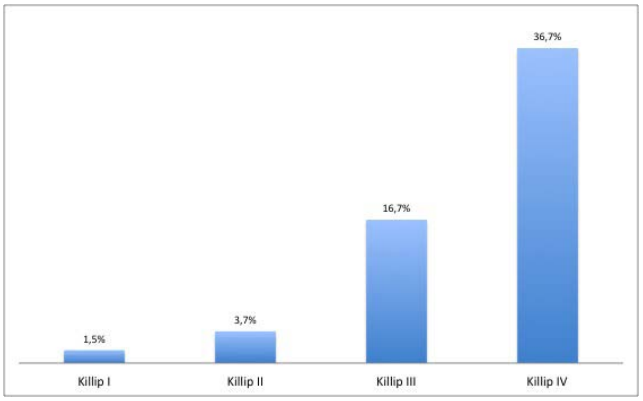
L Vicent[1]; J Velasquez-Rodriguez[1]; MJ Valero-Masa[1]; F Diez-Delhoyo[1]; H Gonzalez Saldivar[1]; F Fernandez-Aviles[1]; M Martinez-Selles[1]
[1]*University Hospital Gregorio Maranon, Cardiology, Madrid, Spain*

Background/Introduction: Primary percutaneous coronary intervention (PCI) has improved outcomes after ST segment elevation myocardial infarction (STEMI), but patients with high Killip class still have a poor prognosis, and those ≥II benefit from a closer monitoring in a specialized cardiac care unit.
Purpose: We aimed to determine the predictors of Killip class in a group of patients admitted for acute STEMI.
Methods: Non-interventional registry in a Coronary Intensive Care Unit. Patients were consecutively included from January 2010 to April 2015. Multivariate analysis was performed to determine independent predictors of high Killip Class.
Results: From 1111 patients, 230 (20.7%) were in class II or higher. Mean age was 64.0 ± 14.0 years and 853 (76.8%) were male. Primary PCI was performed in 991 (89.2%), and 120 (10.8%) only received thrombolysis as acute reperfusion therapy. Independent predictors of high Killip class are depicted in table I. In-hospital mortality increased with Killip class (I 1.5%, II 3.7%, III 16.7%, IV 36.7%).
Conclusion: In patients with STEMI Killip class can be predicted with variables available at the time of presentation and is strongly associated with in-hospital prognosis.

Independent predictors of Killip Class>I

	Killip I, N (%)	Killip>I, N (%)	OR (95% CI)	P value Cox
Previous medical history				
Age >65 years	365 (41.4)	152 (66.1)	2.1 (1.4-3.0)	< 0.001
Female sex	180 (20.4)	78 (33.9)	1.6 (1.1-2.2)	0.017
Diabetes	166 (18.8)	72 (31.3)	1.4 (1.0-2.1)	0.05
History of heart failure	13 (1.5)	20 (8.7)	3.2 (1.4-7.2)	0.006
Chronic kidney disease	46 (5.2)	35 (15.2)	2.0 (1.1-3.6)	0.016
Anaemia	108 (12.3)	74 (33.0)	3.0 (2.0-4.5)	< 0.001
At presentation				
Anterior location	324 (36.9)	127 (55.7)	2.4 (1.8-3.4)	< 0.001
>1 vessel disease	353 (40.2)	129 (56.6)	1.6 (1.1-2.2)	0.008
>2 hours of evolution	565 (64.4)	176 (77.2)	1.6 (1.1-2.4)	0.01
TIMI < 3	739 (84.0)	206 (90.4)	1.8 (1.2-2.7)	0.004
Ventricular fibrillation	13 (1.5)	32 (14.0)	4.7 (2.8-7.8)	< 0.001
LVEF < 40%	148 (16.9)	129 (57.3)	4.6 (3.1-6.7)	< 0.001

OR: Odds Ratio; CI: Confidence Interval, LVEF: Left Ventricular Ejection Fraction. Chronic kidney disease: glomerular filtration rate <60 mL/h Anaemia: haemoglobin <12 g/dL in women and 13 g/dL in men



Mortality according to Killip Class

P1646

Lactate levels in patients admitted in the emergency department with acute decompensated heart failure

D David Cabrita Roque[1]; J Augusto[1]; A Sachetti[1]; D Faria[1]; A Gaspar[1]; L Melo[1]; T Bernardo[1]; J Simoes[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal*

Background: Acute decompensated heart failure (ADHF) may lead to subclinical tissue ischemia due to hypoperfusion from inadequate forward flow or congestion. The aim of this study is to evaluate if the lactate levels are elevated in patients admitted in the emergency department with ADHF and if there is a relation between these levels and in-hospital mortality.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for acute decompensated heart failure. We considered the lactate levels collected in the first medical contact. Profiles were assessed according to the recent guidelines.
Results: 196 patients had lactate levels collected after first medical contact (40.3% male, 75.2 ± 16.3 years). 67 (34.2%) had an elevated lactate level. Of the patients in profile B (wet and warm, n=189), 32.3% had an elevated lactate whereas of those in profile C (wet and cold, n=7), 85.7% had an elevated lactate ($p < 0.001$). There were no differences in hospital mortality among patients with and without elevated lactate levels (4.8% vs 6.1%, respectively, $p = 1.000$), nor in heart rate at admission (mean 93.5 vs 104.4bpm, respectively, $p = 0.440$) or maximum heart rate (mean 124.3 vs 109.8bpm, respectively, $p = 0.960$) during in-hospital stay.
Conclusion: Only one third of patients with ADHF had an elevated lactate on presentation, mainly those in the profile C, a known state of hypoperfusion ("cold"). However, there were no differences in hospital mortality between patients with and without elevated lactate on presentation, probably associated with the fast implementation of therapy in this patients.

P1647

Serum levels of exocrine pancreatic enzyme in patients with heart failure

M Masaru Hiki[1]; T Kasai[1]; S Yatsu[1]; H Matsumoto[1]; A Murata[1]; T Kato[1]; S Suda[1]; H Daida[1]
[1]*Juntendo University School of Medicine, Cardiovascular Medicine, Tokyo, Japan*

Background: Heart failure (HF) can damage systemic organs through the poor perfusion and/or congestion. Recently, interactions between HF and such other organs, especially lungs, kidneys and liver have been focused. However, there are no data regarding interaction between HF and exocrine pancreatic insufficiency which may impair fat and protein absorption and possibly cause malnutrition.
Hypothesis: We hypothesized that serum levels of exocrine pancreatic enzyme as suggestive of exocrine pancreatic function can be lower in patients with HF compared with those without HF, and that there are correlations between serum levels of exocrine pancreatic enzyme and indices of cardiac function in HF patients.
Methods: We collected serum levels of exocrine pancreatic enzyme such as amylase and lipase from patients who admitted to the cardiac intensive care unit (CCU) due to HF or to non-HF causes. Patients undergoing dialysis and those with neoplasms were excluded. Serum levels of amylase and lipase were compared between those two groups. Then, only in HF patients, stepwise multiple linear regression analyses including either natural logarithm transformed serum levels of amylase or lipase as a dependent variable and the other baseline characteristics, blood test and echocardiographic parameters as independent variables was carried out.
Results: Finally, data from 137 patients including 102 HF and 35 non-HF were analyzed. HF patients had significantly lower serum amylase (median [interquratile range], 54 [33] IU/L versus 68 [21] IU/L, P=0.001) and lipase (25 [21] IU/L versus 31 [16] IU/L, P=0.018) as compared with those without non-HF causes. Multivariable regression analysis in HF patients showed that the significant independent correlates of the lower amylase level were lower blood urea nitrogen (BUN) (coefficient, 0.552; $P < 0.001$) and albumin (coefficient, 0.233; P=0.020) levels, greater uric acid (coefficient, -0.328; P=0.001) and B-type natriuretic peptide (BNP) (coefficient, -0.227; P=0.024) levels, and that the significant independent correlates of the lower lipase level were the presence of atrial fibrillation (coefficient, 0.254; P=0.011), the lower BUN level (coefficient, 0.377; $P < 0.001$) and the greater BNP level (coefficient, -0.364, $P < 0.001$).
Conclusion: These findings suggest that HF patients may be suffering from exocrine pancreatic insufficiency in association with the severity of congestion, which may affect malnutrition.

P1648

Hyperadiponectinemia in de novo heart failure is associated with malnutrition

RM Rosa Maria Agra Bermejo[1]; R Gonzalez Ferreiro[1]; A Varela Roman[1]; I Gomez Otero[1]; E Alvarez[1]; M Rodriguez Manero[1]; S Eiras[1]; JR Gonzalez Juanatey[1]
[1]*University Clinical Hospital of Santiago De Compostela, Department of Cardiology, Santiago De Compostela, Spain*

Background: Adiponectin (ADPN) is an adipose tissue hormone that regulates energy metabolism and body composition with cardiovascular protector role. However, in heart failure (HF) patients, high adiponectin levels are paradoxically associated with advanced disease, elevated N-terminal pro B-type natriuretic peptide (NT-proBNP), and increased mortality.
Purpose: The aim of our study was to study the relationship between adiponectin levels and nutritional status in patients with de novo HF.
Methods: We analysed 78 patients admitted consecutively to a cardiology department for de novo HF. Patients were classified according to sex and adiponectin ng/mL levels in three groups: hypo- (Men, 0-11, Women 0-9), normo- (men; 11-20 and women 9-15) and hyperadiponectinemia (men>20, women>15). Nutritional status was measured with the CONUT method, a validated scale based on laboratory testing (albumin; cholesterol; lymphocytes) during hospitalization. The mean of follow up was 416 ± 256 days. Cox regression analyses were employed to calculate the estimated hazard ratio (HR) of death or readmission with 95% confidence interval (CI).
Results: Patients with hyperadiponectinemia had higher presence of hypertension, hyperlipidemia and worse nutritional status (moderate-severely malnourished 50%) compared with those with normo- (17%) or hypoadiponectinemia (33%), $p = 0.019$. We did not find differences regarding BMI among three groups. Moreover, patients with hyperadiponectinemia had worse renal function (creatinine= 1.2 ± 0.3 mg/dl, eGRF= 64.5 ± 22 ml/mi/m2) and lower insulin levels (259.2 ± 62.2 pg/mL) compared with those with hypo (creatinine= 1.0 ± 0.4 mg/dl, eGRF= 76.7 ± 28.5 ml/mi/m2, insulinemia 668 ± 509 pg/mL) or normoadiponectinemia (creatinine= 0.8 ± 0.2mg/dl, eGRF=97.4 ± 46.8 ml/mi/m2, insulinemia 855 ± 70.9 pg/mL) ($p < 0.005$). Also adiponectinemia is strongly related to nutritional status (r=0.411, $p < 0.001$) and proBNP levels (r=0.324, $p = 0.004$) but not with BMI (r=-0.098, $p = 0.394$). Hyperadiponectinemia patients had worse prognosis in terms of death or rehospitalization HR=1.755, CI 95% (1.13-2.77), $p = 0.012$.
Conclusions: In de novo HF, malnutrition state was associated with hyperadiponectinemia that determines a poor outcome in terms of death or rehospitalization.

P1649

Infective endocarditis complicated by heart failure

A Alaeddine Jalled[1]; MAJED Hassine[2]; MEJDI Ben Messoud[2]; MAROUA Mahjoub[2]; ZOHRA Dridi[2]; FETHI Betbout[2]; HABIB Gamra[2]
[1]*University of Tunis El Manar, cardiology departement, La Marsa, Tunisia*;
[2]*University of Monastir, cardiology A departement, Monastir, Tunisia*

Introduction: Despite the progress in the field of antibiotic and the respect for hygiene rules, endocarditis remains a common and serious disease. Heart failure is the most common but also the most serious complication, representing the leading cause of death identified in clinical and autopsy statistics. This heart failure is mainly related to valvular mutilation created by grafting infectious and hemodynamic disturbances
Patients and methods: From the infective endocarditis' register of our service comparing 241 patients and responding to criteria of DURAK DUKE university which collected retrospectively, we included patients with heart failure on admission, namely dyspnea greater or equal to NYHA stage 3. A total of 85 patients were enrolled in the heart failure and 156 in the infective endocarditis group without heart failure group.

Results: The average age of our patients was 42 ± 18 years. A male predominance was noted with a sex ratio of 2.14. Heart failure complicating infective endocarditis of native valve had occurred in 66 cases (77.6%). The preexisting valvular heart disease was the main underlying observed in 38 patients (44.7%).. On admission, 59 patients (69.4%) were in heart failure and heart regurgitation occurred in 29 cases 34.1%. The gateway was suspected in 66 patients (32.9%); the most frequently found was dental in 28 patients (32.9%). The multivariate study of predictors of heart failure occurred identified the following factors; the affected aortic valve, the presence of vegetation, the presence of Staphylococcus aureus and prosthesis disinsertion. Besides antibiotic treatment, 56 of our patients underwent surgical treatment with an average of 24.8 days. The indication for surgery was hemodynamics in 46 cases and septic in 10 cases. The total mortality in our registry was 19.5%, but higher in the group with heart failure (28.2%) with a significant difference p = 0.011. The realization of a multivariate analysis of independent determinants of mortality of infective endocarditis complicated by heart failure group concluded the significant influence of anemia (OR = 5, 95% CI = 0.8 - 27; p = 0.06), Staphylococcus aureus (OR = 5, 95% CI = 0.8 to 29.8; p = 0.07) and the protective role of surgery (OR = 0.15, 95% CI = from 0.025 to 0.99; p = 0.05).
Conclusion: Our results support the conclusion that heart failure remains an independent predictor of hospital mortality at 1 year. It is more common in infective endocarditis of mitral seat and she is associated with severe regurgitation. Early surgery is associated with reduced mortality and should be widely considered to improve results

P1650
Modified systolic index is an independent predictor of acute heart failure and in-hospital mortality in patients with ST-segment elevation myocardial infarction

PM Pedro Azevedo[1]; J Bispo[1]; D Bento[1]; T Mota[1]; D Carvalho[1]; J Guedes[1]; W Santos[1]; S Pereira[1]; J Mimoso[1]; N Marques[1]; I Jesus[1]
[1]*Faro Hospital, Cardiology, Faro, Portugal*

Introduction: Acute heart failure (AHF) and cardiogenic shock (CS) remains a dreadful complication of ST-segment elevation myocardial infarction (STEMI). In these patients, a modified shock index (MSI) ≥ 1.3 have been associated with higher mortality rates and AHF. Our study aims to assess the predictive value of MSI ≥ 1.3 for AHF, in-hospital mortality and 1-year mortality and hospitalization rate in patients admitted with STEMI.
Methods: Retrospective, descriptive and correlational study with all patients admitted with a STEMI in a Cardiology department between the 1st of October 2010 and 31st of August 2015. The baseline characteristics and hospitalization data of patients with MSI (heart rate / mean arterial pressure) ≥ 1.3 were compared to patients with a MSI < 1.3. The 1-year follow-up was made through phone call by a Cardiologist. We performed a univariate and multivariate statistical analysis of in-hospital mortality, mortality and hospitalization rate at 1-year using SPSS.
Results: A total of 1478 patients were included, 1138 (77%) were men with a mean age of 63,93 ± 13,39 years. A MSI ≥ 1.3 was present in 96 (6.5%) patients and was more common in females (10,9% vs 5,2%, p < 0,01) and older patients (65,6 vs 63,8 years, p = 0,2). It was also associated with diabetes mellitus, past history of stroke and dementia.
On admission, patients with a MSI ≥ 1.3 had more frequently an anterior MI (71,9% vs 41,1%, p < 0,001), atrial fibrillation (17,7% vs 4,1%, p < 0,01), a Killip Class ≥ 2 (49% vs 8,3%, p < 0,001) or CS (29,2% vs 1,7%, p < 0,01) and lower hemoglobin levels (13,3 vs 14,1, p < 0,001).
Patients with a MSI ≥ 1.3 had lower left ventricular ejection fraction (43,95% vs 56,46%, p < 0,001), more malignant arrhythmias (6,3% vs 1,6%, p < 0,01), and had less coronary catheterization (74% vs 87,4%, p < 0,001) and percutaneous coronary intervention (67,7% vs 82,2%, p < 0,001). They had more frequently left main occlusion (3,1% vs 0,5%, p = 0,002). There was no relation between a MSI ≥ 1.3 and other coronary artery disease.
These patients were more frequently treated with invasive mechanical ventilation (14,6% vs 3,0%, p < 0,001) and non-invasive ventilation (6,3% vs 0,7%, p < 0,001).
Regarding outcomes, a MSI ≥ 1.3 was strongly associated with in-hospital mortality (28,1%vs4,3%, p < 0,001) but not 1-year mortality (12,8% vs 7,1%, p = 0,15) or hospitalization rate (27,7% vs 17,2%, p = 0,07). On multivariate statistical analysis, a MSI ≥ 1.3 was a strong independent predictor of AHF at admission or during hospitalization (OR 3.66 95% CI 1.7-8.1, p = 0,001) and in-hospital mortality (OR 4.48, 95% CI 1.8-11.1, p = 0,001).
Conclusion: In our study, a MSI ≥ 1.3 was a strong independent predictor of AHF and in-hospital mortality among STEMI patients, although it was not associated with 1-year outcomes. It is an easily accessible tool that can help identify more critical patients and monitor them more closely during hospitalization.

P1651
Hypertonic saline solution in the management of severe decompensated heart failure in the elderly

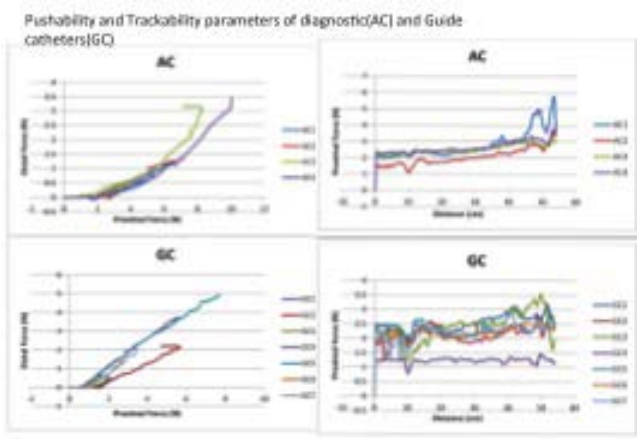
GR Gerald Roul[1]; JJVH Von Hunolstein[1]
[1]*New Civil Hospital, Cardiovascular Medico-Surgical Activities, Strasbourg, France*

Introduction: Low plasma sodium level is frequent in heart failure and is a marker of bad prognosis. Its treatment with hypertonic saline solution has been proposed in previous studies.
Aim: In this study, we compared the outcomes of low plasma sodium level associated with heart failure treated as usual or using hypertonic saline.
Methods: This is an observational, retrospective and single centre study from 2013 to 2015. We included patients admitted for heart failure with low plasma sodium level at entry or treated with hypertonic saline solution during hospitalization.
Results: 167 patients (78 years; 45% of women) were included: group 1 (n = 156 usual care), and group 2 (11 patients treated with hypertonic saline solution). Group 2 patients had a higher BNP and a worse kidney function. Hypertonic saline solution normalized plasma sodium level (137 ± 7 mmol/L vs. 129 ± 3 mmol/L; p < .007), decreased body weight (median 73 kg vs 80; p < .008). Compared to group 1, group 2 patients had a prolonged length of stay (median 21 days vs. 10 days). The hypertonic saline solution group had a high morbidity and mortality rate (odds ratio = 6.8 for mortality or being hospitalized during the 2-year period of the study) explained by the severity of these patients' condition.
Conclusion: Our study does show a benefit of the hypertonic saline solution to rapidly correct sodium level, with kidney function preservation. It underlines the bad outcomes associated with low plasma sodium level. A large-scale randomized controlled study should be realized to conclude.

P1652
Primary and emergency angioplasties with 30 ml contrast using cordis 6F diagnostic coronary catheters and bench evaluation of catheters

MC Mark Christopher Arokiaraj[1]
[1]*Pondicherry Institute of Medical Sciences, Pondicherry, India*

Aims: To safely perform primary and emergency angioplasties with low contrast volume using cordis 6F diagnostic catheters. To perform bench evaluation of cordis guide and diagnostic catheters with 3-bend test, distal tip softness and pushability and trackability tests.
Methods and Results: In 53 patients primary angioplasty, pharmaco-invasive and emergency angioplasties were performed with cordis 6F diagnostic catheters. Angioplasty and stenting was performed in left anterior descending (25), Left main (2), left circumflex (10), ramus (3) and right coronary artery(13) arteries and in total 61 stents were used. The contrast volume was kept to the minimum with only required pictures, which is the routine for the operator. This is to reduce contrast induced nephropathy as well as hemodynamic problems and cardio-renal syndromes. In 75% of cases Iodixanol was used. All injections were given by hand. Regular follow-up of the patients was performed at 30 days. The procedures were performed in femoral route only. Pre-dilatation was performed in 12 cases with semi-compliant balloons (2 mm x 10 mm and lesser sizes) and in 1 case, 2.5 x 10mm in one patient. In cases with difficulty in wire crossing balloon-mediated wire crossing was performed where in the balloon and wire were taken to the tip and with gentle manipulation the wire crosses the lesion. The length of the stents varied from 12 mm to 28mm, and the diameter of the stent varied from 2.25 mm to 4.0 mm. IVUS and OCT were not performed. Aspirin, clopidogrel, tirofiban and low molecular weight heparin were used in appropriate doses. Successful revascularisation of the target lesion was achieved in all cases. No mortality was observed at 30 days. The mean contrast volume was 30ml (± 10ml). Contrast induced nephropathy was observed in only one patient. Cardiogenic shock was seen in 2 cases, which was successfully managed with inotorpes, and IABP support was kept as backup. Distal vessel spasm was seen in 4 cases, which were managed with low dose of nitrates. Mild pulmonary edema was seen in 5 cases, which were managed with medications. Ventilator support was not required in any cases. Mild distal stent edge dissection was seen in one case and it was managed with a stent. Groin hematoma was seen in one case requiring blood transfusion. Distal vessel dissection was seen in one patient, which was managed with additional stent. Rise in creatinine (from 1.3 to 1.8 mg/dl) was seen in only one patient, which subsided in few days. Bench evaluation of the cordis guide and diagnostic catheters was performed with 3-bend tests, distal tip flexion tests and pushability and trackability. The results showed balanced parameters with diagnostic catheters compared to guide catheters.
Conclusions: Emergency angioplasty can be performed safely in patients using diagnostic catheters using low volume of contrast. Low contrast volume usage would result in lower incidence of contrast induced nephropathy and cardiac failures.



P1653

Liver function tests in patients admitted with acute decompensated heart failure

D David Cabrita Roque[1]; J Augusto[1]; A Sachetti[1]; D Faria[1]; A Gaspar[1]; L Melo[1]; T Bernardo[1]; J Simoes[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal*

Background: Episodes of acute decompensated heart failure (ADHF) can affect multiple organs in an unfavorably way, which may have an adverse impact on outcomes. We aim to analyze the prevalence and implications of abnormal liver function tests (LFT) in patients during hospitalization for ADHF.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for ADHF. The liver function tests included aspartate aminotransferase (AST) and alanine aminotransferase (ALT), which were evaluated during hospitalization (maximum values of AST and ALT) and at discharge. The cut-off values were those used by the central laboratory of our hospital (AST 15-37 U/L and ALT 12-78 U/L).
Results: The prevalence of abnormal LFT (above upper limit of normal for AST and ALT) was: during hospitalization AST 34.5%, ALT 14.3%; and at discharge AST 11.2%, ALT 6.2%. Abnormal LFT during hospitalization were associated with a higher risk of in-hospital death (12.4 vs. 0.8%, $p < 0.001$ for AST, 13.5 vs 3.8%, $p = 0.032$ for ALT).
Conclusions: Abnormal LFTs are frequent in ADHF during hospital stay and predict worse outcomes, probably in association with a state of more severe hypoperfusion and/or the use of drugs that affect the liver function. However, whether this association is causal and what are the true underlying mechanisms involved require further study.

P1654

Symptoms and signs of heart failure in patients presenting with acute decompensation who were receiving contemporary guidelines recommended therapy

Y Yuksel Cavusoglu[1]; ME Altinbas[1]; F Mutlu[1]
[1]*Eskisehir Osmangazi University, Eskisehir, Turkey*

Purpose: Evidence-based guidelines recommended therapy improves not only survival, quality of life and functional capacity in heart failure (HF), but it also improves symptoms and signs of HF. In general, symptoms and signs of acute decompensated HF have been reported in all comers admitted to the hospital regardless of having HF medication. In this study, we aimed to evaluate symptoms and signs of HF in patients presenting with acute decompensation who were receiving contemporary guidelines recommended therapy.
Methods: In this descriptive study, 446 patients admitted to the hospital with the diagnosis of acute decompensated HF, NYHA III-IV, LVEF $< 40\%$ and >18 years of age who were receiving contemporary guidelines recommended therapy were included in the analysis and HF patients' clinical characteristics, background therapy and signs and symptoms have been evaluated.
Results: Mean age of HF population was 67 ± 12 years. Comorbidities were CAD, previous MI, hypertension, diabetes, COPD and chronic renal disease in 68.6%, 55.3%, 60.1%, 41.9%, 29.9% and 35.9% of the cases respectively. 24.7% had atrial fibrillation. Mean EF was $25.4 \pm 7.9\%$, NT-proBBNP was 7667 ± 9876 pg/mL, creatinine level was 1.41 ± 0.88 and hemoglobin level was 12.4 ± 2 gr/dL. During admission, the use of beta blocker, ACEI/ARB, MRA, diuretic, ivabradin and digoxin were 93.7% (n = 418), 68.6% (n = 306), 46% (n = 205), 38.6% (n = 172), 12.8% (n = 57) and 21.1% (n = 94) respectively. At the time of initial presentation, 87.4% of patients (n = 390) reported dyspnea, 49.6% (n = 221)- ortopnea, 40.8% (n = 182)- paroxysmal nocturnal dypnea, 39.9% (n = 178)- dizziness, 37.7% (n = 168)- palpitation and 35.2% (n = 157)- chest discomfort. In terms of signs of HF, Juguler venous distension was found in 21.5% (n = 96) of patients, peripheral oedema- in 50.4% (n = 225), pulmonary crepitations- in 54% (n = 241), S3- in 11.7% (n = 52), S4- in 3.8% (n = 17), cardiac murmur- in 41.5% (n = 185), cold extremities- in 10.8% (n = 48), asites- in 18.2% (n = 81) and pleural effusion- in 22.2% (n = 99).
Conclusions: These results suggest that despite to high rates of the use of contemporary guidelines recommended HF therapy including diuretics, the most prevalent symptoms and signs in acute decompensation are still systemic and hemodynamic congestive symptoms and signs, in which dyspnea is the most frequently seen symptom and peripheral oedema and pulmonary crepitations are the most frequently sings of acute decompensated HF in current clinical practice.

P1655

Relationship between early drop in systolic blood pressure through the first 24 hours during admission and worsening renal function in patients with acute heart failure

T Kido[1]; T Okabe[1]; Y Oyama[1]; M Ono[1]; W Igawa[1]; S Ebara[1]; K Yamashita[1]; M Yamamoto[1]; S Saito[1]; K Amemiya[1]; T Yakushiji[1]; N Isomura[1]; H Araki[1]; M Ochiai[1]
[1]*Showa University Northern Yokohama Hospital, Division of Cardiology and Cardiac Catheterization Laboratories, Yokohama, Japan*

Background: Worsening renal function (WRF) is associated with poor prognosis in patients with heart failure (HF). We hypothesized that early drop in systolic blood pressure (SBP) is associated with WRF in patients with acute HF.
Purpose: Our purpose was to identify predictors of WRF including early drop in SBP.
Methods: We retrospectively investigated predictors of WRF in patients hospitalized for acute HF between April 2010 and March 2015. WRF was defined as a relative increase in serum creatinine of at least 25% or an absolute increase in serum creatinine ≥ 0.3 mg/dL from the baseline. SBP was measured at baseline and each 4 hours and early drop was defined as drop in SBP within first 24 hours.
Results: A total of 301 patients with acute HF were enrolled. The mean age was 71 ± 14.5 years and 56% were male. WRF occurred in 118 patients (39%). Univariate Cox regression analysis showed that early drop in SBP (odds ratio (OR), 1.018 per 1 mmHg; 95% confidence interval (CI), 1.010 to 1.026; $P < 0.001$), age, hemoglobin level, dose of intravenous furosemide, inotropic agents, and tolvaptan were associated with WRF. Multivariate Cox regression analysis showed that early drop in SBP (OR, 1.023 per 1 mmHg; 95% CI, 1.012 to 1.035; $P < 0.001$), inotropic agents (OR, 4.77; 95% CI, 1.809 to 13.45; P=0.002) and tolvaptan (OR, 2.96; 95% CI, 1.392 to 6.43; P=0.005) were associated with WRF.
Conclusion: Early drop in SBP may be one of the predictors of WRF in patients with HF.

P1656

Heart rate reduction and diastolic function in patients with decompensated systolic heart failure and left bundle branch block

D Darabantiu[1]; R Lala[1]; A Pop Moldovan[1]; RM Christodorescu[2]
[1]*Vasile Goldis Western University, Arad, Romania*; [2]*University of Medicine & Pharmacy Victor Babes, Timisoara, Romania*

Background and purpose: Patients with systolic heart failure and left bundle branch block (LBBB) have more severe diastolic dysfunction than patients without LBBB. Recent experimental studies have suggested that increased heart rate aggravates diastolic dysfunction in patients with LBBB. The purpose of our study was to evaluate the effect of heart rate reduction on diastolic function in patients with decompensated systolic heart failure and LBBB.
Methods: This prospective study recruited 50 consecutive patients admitted for decompensated heart failure, with left ventricular systolic dysfunction, sinus rhythm and heart rate > 70 b/min under guideline medical therapy, in whom heart rate reducing therapy with ivabradine was initiated. Patients were divided into 2 groups: group 1 (n = 22) with LBBB and group 2 (n = 28) without LBBB. For both groups echocardiography was recorded at baseline and after 6 months of ivabradine therapy. Parameters of diastolic function (mitral E velocity, E/A ratio, e' velocity, E/e' ratio, E deceleration time) were assessed and compared for both groups. Clinical characteristics and concomitant heart failure therapy were also assessed in both groups. Statistics: data were expressed as mean $\pm$ standard deviation or

percentages, comparisons between baseline and follow-up data were done with Student's paired and unpaired t test.
Results: Mean age was 64 ± 13 years in group 1 and 57 ± 11 years in group 2, heart rate at baseline was 88 ± 9 b/min in group 1 and 90 ± 9 b/min in group 2 (p = 0.4). After 6 months heart rate decreased to 68 ± 12 b/min in group 1 and 73 ± 10 b/min in group 2. Echocardiographic changes of diastolic function parameters in both groups of patients are illustrated in the table below. Concomitant heart failure therapy was similar in both groups. Mean ivabradine dose at 6 months was 11 ± 3 mg/day in group 1 and 10.8 ± 3 mg/day in group 2 (p = 0.6).
Conclusion: In patients with decompensated systolic heart failure, LBBB and sinus rhythm, heart rate reduction with ivabradine seems to improve diastolic function at 6 months.

	Group 1 (LBBB +)		Group 2 (LBBB-)			
	Baseline	Follow-up	Differences(p)	Baseline	Follow-up	Differences(p)
E velocity (cm/s)	84±24	75±24	0.09	85±20	80±21	0.4
E/A ratio	1.7±1.1	1.1±0.8	0.02	2.1±1.1	1.5±1.1	0.1
e' velocity (cm)	5.6±1.5	6.8±1.6	0.03	6.4±1.7	7.4±1.6	0.2
E/e' ratio	15.4±4	11.3±4	0.02	13.6±4	11.2±4	0.07

CHRONIC HEART FAILURE

P1657
Asymptomatic left ventricular dysfunction is a predictor of short and long-term mortality among patients with myocardial infarction in southeast Asia: Is there a difference between gender?

J Jakrin Kewcharoen[1]; V Kittipibul[1]; P Suttirut[1]; V Lertsuwunseri[1]; S Srimahachota[1]; A Ariyachaipanich[1]
[1]*Chulalongkorn University, Bangkok, Thailand*

Background: Decreased left ventricular ejection fraction (LVEF) is associated with worse outcomes in patients with ST-elevation myocardial infarction (STEMI). However, little is known about this association in developing countries.
Purposes: The aim of the study was to evaluate the impact of LVEF on mortality rate in patients undergoing primary percutaneous coronary intervention (PCI) and its differences between gender.
Methods: We conducted a retrospective study of all patients with a diagnosis of STEMI who underwent primary PCI at a tertiary care hospital in Thailand from January 2011 to December 2015. Patient characteristics, treatments, and outcomes were gathered. T-test, and Chi-square were used to analyze.
Results: A total of 755 patients (mean age 60.2 ± 13.6 years, 74.8% male, 55.4% hypertension, 30.8% diabetes mellitus and 70% dyslipidemia) were included. Mean LVEF was 50 ± 13%. The LVEF was ≥50%, 35-49% and < 35% in 53.4%, 33.1% and 13.4% of patients. The 30-day mortality rate was higher in patients with LVEF between 35-49% and <35% (Odd ratio 2.3 and 8.4, p = 0.02 and < 0.001, respectively). There were also statistically significant higher 6-month and 1-year mortality rates in patients with lower LVEF. At baseline, the LVEF was not different between male and female (49.7 ± 13.7 vs 50.9 ± 14.3, p = 0.30). LVEF < 35% was associated with 30-day, 6-month and 1-year mortality in both male and female patients (p < 0.05 for all).
Conclusions: In this single center experience, LVEF appeared to be a predictor of short-term and long-term outcomes among patients with STEMI who underwent primary PCI in Thailand. The effect of LVEF on mortality rate was relatively the same between gender.

P1658
Clinical features of patients with heart failure with very reduced ejection fraction (hfvref)

EJJ Eduardo Julian Jose Chuquiure[1]; J Oscar Fiscal-Lopez[1]; R Nayeli Isidro-Hernandez[1]; L Ana Marin-Mejia[1]; N Frida Rodriguez-Quiroz[1]; N Gabriela Mendez[2]; J Maria Jose Chuquiure Gil[3]
[1]*Instituto Nacional de Cardiologia "Ignacio chavez", Mexico City, Mexico*; [2]*Universidad del estado de México, Medicina, ciudad neza, Mexico*; [3]*Instituto Tecnologico de Estudios Superiores de Monterrey, Escuela de Medicina, Monterrey, Mexico*

Purpose: At present the diagnostic criteria of Heart Failure include patients with Left Ventricular Ejection Fraction (LVEF) less than 40%. But in our Unit we detected a population with very low ejection Fraction (<25%) (HFvrEF). The principal purpose is to describe a patients with HFvrEF.
Material and method: We analyzed consecutively Mexican patients from Heart Failure Clinic of the Instituto Nacional de Cardiología. All over 18 years old, both genders with clinical, laboratory and Imaging Diagnosis according 2016 European and AHA-ACC clinical Guidelines. Both Groups based on LVEF criteria: HFvrEF: LVEF < 25% and HFrEF : LVEF >25.1% -40%. We determine retrospectively: Natural History, Clinical characteristics, follow-up from diagnosis, pharmacological treatment, hospitalizations and re-admissions. For statistical difference we declare p value equal or less than 0.05.
Results: According criteria, we describe 109 patients with HFvrEF and 131 with HFrEF. HFvrEF ranges were 8 -25%. Both groups were homogeneous in: General characteristics, Gender, Obesity Rate, Sinus rhythm, Diabetes,Hypertension, Dyslipidemia, Smoker History, Myocardial Infarction and BMI. More Valvular Heart disease patients were seen in HFvrEF group. Transplant and LVAD program were not available for patients.
Mean Follow-up: HFvrEF : 5.80 + 0.63 years (2mo-17.56 y) vs HFrEF: 6.16 + 0.78 years (3mo -18.53y), observing annualized re-hospitalization rates 18.34 vs. 11.80 (OR 1.68 ,p < 0.05). Admissions to Emergency Room (greater than 2) were more frequent in HFvrEF group 5.50% vs. 3.47%. Also in HFvrEF group compared to HFrEF group, a higher event rate was observed at follow up in: Renal Failure (3.67% vs. 1.38%), Dialysis (1.83% vs. 0.69%), PTCA (11.93% vs. 10.42%) and CABG (1.83% vs. 0.96%).
According with new recommendations of 2016 guidelines our therapeutics pattern included: Sacubitril/Valsartan (HFvrEF 16.51% vs HFrEF 6.94%) and Ivabradine (HFvrEF 3.67% vs HFrEF 2.08%).
Conclusions: Of our experience we propose Heart failure Group with Very Low ejection Fraction, Observed under exclusively pharmacological treatment for a mean period of 5.80 years. We determined a higher index of clinical events. We suggest the need to evaluate long-term clinical characteristics such as the new therapeutic strategy.

P1659
Heart failure with mid range ejection fraction (HFmrEF): a retrospective observational study in a single centre in the eastern province of Saudi Arabia

MM Alqaseer[1]; SM Abouzobeida[1]; ZA Al Naser[1]; MA Allwaim[1]; M Hussain[1]; B Mushannen[1]; M Alkharasani[1]; U Ismail[1]
[1]*King Fahad Specialist Hospital, Cardiology Department, Dammam, Saudi Arabia*

Background: The recent ESC/HFA heart failure guidelines have introduced a new suggested classification, where patients are divided into three categories: heart failure with reduced Ejection Fraction (HFrEF), preserved EF (HFpEF), and mid range EF (HFmrEF). The new entity described as HFmrEF includes patient with an EF between 40 and 49%. There is scarcity of research describing this cohort of patients. To better understand this particular patient population, we have analyzed all the heart failure patients in a single center in the Eastern Province of Saudi Arabia who qualify as HFmrEF.
Methods: Retrospective observational study looking at consecutive patients with heart failure who had an echocardiogram done between January 1st and December 1st 2015 with an ejection fraction quantified between 40 and 49%. Demographic data of those patients were collected along with their comorbidities, risk factors, and anti-failure therapies, if any.
Results: 348 patients with HFmrEF were identified. 52.58% were male. Out of 348 patients, 146 were diabetic, constituting 41.95% of the total population. The majority of the patients, 71.26% of the cohort, were hypertensive. 40.51% had renal impairment, defined by an eGFR < 60. 41.09% of the patients had received cardiotoxic cancer therapies and were labeled as chemo-induced cardiomyopathies. With regards to medications, 61.20% were on BB, 56.60% were on ACE-i/ARB, and 18.39% were on MRA. 43.1% were on diuretic therapies. The majority of the patients that were on anti-failure therapies were those with a lower EF ranging between 40-44%.
Conclusion: We present our descriptive data of patients with HFmrEF in a single institution in the astern province of Saudi Arabia. The sample might not be representative as our center is a tertiary cancer and renal transplant facility that may account for the large prevalence of chemo-induced cardiomyopathy and renal impairment. Interestingly, the patients with EF of 40-44% are the ones that are predominantly receiving the conventional anti-failure therapies and treated in a similar fashion to HFrEF patients. Further follow up studies are needed to assess their outcomes.

P1660

A systematic review of clinical prediction rules for the diagnosis of chronic heart failure in the community and their validation in a novel cohort

J Gallagher[1]; D Mccormack[2]; S James[1]; S Zhou[1]; C Keane[1]; C Watson[1]; M Ledwidge[1]; K Mcdonald[1]
[1]University College Dublin, Dublin, Ireland; *[2]University College Dublin, gHealth Research Group, Dublin, Ireland*

Background: Early diagnosis of heart failure in the community may be hampered by lack of access to diagnostics. Clinical predication rules, which have been included in diagnostic guidelines, may help rationalise access to diagnostics for those who are most likely to have heart failure.
Purpose: This study sought to review the literature for clinical prediction models for the diagnosis of patients with heart failure in the community. It also sought to validate the models in a novel cohort of patients with a suspected diagnosis of heart failure referred to a rapid access diagnostic clinic from the community.
Methods: MEDLINE and EMBASE were searched from 1946 to Q2 2016 followed by hand searches of retrieved reference lists, and consultation with experts in the area. Studies were eligible if they contained at least one multivariable model for the diagnosis of chronic heart failure. Studies relating to acute heart failure were excluded. We also sought to validate the models in a novel cohort of patients with a suspected diagnosis of heart failure referred to a rapid access diagnostic clinic.
Results: In total, 5055 articles were identified with nine articles subsequently meeting the eligibility criteria. Three models had undergone internal validation and four had undergone external validation. No clinical impact studies have been completed to date. Area under the curve (AUC) varied from 0.74 to 0.93. Four rules were validated in a novel cohort. AUC varied from 0.60 to 0.65 in the novel cohort for clinical models alone with AUC up to 0.89 in combination with ECG and BNP. The AUC for B-type natriuretic peptide (BNP) was 0.86 (95% confidence interval 83.3%-88.6%).
Conclusion: This review demonstrates that there are a number of clinical prediction rules relevant to the diagnosis of heart failure in the literature. Clinical impact studies are required to compare the use of clinical prediction rules and biomarker strategies in this setting.

P1661

Test-retest-Reliability of explorative measurement of CEC and EPC from peripheral blood in patients with systolic and diastolic heart failure, diabetic nephropathy and arterial hypertension

J Wagner[1]; M Farinnaci[2]; S Beckmann[1]; S Litmeier[1]; F Weisrock[1]; M Fritschka[3]; S Radenovic[1]; D Djawid Hashemi[1]; E Tahirovic[1]; B Pieske[1]; W Dinh[2]; HD Duengen[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; *[2]BAYER Pharma AG, Wuppertal, Germany*; *[3]German Heart Institute of Berlin, Department of Cardiology, Berlin, Germany*

Background: We distinguish between HF with reduced ejection fraction (HFrEF, LVEF < 45%) and preserved EF (HFpEF, LVEF≥45% and echocardiographic evidence of diastolic dysfunction).HF in particular is the most common reason for elderly for hospitalization and its prevalence is rising.
Circulating endothelial cells (CEC) and endothelial progenitor cells (EPC) have been described as new non-invasive markers of endothelial damage. They are measureable in peripheral blood and correlate with other markers of endothelial function. Therefore, CEC and EPC can depict the presence and extent of vascular damage.
Ability to estimate, quantify and observe changes in CEC and EPC levels reliably will open new doors in the screening, treatment and follow-up of patients with heart failure and other cardiovascular diseases.
However, uniform procedures to isolate and determine the number of CEC still have to be established.
Aim: We carried out a test-retest-study in which we applied the same method of estimating CEC levels twice and compared the results.
Methods: Endo-CEC was an observational trial in HFrEF patients, HFpEF patients, patients with diabetic nephropathy and patients with arterial hypertension. Blood samples were obtained from in total 101 patients and CECs and EPCs were determined in the peripheral blood from 25 HFpEF patients, 25 HFrEF patients, 25 patients with diabetic nephropathy and 26 patients with arterial hypertension.
To evaluate the test-retest-reliability blood was taken at two points of time and CEC and EPC levels were estimated and expressed both in CEC/EPC per ml and as a percentage of peripheral blood mononuclear cells.
Results: Out of 101 patients included in this analysis, 25 had Diabetic nephropathy of which 21 (84%) were male and 4 (16%) were female, out of 25 HFrEF patients, 20 (80%) were male and 5 (20%) were female. In the group of HFpEF patients, 15 (60%) were male and 10 (40%) were female while the group of arterial hypertension was evenly distributed with 14 (54%) men and 12 (46%) women.
Comparing the CEC/ml and CEC/PMNC levels of the visits, no correlation between the two visits could be detected (ICC CEC/ml: 0.077; ICC CEC/PMNC 0.19).
The intraclass correlation of EPC measurements was statistically significant in each group (EPC/ml: Arterial Hypertension: ICC=0.683; DiabNeph; ICC=0.946; HFpEF: ICC=0.665; HFrEF: 0.946).
Conclusion: This method of determining the number of CEC via flow cytometry is not reliable to use it as a prognostic marker or follow-up-parameter for the treatment period of heart failure or diabetic nephropathy patients.
Therefore, there is still need to enhance the method of measuring CECs by identifying disturbing factors or reasons.
As understanding and estimating the occurrence of CEC and EPC promise high potential for further treatment and supervision of heart failure and other diseases associated with endothelial dysfunction, there is absolute necessity to do further research.

P1662

Time trends in the use and appropriateness of natriuretic peptide testing in primary care

F H Frans Hendrik Rutten[1]; MJM Valk[1]; NP Zuithoff[1]; BJ Broekhuizen[1]; A Mosterd[1]; AW Hoes[1]
[1]University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands

Diagnosing heart failure (HF) is difficult, relying on medical history, symptoms and signs only. Clinical guidelines recommend natriuretic peptides (NPs) as an additional diagnostic test, notably to exclude HF in suspected patients. NP testing is available since 2003 for primary care in the Netherlands, but little is known about its uptake.
Aim: To evaluate the trend in ordering and appropriateness of NP testing in primary care.
Methods: An observational study performed between January 2005 and December 2013. Nine Dutch general practices participated, with 21,000 registered persons (≈4,300 aged 65 years and over). The total number of patients undergoing NP testing each year was calculated per 1,000 patient years (PY) based on the total practice population. NP-levels were used to assess whether NP-testing was applied to exclude or confirm HF.
Results: The number of NP testing increased from 2.5 per 1,000 PY in 2005 to 14.0 per 1,000 PY in 2013, with a peak in 2009 of 15.6 per 1,000 PY. The proportion of subjects with NTproBNP below 125 pg/mL (the exclusionary threshold recommended by the European Society of Cardiology HF guidelines) was on average 30%, and highest in the first year with 47%.
Conclusions: After a rapid uptake of NP testing in primary care from 2005 onwards, the use of it seemed to stabilize after 2009. Although guidelines recommend NP testing to rule out heart failure, the percentage of patients with NTproBNP < 125 pg/mL suggests that GPs use it more often as a confirmatory test.

P1663

Non-invasive monitoring of peripheral and cardiac influence on exercise limitation in patients with heart failure with preserved ejection fraction

SB Beckmann[1]; F Weisrock[1]; M Fritschka[2]; J Wagner[1]; D Djawid Hashemi[1]; E Tahirovic[1]; S Radenovic[1]; A Busjahn[3]; B Pieske[1]; T Krahn[4]; W Dinh[4]; HD Duengen[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; *[2]German Heart Institute of Berlin, Department of Cardiology, Berlin, Germany*; *[3]Health Twist, Berlin, Germany*; *[4]BAYER Pharma AG, Pharmaceutical Division, Wuppertal, Germany*

Background: Heart failure (HF) is a major reason for mortality and morbidity in societies all over the world and will gain importance in an aging society. About half of HF patients suffer from heart failure with preserved ejection fraction (HFpEF) which is till now neither fully understood nor treatable. The main symptom of these patients is exercise limitation. Current data provides evidence that this limitation is caused by both cardiac and peripheral influences. Monitoring of these influences in cardiopulmonary exercise testing (CPET) can therefore be of big interest, e.g. when assessing effects of a yet to develop HFpEF therapy.
Methods: To provide an insight into the limitations caused by HFpEF, we recruited 51 subjects of same gender and BMI distribution that suffered from either arterial hypertension (HT) without any sign of HF ($n = 24$, 58% male, BMI 29.3 ± 6.4) or HFpEF ($n = 27$, 56% male, $p = 1.000$, BMI 28.2 ± 4.1, $p = 0.455$) for the ENDO-CEC trial. To assess their individual grade of exercise limitation all subjects performed a standardized six minute walking test (6-MWT) and completed CPET protocol in which non-invasive cardiac output monitoring (NICOM) by bioreactance was conducted simultaneously.
Results: As expected, HFpEF subjects were significantly limited in all exercise related parameters. They reached a lower maximum power stage at CPET (HT: 121 ± 10, HFpEF: 100 ± 20 Watt, $p = 0.001$), had a lower maximum cardiac index (HT: 6.8 ± 1.3, HFpEF 6.0 ± 1.2 l/min/m^2, $p = 0.029$), a lower VO2 at maximum exertion (HT: 22.7 ± 5.9, HFpEF: 17.9 ± 2.0 ml/kg/min, $p = 0.001$) and a higher

VE/VCO2 slope (HT: 29.8 ± 4.1, HFpEF: 33.0 ± 4.8, p = 0.019). Additionally they covered a shorter distance in 6-MWT (HT: 538 ± 81, HFpEF 470 ± 67m, p = 0.005). Non-invasive monitoring of cardiac function shows us that the lower maximum cardiac index in HFpEF patients is not caused by reduction in stroke volume recruitment (HT: 151 ± 16, HFpEF 176 ± 53, percentage of maximum stroke volume compared to minimal stroke volume, p = 0.036) but only by a reduced peak heart rate (HT: 81 ± 10, HFpEF: 71 ± 14 percent of predicted maximum heart rate, p = 0.011). HFpEF subjects were furthermore slightly but insignificantly limited peripherally, meaning in their arteriovenous oxygen difference (AVDO2) calculated using the Fick principle (HT: 134 ± 33, HFpEF 121 ± 28, milliliter oxygen difference per liter blood flow per minute p = 0.155). When looking at the AVDO2 alone one finds that 57% of all HFpEF subjects had an AVDO2 below average with only 33% of HT subjects respectively. The lowest AVDO2 values were all reached by HFpEF subjects while the highest values were reached by HT subjects.
Conclusion: NICOM during CPET can show that HFpEF subjects are both centrally and to a certain extent peripherally limited during exercise compared to HT subjects. This is why a combined CPET and NICOM assessment can be of use for monitoring changes in HFpEF patients, e.g. in interventional pharmacological trials.

P1664
Arterial stiffness indices in a chronic heart failure population: a comparison between preserved and reduced ejection fraction population

L C Luiz Claudio Danzmann[1]; TS Moreira[1]; EL Garcia[2]; RSA Fonseca[1]; MG Menezes[2]; V Predebon[1]; BO Burmeister[1]; AJ Lagoeiro Jorge[3]; ET Mesquita[3]; LJ Santos[1]; E Bartholomay Oliveira[1]
[1]Universidade Luterana do Brasil, Porto Alegre, Brazil; *[2]Hospital de Clínicas de Porto Alegre - UFRGS, Porto Alegre, Brazil*; *[3]Universidade Federal Fluminense, Niteroi, Brazil*

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Background: patients with heart failure with preserved ejection fraction (HFpEF) have important influence of arterial stiffness (AS) that may impair the left ventricle-arterial coupling.
Purpose: to test differences between AS indices of a population with HFpEF and heart failure with reduced ejection fraction (HfrEF).
Method: the population were outpatients met heart failure (HF) Boston Criteria, clinically stable, consecutivelly admited in a HF clinic, wich were dichotomized according to LVEF measured by echocardiography. AS indices were estimated by previously validated logarithmic equation from the measurement of blood pressure (BP) by brachial oscillometric method (Wassertheurer S, et al.). The indices studied were the central blood pressure (Central SBP); total vascular resistance (Vasc Res Total); BP augmentation and pulse wave velocity (PWV). To test the difference between the means was used the Student's T test, qui^2 and a P $<$0.05 was considered statistically significant.
Results: 77 patients were included, mean age was 63 ± 13 years old, 58% were male, and 52.2% were ischemic and 52% were NYHA class II. The HFpEF population had higher prevalence of hypertension (71,4% x 92,3%, P=0,02). The indices central SBP and Total Vasc Res were significantly higher in patients with HFpEF.
Conclusion: In this preliminary analysis of our population of outpatients with heart failure we found out a the indices Central SBP and Total Vasc Res significantly higher in the group with HFpEF.

Arterial stiffness in HFrEF and HFpEF

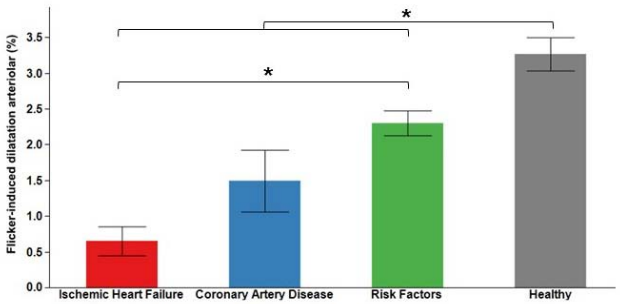
Arterial stiffness indices	LVEF $<$ 50%	LVEF≥50%	P
Central SBP (mmHg)	109,22±18,33	119,57±18,75	0,03
Total Vasc Resistance (mmHg/ml)	1,25±0,19	1,37±0,25	0,04
Augmentation BP(mmHg)	8,68±7,87	12,76±10,27	0,07
PWV (m/s)	7,59±1,85	8,10±1,46	0,25
Central PP (mmHg)	34,80±14,5	38,90±14,6	0,25

HFrEF- heart failure with reduced ejection fraction; HFpEF-heart failure with preserved ejection fraction; LVEF - left ventricle ejection fraction; SBP-systolic blood pressure; Vasc-vascular; BP - blood pressure;PWV-pulse wave velocity; PP- pulse pressure.

P1665
Severe retinal endothelial dysfunction in patients with ischemic cardiomyopathy

J Jens Barthelmes[1]; MP Naegele[1]; V Ludovici[1]; I Sudano-Noll[1]; F Ruschitzka[1]; AJ Flammer[1]
[1]University Heart Center, Cardiology, Zurich, Switzerland

Background: Heart failure (HF) is the most prevalent heart disease worldwide with coronary artery disease (CAD) being the most frequent aetiology. Endothelial dysfunction is associated with cardiovascular risk factors; it is important for the development and progression of atherosclerosis and its presence is a prognostic marker for future cardiovascular events. Endothelial function is commonly measured by Flow-mediated vasodilatation (FMD) of the brachial conduit artery. Retinal vessel analysis (RVA) is a novel and unique method allowing to assess microvascular function by measuring endothelial dependent flicker-light induced vasodilatation (FLID) using videography of the retinal vessels. However, whether retinal vascular function is associated with the severity of CAD is not known.
Purpose: We therefore studied FLID of the retinal arteries in patients with severe disease (heart failure due to CAD), in patients with documented CAD, and in patients with CV risk factors, as well as in healthy controls.
Methods: Patients were examined with a dynamic vessel analyser (Germany). Mydriasis was induced with 0.5% tropicamide in one randomly selected eye. Retinal arteriolar dilatation was measured after provocation with 12.5 Hz optoelectronic flicker light. Temporal segments of one retinal arteriole and venule that were 0.5 to 2 optic disc diameters away from the optic disc were analysed. After acquisition, the results from the three flicker periods were averaged and percent dilatation of arteriole from baseline (i. e. arterial FLID) was calculated.
Results: 277 participants (median age M=63.8 ± SD=8.0, 36.8% female) were included in this study (41 patients with CAD and heart failure [LVEF mean 35.4 ± 11.5%, median NYHA=II], 18 patients with CAD, 142 with cardiovascular risk factors and 76 healthy controls). RVA revealed significant group differences (ANOVA F(3, 67.94)=25.7, p $<$ 0.001) in arterial flicker-light induced vasodilatation: healthy controls M=3.27% ± SD=2.02%; risk factor patients 2.30 ± 2.08% , CAD patients 1.42 ± 1.76%, and ischemic HF: 0.65 ± 1.30%, cf. Figure 1. Post-hoc Tukey tests showed significant group differences in arterial FLID between healthy individuals and all other groups (max. p = 0.0034) as well as the risk factors group and ischemic HF (p $<$ 0.001).
In FMD no significant differences (ANOVA F(3, 273)=1.91, p = 0.1278) were found between groups although the same trend from healthy to HF was visible.
Conclusions: In this preliminary study, we demonstrate significant and profound retinal microvascular dysfunction in patients with heart failure due to CAD, although all patients were treated with state-of-the art medication. Furthermore, FLID seems to mirror the severity of CAD, with gradual reduction from healthy, to patients with RF and overt CAD disease. Therefore, dynamic retinal vessel changes to flicker light is a promising new tool for the assessment of the severity of disease in CAD. More studies in this field are warranted.



Progressing microvascular dysfunction

P1666
Lipids, oxidative stress and inflammation as sex-specific predictors of systolic left ventricular dysfunction in acute coronary syndrome

N Semerdzieva[1]; S Denchev[2]; M Gospodinova[2]; S Dimitrov[3]; V Lozanov[4]; R Abrashev[5]; J Hristova[6]
[1]University Hospital Alexandrovska, Clinic of Cardiology, Sofia, Bulgaria; *[2]Medical Insitute of the Ministry of Internal Affairs, Clinic of Cradiology, Sofia, Bulgaria*; *[3]Second MHAT, Department of Invasive Cardiology, Sofia, Bulgaria*; *[4]Medical University of Sofia, Department of Biochemistry, Sofia, Bulgaria*; *[5]Bulgarian Academy of Sciences, Stefan Angeloff Institute of Microbiology, Sofia, Bulgaria*; *[6]Medical University of Sofia, Central Clinical Laboratory, Sofia, Bulgaria*

Backgroud: Antioxidant and lipid-lowering effects of estrogen are mechanisms for the resistance of women to atheroma growth. Oxidative stress and inflammation have sex-specific influence on acute coronary syndrome (ACS) prognosis.
Purpose: The study examined the relationship of lipids with oxidative, inflammatory markers and coronary disease severity and their significance as predictors for development of left ventricular systolic dysfunction after ACS.

Methods: Indices of systolic function, serum lipids (total cholesterol, TChol; high-density lipoproteins, HDL; low-density lipoproteins, LDL; triglycerides, TG), oxidative (oxidized LDL, oxLDL; extracelluar superoxide dismutase activity, ecSOD) and inflammatory (white blood cell count, WBC; high-sensitive C-reactive protein, hsCRP) markers were measured in 274 (128 women, 46.7%), 111 (40.5%), 68 (24.8%), 200 (72.9%) and 173 (61.1%) acute coronary syndrome patients, respectively. The methods used were 2D-echocardiography, enzyme and immunologic laboratory tests. Repeated echocardiography at the six month was available in 147 (43.6%) patients. SYNTAX scores were calculated based on 241 (87.9%) coronary angiographies performed. At baseline 65.8% patients were on statin therapy.
Results: In the female group several serum lipid fractions correlated considerably with coronary atherosclerosis severity (r= - 0.300, p = 0.033 for HDL; r= 0.336, p = 0.016 for TG), acute rise of oxLDL (r=0.268, p = 0.049 for TChol; r=0.359, p = 0.016 for TG) and hsCRP (r=0.369, p = 0.007 for TG); in the male group the only significant association was of TChol with leukocytosis (r=0.234, p = 0.043). Among the acute (WBC, SYNTAX score in men; WBC, hsCRP and SYNTAX score in women) and chronic systolic dysfunction predictors (LDL, TG, hsCRP, SYNTAX scores in men; TChol, WBC, SYNTAX scores in women), after multivariate regression analysis only SYNTAX score predicted abnormal ejection fractions in acute phase in male patients (OR 1.066; CI 1.102-1.124; p = 0.016); inflammatory markers were related to both the acute (hsCRP OR 1.036; 95% CI 1.003-1.070; p = 0.032; WBC OR 1.230; CI 1.024-1.478; p = 0.027) and chronic (WBC OR 1.357; 95% CI 1.002-1.837; p = 0.049) contractile dysfunction in female patients. The recorded incidence of systolic dysfunction was independent of the usage of statin therapy at baseline (men - 23.1% vs 41.7%, p = 0.103; women - 17.5% vs 30.4%, p = 0.232).
Conclusion: In ACS lipids may have indirect sex-specific role for myocardial damage through oxidative stress and inflammation. Inflammatory markers are characteristic for female sex predictors of acute and chronic systolic dysfunction.

P1667

Wearable defibrillator protected optimization of therapy and development of LVEF in newly diagnosed heart failure

HN Naegele[1]; DS Stierle[1]; MAK Khan[1]; KK Krause[1]
[1]*Albertinen Hospital, Heart Centre, Dpt. Heart Failure & Device Therapy, Hamburg, Germany*

Introduction: Guidelines recommend that prophylactic defibrillator (ICD) implantation in patients with newly diagnosed heart failure (HF) should be postponed after an intervention and a period of optimization of medical therapy. The wearable defibrillator (WD) offers arrhythmic protection during that time. Duration and efficacy of such a strategy is currently under discussion.
Method: We analyzed data of all patients who received a WD in the years 2014-2016 in our center (n = 141) for newly detected HF (mean LVEF 26 ± 8%) under further medical therapy only (n = 62) or an additional intervention (coronary stenting, bypass or valve surgery; n=79). Patients were re-evaluated at 1 and 3 month, or later and medical therapy was up-titrated whenever possible.
Results: Mean wear time of the WD was 65 ± 39 days. Neither death nor any arrhythmia needing shock therapy was observed. In 72% of patients the LVEF increased >35% and ICD implantation could be omitted. Some patients needed >6 month for that improvement. LVEF increased similarly in interventional (+ 53%) and medically treated patients (+ 73%).
Discussion: Therapy can be safely optimized in newly diagnosed HF patients with reduced LVEF. ICD implantation can be omitted in the majority of these patients. The probability of a WD discharge seems to be low in this cohort.

P1668

Remote results of percutaneous coronary interventions at patients chd with reduced of the left ventricle contractility

HG Fozilov[1]; T Abdullaev[1]; I A Igor Tsoy[1]; RSH Bekbulatova[1]; AM Karimov[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

The purpose: to study clinical efficiency percutaneous coronary interventions and its influence on myocardial contractility at pts CHD with low left ventricle ejection fraction (LVEF) in the remote period (12-24 Mec) without estimate viability of the myocardium.
Materials and Methods: 1266 pts with various forms of CHD were included. At pts CHD with reduced of LV contractility of the left ventricle 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 LVEF (less than 45 %) at which it was possible to study the remote results. Pts of a male have made - 80.0 % (52), and female – 20.0 % (13). The age of pts fluctuated from 39 until 76 years, and has on the average made 59.5 ± 8.4 years. From the standard risk factors most often met an arterial hypertensia - at 87.7 %, (57) pts, hyperlipidemia – at 90.7 % (59); a diabetes mellitus at 40 % (26) pts. The LVEF fluctuated from 27.3 % to 45%, and has on the average made 38.5 ± 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 of pressure II-IV FC, and in 15.4 % (10) cases at an unstable angina. Three-vascular defeat of a coronary channel took place in 47.7% (31) cases, two-vascular in 29.2% (19) and one-vascular defeat in 23.1% (15) cases. At pts with multivascular defeat (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 revasculization were performed. 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) bioresorbable vascular skaffolds.
Results: In our research frequency of angiographic success at implantation stents at pts CHD with low LVEF 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 remote period the LVEF fluctuated from 30% to 61.5 %, and has on the average made 43.5 ± 6.9 % (p=0.000). Increase the fraction of emission LV was observed at 60% (39) pts, decrease at 15.4 % (10) pts and at 10.8 (7) pts of LV ejection fraction has not changed. The lethal outcome has developed at 8 (12.3%) pts, operation CABG is executed at 1(1.5%) the pt.
The conclusion: Thus, frequency of clinical success at a hospital stage of supervision has made 85.7% (59) cases. In the remote period authentic increase of an average index of fraction of ejection left ventricle to 43.5% ± 6.9 % was marked at initial 38.5 ± 4.9 % (p=0.000).

P1669

Heart failure nurses, luxury or necessity? a substudy of the INTERACT-in-hf (improving knowledge transfer to efficaciously raise level of contemporary treatment in heart failure) study

K Baldewijns[1]; HP Brunner La Rocca[2]; S Bektas[2]; L De Maesschalck[1]; J Boyne[2]
[1]*Thomas More Kempen, Mobilab, Geel, Belgium*; [2]*Maastricht University Medical Centre (MUMC), Department of Cardiology, Maastricht, Netherlands*

Background: The complex nature of heart failure (HF) and its high burden challenge the management of national health systems. To address these questions, international associations of cardiology developed guidelines for best practice in heart failure care. However, implementation of these guidelines is a challenge, partly due to health care organizations.
The INTERACT-in-HF study was set up to investigate current practice in chronic HF care from different perspectives in three different European regions (Flanders (Belgium), region Maastricht and Aachen). This study showed that HF nursing is well established in the Netherlands and less established in Flanders and Germany.
Purpose: The ESC guidelines state that it is important to provide HF-patients with disease specific information in order to improve self-care and to make them able to make their own justified lifestyle decisions. Educating patients is supposed to be an important role of HF-nurses.
This substudy investigates the knowledge and implementation of guidelines concerning patient education and the role of HF-nurses according to patient education.
Methodology: A quantitative research design was used. All HF-nurses in Flanders, the Netherlands and Germany, being members of respectively the Belgian working group on cardiovascular nurses, the Dutch Nursing Cardiovascular Association and German association of HF-nurses, were approached in order to fill in a digital questionnaire about their knowledge and implementation of guidelines concerning patient education.
Data were analysed using SPSS v 23.0 (IBM).
Results: 23 Flemish, 59 Dutch and 7 German HF-nurses with cardiology experience participated in our survey. Almost every HF-nurse knows and implements the ESC-guidelines and their own national guidelines. Little regional differences were found between HF-nurses concerning knowledge and implementation of existing guidelines. Flemish nurses educate their patients significantly more about vaccination than their Dutch or German colleagues (X2, p = 0,003) and information about sexuality is mentioned less by all of them.
Conclusion: Despite the fact that ESC guidelines recognize the role of HF-nurses, few of them are actually active in Flanders and Germany. Though there are regional differences in health care organization between the Netherlands, Flanders and Germany, all HF-nurses in the participating centres offer education, and little difference was found regarding knowledge and implementation of guidelines.

P1670

A French national observational study on 2013 ESC Heart Failure guidelines: Impact on therapeutic management of chronic heart failure patients by office based cardiologists: RECO-Coeur study

P De Groote[1]; J Gauthier[2]; A Achouba[3]
[1]*Lille University Hospital, Institut Coeur-Poumon, Lille, France*; [2]*CNCF, Cannes, France*; [3]*Novartis Pharma S.A.S, Rueil-Malmaison, France*

On behalf of: RECO-Coeur study

Aim of the study: to determine the prescription rates of different drugs in a group of ambulatory patients with stable chronic heart failure (CHF) in NYHA class II-IV followed by French cardiologists.
Methods: Non-interventional, multi-center, cross-sectional study carried out with office based French cardiologists. Each investigators had to include the first 8 consecutive eligible patients seen in outpatient. Data from medical records and study visit were collected and recorded through an electronic case report form.
Results: 263 cardiologists included from 07/15/2015 to 10/28/2016, 2562 patients, age: 73.4 ± 11.9 years old, 1624 (63.4%) male, NYHA class II: 66%, hypertension: 62%, diabetes mellitus: 28,5%, renal impairment: 21%, coronary artery disease: 43%, peripheral arterial disease : 14%, COPD: 15,5%, depression or cognitive disorder: 10%. Mean LVEF was 43.1 ± 12 %, 941 patients (37%) had a LVEF < 40%, 845 (33%) a LVEF between 40 and 50% and 776 (30%) a LVEF ≥ 50%.
Prescription rates and doses achieved for each classes of drugs are presented in the Table.
In conclusion: there is no great difference in prescription rates of CHF drugs in subgroups of patients divided according to LVEF. In comparison to previous French registries, in patients with LVEF < 40%, there is a small increase in prescription rates of recommended CHF drugs and in recommended doses but there is still room for improvement, particularly for betablocker therapy.

Treatment of the study population

Drugs	LVEF < 40%	LVEF 40-50%	LVEF ≥ 50%
ACE-I	66%	59%	45.5%
Target doses	49%	51%	52%
≥50% target doses	31%	29%	32%
ARB	19%	22%	28%
Target doses	22%	27%	28%
≥50% target doses	31%	30%	28%
Betablockers	84%	81%	73%
Target doses	27%	24%	23%
≥50% target doses	37%	39%	39%
MRA	35.5%	26%	21%
Diuretics	76%	66%	74%
Ivabradine	5%	6%	3%
LCZ696	2.7%	2%	0.1%
Digoxin	5%	6%	10%

P1671

Optimisation of guidelines adherence is associated with better prognosis in outpatients with heart failure with low ejection fraction (HFrEF): the QUALIFY registry

M Michel Komajda[1]; MR Cowie[2]; L Tavazzi[3]; P Ponikowski[4]; SD Anker[5]; GS Filippatos[6]
[1]*AP-HP - Hospital Pitie-Salpetriere, University Pierre & Marie Curie Paris VI, Dept of Cardiology, Paris, France*; [2]*Imperial College London, Royal Brompton Hospital, London, United Kingdom*; [3]*Maria Cecilia Hospital-GVM Care and Research, Ettore Sansavini Health Science Foundation, Cotignola, Italy*; [4]*Wroclaw Medical University, Faculty of Public Health, Wroclaw, Poland*; [5]*University Medical Center Gottingen (UMG), Innovative Clinical Trials, Department of Cardiology and Pneumology, Gottingen, Germany*; [6]*Attikon University Hospital, Athens, Greece*

On behalf of: QUALIFY Investigators
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Aim: Implementation of HF guidelines is associated with improvement in outcomes but remains suboptimal in clinical practice. We assessed the impact of physicians' adherence to treatment guidelines on clinical outcomes in HFrEF.
Methods and results: QUALIFY is an international prospective observational survey of 7.092 CHF outpatients recruited 1-15 months after HF hospitalization from 36 countries. We analysed the relationship between 6 month outcomes and baseline adherence score for the use of ACEIs or ARBs, BBs, MRAs and ivabradine (if indicated) in in 6669 patients with data available at six months. Score was calculated for each patient by summing the points attributed: 0 for non-prescription in the absence of contraindications, 0.5 point for the use of < 50% of target dosage (TD) (< 100% of TD for MRA) or 1 point for use in ≥ 50% of TDs (TD for MRA). The table presents the relationship between 6 month outcomes and adherence score (Cox proportional hazards regression model on time to event - multivariate analysis conducted by selecting only covariates significant at 1% in univariate analysis).
Conclusion: Among outpatients with HFrEF, a good adherence to pharmacologic treatment guidelines as determined by prescription of ACEI/ARB, BB, MRA, ivabradine with at least 50% of recommended dosages was associated with improved clinical outcomes during 6 month follow up.

	Univariate analysis	Multivariate analysis		
Adherence score	HR [95%CI]	P for group effect	HR ratio [95%CI]	P for group effect
All cause death				
		0.0048		0.001
Moderate vs Good	1.64[1.14;2.34]		1.85[1.26;2.72]	
Poor vs Good	1.96[1.30;2.97]		2.21[1.42;3.44]	
CV death				
		0.0056		0.003
Moderate vs Good	1.85[1.23;2.81]		2.06[1.32;3.20]	
Poor vs Good	2.08[1.29;3.34]		2.27[1.37;3.77]	
HF hospitalization or HF death				
		0.0170		0.024
Moderate vs Good	1.26[1.05;1.52]		1.22[1.01;1.47]	
Poor vs Good	1.34[1.07;1.67]		1.36[1.08;1.71]	

Good adherence score (n = 1543); Moderate adherence >0.5 - <1 (n = 3631); Poor adherence score ≤ 0.5 (n = 1495)

P1672

LCZ696 compassionate use progamme at mater dei hospital, malta

A M Alice May Moore[1]; L Buttigieg[1]; S Xuereb[1]; RG Xuereb[1]
[1]*Mater Dei Hospital, Cardiology, Msida, Malta*

Background: LCZ696 is a combination drug for use in Heart Failure with reduced ejection fraction (HFrEF) consisting of valsartan and sacubitril. It has been included in the treatment algorithm of the 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. The trial PARADIGM-HF has shown a 20% risk reduction in death from CV cause and 21% HF hospitalization risk reduction when LCZ696 was compared to Enalapril.
Purpose: to assess the effect of LCZ696 in HF patients included in the Compassionate Use Programme at Mater Dei Hospital.
Method: Patients that attend the HF Clinic were selected between October 2015 and May 2016. Inclusion criteria included: Age>18; NYHA Class II-IV; LVEF < 35%; at least one hospitalization for HF within the last 12 months; ACE-inhibitor or ARB therapy with a stable dose for prior 4 weeks. The patients were reviewed regularly at the HF clinic. Symptomatology, blood pressure, renal function, potassium and NT pro BNP levels were monitored.
Results: A total of 21 patients were included: 16 males, 5 females. The average age was 56.8 years. 71% had a diagnosis of dilated cardiomyopathy and in 29% the cause of HF was ischaemic heart disease. The mean ejection fraction (EF) was 24%. The choice of the starting dose depended on renal function, potassium levels and blood pressure readings. 29% of patients were started on 50mg twice daily, whereas 71% were started on 100mg twice daily. 81% of patients reached target dose within an average time of 37.5 days. The patients who were started on a lower dose required an average of 60 days to reach target dose, compared to an average of 32 days to target dose in patients who were initiated on 100mg twice daily. 19% of patients did not reach target dose in view of hypotension and hyperkalaemia respectively.
57% had a significant decline in NT pro BNP levels after 6 months of treatment with LCZ696. We managed to stop loop diuretics in 15% of patients and reduce the dose in 45%. Since starting LCZ696, only 2 patients required hospitalization for HF exacerbation. 30% of patients experienced hypotension and 33%hyperkalaemia. Only 1 patient had a significant deterioration in renal function. LCZ696 had to be stopped in 2 of the patients. This was due to significant impairment in renal function and persistent hyperkalaemia respectively despite adjustment of other medication.
Conclusion: The introduction of LCZ696 had an overall positive effect on HF management with reduction in NT pro BNP levels, number of hospitalizations and reduced need of loop diuretics. Further follow-up will include the use of Kansas

City Cardiomyopathy Questionnaire to assess effect on quality of life and repeat of echocardiograms to assess ejection fraction after treatment with LCZ696.

P1673
Comparison of ischemic and non-ischemic heart failure outpatients in a Turkish cohort

C Cihan Altin[1]; H Kaya[2]; L Bekar[3]; H Altay[1]; MB Yilmaz[2]
[1]Baskent Univercity Faculty of Medicine, Ankara, Turkey; *[2]Cumhuriyet University, Cardiology, Sivas, Turkey*; *[3]Hitit University, Cardiology, Corum, Turkey*

On behalf of: TREAT-HF investigators

Purpose: to compare the data of ischemic and non-ischemic subgroups of outpatients with chronic stable heart failure (HF).
Methods: The data of 1253 outpatients with the mean age of 61.58 ± 13.70, obtained from Turkish Research Team-HF (TREAT-HF) multi-centered, prospective, observational, cohort study were analyzed to compare ischemic and non-ischemic subgroups.
Results: Comparison of ischemic (n = 564, male 76.8%) and non-ischemic (n = 689, male 66.9%) subgroups regarding demographics, clinical characteristics, risk factors, symptoms and medications were given in Table. Medications except high usage of statin, acetylsalicylic acid in ischemics diuretic, digoxin in non-ischemics, and achieving the target dose rates were similar between the groups.
Conclusion: Medications which improve survival in HF including newly recommended drugs like ivabradine usage and achieving the target dose rates were similar between the groups but the rates still seem not to be enough according to current guidelines.

Table: Comparison of our study groups

	Non-ischemic (n = 689)	Ischemic (n = 564)	P value
Age (years)	59.80±14.92	63.66±11.78	< 0.001
Heart Rate (bpm)	82.20±17.26	80.28±18.15	0.076
Ejection Fraction (%)	30.34±8.36	32.46±7.92	< 0.001
Hypertension (%)	23.1	41.1	< 0.001
Diabetes Melitus (%)	14.4	31.6	< 0.001
Dispnea (%)	58.1	49.7	0.003
Edema (%)	26.2	20.4	0.017
Angina (%)	22.8	27.4	0.065
Medical therapyβ-blocker (%)	-83.3	-80.4	-0.217
Ivabradine (%)	13.5	11.3	0.334
Diuretic (%)	77.8	66.0	< 0.001
MRA (%)	53.3	48.4	0.108
ACEI/ARB (%)	70.1	72.3	0.415
Acetylsalicylic acid (%)	61.7	77.3	< 0.001
Statin (%)	30.8	48.7	< 0.001
Digoxin (%)	30.0	16.3	< 0.001
Trimetazidine(%)	10.5	11.6	0.551
Achieving target dose of (%)-β-blocker-ACEI/ARB	-20.626.6	-16.127.6	-0.0720.734

ACEI: Angiotensin converting enzyme inhibitors, ARB: Angiotensin II receptor blockers, MRA: Mineralocorticoid receptor antagonist.

P1674
Quality of life predicts exercise capacity in heart failure patients

A Artan Ahmeti[1]; A Batalli[1]; E Haliti[1]; A Poniku[1]; P Ibrahimi[1]; S Elezi[1]; MY Henein[2]; G Bajraktari[1]
[1]University Clinical Centre of Kosovo (UCC), Department of Cardiology, Pristina, Kosovo Republic of; *[2]Umea University Hospital, Umea, Sweden*

Background and Aim: Chronic heart failure (HF) is associated with poor quality of life (QoL). The Minnesota Living with HF Questionnaire (MLHFQ) is the most widely used measurement for assessing the QoL in HF patients. This prospective study aimed to assess relationship of QoL with clinical, echocardiographical and exercise capacity in HF patients.
Methods: The study subjects were 103consecutive HF clinically stable patients (63 ± 10 years, 56 female, 48% hypertensive and 26% ischaemic etiology, classified as NYHA I-III). The MLHF questionnaire was administered during the same day of complete clinical, biochemical and echocardiographic assessment of the patient. A six minute walk test (6-MWT) distance was performed in all patients. Patients were divided into two groups based on the 6-MWT distance (Group I: ≤ 300 m and Group II: >300 m).
Results: The MLHFQ correlated with 6-MWT (r=0.45, p < 0.001) and was higher in female patients (p = 0.015). The NYHA class (P=0.001) and lateral left ventricular long axis amplitude (p = 0.004) differ in MLHFQ tertiles.
Increased MLHFQ [1.070 (1.025-1.117), p = 0.002], older age [1.106 (1.022-1.196), p = 0.012], enlarged left atrium [2.448 (1.171-5.120), p = 0.017] and the presence of diabetes [4.857 (1.287-18.338), p = 0.02] independently predicted poor 6-MWT performance in HF patients. A MLHFQ ≥50 was 74% sensitive and 62% specific (AUC 0.75, p < 0.001) in predicting poor exercise capacity in HF patients.
Conclusions: Quality of life assessed by MLHFQ is the best correlate of exercise capacity assessed by 6-MWT. These findings suggest that exercise capacity and quality of life indices are closely related in HF patients.

P1675
Building bridges between primary and secondary/tertiary care: technology driven integrated care in the area of heart failure

E Etain Quigley[1];
K Mcdonald[2]; M Ledwidge[2]; C Keane[2]; J Gallagher[2]; S James[2]; C Hecht[1]
[1]University College Dublin, Applied Research for Connected Health, Dublin, Ireland; *[2]St Vincents University Hospital, Heart Failure Unit, Dublin, Ireland*

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Background: Heart failure (HF) is a significant public health issue with more than 20 million people around the world affected by the disease. The increasing prevalence rates for HF and the other chronic diseases has led to the development of new policy frameworks in many countries and these have emphasised the need for integrated care and a greater role for primary care in disease management.
The HF Virtual Clinic (HFVC) provides access for General Practitioners to specialist opinion and thus assists with the management of patients in the community. In this respect the HFVC enhances integrated care and meets the demands of the new chronic disease frameworks related to HF. The HFVC was designed in line with the Extension of Community Healthcare Outcomes (ECHO) Project which was established in the US with the aim of supporting collaborative medical education and care management. ECHO facilitates clinician empowerment by providing support within the community thus reducing the need for secondary/tertiary care referrals.
Purpose: The purpose of this paper is to outline findings from an evaluation conducted on an HFVC in Ireland. The paper highlights the simple and yet effective approach that this model adopts and is a prime example of where technology can enhance integrated care and support General Practitioners in optomising their skillset.
Methods: This study adopted a mixed methods approach, combining quantitative surveys, a vignettes based decision making approach, and qualitative interviewing. The HFVC had been in operation in Ireland for approximately 24 months at the time of data collection and had thus provided somewhere close to 48 sessions. A total of 17 General Practitioners were involved with the study.
Results: The HFVC was considered to be a positive and supportive integrative care model. It was perceived as a professionally useful means of disseminating and gathering patient management and condition relevant information. Participants discussed the models ability facilitate peer interaction and a group learning environment. It was outlined as a means of connecting primary/secondary/tertiary care and thus facilitating integrative care. Participants highlighted the models impact in terms of increasing General Practitioner's knowledge base and confidence when treating and managing patients in the community. The model was outlined as a key strategy for reducing referrals to secondary and tertiary care systems.
Conclusion: This paper highlights the potential for such a model in terms of bridging the gap and increasing expertise across primary, secondary and tertiary care. It is an example of where technology can facilitate efficient and effective communication pathways which have the potential to benifit the patient as well as the system.

P1676
Characteristics, treatments, and outcomes of patients hospitalized for heart failure: a report from the OPTIMIZE-HF Registry (Azerbaijan)

G Gulnaz Dadashova[1]
[1]Scientific Research Institute of Cardiology, Heart Failure, Baku, Azerbaijan

Objectives: The aim of this study was to investigate characteristics, treatments, and outcomes of patients with reduced systolic function heart failure (HF).
Methods: This is a single-centre retrospective analysis of 50 patients admitted with decompensated heart failure over 1 year from November to March 2016. We evaluated clinical characteristics of patients according to left ventricular ejection fraction at least 50 or less than 50%. Outcomes as defined by evolution of NYHA class, quality of life (by Minnesota),1-year mortality and re-hospitalization rates for heart failure were compared between the before discharge , and then after 12 months.
Results: The median age was 57.1 years, 66% were men, and 46% had ischemic etiology. Comorbidities were frequent, including hypertension in 82%, diabetes mellitus in 53%, and chronic obstructive pulmonary disease in 29%. HF origin was ischemic in 46% of enrolled patients. The mean range of heart rate (HR) was before discharge 93.1 ± 1.7, after 12 month 73.8 ± 0.6. Ivabradine was administered in 52.1%. Mean left ventricular ejection fraction was 0.41 ± 1.1. After 1 year mortality occurred in 30%. Multivariable predictors of mortality included age, heart rate, systolic blood pressure (SBP) , creatinine. A scoring system was developed to predict mortality. It was found that among hospitalized patients with heart failure has taken an important place modern neurohormonal therapy. ACE inhibitors are used more often than ARB ($p < 0.001$). Aldosterone antagonists eplerenon are used much less frequently in comparison with spironolactone (<0.001). More likely to prescribe loop diuretics than thiazide ($p < 0.001$). Often administered digoxin, levosimendan was not used. Rate of re-hospitalization 1 after year was 34%.There were no significant relationships between discharge use of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker or beta-blocker and before discharge and after 1 year mortality and rehospitalization rates in patients with HF.
Conclusions: Risk of in-hospital mortality for patients hospitalized with HF remains high and is increased in patients who are older and have low SBP or sodium levels and elevated heart rate or creatinine at admission. Postdischarge clinical outcomes also did not significantly vary by day of hospital discharge. Application of this risk-prediction algorithm might help identify patients at high risk for in-hospital mortality who might benefit from aggressive monitoring and intervention.

P1677
Diagnosis of myocardial viability in patients with chronic heart failure: search for the best methods

Y Rustamova[1]; V Azizov[1]; D A Daniil Maximkin[2]; A Faibushevich[2]
[1]Azerbaijan Medical University, Baku, Azerbaijan; *[2]Peoples Friendship University of Russia (RPFU), Moscow, Russian Federation*

AIMS: to reveal the significance and efficiency of different diagnostic methods of myocardial viability.
Methods and Results: 214 patients are included in study. Inclusion criteria: stable angina class II-III(CCS): occlusion or subtotal stenosis of one or more coronary arteries by angiography,previous myocardial infarction (OMI) associated with congestive heart failure (CHF). Patients with acute coronary syndrome, multivessel disease (SYNTAX score ≥32) were excluded of the study.All patients are randomized in 3 groups. At 1group (n = 76) myocardial viabilitywas determined by cardiac magnetic resonance (CMR) with delayed enhancement,at 2 group (n = 78) – two-dimensional low dose Dobutamine stress echocardiography (LDDSE), at III group (n-60) both of methods. Coronary revascularization was performed to all patients with viable myocardium. Late follow-up of intervention was planned for 18 months after procedure.
The mass of hibernating myocardium was able to identify only in groups I and III, where in indicators was 36 and 44% accordingly ($p > 0.05$). At hospitalization period patients surviving was 100% with no complications. Late follow-up were done in 193 of 214 patients, from which 70 included in I group, 68 – II group, 55 – III group. Control methods matched to initials. Summary frequency of cardiovascular complications was 2.8, 8.8 and 5,45% according to groups ($p < 0,5$), but by frequency of non-fatal MI wasn't revealed any significantly differs, but repeated intervention on stented segment of arteries differs at I and II groups (1,4 and 5.9% accordingly; $p < 0.05$).To the end of observation dynamic of recovery of wall motion abnormality was more significant at I and III groups, nearly more than 30% compared to the II group($p < 0.05$). Positive myocardial remodeling and significant increasing of EF (Ejection Fraction) was marked in all groups. Strong positive correlation between duration of myocardium hibernation and its function's recovery time was revealed. ($r=0.54$, $p < 0.05$). I and III groups patient's hibernating myocardium mass was significantly decrease to 37 and 34% accordingly ($p < 0.05$)
Conclusions: CMR with delayed enhancements safe and effective method of detection of myocardial viability, compared to low dose Dobutamine stress-echocardiography allows significantly better estimate dynamic functional recovery of hibernating myocardium and it's remodeling after coronary revascularization.

P1678
Safety and effectiveness of sacubitril/valsartan in real-life practice

J Jenna Berger[1]; T Huynh[1]; V Nguyen[1]; M Rasti[1]; V Cyr[1]; N Giannetti[1]
[1]McGill University Health Centre, Montreal, Canada

Introduction: The most recent medical addition to heart failure management, in those with reduced left ventricular ejection fraction, has been the use of Sacubitril/Valsartan.
Methods: Several clinical parameters were investigated, including some that were not studied in PARADIGM. Our goal was to perform a single center, retrospective, descriptive study, evaluating our patients' clinical outcomes, on Sacubitril/Valsartan.
Results: Demographics From December 2015-December 2016: Sacubitril/Valsartan was initiated in 140 patients. More than half of the patients (51%) suffered from ischemic cardiomyopathy; 21% were females. The mean age and left ventricular ejection fraction were 62 and 25%, respectively. The majority were NYHA 2 and 28% were NYHA 3.
Diuresis Following initiation of Sacubitril/Valsartan, 16% were able to have doses of diuretics decreased, 12% had to have diuretics dosage increased, 58% had unchanged doses of diuretics (6% were not on diuretics before initiation of Sacubitril/Valsartan). Blood pressure Sacubitril/Valsartan was initiated in 19 patients with systolic blood pressures of less than or equal to 100mmHg. The lowest measured blood pressure at initiation was 84/53. The medication was well tolerated in 79% of these patients and 52% were able to have up-titration of Sacubitril/Valsartan Left ventricular Ejection Fraction Of 31 patients who obtained repeat left ventricular ejection fraction (LVEF) measurement, 13 (42%) had improved LVEF.
Cardiac Transplantation On our transplantation and Ventricular assist device (VAD) list, 17 patients were on Sacubitril/Valsartan. 4 of these patients were deactivated from the transplant list, once on Sacubitril/Valsartan due to improving clinical status. 3 of these patients reached maximal dose Sacubitril/ Valsartan, while 1 patient reached medium dose.
Conclusion: In this single-center retrospective cohort study, we showed that Sacubitril/Valsartan was well tolerated even in patients with baseline hypotension. We observed decreases of diuretics requirement and improvement in LVEF in several patients. Moreover, there was no further need for cardiac transplantation and/or LVAD in some patients. Overall, our data suggested that Sacubitril/Valsartan had good safety and effectiveness in "real-life" practice.

P1679
Efficacy and safety of angiotensin II receptor-1 blockers administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

V Evdokimov[1]; A Evdokimova[1]; E Kovalenko[1]; E Fedorova[1]; K Tebloev[1]
[1]State University of Medicine & Dentistry, Moscow, Russian Federation

Purpose: to compare clinical efficacy and safety of sartans in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease.
Methods: after enrollment in this trial 48 patients (31 men and 17 women), aged 63.6 ± 4.9 years, with CHF classes II to III combined with moderate to severe COPD (GOLD-2015) with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized into two groups – losartan (56 ± 6,5 mg daily, n=22) and candesartan (10 ± 2,7 mg daily, n=26). Patients of both groups received the complex CHF treatment comprising torasemide, nebivolol, cardiac glycosides (if necessary) and basic COPD therapy (LABA + LAMA). Echocardiography, exercise tolerance (6-min walk distance), 24-hour electrocardiography and blood pressure monitoring were assessed at baseline and after 6 months of treatment, respiratory function test was assessed at baseline, after 1 month and after 6 months. The quality of life was evaluated by MYHFQ, SGRQ and mMRC.
Results: after 6 months of therapy the improvement of clinical condition and quality of life were marked in both groups. In 1st and 2nd group LVEF was increased by 8.5% and 11.2%, pulmonary hypertension decreased by 9.2% and 12.4%, episodes of silent myocardial ischemia decreased by 21% and 26.8%, respectively. Towards the end of the observation period, there was no deterioration of respiratory function during therapy in both groups, 6-min walk distance increased by 19.6% and 26,2% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (15.7% and 16.4%) and MYHFQ score (22.8% and 28.4%), significant improvements in MMRC dyspnea grade (17.2% and 20% respectively). All treatments were well tolerated and side effects of therapy in patients in all groups was comparable.
Conclusions: the losartan and candesartan inclusion in the structure of complex therapy in patients with CHF combined with COPD raises efficiency of treatment, improves quality of life and basic parameters of central hemodinamics. Efficacy and

safety of losartan and candesartan in patient with CHF due to CAD combined with COPD are similar.

P1680
Ivabradine and heart failure: experience from a real practice

L Lilyana Mircheva[1]; YY Yotov[1]; YB Bocheva[2]
[1]*Medical University of Varna, Varna, Bulgaria*; [2]*University Hospital St. Marina, Clinical Laboratory, UMHAT St. Marina, Varna, Bulgaria, Varna, Bulgaria*

Introduction: Chronic heart failure (CHF) is the most common diagnosis at admission in patients above 65 years. The introduction of ivabradine as a new medication is expected to cope with HF.
Aim: To assess the effect of ivabradine (Iv) after 6 months in patients with CHF NYHA class III-IV post hospitallization.
Materials: We followed 180 patients with CHF for 6 months in an out-patient program. Of them, 80 were in sinus rhythm (SR). The baseline and 6 months levels of NTproBNP, ejection fraction (EF), 6 min walking test (6MWT), NYHA functional class, and renal function were evaluated.
Results: Iv was initiated in 40.3% of patients with SR. After 6 months, the 6MWT improvedt (62.5 m in the Iv vs 23.5 m in the non-Iv group; $p = 0.043$), NTproBNP reduced with median 680 pg/ml and 552,5 pg/ml ($p = NS$), respectively, and EF increased in Iv with 4.02% and decreased with 1.14% in non-Iv, $p = 0.06$. After 6 months, 77% of the Iv patients were in class II, whereas only 45% of the controls were in class I-II ($p = 0.023$).
Conclusions: Ivabradine in CHF leads to subjective improvement, increases the systolic function, improves the quality of life and functional NYHA class.

P1681
Mapping heart failure: patient-level costs of an integrated care pathway

D Daniel Regan[1]; E Quigley[2]; C Keane[3]; M Walshe[3]; J Gallagher[3]; P Kalra[4]; M Ledwidge[3]; M Cowie[5]; K Mcdonald[3]
[1]*University College Dublin, School of Psychology, Dublin, Ireland*; [2]*University College Dublin, Applied Research for Connected Health, Dublin, Ireland*; [3]*St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*; [4]*Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*; [5]*Royal Brompton Hospital, London, United Kingdom*

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Background: Heart failure (HF) is a significant public health issue worldwide. The global economic cost of HF (2012) was $108 billion, with direct costs accounting for 60%. In Ireland total costs of HF (2012), were estimated at €660 million. In spite of high costs, a comprehensive understanding of the HF care-pathway (HF-CP) is currently lacking.
Purpose: To address this, comprehensive maps of HF patient care were developed, relating to: 1) immediate pre-hospitalisation, 2) in-hospital (emergency department/inpatient at an Irish public university hospital), and 3) post-discharge. These maps were then used to calculate the granular cost of patients' journeys.
Method: An interdisciplinary approach was adopted: Time-driven activity-based costing (TDABC) from economics/accountancy, and vignette-based surveying from the social sciences. Within a framework of seven patient vignettes ('paper patients'), developed to represent 'typical' severe/acute decompensated HF patients, TDABC was used to identify the granular activities in the pathway.
Activity-data were collected through participant observations and approximately 100 semi-structured interviews with healthcare professionals (HCPs). Cost-data were collected from publicly available sources, and from the hospital finance department.
Results: Individual-level maps (per HCP-role), were developed, and when combined, produced an integrated HC-CP. Costs per vignette patient ranged from €2,868.92 to €9,427.11. Findings suggest that bedday costs, while still a key factor, are less costly than often estimated. The admission process/referral system of HF patients at the ED level was identified as another cost driver.
Conclusions: Mapping of an integrated HF care pathway through the Irish public healthcare system was conducted for the first time. Recommendations for management and future research are outlined.

P1682
Are our heart failure patients with preserved ejection fraction ready to be included in trials?

B Neves[1]; N Hammoudi[1]; F Pousset[1]; P Balagny[1]; L Legrand[1]; M Komajda[1]; R Isnard[1]
[1]*Hospital Pitie-Salpetriere, Cardiology Department, Paris, France*

Introduction: Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous entity and many clinical trials have been done so far, all with negative results. Heterogeneity is pointed out as an explanation for this, making inclusion and exclusion criteria especially important in this setting. Our aim was to evaluate the inclusion and exclusion rates of a cohort of patients admitted for HFpEF if they would be proposed to enter three major trials on HFpEF (I-PRESERVE, TOPCAT and PARAGON).
Methods: A cohort of patients admitted for HF decompensation between June 2015 and June 2016 on a tertiary HF center was analyzed. Electronic medical records and echocardiograms were analyzed for data introduction. HF was defined as current ESC criteria guidelines. We selected patients with left ventricular ejection fraction (LVEF) ≥45% and excluded a priori those with history of previously reduced LVEF, more than moderate valvular heart disease, constrictive pericarditis, congenital heart disease and previous cardiac transplantation. We applied inclusion and exclusion criteria of 3 major trials to this population
Results: Among 176 patients with HFpEF criteria and LVEF ≥45% and without taking into account longitudinal blood pressure values criteria, rates of inclusion would be 25% for PARAGON, 47% for TOPCAT and 84% for I-PRESERVE. The main reasons for exclusion were rapid atrial fibrillation (21% in TOPCAT), anemia (19% in PARAGON), COPD (15% in TOPCAT and PARAGON), elevated creatinine (13% in TOPCAT and 4% in I-PRESERVE) and lower age (7% in I-PRESERVE and 3% in TOPCAT and PARAGON).
Conclusions: The low inclusion criteria rate on this real world cohort illustrates the complexity of addressing these patients and raises uncertainty about these important clinical trials conclusions when generalized. Disease heterogeneity and associated comorbidities should be taken into account on future clinical trials to make clinical practice decisions easier.

P1683
CHIC trial: Can a single outpatient visit, 8 to 15 days after the hospitalization for acute heart failure, decrease the number of re-hospitalizations?

A Gueye[1]; J Charles[1]; O Milleron[1]; C Bouleti[1]; F Arnoult[2]; I Dehedin[1]; K Ghezali[1]; G Phan[1]; G Caligiuri[1]; C Morgant[1]; A Dechanet[3]; F Tubach[3]; G Jondeau[1]
[1]*Hospital Bichat-Claude Bernard, Equipe Insuffisance Cardiaque, Paris, France*; [2]*Hospital Bichat-Claude Bernard, service d'exploration fonctionnelle, Paris, France*; [3]*Hospital Bichat-Claude Bernard, Unité de Recherche Clinique Paris Nord, Paris, France*

On behalf of: Equipe Insuffisance Cardiaque, Service de cardiologie, Hôpital Bichat Claude Bernard

Among people suffering from congestive heart failure (CHF), the first 6 months after a hospitalization is the most critical period for the risk of recurrences.
This prospective randomized study aims to evaluate if a single outpatient visit, with echocardiography 8 to 15 days after discharge for CHF hospitalization, decreases the number of re-hospitalizations during the following 6 months.
Between 2013 and 2016, 326 patients hospitalised for acute heart failure in Bichat Hospital, with either a none-optimal treatment for CHF according to the practitioner in charge or NT-proBNP value upper than 3500 ng/l at discharge were included. These 233 men and 93 women were randomized 1/1 into 2 groups, one "interventional" (162 with scheduled additional outpatient visit, ECG and echocardiography 8 to 15 days after hospitalization) and one "standard" (165 pursuing the standard of care). Follow-up included phone calls at 3 and 6 months after hospital discharge.
In the first 100 patients included, age ranged from 26 to 97 years old (mean age 68 ± 14), and hospitalisation lasted 2 to 77 days (mean 13 ± 8). Reasons for inclusion were high Nt-ProBNP in 44% or non-optimal therapy at discharge in 56%. Hypertension was present in 63% and diabetes mellitus in 48%. Decompensation was de novo in 51%. LVEF was preserved in 27%. Main aetiologies of heart failure were ischemic and dilated cardiomyopathy (1/3 of cases each) and cardiac arrhythmias in 14%.
At discharge, 74% of patients received an ACEI, 15% an ARB (renin angiotensin system blocker 89%), and 91% a beta-blocker. Follow-up is started and complete baseline data will be presented during the meeting. Prevalence of heart failure with preserved ejection fraction appears to be lower than anticipated in patients not selected in the Cardiology department, but these patients were considered as being amenable to optimisation of therapy in the idea of the practitioner in charge.

P1684
General practitioner perceptions of services for patients with advanced heart failure: a qualitative study

J J Jingwen Jessica Chen[1]; KO Orr[1]; CS Stone[2]; JD Doherty[2]; LG Graham[2]; KMG Mcglade[1]; PD Donnelly[3]
[1]*Queens University Belfast , Medicine, Dentistry and Biomedical Science, Belfast, United Kingdom*; [2]*Marie Curie Hospice, Belfast, United Kingdom*; [3]*South Eastern Health and Social Care Trust , Cardiology, Belfast, United Kingdom*

On behalf of: Queens University Belfast Research Group

Background: The holistic needs and healthcare service support of patients with advanced heart failure are often neglected. Collaboration and communication between Primary Care, Cardiology and Palliative Care Services is likely key in meeting the multidimensional needs of patients. It is unclear if such a model of care exists in this region.
Purpose: This qualitative study assessed current services models available within one geographical region and explored the adequacy of these models in meeting the needs of patients and carers with heart failure, as perceived by General Practitioners (GPs).
Method: Semi-structured interviews were conducted with GPs recruited via the medical school and postgraduate deanery. Selected GPs represented each healthcare trust area in the region, ensuring a snapshot of perception was achieved. Interviews were transcribed, independently coded using NVivo 9TM and analysed using a six-step thematic analysis approach. Key themes were identified inductively.
Results: Twenty semi-structured interviews were conducted between June and August 2016. A number of recurring themes emerged. Care provided by the heart failure nursing team (HFT) was highly regarded. However, access to this service was limited to patients under the care of a Cardiologist, thus excluding those with advanced disease no longer seen by a Cardiologist. This lack of community facing HFT was associated with inadequate handover of care from the HFT to GPs at discharge. Such a disjointed primary and secondary care service model has created a perception that access to timely advice and appropriate services for patients, is limited in an elective setting, frequently resulting in inappropriate admission for acute service support. Discussions about end of life care are frequently neglected by Cardiologists and GPs. GP's reported that this may be due to poor awareness of the need for these discussions and lack of clarity regarding who is responsible. It was reported that at all stages of heart failure management, the emphasis is on medical treatment, rather than holistic assessment of underlying needs. Linked to this was a poor awareness of the role of Specialist Palliative Care (SPC) services in the management of heart failure in the community. GP's perceptions that SPC services are overstretched, cancer focused and lack expertise in heart failure lead to its limited utilisation. Barriers to referral for SPC include difficulties identifying palliative care needs and a fear of causing distress.
Conclusions: GPs describe significant shortcomings in the delivery of holistic care to patients with advanced heart failure in the region. There is a clear need to review existing service models within the region, with a focus on collaborative service planning, education, effective communication, role delineation and greater access to specialist palliative care.

P1685

Personalized approach to heart failure with preserved ejection fraction (HFpEF), the Maastricht experience

MA Barandiaran Aizpurua[1]; VPM Van Empel[2]; BLM Schroen[3]; M Van Bilsen[1]
[1]Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands; *[2]Maastricht University Medical Centre (MUMC), Cardiology , Maastricht, Netherlands*; *[3]Maastricht University, Cardiology , Maastricht, Netherlands*

Background: Heart failure (HF) with preserved ejection fraction (HFpEF) is one of the main dilemmas in modern cardiology. The recently postulated paradigm gives to co-morbidities a central role being the cause of low grade systemic inflammation producing endothelial and microvascular dysfunction, alteration of myocardial signalling and involvement of other organs; lungs, skeletal muscle and kidneys.
Purpose: The absence of effective treatment leads to pursue a different approach to the HFpEF patient. Multidisciplinary strategies have been proven to reduce mortality and hospitalization significantly and are recommended by the ESC HF guidelines. Nevertheless these efforts have mostly been focused on HFrEF. A multidisciplinary, individualized approach to HFpEF patients could be the answer that is lacking.
Methods: In Maastricht University Medical Center a specific HFpEF out-patient clinic have been implemented. Suspected patients are referred from their general practitioner, cardiologist or another medical specialist to the HFpEF out-patient clinic. An intense and complete medical assessment is performed: electrocardiogram, cardiac echography, lung function test, six-minute walking test, exercise testing, twenty-four hour Holter monitoring, ApneaLink, Hospital Anxiety Depression Subscale score and laboratory tests including biobank analysis. If coronary artery disease is suspected a coronary computed tomography or coronary angiography will be performed. The patient gest a medical consultation with a dedicated HF specialist. Once a week in a multidisciplinary meeting all patients get discussed with all HF specialist and internal medicine or pulmonologists if needed. If co-morbidities have been diagnosed, these will be treated. Sometimes the diagnosis of HFpEF remains uncertain. In these cases, a right heart catheterisation will be performed.
Results: After one year we have screened 144 patients of which 115 had HFpEF according to the last ESC HF guidelines. In the baseline characteristics, we can observe most patients are women (67,8%), obese 48,3% with a BMI above 30 kg/m2 and 15,7% above 35 kg/m2, have hypertension (84,3%), type II diabetes (37,4%), atrial fibrillation (61,7%), sleep apnoea (47,8%) and iron deficiency (50%). Echographically most patient have an increased left atrium volume index (85,2%) increased E/E' above 13 (37,1%). Increased left ventricular mass index is only present in 20% of the patients. The mortality rate after 1 year is 5,4%, the half related to cardiovascular disease; pulmonary hypertension of right ventricular failure. 31 patients got hospitalized in the first year (26,9%).
In conclusion, the characteristic of our HFpEF population does not differ from the patients included in the main HFpEF trials. However, our mortality and hospitalization rate are lower. This could be related to a diagnosis in an earlier stadium, selection bias or to an intensified treatment regime of the different co-morbidities.

P1686

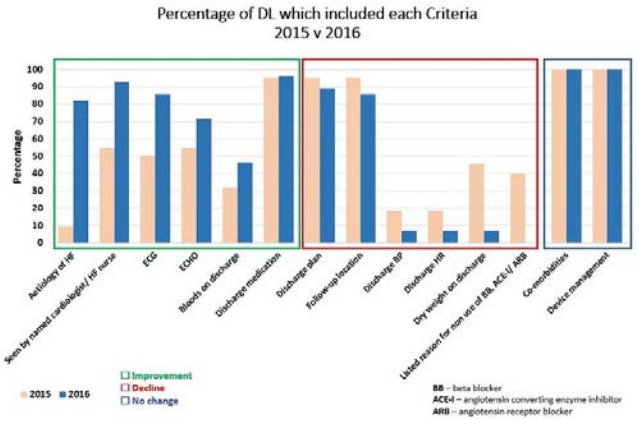
Hospital discharge letter quality - An important standard between hospital and community heart failure teams

A Aysha Gomaa[1]; D R Duncan[2]
[1]Barts and The London School of Medicine and Dentistry, London, United Kingdom; *[2]Mid Essex Hospital NHS Trust, Cardiology Department, Chelmsford, United Kingdom*

Introduction: Heart failure (HF) admissions are increasingly prevalent. Discharge Letters (DL) are an important communication between secondary care and community teams for the ongoing management of HF patients, and as a dataset for National HF audits. This audit sets out to assess the quality of DL at a district general hospital in the UK.
Methodology: DL for patients admitted with symptoms of HF to the joint cardiology and renal ward were analysed for meeting criteria (figure 1) deemed as 'good practice standards' by the National Institute for Cardiovascular Outcomes Research (NICOR) and National HF Audit. The initial audit evaluated DL from September 2015 and was re-audited in September 2016 following actions to improve quality of DL. These included promoting the aide-memoire of the required criteria through a screensaver on trust computers, hospital doctor induction and placing hard and electronic versions on computers.
Each criterion was scored using a 3 point scoring system and a total score was calculated and standardised by converting to a percentage. The scores were analysed by looking at the total DL score as well as analysis by criteria.
Results: September 2016 DL scores showed an improvement compared to 2015 (p-value = 0.359) as shown in table 1; 93% of DL had a score over 50% in 2016 compared to only 45% in 2015. A notable increase can be seen in the percentage of DL which included each criteria in 2015 and 2016 (figure 1), most markedly the first four criteria. Patient vital signs and medication are areas requiring more work.
Conclusion: This audit demonstrates that educational activities improve inclusion compliance of the majority of HF data standards within DL. This is likely to improve communication between hospital and community HF teams which is important in optimising the management of HF patients. Compliance in data standards within DL still has room for improvement, and further systems to improve this can be explored.

DL Scores 2015 v 2016

	2015	2016	% change
Number (n) of HF DL (total)	11 (131)	14 (135)	
Highest score	92.3	84.6	- 8
Lowest score	30.8	46.2	+ 50
Average score	55.4	61.7	+ 14
n DL scoring 25 - 49.9%	6	1	- 83
n DL scoring 50 - 74.9%	2	12	+ 500
n DL scoring 75 - 100%	3	1	- 67



Criteria included in DL 2015 v 2016

P1687

Heart failure specialist versus general cardiologist in the management of chronic heart failure in Russia

E Elena Lyasnikova[1]; M YU Sitnikova[1]; MA Trukshina[1]; AV Yurchenko[1]; DV Duplyakov[2]; EV Shlyakhto[1]
[1]Federal Almazov Medical Research Centre, Heart Failure Department, St-petersburg, Russian Federation; *[2]Samara Regional Cardiology Dispanser, Samara, Russian Federation*

Purpose: HF is responsible for considerable mortality rates and resource utilization. The aim of this study is to identify differences in HF management practices and outcomes between general cardiologists and cardiologists specializing in the treatment of patients with HF in real Russian clinical practice (from the Russian hoSpital Heart Failure Registry (RUS-HFR).
Methods: HF patients (included in the RUS-HFR from Oct 2012 to Jan 2014) discharged from cardiology wards and were followed-up (FU) in outpatient HF clinic (1 group - St.Petersburg(n = 74) were compared to patients who were under the supervision of a general cardiologists (2 group – St.Petersburg (n = 186), 3 group – Samara (n = 130). Mean age 59.0 ± 8.3 yrs; 80% men; most patients with HF III NYHA, LVEF≤40%. The average duration of FU was 30 month.
Results: After 2.5 yrs the survival of patients was 77% vs 65% ($p>0.05$) vs 40% ($p<0.01$) and HF hospitalizations were 33% vs 28% ($p>0.05$) vs 103% ($p<0.01$) in the groups 1,2,3, respectively. Among all groups more than 88% and 79% patients regularly visited the doctor and had HF NYHA II-III. There were important differences between the practice patterns of cardiologists and HF specialists. HF specialists treat patients more aggressively. Cardiologists reported that 68%-78%, 81-85%, 52-54% and 60-79% of their patients were taking RAS blockers,β-AB, MRAs and diuretics compared to 89%, 91% , 63% and 88% by HF specialists. Also, HF specialists were more likely than cardiologists to titrate RAS blockers and β-AB to higher doses: 46% vs 26-38% and 74% vs 52-56%, even in the presence of renal dysfunction and hypotension.
Conclusion: Cardiologists and HF specialists in Russia generally manage their patients in conformity with guidelines. However, in many areas, such as RAS blockers and β-AB use, HF specialists do so more aggressively. These approaches may, in part, explain the success of the outpatient HF clinic model in post-discharge mortality and raise the question of improve HF management in RF through to organize network of HF specialists and HF clinics throughout the country.

P1688

Left ventricular assistance device for destination therapy: results in the west region of France

P Pierre Teruin[1]; L Mabire[1]; M Michel[1]; JC Roussel[1]; T Senage[1]; E Flecher[2]; A Belin[3]; JN Trochu[1]
[1]University Hospital of Nantes Nord Laennec, Nantes, France; *[2]Hospital Pontchaillou of Rennes, Rennes, France*; *[3]University Hospital of Caen, Caen, France*

Background: Left ventricular assist device (LVAD) for destination therapy is a validated procedure in patients with advanced heart failure and contraindicated for transplantation. The aim of our study was to implement a destination therapy registry for patients implanted with an LVAD in 3 teaching hospitals of the west region of France from December 2005 to October 2015.
Results: 63 patients, 65 ± 7 years old, contraindicated for cardiac transplantation and implanted with a continuous flow LVAD as destination therapy were included. Preoperatively 92% were in NYHA class 3B or 4, 77% had a 3 or 4 INTERMACS profile, 61% had a stage 3 or 4 renal insufficiency, 38% liver failure, 35% type 2 diabetes, 19% peripheral arterial disease and 17% chronic pulmonary disease. Contraindications to transplantation were age (68%) and comorbidities (35%). Postoperatively, 78% of the patients were in NYHA class 2. Most common adverse events included bleeding (76%), ventricular arrhythmias (63%), right ventricular dysfunctions (56%), strokes (38%), driveline infections (25%) and pump thrombosis (13%). At 24 ± 24 months of follow-up, 56% of patients had died and 3 had been transplanted. 28% of early deaths were related to right ventricular failure (56%) and 18% of total deaths were related to pump failure. Overall survival was 65.4 ± 6.1% at one year and 53.9 ± 6.7% at 2 years. Increases in pre-implant mean pulmonary arterial pressure, pulmonary vascular resistance, and total bilirubin were significantly correlated ($p<0.05$) with lower survival.
Conclusion: Our study constitutes a French register of 63 patients implanted with LVAD as destination therapy, with results comparable to literature. Despite frequent complications, LVADs allow an improvement in survival and functional capacities.

P1689

NT pro BNP - a decision factor in preventing heart failure at diabetic patients

I Dimitriu[1]; D Voiculescu[1]; A Lacraru[1]; C Sinescu[1]
[1]Carol Davila University of Medicine and Pharmacy , Cardiology, bucharest, Romania

Background: To prove the importance of NTproBNP for preventing heart failure at diabetics.
Materials and Methods: We included 174 patients who were presented at hospital during two years, with diabetes. We excluded patients who are already diagnosed with heart failure or who had current symptoms of heart failure. We randomized patients into 2 equal groups: a control group and an intervention group. NTproBNP value was determined for all patients. In the intervention group patients were treated according to the NTproBNP. Patients with NTproBNP <125 pg/dl (38 patients) received standard treatment for their symptoms. Patients with NTproBNP>125 pg/dl (49 patients) were the ones on which we intervened to prevent heart failure. They were investigated by cardiac ultrasound and other tests and they received specific treatment. Patients in the control group received standard treatment regardless of the NTproBNP value.
Results: After two years, the end points were: diagnosis of heart failure left ventricular dysfunction, death from any cause, the rate of hospitalizations for cardiovascular pathology. After two years in the control group were eighteen (20.6%) patients who developed heart failure compared to ten (11.42%) patients in the intervention group. Twenty-eight (27.5%) patients were diagnosed with left ventricular systolic dysfunction, compared to eighteen (20.6%) in the intervention group. Also, and rate of admissions for cardiovascular pathology was higher in the control group thirty-four (39%) versus twenty-seven (31%) in the intervention group.
Conclusions: Patients in the intervention group, in which the value of NTproBNP was used in choosing therapeutic management, had lower rate of incidence of heart failure or cardiovascular events than patients in the control group. The NTproBNP value in patients without heart failure can detect patients at risk of developing heart failure. And more, medical intervention guided by NTproBNP can prevent or delay heart failure.

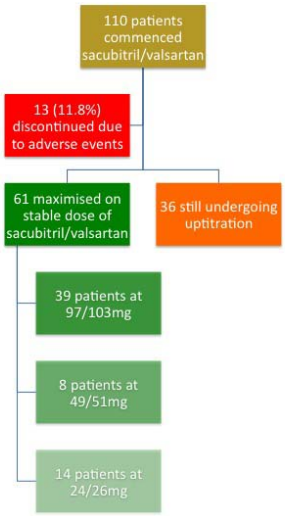
P1690

Use of sacubitril/valsartan in a dedicated heart failure centre - real world experience from the first 110 patients

M J Barrett[1]; S Earls[2]; S Zhou[2]; K Mcdonald[2]
[1]St Vincent's University Hospital, Cardiology, Dublin, Ireland; *[2]Heartbeat Trust, Dublin, Ireland*

Background/Introduction: Sacubitril/valsartan is a novel therapy which has been shown to reduce major adverse cardiovascular events and mortality in patients with reduced ejection fraction heart failure (HFrEF). Most data regarding tolerability comes from clinical trials. Experience in a real world population is less-well described.
Purpose: To assess the tolerability and success in achieving maximum target dose of sacubitril/valsartan, as well as detailing the side effect profile in a real world population.
Methods: Sequential patients attending a dedicated specialist heart failure unit with a therapeutic indication for sacubitril/valsartan were included. Electronic records (including electronic prescriptions) were reviewed to determine final achieved dose in patients who were maintained on sacubitril/valsartan. Any patient who had sacubitril/valsartan discontinued had the reason for discontinuation recorded along with any relevant laboratory or clinical investigations at the time.
Results: 110 patients were deemed suitable to commence sacubitril/valsartan. Of these, 9 (8.2%) were commenced on 49/51mg twice daily and the remaining 101 (91.8%) on 24/26mg twice daily.

At follow-up, 61 patients had been stabilised at maximum tolerated therapy. Of these, 39 (63.9%) achieved the maximum dose of 97/103mg twice daily. A further 8 patients (13.1%) reached the 49/51mg dose and 14 (22.9%) remained on the 24/26mg strength without tolerating a dose increase. 36 patients (32.7%) were still in the process of being uptitrated to the maximum tolerated dose.
13 patients (11.8%) discontinued sacubitril/valsartan. The commonest reason was a composite of hypotension, presyncope or sycnope (9/13, 69.2%). In this group, the mean drop in systolic blood pressure (SBP) at follow-up after commencement of sacubitril/valsartan was 17mmHg (range 0-45mmHg).
In patients in whom blood pressure effect was the predominant reason for discontinuation, half were noted to be concommitantly prescribed non-cardiac medications in which hypotension was a known side effect.
Other reasons for discontinuation included gastrointestinal disturbance (n = 3), acute kidney injury (n = 1), hyperkalaemia (n = 1) and back pain (n = 1). 2 patients had more than one indication for discontinuation of sacubitril/valsartan.
Conclusion(s): Sacubitril/valsartan is a well-tolerated medication in the majority of patients in our heart failure population. True hypotension was the dominant cause for discontinuation. Caution should be taken to consider reducing diuretics if clinically justifiable or rationalise other medications with anti-hypertensive side-effects to ensure that suitable patients only have the medication discontinued if truly intolerant.
Reassuringly, rates of hyperkalaemia and kidney injury were not higher than for standard angiotensin-blocking therapy and only a single patient developed an idiosyncratic side-effect.



P1691

Advanced age attenuates the aggravating role of salt on acute coronary syndrome patients with heart failure; results from hellenic heart failure study.

M Kouvari[1]; C Christina Chrysohoou[2]; H Kosyfa[1]; G Kalogirou[1]; P Aggelopoulos[1]; A Filippou[3]; S Iosifidis[3]; E Tsiamis[1]; D Tousoulis[1]
[1]*University of Athens, First Cardiology Clinic, School of Medicine, Athens, Greece*; [2]*University of Athens, Athens, Greece*; [3]*Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

On behalf of: Hellenic Heart Failure study

Background/Introduction: Dietary salt restriction is arguably recommended in the prevention and management of heart failure. Nonetheless, salt is a dietary product which is highly associated with appetite. Considering that anorexia and cardiac cachexia is usually presented in heart failure patients, namely those in advanced age, to what extend salt restriction is a recommendation for all remains questionable.
Purpose: the role of discretionary and hidden salt intake on 10 year prognosis of Acute Coronary Syndrome (ACS) patients was investigated.
Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, 10y follow-up (2006-2016) was performed in 745 participants. A validated food frequency questionnaire was used, to assess, among other dietary habits, discretionary salt intake (i.e. addition in cooking or in table) as well as consumption of major hidden-salt food sources (i.e. processed / fried meat products, canned food, feta cheese, yellow-cheese, salted nuts, bread and other bakery products).
Results: 10y fatal/non fatal ACS events were 60% in heart failure patients who reported use of salt shaker in table and 47% in patients who avoided this habit (p = 0.03). Multivariate logistic regression analysis highlighted that patients who reported were twice as likely to develop a new cardiac episode within the decade (OR=2.19 95% CI (1.12, 4.3), p = 0.02). Principal component analysis was performed for major hidden-salt-sources. Salt addition during cooking did not reach significance. Two out of four patterns identified, reached significance in a multivariate analysis; a pattern characterized by processed/fried meat products, fast food and salty yellow cheese was associated with unfavorable ACS prognosis (OR=1.4 95%CI (0.97, 2.04)) whilst a pattern with healthier food choices (i.e. nuts, canned fish/vegetables, olives and feta cheese) was inversely associated with 10 year recurrent events (OR=0.55 95%CI (0.37, 0.82)). A significant interaction was observed between age and addition of salt in table as well as the aforementioned hidden salt patterns (all ps for interaction>0.05). Stratified analysis revealed that use of salt shaker retained its significance only in younger patients (OR=2.80 95% CI (1.18, 5.3), p = 0.02). Additionally, the potential protective effect of healthy, yet rich in salt, food choices reached significance in patients >65 years old (OR=0.27 95% CI (0.10, 0.71), p = 0.008).
Conclusion: salt, mainly this added in table, seemed to have an aggravating role in 10y prognosis of heart failure. Nonetheless, considering its detrimental role in appetite, instead of a general strict restriction, priorities should be set for a more efficient treatment approach.

P1692

Oral use of high doses of Furosemide as an alternative to intravenous or subcutaneous way in patients with severe Congestive Heart Failure

M Magdalena Fernandez Martinez De Mandojana[1]; S Llavina Farres[1]; J Muguerza Iraola[1]; B Ferro Castro[1]; I Serna Diez[1]; M Del Hierro Baleztena[1]; L Juaristi Azpiazu[1]; A Gonzalez Penagaricano[1]; E Coll Viciosa[1]; D Camacho Madueno[1]; A Aranzabal Lasagabaster[1]; ML Txakartegi Ibarloza[1]; J Taboada Gomez[2]; A Sanchez Gonzalez[1]; G Uranga Hernandez[1]
[1]*OSI Debabarrena - Mendaro Hospital, Home Hospitalization, Mendaro, Spain*; [2]*Hospital Comarcal de Mendaro, Preventive Medicine, Mendaro, Spain*

Background/Introduction: ACCF/AHA 2013 Heart Failure guidelines recommend initial dosing of oral Furosemide of 20-40 mg, once or twice daily, and a maximum total daily dose of 600 mg. In the last few years, several patients with severe Congestive Heart Failure had income in our Home Hospitalization Service with high doses of continuous parenteral Furosemide infusion. When we got the patient stability, we explored the option of using the oral way to administer high doses in an attempt to use a non-invasive way in patients with a long term treatment.
Purpose: The aim of this work is to describe our experience in a local Home Hospitalization Service in the orally use of high doses of Furosemide (higher than 750 mg daily) as an alternative to intravenous or subcutaneous use, in patients with severe Congestive Heart Failure (NYHA 3-4) and a high probability of death within the first year (PALIAR INDEX 3-4). We also want to study the impact of this therapy over renal function, survival rates and hospital return rates.
Methods: We conduct a retrospective study of 33 months of following (2013-2016). We recruited patients with severe Congestive Heart Failure, NYHA 3-4 and PALIAR INDEX 3-4, who required high doses of continuous parenteral Furosemide (iv/sc) to stabilize and have been sequenced with oral Furosemide at equivalent doses for which we used the vials of 250 mg diluted in water that patient takes along the day (respecting sleep).
Results: Our cohort included 32 patients with an average age of 83 (SD: 6,41) years. Sixty eight percent were men. Regarding to the etiology, almost the 50% were due to valvular disease. The median of monitoring was of 284,5 days (IQR: 332) and an average daily dose of Furosemide of 800 (SD: 575) mg. Baseline creatinine was 1.72 and after a month of treatment there was a slightly increase (1.76) but was not statistically significant. Sixty two percent of patients suffered hypokalemia that recovered with supplementary intakes. The readmission rate was of 37%. The global mortality was of 56%.
Conclusion(s): In our limited experience, we have found that the use of high doses of oral furosemide in patients with severe Congestive Heart Failure is a good therapeutic option, with very good clinical and analytical tolerance.

P1693

Why are heart failure patients in a district general hospital not being discharged on mineralocorticoid receptor antagonists?

E H Elen Hanna Hughes[1]
[1]*Countess of Chester Hospital, Cardiology, Chester, United Kingdom*

Background: The UK National Heart Failure Audit found that all criteria for the management of chronic heart failure patients were being met in a district general hospital, except the recommendation that patients with heart failure with reduced

ejection fraction should be treated with a mineralocorticoid receptor antagonist (MRA) if they are still symptomatic and have an ejection fraction of <35%. The project looked to try and ascertain why less than the national average of patients in a district general hospital were being discharged on MRAs, and whether there were any practical measures that could be put in place to ensure the national guidelines are being met in future to help optimise the treatment of the chronic heart failure patients.
Purpose: The project was undertaken to try and address any factors that might be contributing to a district general hospital's below-average rate of prescription and discharge on MRAs. It was also done to see whether any practical measures could be implemented to ensure optimal treatment of the chronic heart failure patients in a district general hospital.
Methods: The data from the National Heart Failure Audit was extrapolated and used in order to analyse any variables that may be contributing to the difference in the numbers of patients being discharged from hospital on MRAs elsewhere in the country compared to the district general hospital. The data provided a sample size of 81 patients.
Results: The biggest factor in patients not being discharged on an MRA was their place of care. A majority (55%) of patients who were discharged on an MRA were discharged from a dedicated cardiology ward. Those patients who were not discharged on an MRA were mainly cared for on other wards (68%), implying that specialist cardiology care is vital in discharging patients appropriately on an MRA.
Conclusion: There is evidence to support the hypothesis that a patient's place of care impacts their optimal drug therapy for chronic heart failure. One of the outcomes of the project is to aim to increase awareness and education regarding the use of MRAs in chronic heart failure among non-cardiological medical specialties, in order to optimise chronic heart failure management post-discharge.

P1694
Pending heart failure clinic opening: care performance measures in real-life practice

S Padaryan[1]; S Galochkin[1]; N Soseliya[1]; E Shavarova[1]; S Villevalde[1]; A Milto[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Aim: to compare real clinical practice with current guidelines for the diagnosis and treatment of chronic heart failure (HF) before the HF Clinic opening.
Material and methods: all patients admitted for two Moscow city clinical hospitals with decompensated HF from January to May 2015 were included into the registry (n = 484). Clinical, demographic, laboratory and instrumental characteristics and medical treatment before and during hospitalization were evaluated, as well as recommendations contained in the discharge summary. Performance measures included left ventricular ejection fraction (LVEF) documentation in medical history, any beta-blocker for patients with HF with reduced EF (HFrEF); evidence-based beta-blocker for patients with HFrEF; inhibitor of the renin-angiotensin-aldosterone system (RAAS) for patients with HFrEF; warfarin for patients with atrial fibrillation; aldosterone antagonist for patients with HFrEF; implantable cardioverter-defibrillator for patients with EF ≤35%; and referral to outpatient disease management.
Results: the median age was 73 years (39, 95); men – 45%. 97% of patients had HF II- IV (NYHA), among them 26% - HF II, 64% - HF III, 10% - HF IV (NYHA). Echocardiography was done in 100% patients with HF. EF<40% was found in 44% of patients. 21% of the patients did not receive medical treatment before admission. 56% of patients with HFrEF received ACE inhibitors/angiotensin receptor blockers (ARBs), of which only 25% - in effective dose. beta-blockers were prescribed in 67% of HFrEF patients, among them 25% - in the target dose, two-thirds were treated with evidence-based beta-blocker. 38% of patients needed in mineralocorticoid receptor antagonists (MRA) received spironolactone. During hospitalization 82% of HFrEF patients received ACEI therapy, 11% – ARBs, 92% – beta-blockers, 89% – MRA, 83% – loop diuretics and 15% – thiazide diuretics. According to the discharge summary 5% of patients did not receive post-discharge inhibitor RAAS without explanation in the medical documentation. Evidence-based beta-blocker was prescribed to 70% of HFrEF patients. Spironolactone was recommended after discharge in 89% of HFrEF patients. Warfarin for patients with atrial fibrillation and high CHA2DS2-VASc score risk was recommended in 52%. Necessity of cardioverter-defibrillator implantation for patients with EF ≤35% was discussed in 4% of discharge summaries. All discharge summaries contained recommendation of outpatient clinic visit but only in 15% of them exact date and place were mentioned.
Conclusion: Treatment of HF is one of the main areas targeted for improvement. Such registry is a valuable tool for optimizing the management of HF patients.

P1695
The difference between drug usage in patients with HFrEF and HFmrEF: results from TREAT HF

A Celik[1]; H Kaya[2]; L Bekar[3]; H Gunes[4]; MB Yilmaz[2]
[1]*Mersin University, Cardiology, Mersin, Turkey*; [2]*Cumhuriyet University, Cardiology, Sivas, Turkey*; [3]*Hitit University , Cardiology, Corum, Turkey*; [4]*Kahramanmaras Sutcu Imam University, Cardiology, Kahramanmaras, Turkey*

On behalf of: TREAT HF

Purpose: Heart failure with mid-range ejection fraction (HFmrEF) is a new defined type of heart failure. There was no clear data and no evidence about the usage of heart failure drugs in this population. TREAT HF (Turkish Research Team-HF) data were analyzed for the assessment of any usage difference between heart failure drugs in patients with HF and reduced ejection fraction (HFrEF) and HFmrEF.
Methods: TREAT HF is a network which undertakes multicenter, national, observational studies designed to evaluate HF patient's clinical characteristics and current treatment modalities. 1074 patients with the diagnosis of HFrEF and HFmrEF were included in this analysis. 84 of these patients had HFmrEF and 990 of them had HFrEF according to their left ventricular ejection fraction (LVEF) and additonal ESC criteria.
Results: Patients with HFrEF had higher usage of ACEi/ARB, digoxin and loop diuretics than patients with HFmrEF (Table 1). No significant difference were seen in patients with HFrEF and HFmrEF according to the usage of beta blockers, MRAs, tiazide diuretics, and ivabradin.
Conclusions: These results show that beta blockers, MRAs, tiazide diuretics and ivabradin usage of patients with HF did not change according to LVEF. But the HF patients with reduced EF were using higher rate of ACEi/ARBs, digoxin and loop diuretics than with mid-range EF.

The drug usage of patients with HF

Drug usage (%)	HFrEF (N=990)	HFmrEF(n = 84)	P value
ACEi/ARBs	72.5	60.7	0.031
Beta blockers	82.3	76.2	0.107
MRAs	50.7	47.6	0.650
Ivabradin	13	8.4	0.300
Digoxin	24.1	11.9	0.010
Loop diuretics	73	60.7	0.022
Tiazide diuretics	34.7	37.3	0.633

P1696
The effects of prolonged daytime fasting on clinical and laboratory parameters of heart failure patients treated with diuretics

G Gabra[1]; B Bassam Atallah[2]; ZG Sadik[2]; R Ferrer[3]; J Stapleton[3]; M Soliman[1]; F Bader[1]
[1]*Cleveland Clinic Abu Dhabi, Cardiovascular Medicine, Abu Dhabi, United Arab Emirates*; [2]*Cleveland Clinic Abu Dhabi, Pharmacy Services, Abnu Dhabi, United Arab Emirates*; [3]*Cleveland Clinic Abu Dhabi, Nursing, Abu Dhabi, United Arab Emirates*

Background: Religious fasting during the month of Ramadan necessitates that one refrains from eating and drinking during daytime. Since Ramadan is determined by the lunar calendar (354 days), it will start 11 days earlier each year on the solar calendar. In 2016, Ramadan fell in June and fasting was for about 15 hours daily. Although not mandated by sick patients, some still insist on fasting. We investigated whether this negatively affects chronic heart failure (CHF) patients on diuretics.
Methods: Patients with CHF requesting to fast were told to decrease their diuretic dose by half. We then prospectively followed them for clinical as well as laboratory parameters at the beginning and at the end of the month.
Results: A total of 23 systolic CHF patients were included (17 males and 6 females). Mean age was 54.4 ± 11.5 years. The mean baseline dose of furosemide was 108 ± 133.3 mg daily. All patients reduced their dose by half. There were no admissions for heart failure among study patients. There was no significant change in weight from baseline (87.4 ± 21.8 kg vs. 88.1 ± 21.5 kg, p = 0.47), neither was there a significant change in renal function, serum Hb, as well as serum electrolytes (table 1).
Conclusion: Despite long hours with no oral intake, patients with CHF tolerated fasting well while requiring less diuretics. Larger studies are needed to determine if patients would normally drink less fluids if treated with less diuretics and if self-management with diuretics influences outcomes compared to strict regimens.

Table 1

Variable	Before	After	p Value
Weight (Kg)	87.4 ± 21.8	88.1 ± 21.5	0.47
Hb (g/dL)	13.35 ± 1.69	13.41 ± 1.67	0.76
Na+ (mmol/L)	137.96 ± 3.6	137.9 ± 4.2	0.90
K+ (mmol/L)	4.64 ± 0.47	4.64 ± 0.62	0.99
BUN (mmol/L)	7.87 ± 3.90	6.74 ± 2.96	0.08
Cr (μmol/L)	100.82 ± 48.42	93.95 ± 33.61	0.24
Mg ++ (μmol/L)	0.84 ± 0.10	0.82 ± 0.10	0.38

Variables before and after a month of daytime fasting. Values are expressed in mean ± SD

P1697

Impact of Ivabradine to improve the heart rate variability in patients with chronic heart failure

K Hristova[1]; R Marinov[1]; RB Singh[2]; G Cornelissen[3]; TZ Katova[1]; V Kostova[1]
[1]National Heart Hospital, Sofia, Bulgaria; *[2]Halberg Hospital and Reaserch Institut , Moradabad, India*; *[3]University of Minnesota, Minneapolis, United States of America*

Heart Rate Variability (HRV) is a noninvasive and sensitive technique to evaluate cardiovascular autonomic control and major determinant of cardiovascular health.Reduced HRV is an independent risk factor for heart disease and increased risk of mortality after a diagnosis of CHF or LV dysfunction

The aim of the study is to analyze this circadian pattern in the HRV in patients with CHF and severe LV dysfunction (EF < 35%) in patients with HFrEF and analyzed the effect of Ivabradyne to improve the reduced HRV.

Methods: Were evaluated 30 pts mean ages 58.5 ± 3.5y with EF% 33.5 ± 2.3 % in sinus rhythm. Holter ECG monitoring for 48 hours were performed in all pts in order to analyze the HRV before treatment with Ivabradin (7,5 mg two times per day),1.st week and also a month after therapy. HRV was assessed based on the RR intervals and ECG signal was recorded using leads, to obtain a predictive value of reduced HRV by measuring 48 h standart deviation of N-N intervals (SDNN), also HRVindex, derived by dividing total heart rate intervals by the high of histogram. The echocardiography with speckle tracking imaging was performed basal and 1mFU in order to extract longitudinal strain.

Results: All patients with HFrEF are with reduced SDNN -55, 6 ± 5 ms and reduced GLS- 12.93 ± 3 %. The highest value for SDNN (>70 ms) and HRV index are around 6.00 am and the lowest value are around 6.00 pm (< 40 ms). Considering results from all SDNN and HRV index before and after treatment with Ivabradine, the lowest values occurs, on average, around 06:00 p.m., circadian rhythm is found for all parameters before treatment and follow up (1wFU, 1mFU). After 1mFU therapy with Ivabradyn were found significant improvement ot reduced HRV - SDNN 65.5 ± 3.6 ms , also in HRV index – 41.1 ± 1.2 ms. Reduced HRV is fairly correlated with EF % ($p < 0.01$, r= 0.65) and GLS % ($p < 0.01$, r=0.47) .

Conclusions: This is the first study to assess global physiological consequences of the circadian clock specifically within the myocardial deformation and HRV.We provide evidence that the cardiomyocyte circadian clock influences not only heart rate and the responsiveness of the heart to increased workload, but and circadian pattern of regional dysfunction and deformation, which is important for global ventricular function. Ivabradin has positive effect to increase reduced HRV in patient with HFrEF.

Circadian clock and variability

1mFU	06:00	12:00	18:00	24:00
GL Strain (%)	-13.22±3.19	-12.99±2.3	-12.76±3.19*	-12.95±2.86
SDNN	-65.93±4.91	-40.78±5.45	-28.42±6.73*	-30.53±4.45
HRVindex	41.99±1.26	40.06±1.12	37.04±1.34*	39.31±1.28

P1698

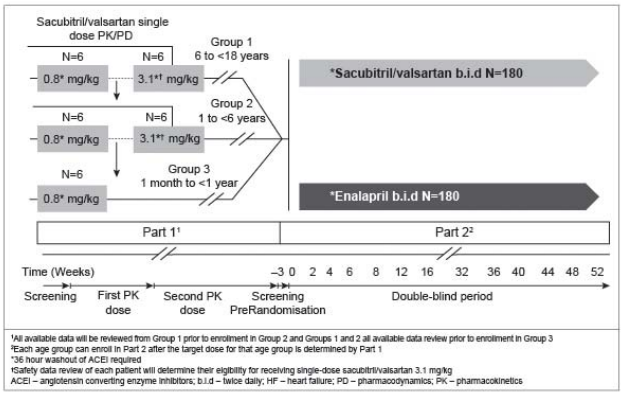
Effects of sacubitril/valsartan vs. enalapril in paediatric patients with heart failure due to systemic LV systolic dysfunction: Design and rationale of the PANORAMA-HF study

R Shaddy[1]; F Chen[2]; C Canter[3]; N Halnon[4]; J Rossano[1]; P Kantor[5]; D Bonnet[6]; M Burch[7]
[1]The Children's Hospital of Philadelphia, Philadelphia, United States of America; *[2]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*; *[3]Washington University, MO, United States of America*; *[4]UCLA, Los Angeles, United States of America*; *[5]University of Alberta, Edmonton, Canada*; *[6]Necker Hospital University, Paris, France*; *[7]Great Ormond Street Hospital for Children, London, United Kingdom*

Background: Paediatric heart failure (HF) is characterised by significant morbidity and mortality, frequent hospitalisation, and poor quality of life. The rationale for medical therapy of paediatric HF primarily comes from adult studies. Sacubitril/valsartan (LCZ696) reduced mortality and delayed HF progression vs. enalapril, and was generally well tolerated in the PARADIGM-HF trial in adults with HF with reduced ejection fraction.

Study Design: This multicentre study will use an adaptive seamless, two-stage design (Figure). In part 1, an open-label, single-dose study with 36 paediatric HF patients (1 month to < 18 years) stratified into 3 age groups (Group 1: 6 to < 18 years; Group 2: 1 to < 6 years; Group 3: 1 month to < 1 year) will receive sacubitril/valsartan in a sequential overlapping fashion and in descending age group order. The doses for Group 1 and 2 (0.8 mg/kg and 3.1 mg/kg) corresponds to ˜50 and 200 mg dose of sacubitril/valsartan in an adult with 65kg bodyweight. Group 3 will only be assessed with the 0.8 mg/kg dose of sacubitril/valsartan. The dose for Group 2, and subsequently for Group 3, may be adjusted based on safety information from the previous group(s). Pharmacokinetics/pharmacodynamics and biomarkers (N-terminal pro-B-type natriuretic peptide and cyclic guanosine monophosphate) will be evaluated. Part 2 is a 52-week randomised, double-blind, parallel-group, active-controlled study. Eligible patients (N=360) will be stratified by age and functional classification and randomised to receive either sacubitril/valsartan or enalapril (target dose: 0.2 mg/kg twice daily (b.i.d); maximum dose 10 mg b.i.d). As there is no generally agreed, validated clinical efficacy endpoint for this patient population, a Global Rank primary endpoint has been developed; this will be derived by ranking patients (worst to best outcome) according to clinical events such as death, listing for urgent heart transplant or mechanical life support, worsening HF, and measures of functional assessment (New York Heart Association/Ross) and patient-reported outcomes (Patient Global Impression of Severity and the paediatric Quality of Life Inventory [physical functioning]). Additional patients will be enrolled to ensure that a minimum of 80 patients with clinical events are obtained. Safety areas of interest include identified risks common to both sacubitril/valsartan and enalapril such as hypotension, hyperkalaemia, worsening renal function, and angioedema.

Conclusion: This adaptive study design will determine if sacubitril/valsartan can offer a greater clinical benefit vs. enalapril in children with HF.



P1699

Safety of sacubitril/valsartan in patients receiving statins in the PARADIGM-HF trial

H Streefkerk[1]; D Anand[2]; W Zhou[2]; B Balas[1]; H Schwende[1]; V Shi[2]
[1]Novartis Pharma AG, Basel, Switzerland; *[2]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*

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Background: Sacubitril/valsartan (S/V) reduces mortality and morbidity in patients with chronic heart failure with reduced ejection fraction (HFrEF). Healthy human studies showed that co-administration of S/V increased the Cmax of atorvastatin and its metabolites by up to 2-fold and AUC by up to 1.3-fold but did not find a similar increase with simvastatin. Both statins are widely used in patients with HFrEF.
Purpose: To determine if concomitant use of statins with S/V was associated with a higher incidence of adverse events (AEs) in the PARADIGM-HF trial.
Methods: In the double-blind (DB) PARADIGM-HF trial, 8442 eligible patients with symptomatic HFrEF were randomised, after consecutive run-in with enalapril (ENA) and S/V, to receive S/V or ENA in addition to other background therapy. In this post hoc analysis, potentially statin-related AEs and serious AEs (SAEs) were compared by treatment group, statin use (yes/no) at baseline and statin dose level (highest dose defined as 80 mg atorvastatin or simvastatin) in patients treated in DB period. The homogeneity of risk ratios (RR, S/V vs. ENA) of potentially statin-related AEs was evaluated by Breslow-Day test.
Results: Of the 8432 patients exposed to study treatment, 4653 (55.2%) received statins at baseline (most frequently atorvastatin or simvastatin). Common statin-related AEs including rhabdomyolysis, hepatitis and pancreatitis were low in both S/V and ENA groups (table). Rhabdomyolysis was reported in the S/V (n = 4) and the ENA (n = 3) group, with 1 case in each treatment group occurring without statin treatment. Medical review of rhabdomyolysis cases reported with S/V did not support a potential causal association with the drug (either an improbable temporal relationship with study drug, or presence of confounding factors). None of the assessed statin categories including statin vs. no statin, highest dose statin, atorvastatin, simvastatin or the combination demonstrated a statistically significant signal ($p < 0.05$) for an interaction between S/V and statins. The overall incidences of AEs and SAEs were higher in patients on a highest dose statin than in patients not taking statins but generally comparable between S/V and ENA treatment groups. The rate of overall AEs and potentially statin related AEs were also consistent across the frequently used statins.
Conclusions: Irrespective of concomitant statin treatment or statin dose level, no clinically meaningful differences in the AE profile were seen between S/V and ENA groups.

	Any statin dose		Highest-dose statins		No statin	
Preferred term	S/V N=2369	ENA N=2362	S/V N=188	ENA N=192	S/V N=1834	ENA N=1867
Any AE	1968 (83.07)	1994 (84.42)	172 (91.49)	174 (90.63)	1451 (79.12)	1509 (80.82)
Musculoskeletal pain	40 (1.69)	28 (1.19)	5 (2.66)	6 (3.13)	9 (0.49)	20 (1.07)
Arthralgia	85 (3.59)	79 (3.34)	8 (4.26)	4 (2.08)	41 (2.24)	40 (2.14)
Back pain	104 (4.39)	84 (3.56)	13 (6.91)	7 (3.65)	60 (3.27)	54 (2.89)
Myalgia	23 (0.97)	24 (1.02)	2 (1.06)	1 (0.52)	6 (0.33)	14 (0.75)
Rhabdomyolysis	3 (0.13)	2 (0.08)	1 (0.53)	0	1 (0.05)	1 (0.05)
Pancreatitis	1 (0.04)	4 (0.17)	1 (0.53)	0	1 (0.05)	4 (0.21)
Pancreatitis acute	8 (0.34)	2 (0.08)	1 (0.53)	1 (0.52)	0	2 (0.11)
Hepatitis	2 (0.08)	1 (0.04)	0	0	1 (0.05)	2 (0.11)

Data are n (%)
AE, adverse event; ENA, enalapril; S/V, sacubitril valsartan

P1700

Achievement of optimal medication doses during the heart failure titration process

S O'leary[1]; M Griffin[2]; J O'neill[3]; M Bermingham[1]; C Blaine[3]; G Ryan[3]
[1]University College Cork, School of Pharmacy, Cork, Ireland; *[2]Connolly Hospital Blanchardstown, Pharmacy Department, Dublin, Ireland*; *[3]Connolly Hospital Blanchardstown, Heart Failure Clinic, Dublin, Ireland*

Background: Patients newly diagnosed with heart failure (HF) are initiated on disease-modifying drug therapies and are gradually up-titrated to target doses. The success of this approach varies with studies reporting between 31-53% of patients achieving ACE inhibitor or angiotensin receptor blocker (ACEi/ARB) target dose and between 18-91% of patients achieving beta-blocker target dose.
Purpose: To determine (i) the extent to which prescribing of recommended HF therapies and achievement of target doses of these agents is accomplished in patients attending a nurse-led outpatient HF clinic and (ii) the rate of adverse effects experienced by patients and the effect of adverse effects on titration to target doses.
Methods: This was a retrospective cohort study of HF patients post- de novo HF hospitalisation who first attended a nurse-led outpatient HF clinic in an Irish teaching hospital from January 2014 - June 2015. Chart review confirmed medications and doses prescribed, clinical and biochemical parameters. Target dose was defined from the 2012 European Society of Cardiology heart failure guidelines where available or from the Summary of Product Characteristics of the originator product.
Results: Data were available for 51 patients (average age 65.3 ± 14.5 years, 67% male). Of these, 42 patients had heart failure with reduced ejection fraction (HFrEF) and 9 had heart failure with preserved ejection fraction (HFpEF). Median duration of titration was greater in HFrEF patients (89 days) compared to HFpEF patients (47 days). At the end of the titration period, an ACEi/ARB was prescribed to 93% of HFrEF and 78% of HFpEF patients. A beta-blocker was prescribed to 93% of HFrEF and 67% of HFpEF patients. In the HFrEF group 33.3% of patients were titrated to target ACEi/ARB dose, 9.5% to target beta-blocker dose and 4.8% to the target dose of both medications. An adverse effect was experienced by 92.2% of all patients during titration. The most common adverse effects were excessive reduction in blood pressure (n = 31, 60.8%), excessive reduction in heart rate (n = 26, 51.0%), high serum potassium level (n = 18, 35.3%) and deterioration in renal function (n = 20, 39.2%). No patient experienced adverse changes to pulmonary function. Taking into account titration limiting adverse effects, an individualised maximum tolerated ACEi/ARB and beta-blocker dose was reached in 90.5% and 78.6% of HFrEF patients respectively.
Conclusion: Over an average period of three months, a nurse-led HF clinic successfully titrated HFrEF patients to target medication doses which were maintained over one-year follow-up. The majority of patients were titrated to maximum tolerated doses of HF medications however there remain patients who are not reaching these individualised doses. Adverse effects were the main burden preventing titration in both HF patient groups.

P1701

Frusemide adjustment in heart failure HF) during ramadhan: effectiveness and safety pilot study.

MK Othman[1]; SL Yang[2]; HB Liew[1]; CH Yen[2]; KK Chow[1]; JRJ Jinuin[1]; BC Beh[1]; MH Mohd Asnawani[1]; SL Tan[3]; JH Chi[3]; QL Goh[3]
[1]Queen Elizabeth II Hospital, Cardiology, Kota Kinabalu, Malaysia; *[2]Clinical Research Centre Queen Elizabeth II, Kota Kinabalu, Malaysia*; *[3]Queen Elizabeth II Hospital, Pharmacy, Kota Kinabalu, Malaysia*

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Background and Objectives: Compliance to medication and fluid restriction are important to prevent HF exacerbations1. During Ramadhan months, Muslim are fast from dawn to sunset2. There are no published guidelines/consensus in adjustment of medication during Ramadhan. Our study aim to evaluate the effectiveness and safety of standardized approach to individualise HF medications to twice-a-day regime, especially frusemide.
Methodology: Thirty patients recruited from outpatient HF clinic in a tertiary hospital. Convenience sampling for both fasting (n = 17) and non-fasting (n = 13) patient whom fulfilled selection criteria. Subjects were followed up before, during and after Ramadhan. Clinical variables and HF outcomes were measured at baseline and follow-up. Frusemide is adjusted to bid regime with 2/3 total daily dose at break of fast.
Findings: Mean age was 56.3 year-old; 90% male. Half of the patients have ischemic cardiomyopathy. 86.7% in sinus rhythm. Comorbidities includes hypertension (70%), diabetes mellitus (40%), dyslipidemia (43.3%), chronic kidney disease (23.3%) and thyroid dysfunction (3.3%). Pre-exsiting HF medication includes beta blocker (94%), ARB/ACEi (88%), MRA (94%), nitrates (24%) and frusemide dose were 70% od, 18% bid and 12% tid. Majority (88%) were steady medication for minimum 6 months. All patients were warm and dry at baseline. 60% has no prior HF-related hospitalization. Among fasting patients, there were no differences throughout study in blood pressure, heart rate and body weight. However, one hospitalization due to dehydration secondary to overdiuresis, another patient required frusemide uptitration as outpatient. Majority (87%) were able to comply to adjusted regime. 14% of the patient reported not thirsty and 43% very thirsty.
Conclusions: In our study, individualized frusemide adjustment among HF patient during Ramadhan is well-tolerated, effective and safe. However this study is limited by small sample size therefore further study is required to support wider practice recommendation.

P1702

Rationale and design of TRANSITION: a multi-center, randomised, open-label study comparing pre- versus post-discharge initiation of sacubitril/valsartan in hospitalised patients with ADHF and HFrEF

DP Figal[1]; R Wachter[2]; M Senni[3]; J Belohlavek[4]; A Noe[5]; D Carr[5]; D Butylin[5]
[1]Hospital Universitario Virgen de la Arrixaca, Universidad de Murcia, Murcia, Spain; *[2]Department of Cardiology, University Hospital Göttingen, Gottingen, Germany*; *[3]Heart Failure and Heart Transplant Unit ASST Papa Giovanni XXIII , Bergamo, Italy*; *[4]General Teaching Hospital, Charles University in Prague, Prague, Czech Republic*; *[5]Novartis Pharma AG, Basel, Switzerland*

On behalf of: TRANSITION study investigators
Funding Acknowledgements: This study was funded by Novartis Pharma AG

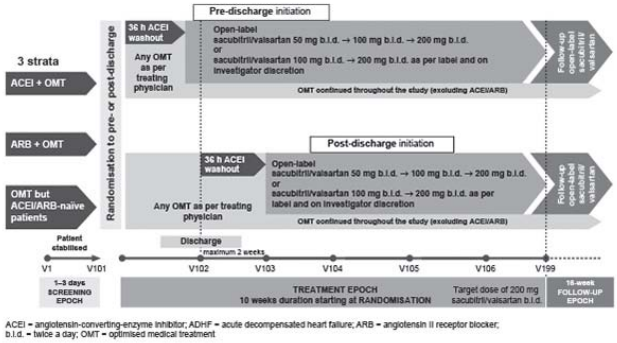
Background: Despite short-term symptomatic improvement with current treatments, the prognosis for hospitalised patients with acute decompensated heart

failure (ADHF) remains poor, with over 15–20% mortality and 30–40% readmission rates in the first year post-discharge. In the PARADIGM-HF trial, the angiotensin-receptor-neprilysin inhibitor sacubitril/valsartan was well tolerated and, compared with enalapril, was found to provide highly significant reductions in rates of mortality and HF hospitalisation, and to delay HF progression. Given that PARADIGM-HF enrolled only patients who were ambulatory at the time of inclusion, there is limited evidence at present on the safety and tolerability of initiating sacubitril/valsartan treatment in patients hospitalised due to ADHF.

Methods: TRANSITION is a randomised, multi-centre, open-label clinical trial designed to compare pre- versus post-discharge sacubitril/valsartan treatment initiation in patients hospitalised for ADHF, including patients with newly diagnosed HF. The study aims to randomise 1000 hospitalised patients with HF with reduced ejection fraction (HFrEF, LVEF ≤ 40%) after hemodynamic stabilisation (defined as no need for intravenous diuretics in 24 hours prior to screening and systolic blood pressure > 110 mmHg for at least 6 hours prior to randomisation). All patients are stratified by pre-admission treatment status: on an angiotensin converting enzyme inhibitor (ACEI), on an angiotensin receptor blocker (ARB), or ACEI/ARB-naive. Patients are randomised 1:1 within each stratum for initiation of sacubitril/valsartan treatment either pre-discharge (no later than 12 hours before discharge) or within 1–14 days post-discharge. The study design is represented in Figure 1. The primary endpoint is the proportion of patients achieving the target dose of 200 mg sacubitril/valsartan twice daily at 10 weeks after randomisation. Key exploratory endpoints will assess among others, patterns of biomarkers (N-terminal pro B-type natriuretic peptide and high-sensitivity-troponin-T), signs and symptoms, re-hospitalisations and other health resource utilisation parameters.

Current status: Presently, 244 patients have been randomised in 16 countries and 132 centres at the time of abstract submission.

Conclusion: TRANSITION study will provide evidence on the safety and tolerability of initiating sacubitril/valsartan treatment pre-discharge or shortly after discharge, in hemodynamically stabilised patients with HFrEF hospitalised for ADHF.



ACEI = angiotensin-converting-enzyme inhibitor; ADHF = acute decompensated heart failure; ARB = angiotensin II receptor blocker; b.i.d. = twice a day; OMT = optimised medical treatment

STUDY DESIGN

P1703

A double-blind, randomised, two arm parallel group trial to determine the effects of torasemide versus furosemide on one marker (PIP) of cardiac fibrosis in patient with HFpEF and T2DM

T D Trippel[1]; S Von Linthout[1]; R Lindhorst[1]; A Sandek[2]; A Bobenko[1]; B Pieske[1]; F Edelmann[1]; C Tschoepe[1]
[1]*Charite - Campus Virchow-Klinikum, Department of Internal Medicine-Cardiology, Berlin, Germany*; [2]*University Medical Center Gottingen (UMG), Department for Cardiology and Pneumology, Gottingen, Germany*

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Background: Heart failure with preserved ejection fraction (HFpEF) accounts for 50% of HF cases. HFpEF is associated with diastolic dysfunction and myocardial remodeling. Serum propeptide of procollagen type I (PIP) strongly correlates with the turnover of extracellular cardiac matrix proteins and ongoing cardiac remodeling and PIP may reflect the rate of extracellular synthesis of collagen type I as a surrogate parameter. Loop diuretics such as torasemide and furosemide have been described to alter PIP levels. We evaluated the effects torasemide vs. furosemide on serum PIP levels in patients with HFpEF and diabetes mellitus type II.

Material and Methods: We performed a monocentric, double-blind, randomized, two-armed, parallel-group, active controlled clinical trial in 35 patients to determine the effects of a 9 month treatment with torasemide 5 mg (test medication) versus furosemide 20 mg (active control) on one marker (PIP) of cardiac fibrosis.

Results: 15 of enrolled patients were female (42%), mean age in DROP-PIP was 69 yrs, mean was BMI 34,7 kg/m2, 83% were NYHA class II/III. Echocardiographic characteristics at baseline showed a mean LVEF 61%, LVMI 121,7 g/m2, E/E' 14, and LAVI of 40 ml with a NT-proBNP of 174 ng/l and a 6MWT distance of 421 m. 28 patients completed the trial per-protocol. On average patients treated with Furosemide experienced a non-remarkable absolute increase for PIP of 1.15 ± 38.1 (paired t-test, $p = 0.9062$), in contrast Torasemide treated patients show a negligible absolute reduction of -1.25 ± 29.1 ($p = 0.8854$) in the per -protocol population. Both Treatment groups did not show a significantly different treatment effect regarding a change in absolute PIP levels from baseline to follow-up ($p = 0.8583$). Key secondary endpoints were neutral.

Conclusion: In the present patient population with HFpEF and T2DM, loop diuretic therapy did not significantly affect PIP serum levels as a marker of cardiac fibrosis. Torasemide and furosemide did not show significant differences in the effect exerted on serum PIP level.

P1704

Comparative efficacy of long-term digoxin and ivabradine therapy on prognosis, left and right heart functional parameters in patients with chronic heart failure and preserved ejection fraction

LR Liana Tumasyan[1]; KG Adamyan[1]
[1]*Institute of Cardiology, Yerevan, Armenia*

The aim of study was to assess the comparative efficacy of long-term digoxin (D, 0.25 mg) and ivabradine (I, 15 mg) therapy on prognosis, left (LV) and right ventricular (RV), left atrial (LA) and right (RA) atrial parameters, NT-pro-BNP and high sensitivity C-reactive protein (hsCRP) levels in pts with III NYHA functional class chronic heart failure (CHF) and preserved LV ejection fraction (PEF).

Methods: 165 pts (age 63.2) with symptomatic CHF and PEF in sinus rhythm with heart rate (HR)>70 bpm were randomly assigned to groups A ($n = 55$, receiving D), B ($n = 53$, receiving I) and C ($n = 57$, non-receiving both drugs) in addition to ACE inhibitors, beta-blockers and diuretics. RV fractional area change (FAC), tricuspid annulus plane systolic excursion (TAPSE), pulmonary artery (PA) ejection (ET) time, RA and LA functional index (FI), relation of pulmonary vein (PV) systolic and diastolic fraction (S/D), PV systolic contribution (SC),difference between duration of reversal atrial flow (Ar) and late (A) transtmitral filling, NT-pro-BNP and hsCRP levels were assessed at baseline, 12, 24 and 36 months.

Results: 1-year, 2-year and 3-year mortality were 29.1%, 36.4% and 43.6%; 30.2%, 37.7% and 45.5%; 35.1%. 42.1% and 52.6% in groups A, B and C, respectively. 1-year, 2-year and 3-year hospitalization rates were 41.8%, 52.7% and 61.8%; 43.4%, 54.7% and 62.3%; 63.2%, 75.4% and 82.5% in groups A, B and C, respectively. Event-free analysis showed lower probability (RR reduction) of 1- year, 2- year and 3-year hospitalization at 33.9% and 31.3%; 30.1% and 27.5%; 25.1% and 24.5%, respectively, in groups A and B compared to group C ($P < 0.05$) and trend to reduction of 1-year, 2-year and 3-year mortality at 17.1% and 14%, 13.5% and 10.5%, 13.5% and 17.1%. 1-year I and D treatment increased (%) RV FAC at 28.5 and 27.2, TAPSE at 42.1 and 40.1, PA ET at 17.9 and 16.2, PV SC at 39.9 and 38.1, RA FI at 48.8 and 46.4, LA FI at 46.7 and 45.4, PV S/D at 35.2 and 33.4, decreased Ar-A at 82.7 and 79.1, levels of NT-pro-BNP at 36.1 and 34.9 and hsCRP at 40.1 and 39.9 ($p < 0.05$ for all). Reduction of NT-pro-BNP, hsCRP≥40% and HR≥25% was associated with significant improvement of morbidity compared to decrease of NT-pro-BNP, hsCRP < 25% and HR < 15% (RR 0.35, 0.33 and 0.32, $p < 0.05$), respectively. Similarly, changes of RA and LA FI, PV SC≥50%, PAET at≥25% and Ar-A ≥80% were associated with significant improvement of hospitalization compared to changes of RA and LA FI, PV SC < 30%, PAET < 15% and Ar-A < 60% (RR 0.37, 0.36, 0.35, 0.34, and 0.33, $p < 0.05$, respectively).

Conclusions: 1) Changes of Ar-A ≥80%, RA and LA FI, PV SC≥50%, NT-pro-BNP, hsCRP≥40; PAET and HR≥25% identified pts with hospitalization risk reduction. 2) I and D use associated with similar significant reduction of morbidity and trend to reduction of mortality due to significant improvement of RV, LA and RA functional parameters, neurohormonal and inflammation status and HR reduction.

P1705

Results of a single center experience on 200 consecutive patients treated with Entresto (sacubitril/valsartan).

A Canu[1]; V Maurin[1]; P Dos Santos[1]; F Picard[1]
[1]*University Hospital of Bordeaux, Bordeaux, France*

Background: Guidelines for the treatment of chronic heart failure (HF) currently recommend Entresto as replacement of ACE-I or ARB in patients with HFrEF who remain symptomatic despite optimal treatment to reduce the risk of HF hospitalization and cardiovascular death. However, the detail of the improvement sequence of patients treated by angiotensin receptor neprilysin inhibitor remains unknown due to the lack of data during the run in period before the randomization in the PARADIGM trial.

Objective: We report the results of our monocentric cohort of 200 consecutive systolic HF patients treated with Entresto. Between October 2015 and September 2016, 200 patients received Entresto, 180 were evaluated one month after introduction, 157 three months after, and 99 after six months of follow up.
Results: All patients were in stable hemodynamic condition with an optimized pharmacological therapy at baseline (95% were treated with ACE-I or ARB, 93.5% with betablocker and 80% with MRA). 81% were men, mean age was 59 years old. 51% of patients had ischemic HF and the median duration of HF was 8.5 years. 2.5% of the patients were in NYHA class 1 (but with poor prognosis factor such as elevated BNP level), 68% were in class 2, and 29.5% in class 3. During the follow-up period, 8.5% patients discontinued treatment for adverse events, 6% were heart transplanted, and 6% died of cardiovascular cause. Entresto was initiated at half dosage or less depending on the fragility of the patient, (78% at 49 mg/51 mg twice daily and 22% at 24 mg/26 mg twice daily). Patients attended a first follow-up appointment after one month of treatment. If tolerance was good, dosage of sacubitril/valsartan was increased. At 3 months, 82% of patients received the target dose of 97 mg/103 mg, 14% the half dose (49/51mg) and 4% the low dose (24/26mg). After 1 month of treatment, functional class improved significantly with 4.5% NYHA 1, 81% NYHA 2, and 14.5% NYHA 3 ($p = < 0.001$), as the 6 minutes walk distance (511 vs 461m, $p < 0.0001$). These improvements occurred from the first month of treatment with the half dosage of sacubitril/valsartan and were still significantly present after six months of follow up. Regarding tolerance, systolic blood pressure decreased (105 vs 109mmHg, $p < 0.001$) and serum creatinine increased significantly after one month of treatment (117 vs 108 μmol/L, $p < 0.001$). After six month of treatment, the dose of furosemide decreased (114mg vs. 74mg, $p < 0.0001$) and the BNP did not significantly change (587pg / ml vs. 709, $p = 0.14$).
Conclusion: The results of this "real life" cohort confirm the benefits of the treatment by Entresto in stable systolic heart failure patients. These changes seem to appear very early after introduction of the treatment and to be maintained over time.

P1706
Collaboration cardiologists-pharmacists for improving heart failure medication management.

Y Yohan Audurier[1]; B Mathieu[1]; N Chapet[1]; F Leclercq[2]; JL Pasquie[2]; A Jalabert[1]; G De Barry[1]; C Breuker[1]; K Solecki[2]; F Roubille[2]
[1]University Hospital Arnaud de Villeneuve, Pharmacy department, Montpellier, France; *[2]University Hospital Arnaud de Villeneuve, Cardiology department, Montpellier, France*

A recent retroactive study led by the unit of cardiology of our universitary hospital center had shown an underprescription for patients with heart failure (HF). So, we decided to confirm these results with a prospective study. For improving medication management, one senior pharmacist and one junior pharmacist, located in the unit, were associated to the cardiology medical team.
The aim of this study was to identify factors of underprescription for drugs recommanded in HF pharmacotherapy (ESC 2012 then 2016). In the same time, listed therapeutic optimization realized by the collaboration between clinical pharmacists and cardiologists.
This prospective study is currently in progress. Preliminary results were extracted on nine month (march to december 2016). Each patient admitted in cardiology units (79 beds) with a diagnostic of HF were checked by pharmacy team. All discrepencies with recommandations established by ESC about HF medication management were registred. Reasons of underprescription were recorded and if necessary a proposition of correction was addressed to the prescriber.
In the preliminary results 395 patients were included. During hospitalization, 129 patients (32.7%) didn't have B-blocker prescription and 186 patients (47.1%) didn't have ACE inhibitor/Angiotensin II receptor antagonist prescription. Mains reasons of underprescription were HF with preserved ejection fraction (EF), hemodynamic intolerance, acute renal failure, asthma/chronic bronchopneumonia, atrioventricular block, aortic stenosis. Moreover, 137 patients had spironolactone or eplerenone in their prescription (34.68%). Others drugs recommanded were less prescribed, sacubitril/valsartan (22), ivabradine (7), digoxine (6). Several patients didn't have medical reason for these discrepencies, so 24 pharmaceutical optimizations (PO) had been realized : 12 concerned ACE inhibitors, 9 B-blockers, 1 sacubitril/valsartan and 1 about ivabradine. These PO concerned introduction drugs or dose increasing.
Discussion: We can see that medication management of HF wasn't perfect. Most of underprescriptions were medically justified but an important number didn't have medical reason of this lack. The collaboration between physicians and pharmacists can improve medication management of HF patients. Others results are in progress especially about proportions of underprescription reasons for patients with reduced EF and iron supplementation.
Conclusion: This collaboration is a complete success, physicians and pharmacists will continue to work together about medication management of HF and others studies about therapeutic education are in progress.

P1707
Loop diuretic down-titration in stable chronic heart failure: role for spot urinary chloride analysis?

FH Frederik Hendrik Verbrugge[1]; P Martens[1]; L Boonen[1]; P Nijst[1]; D Verhaert[1]; P Noyens[1]; P De Vusser[1]; M Dupont[1]; WHW Tang[2]; W Mullens[1]
[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium; *[2]Cleveland Clinic Foundation, Cardiovascular Medicine, Cleveland, United States of America*

Background: Loop diuretic efficiency, defined as natriuresis per dose of loop diuretics administered, is a powerful predictor of clinical outcome in chronic heart failure (CHF), irrespectively of underlying renal function. A poor natriuretic response to loop diuretics may indicate either true diuretic resistance, which is associated with residual congestion and poor clinical outcome, or alternatively thorough decongestion and relative sodium depletion. Therefore, a preserved natriuretic response to loop diuretics in CHF may indicate subclinical congestion or high salt intake, indicating the need for continued diuretic treatment.
Purpose: This study investigated spot urinary chloride concentration, assessed with a simple point-of-care test strip, in euvolemic CHF patients after intake of maintenance loop diuretics. It was hypothesized that lower urinary chloride levels would predict successful down-titration. Urinary chloride instead of sodium concentration was measured because no point-of-care test is available for sodium and both urinary sodium and chloride are strongly correlated.
Methods: This prospective cohort study included 50 ambulatory CHF patients on maintenance loop diuretic therapy without recent (<3 months) hospital admission, clinical signs of volume overload, or recent adjustment in neurohumoral blocker or diuretic therapy. Spot urinary samples were collected immediately after loop diuretic intake. Subsequently, maintenance loop diuretic dose was reduced with 50% or stopped if ≤40 mg furosemide equivalents. Successful down-titration was defined as persistent dose reduction after 7 days, without body weight increase >1.5 kg. Patients were followed for up to 30 days.
Results: Urinary chloride concentration was 3,045 ± 1,271 mg/L overall. Patients with a higher versus lower urinary chloride concentration showed not differences in baseline characteristics, took the same dose of loop diuretics [40 mg (20 40 mg) furosemide equivalents; P-value=0.509] and had similar plasma NT proBNP levels [1,179 ng/L (311 2,195 ng/L) versus 900 ng/L (255 1,622 ng/L), respectively; P-value=0.461]. Down-titration was successful in 72% versus 76% in both groups, respectively (P-value=1.000). At 30 days, loop diuretic dose remained reduced in 59% versus 76% of patients, respectively (P-value=0.238). The proportion of patients that was free from any diuretic therapy at 30 days was 45% versus 62% in the high versus low chloride concentration group (P-value=0.265).
Conclusion: Successful loop diuretic down-titration could be performed in 3 out of 4 euvolemic CHF patients, irrespectively of urinary chloride concentration on spot samples collected after diuretic intake. The need for long-term diuretic use may be reduced in patients with low urinary chloride concentrations.

P1708
One-year outcome in patients with heart failure with mid-range ejection fraction hospitalized due to worsening heart failure

M Michal Marchel[1]; A Tyminska[1]; A Kaplon-Cieslicka[1]; K Ozieranski[1]; M Peller[1]; P Balsam[1]; MG Crespo-Leiro[2]; AP Maggioni[3]; J Drozdz[4]; KJ Filipiak[1]; G Opolski[1]
[1]Warsaw Medical University, Warsaw, Poland; *[2]Complexo Hospitalario Universitario A Coruña (CHUAC), A Coruna, Spain*; *[3]Centro Studi ANMCO (Associazione Nazionale Medici Cardiologi Ospedalieri), Florence, Italy*; *[4]Medical University of Lodz, Lodz, Poland*

Background: Heart failure (HF) comprises a wide range of patients (pts), from those with normal to those with reduced left ventricular ejection fraction (LVEF). According to 2016 European Society of Cardiology (ESC) HF guidelines, pts with LVEF in the range of 40-49% represent a "grey area," which is defined as heart failure with mid-range ejection fraction (HFmrEF). Little is known about the clinical characteristics and prognosis in the HFmrEF group.
Purpose: Our aim was to determine the incidence of HFmrEF in the group of pts acutely hospitalized due to worsening heart failure as well as to assess the prognosis and prognostic factors in this group.
Method: This study was based on two multicenter prospective observational surveys of the ESC: ESC-HF Pilot Survey and ESC-HF Long-Term Registry conducted in 211 European cardiology centers, including 35 centers from Poland. The current study included Polish pts from both ESC registries, admitted to hospital for new-onset or worsening HF. Pts were divided into three groups based on LVEF: the HFpEF group (LVEF ≥50%), the HFmrEF group (40-49%) and the HFrEF group

(< 40%). We compared in-hospital and one-year outcomes in all 3 groups. The primary endpoint was all-cause death at one year. The secondary endpoint was a composite of all-cause death and hospital readmission for HF worsening at one year. We assessed the frequency of the primary and the secondary endpoints and their predictors in the HFpEF, HFmrEF and HFrEF group.
Results: We included 1306 pts. 230/1306 pts with HFmrEF represented 17,6%, 340/1306 HFpEF 26,0% and 736/1306 HFrEF 56,4% of the whole analyzed group. Median LVEF in HFmrEF was 43% (40-45). Median hospitalization length was 7 (4-11) days. 10,7% HFmrEF pts met the primary endpoint, comparing to 17,5% in HFrEF and 14,4% in HFpEF (p = 0,02) pts. 33,7% met the secondary endpoint, comparing to 41,1% and 30,3% for HFrEF and HFpEF respectively (p = 0,09). A history of revascularization (PCI or CABG) and NYHA class at admission were predictors of the primary (HR 0,11; 95%CI 0,01-0,85, p = 0,04 and HR 2,58; 95%CI 1,14-5,82, p = 0,02 respectively) and secondary (HR 0,11; 95%CI 0,01-0,91, p = 0,04 and HR 1,77; 95%CI 1,13-2,77, p = 0,01 respectively) endpoints, while male gender was a predictor for the secondary endpoint (HR 0,47; 95%CI 0,28-0,79, p = 0,01) in HFmrEF.
Conclusions: Patients with HFmrEF represent one sixth (17,6%) of all HF patients hospitalized due to acute decompensation. 34% of HFmrEF either died or were rehospitalized in one year and 11% died in 12 months. Revascularization in the past was associated with a more favorable patients' outcome.

P1709
Heart failure with recovered ejection fraction: clinical characteristics, determinants and prognosis.

RM Rosa Maria Agra Bermejo[1]; E Gonzalez Babarro[2]; E Gonzalez Babarro[2]; JN Lopez Canoa[1]; JN Lopez Canoa[1]; A Varela Roman[1]; A Varela Roman[1]; I Gomez Otero[1]; I Gomez Otero[1]; M Oro Ayude[1]; M Oro Ayude[1]; P Parada Vazquez[1]; P Parada Vazquez[1]; I Gomez Rodriguez[2]; I Gomez Rodriguez[2]; O Diaz Castro[2]; O Diaz Castro[2]; JR Gonzalez Juanatey[1]; JR Gonzalez Juanatey[1]
[1]University Clinical Hospital of Santiago De Compostela, Department of Cardiology, Santiago De Compostela, Spain; *[2]Hospital Center of Montecelo, Cardiology, Pontevedra, Spain*

Background: The magnitude and the prognostic impact of recovering left ventricular ejection fraction (LVEF) in patients with heart failure (HF) and systolic dysfunction is unclear.
Purpose: The aim of our study was to evaluate the clinical characteristics and prognosis of patients with HFrecEF in a HF population.
Methods: We selected 449 consecutive patients with the diagnosis of HF and evaluation of LVEF in the previous 6 months, who were referred to two HF units. Patients with systolic dysfunction were only considered if a second echocardiogram was performed during the follow-up.
Results: At the time of diagnosis, 207 patients had LVEF >40% (HFpEF) and 242 had LVEF ≤40% (HFrEF). After 1 year, the LVEF was re-evaluated in all 242 patients with a LVEF ≤40%: in 126 (52%), the second LVEF was >40% (HFrecEF), and the remaining 116 (48%) had LVEF ≤40% (HFrrEF). After 58 ± 27 months of follow-up patients with recovered LVEF had a significantly lower mortality rate (HFpEF vs. HFrecEF: Hazard Ratio (HR)=.,286, 95% confidence interval (95%CI), 1.264–4.145, p = 0.019; HFrrEF vs. HFrecEF: HR=2.222, 95%CI, 1.189–4.186, p < 0.001) and hospitalization rate (HFpEF vs. HFrecEF: HR=1.411, 95%CI, 1.046–1.903, p = 0.024; HFrrEF vs. HFrecEF: HR=1.388, 95%CI, 1.002–1.924, p = 0.049). The following are predictors of LVEF recovery: younger age, lower functional class, treatment with renin-angiotensin-aldosterone system inhibitors and beta-blockers, absence of defibrillator use, and non-ischemic etiology.
Conclusions: Approximately half of the patients with HF and reduced LVEF who were re-evaluated after one year showed significant improvement in their LVEF, having a more favourable prognosis than HF with preserved and reduced ejection fraction.

P1710
Features of congestive heart failure in patients with post-MI one year after

AI Chesnikova[1]; ES Godunko[1]; VA Safronenko[1]; OE Kolomatskaya[1]; AV Khripun[1]; VP Terentyev[1]
[1]State Medical University of Rostov-on-Don, department of internal medicine 1, Rostov-on-Don, Russian Federation

It is on record that myocardial infarction (MI) contributes to the development of congestive heart failure (CHF) in most patients due to the maladaptive character of cardiac remodeling with progressive left ventricular dilation, violation of its geometry and decreased pumping function. It is important to measure the concentration of NT-proBNP to confirm congestive heart failure especially with preserved left ventricular ejection fraction. NT-proBNP secretion increases in accordance with the intensity of post-infarction heart changes.
The aim of the study was to investigate features of congestive heart failure in patients with post-MI one year after with distinct methods in the acute period.
Methods: 101 patients with acute myocardial infarction with ST- segment elevation were enrolled in the study. Their congestive heart failure clinical signs were assessed as well as their exercise tolerance and level of NT-proBNP at hospital discharge and one year after. Mean age was 56 ± 9, 99 years; with 81.9 % of men. All the patients depending on availability and revascularization method in acute myocardial infarction 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 NT-proBNP level exceeding the threshold. NT-proBNP ≥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 NT-proBNP was significantly lower in patients who underwent PCI (150 ± 90, 1 pg / ml), compared with an average level of NT-proBNP 470 ± 117, 6 pg / ml in patients without reperfusion (p = 0.000). In addition, there is a clear tendency towards accuracy by comparing the average NT-proBNP level of Groups 1 and 2 (p = 0.072) with the lowest value in patients with a history of PCI.
Analysis of CHF clinical manifestations showed that in patients of Group 1 and 2 after a year of observation there was a significant decrease in the average score on the rating scale of clinical state by 24% (p = 0.000) and 30% (p = 0.000) respectively and an increase in the average distance in the six-minute walk test (SMWT) in Group 1 by 10.5% (p = 0.000), in Group 2 - by 11.7% (p = 0.000). This indicates a reduction in the severity of CHF symptoms and enhanced exercise tolerance. However, in patients of Group 3 there was observed deterioration in exercise tolerance (p = 0.021) and more pronounced CHF symptoms (p = 0.022) over time.
Conclusion: Patients with PCI had a lower NT-proBNP level as well as less pronounced congestive heart failure as compared with the values in the experimental groups. Thus, it can be argued that there is a positive effect of the invasive strategy on congestive heart failure development and progression.

P1711
Prognostic value of different cardiohepatic syndrome variants during the chronic heart failure

Y Yuliya Shaposhnikova[1]; I A Ilchenko[1]; L Bobronnikova[1]
[1]Kharkiv National Medical University, Kharkiv, Ukraine

The aim of the study was to assess the influence and prognostic values of different variants of cardiohepatic syndrome (CHS) during the chronic heart failure (CHF). Design and method: A prospective analysis of the main symptoms and signs of CHF within 1 year in 86 patients were done (35 female (40.7%), 56.5 ± 10.7 years (M ± SD)). 52 patients with essential arterial hypertension (AH), 38 with atrial fibrillation (AP), 18 with myocardial infarction in anamnesis. Only ALT and/or AST increase was considered as hepatocellular CHS, only GGT and/or alkaline phosphatase (AP), direct (BDP) and / or total bilirubin (TB) increase – as cholestatic CHS. The simultaneous increase of markers of cytolysis and cholestasis was considered as mixed CHS.
Results: CHS was observed in 76 (91.9%) patients, mixed CHS prevailed - 51 patients (67.1%), less was cholestatic CHS - 23 patients (30.3%), only 2 patients were identified hepatocellular CHS (2.6%) presented. Cholestatic CHS more often than mixed CHS developed in obese patients (respectively 63.2% and 25.8%), in patients with diabetes (respectively 46.1% and 29.5%), chronic obstructive pulmonary disease (respectively 42.1% and 23.6%). Meanwhile mixed CHS more than cholestatic CHS developed in smokers (respectively 61.7% and 29.3%); in patients with atrial fibrillation (respectively 64.1% and 31.7%). Patients with mixed CHS worse than hepatocellular CHS was myocardial contractility (ejection fraction decrease, respectively: 60.4% and 32.7%). Manifestations of CHF associated not only with systemic congestion but also with peripheral edema more likely were observed in patients with hepatocellular CHS. Violations of the functional state of the liver were most significant in mixed CHS in comparison with cholestatic CHS and hepatocellular CHS. They characterized by more significant AST increase (respectively: 42.8 ± 2.4; 22.5 ± 2.1; 36.8 ± 2.7 U / L), ALT (respectively: 49.4 ± 4.8; 32.8 ± 1.7; 20.8 ± 1.8 U / l), DB (respectively: 10.8 ± 2.2; 8.2 ± 0.4; 4.4 ± 2.0 mmol / l) and TB (respectively: 29.8 ± 1.3; 26.4 ± 2.0; 14.4 ± 1.7 mmol / l). Also mixed CHS it was worse than cholestatic and hepatocellular CHS coagulation and blood parameters (prothrombin index, respectively: 69.8 ± 2.4; 78.2 ± 3.6; 82.5 ± 4,3%) and hypoalbuminemia (respectively: 36.8 ± 1.8; 47.2 ± 2.1; 43.4 ± 1.7 g / l). Indicators CHF markers - NT-proBNP were worse in patient with mixed CHS than cholestatic CHS (respectively: 879.48 ± 26.16 ng / ml; 642.52 ± 34.28 ng / ml control 154.22 ± 12.14 ng / ml (p < 0.05). The frequency of readmissions during the year was comparable in patient with mixed CHS and cholestatic CHS, but mortality was higher in patients with cholestatic CHS than with hepatocellular CHS (respectively 26.4% and 18.4%).
Conclusions: Patients with CHF and mixed variant CHS have a worse prognosis

and significantly worse functional state of the liver that is associated with higher levels of NT-proBNP.

P1712

Validation of the seattle heart failure model (SHFM) in an Iranian heart failure population

MH Soltani[1]; M Mirzaei[1]; M Seyed Hosseini[1]; R Omidvar[1]; A Dehghani[2]
[1]*Shahid Sadoughi University of Medical Sciences, Yazd, Iran (Islamic Republic of)*; [2]*Shahid Beheshti University of Medical Sciences, Department of Statistics, Shahid Beheshti University, Tehran, Iran (Islamic Republic of)*

Background: The accuracy of Seattle Heart Failure Model (SHFM) in Iranian heart failure patients is unclear. This study aims to validate SHFM for Iranian heart failure patients.
Methods and Results: We evaluated SHFM for 176 ambulatory patients with systolic heart failure (ejection fraction ≤40%), who presented to a Heart Center clinic located in Iran. Their one year mortality chance was calculated by the SHFM on their enrollment in the study. The patients were followed for one year for all cause mortality. All cause mortality was compared with predicted SHFM mortality to assess validity of the tool.
The mean age of participants was 58.2 ± 10.5 years and 119 (67.6%) were male. Mean ejection fraction was 24.7 ± 6.1. Etiology of heart failure in 61% of the patients was ischemic and 123 patients were in NYHA class II. Eight patients died during one year follow up. Sensitivity of the model for our population was 97% and specificity was 87.5%. The positive predictive value was 95.6% and negative predicted value was 20%. The overall accuracy of the model was 73.2%.
Conclusion: The SHFM can predict the one-year survival of Iranian heart failure patients reasonably accurate. However, the mortality prognostic ability of the model is poor in our population.

P1713

Frailty conferred incremental prognostic significance in Chinese heart failure patients with advanced heart failure

K Fan[1]; M Wong[1]; K Cheng[1]; C Chow[1]; KL Leung[1]
[1]*Grantham Hospital, Hong Kong, Hong Kong SAR People's Republic of China*

Background: Despite increased emphasis on comprehensive management of heart failure (HF), current assessment of HF focuses solely on disability. Frailty has been increasingly recognized as an important indicator of adverse prognosis in HF patients (pts). Recipients of heart transplants or ventricular assist device (VAD) are the best population to assess for potential improvement of HF-related frailty. Frailty among advanced HF in Chinese patients is unknown.
Method: Patients referred for consideration of heart transplantation or left ventricular assist device (LVAD) from May 2015 to Oct 2016 underwent frailty assessment. Physical frailty was defined as a positive response to 3 or more of the following 5 components: weak hand grip strength, 6-minute walk test <400m, poor appetite, physical inactivity and exhaustion. Cognitive assessment (Montreal Cognitive Assessment-Hong Kong version) and depression screening (Hospital Anxiety and Depression Scale) were also performed with positive response being MoCA score <22 and depression score ≥8 respectively. Total frailty score ranges from 0-7. All patients were prospectively followed for clinical outcomes.
Results: Fifty pts (38 men: 12 women; mean age 48.4 ± 10.4 years; left ventricular ejection fraction 21.1 ± 13.6%; 54% New York Heart Association Class IV; 42% required inotropic support) underwent frailty assessment. Physical frailty could be identified in 27 (54%) pts while 17 (34%) pts obtained total frailty score ≥4. Overall frailty score ≥ 4 was associated with positive clinical events ($p = 0.041$) including death (n = 2), LVAD implantation (n = 7), heart transplant (n = 4) and left ventricular reduction surgery (n = 2).
Conclusion: Frailty is prevalent among non-elderly younger Chinese patients with advanced heart failure referred for heart transplantation or LVAD implantation. It provides added prognostic value in HF pts at risk for poor outcomes and high medical consumption.

P1714

Is serum uric acid level an independent predictor for prognosis in advanced systolic heart failure patients with diabetes mellitus?

G Guliz Kozdag[1]; D Ural[2]; O Argan[3]; I Karauzum[1]; K Karauzum[4]; E Ural[1]; U Bildirici[1]; T Kilic[1]; T Sahin[1]; A Agacdiken Agir[1]
[1]*Kocaeli University, Faculty of Medicine, Department of Cardiology, Kocaeli, Turkey*; [2]*Koc University, Cardiology, Istanbul, Turkey*; [3]*Izmit Seka Public Hospital, Cardiology, Kocaeli, Turkey*; [4]*Kocaeli Government Hospital, Cardiology, Kocaeli, Turkey*

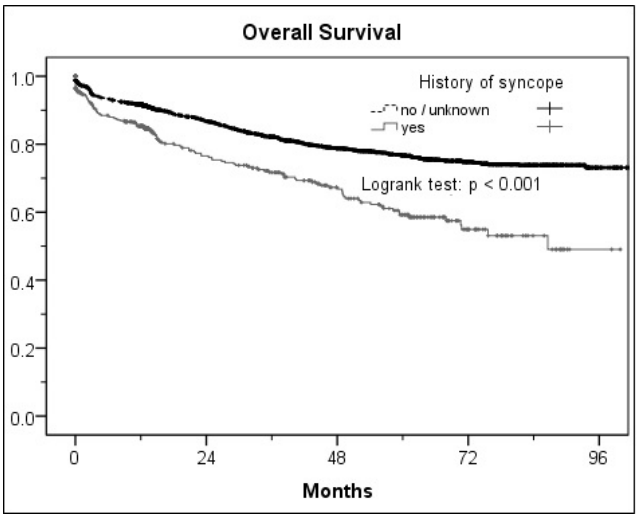
Heart failure (HF) is a major public health problem responsible for high morbidity and mortality rates. Therefore, the importance of survival predictors in directing the treatment of HF is gradually increasing. Serum uric acid levels elevated in patients with heart failure. %30-40 of patients with HF has diabetes mellitus. Our objective was to evaluate the association between levels of uric acid and mortality in advanced HF patients with diabetes mellitus.
Study Design: 250 patients (mean age 67 ± 10 years, 151 male, 99 female, mean ejection fraction (EF) 25 ± 9%) with advanced systolic heart failure and diabetes mellitus were included to the study. Clinical, echocardiographic, and biochemical parameters were measured at baseline, and all patients were followed. Cardiac death was established as the end point of the study.
Results: 121 patients (48 %) of the cohort died during a median follow-up duration of 52 months. Serum uric acid levels were significantly higher in the deceased patients compared to the patients who survived in advanced HF patients with diabetes (8.4 ± 2.3 vs. 7.0 ± 1.8 mg/dl, $p < 0.001$).
After adjusting for multiple confounders multivariate Cox regression analysis showed that the serum uric acid level was the strongest parameter predicting prognosis (HR-1.21, 95% CI 1.11- 1.31, $p < 0.001$) in the patient group.
Conclusion: Serum uric acid level is a very important predictor to determine mortality in advanced systolic HF patients with diabetes mellitus.

P1715

The history of syncope as a risk factor for hospitalization and mortality - A robust predictor for all heart failure patients?

D Hashemi[1]; M Blum[1]; M Mende[2]; S Stoerk[3]; CE Angermann[4]; S Pankuweit[5]; R Wachter[6]; F Edelmann[1]; B Pieske[1]; HD Duengen[1]
[1]*Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany*; [2]*University of Leipzig, Institute for Medical Informatics, Statistics and Epidemiology (IMISE), Leipzig, Germany*; [3]*University of Wuerzburg, Department of Internal Medicine I, Wurzburg, Germany*; [4]*Comprehensive Heart Failure Center (CHFC), Wurzburg, Germany*; [5]*University Hospital Giessen and Marburg, Department of Internal Medicine-Cardiology, Giessen, Germany*; [6]*University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*

Introduction: Data from small cohorts suggested that a history of syncope (HoS) of any origin is associated with a higher risk for sudden death in patients (pts) with advanced heart failure (HF). It is known that among HF pts with a HoS left-ventricular (LV) systolic dysfunction is more prevalent than in those without HoS. However little is known about the role of syncopes in pts with HF with preserved EF (HFpEF) despite approximately 50% of HF pts account for HFpEF. We aimed for the differences between the HF entities and the prognostic effect in a large pooled patient cohort.
Methods: We pooled data from 4659 subjects from several heart failure trials of the competence network HF. Excluding insufficient follow-up details we evaluated 4256 pts (1576 HFrEF, 584 HFpEF). HFrEF was defined as LVEF < 35% plus at least one symptom due to HF, HFpEF as LVEF>50% plus E/é>15 plus at least one symptom due to HF. We evaluated baseline characteristics including age, sex, NYHA class, medication, co-morbidities, device therapies, lab work and echo parameters plus HoS with a logistic regression model.
Results: 13.2% of the pts reported a HoS. We learned that pts with HoS took more often distinct medication (diuretics, antiarrhythmics and glycosides), were more often female, older, hypotensive, anemic and suffered from both CKD and structural heart disease. NYHA classes were positive correlated with syncopes. Our data confirms that the HoS was more prevalent in HFrEF pts than in controls ($p < 0.001$) and in HFpEF pts ($p = 0.029$). In contrast, in HFpEF pts. it was not different from healthy controls ($p < 0.125$). After adjustment for age, gender, NYHA Class, medication, device therapy, history of CAD or AMI, present anemia and depression, our results remained consistent and showed that HoS is independent from these confounders. Pts with HoS at baseline were more likely to suffer 1.from syncope during follow-up regardless of HF entity (noHF [$p = 0.004$], HFrEF [$p < 0.001$], HFpEF [$p < 0.001$]), 2. from a worse overall ($p < 0.001$) and 3. a worse hospitalization-free survival ($p < 0.001$) after 96 months.
Discussion: Taking into account the lower prevalence of HoS in HFpEF pts the explanation for syncopes in HF pts remains unclear. With stroke volume being impaired in both HFrEF and HFpEF chronic borderline cardiac output is unlikely to describe the mechanism of action. It has been shown that a low LVEF is associated with arrhythmia and sudden cardiac death. This explains the high numbers of ICDs, RV and LV pacemakers and antiarrhythmic drugs in our HFrEF data. The idea of arrhythmic episodes leading to hemodynamic instability among the HFrEF population as an explanation for both HoS and worse outcome is confronted with the statistical adjustment for ICD therapy in these pts which did not reduce the effect of HoS. In conclusion, the pathophysiology remains undefined and further assessment of HoS as a highly promising tool in the setting of HF in prospective trials is required.



Overall Survival

P1716

Endothelial progenitor cells and apoptotic endothelial cell-derived microparticle as biomarker of chronic heart failure phenotype

A E Alexander E Berezin[1]; A Kremzer[1]; T Berezina[2]; T Samura[1]
[1]State Medical University, Zaporozhye, Ukraine; [2]Private medical center VitaCenter, Zaporozhye, Ukraine

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 angiogenic endothelial progenitor cells (EPCs) and apoptotic endothelial cell-derived microparticles (EMPs) would be able to differentiate HF with reduced (HFrEF) and preserved (HFpEF) ejection fraction.
Methods: One hundred sixty four chronic HF subjects met inclusion criteria. Patients with global left ventricular ejection fraction ≥50% were categorized as the HFpEF group (n = 79) and those with ≤45% as the HFrEF group (n = 85). Therefore, to compare the circulating levels of biological markers 35 control subjects without HF were included in the study. All control individuals were age- and sex-matched chronic HF patients. The serum level of biomarkers was measured at baseline. The flow cytometric technique was used for predictably distinguishing circulating cell subsets depending on expression of CD45, CD34, CD14, Tie-2, and CD309 antigens and determining endothelial cell-derived microparticles. CD31 + /annexin V + was defined as apoptotic endothelial cell-derived MPs, MPs labeled for CD105 + or CD62E + were determined as MPs produced due to activation of endothelial cells.
Results: In multivariate logistic regression model T2DM (R2 = 0.26; P=0.001), obesity (R2 = 0.22; P=0.001), previous MI (R2 = 0.17; P=0.012), galectin-3 (R2 = 0.67; P=0.012), CD31 + /annexin V + EMPs (R2 = 0.11; P=0.001), NT-proBNP (R2 = 0.11; P=0.046), CD14 + CD309 + cells (R2 = 0.058; P=0.001), and CD14 + CD309 + Tie-2 + cells (R2 = 0.044; P=0.028) were found as independent predictors of HFpEF. 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) were independent predictors for HFpEF.
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 HFpEF compared with NT-proBNP and clinical data / cardiovascular risk factors alone.

P1717

N-terminal fragment of proBNP holds prognostic value in very elderly patients with systolic heart failure

A Alessandro Valleggi[1]; G Vergaro[1]; A Aimo[2]; C Arzilli[1]; R Poletti[1]; A Giannoni[1]; A Gabutti[1]; L Zyw[1]; C Prontera[1]; C Passino[1]; M Emdin[1]
[1]Gabriele Monasterio Foundation, Department of Cardiovascular Medicine, Pisa, Italy; [2]Azienda Ospedaliero-Universitaria Pisana, Cardiotoracico, Pisa, Italy

Background: Natriuretic peptides (namely brain natriuretic peptide, BNP and N-terminal fragment of proBNP, NT-proBNP) are widely recognized as useful biomarkers for diagnostic, prognostic and therapeutic management of heart failure (HF) patients. Nonetheless, few data are currently available on their prognostic role in the very elderly population, likely representing a significant subset of HF patients in the next future.
Purpose: We aimed to test whether the prognostic value of NT-proBNP was maintained independently from age in a large systolic HF cohort.
Methods: We prospectively enrolled 2364 patients with systolic HF, defined as left ventricular ejection fraction (LVEF) ≤50% (age 68 ± 13 years, 75% males, LVEF 35 ± 10% [mean ± SD]), who underwent a complete clinical, biohumoral and echocardiographic evaluation. Patients were then followed-up for the combined end-point of cardiac death and heart transplantation. The prognostic value of NT-proBNP was assessed in the subgroups aged either <80 or ≥80 years by means of Cox regression analysis.
Results: In our cohort, 395 (17%) patients aged ≥80 years. Compared to younger patients, the very elderly subgroup had more severe symptoms (NYHA class III/IV 59% vs 37%, p < 0.001), higher LVEF (36 ± 9% vs 34 ± 10%, p = 0.002), worse kidney function (estimated glomerular filtration rate by Cockcrof-Gault formula, eGFR 33 ± 18 vs 67 ± 35 ml/min/1.73m2, p < 0.001) and higher NT-proBNP (3182 ng/L, 1496-7543 vs 1181 ng/L, 432-2979 [median, IQR], p < 0.001); further, they were less frequently treated with ACE inhibitors (ACEi) or angiotensin receptor blockers (ARBs) and mineralocorticoid receptor blockers (75% vs 87%, p < 0.001 and 55% vs 63%, p = 0.004, respectively). During the follow-up period (39 months, IQR 17-80), the end-point occurred in 514 patients (487 deaths, 27 heart transplantations). At multivariate analysis, eGFR (p = 0.022), VE/VCO2 slope at cardiopulmonary test (p = 0.029) and NT-proBNP (p = 0.036) were independently associated with the end-point in younger patients. NT-proBNP was also an independent predictor of cardiac death and transplantation in patients aged ≥80 years (p < 0.001), together with haemoglobin (p = 0.034), LV end-systolic/diastolic diameters (p = 0.002 and p = 0.008, respectively) and lack of therapy with ACEi/ARBs (p = 0.001). At receiver operating characteristic analysis, the best prognostic cut points were set at 1646 ng/L (AUC 0.707, sensitivity 64%, specificity 67%) and at 4055 ng/L (AUC 0.637, sensitivity 62%, specificity 63%) in patients aged <80 and ≥80 years, respectively.
Conclusions: NT-proBNP holds long-term independent prognostic value in very elderly systolic HF patients. A higher prognostic cut-off is likely to be considered in such population, possibly because of the higher prevalence of comorbidities (in particular kidney failure) influencing circulating NT-proBNP levels.

P1718

Low serum chloride levels in patients with heart failure: clinical associations and prognostic significance

JJ Cuthbert[1]; P Pellicori[1]; AL Clark[1]
[1]University of Hull, Academic Cardiology, Hull, United Kingdom

Background: Low serum chloride levels might be common in patients with chronic heart failure (CHF). It may be a consequence of treatment or a marker of disease severity.
Aim: We assessed the prevalence, clinical associations and prognostic significance of low serum chloride in patients referred to a heart failure (HF) clinic with suspected HF.
Methods: Patients with baseline echocardiogram and serum chloride were evaluated (n = 5613). CHF was defined as the presence of signs or symptoms compatible with the diagnosis and either left ventricular systolic dysfunction (LVSD), defined as heart failure with reduced ejection fraction (HeFREF) or LVSD absent or at most mild and NT-pro-BNP >125 ng/L, defined as heart failure with normal ejection fraction (HeFNEF). Hypochloraemia was defined as greater than 2 standard deviations below the mean chloride level in normal distribution (< 96 mmol/L).
Results: Of the 5613 patients, 908 patients did not have HF, 1988 had HeFREF, and 2717 had HeFNEF (table 1). The prevalence of hypochloraemia in patients with HF was 10.7%; it was more common in HeFREF (12.6%) than HeFNEF (9.3%) (P < 0.001). Compared to those in the higher quartiles, patients in the lowest quartile of serum chloride (median 96 mmol/L (range 76-99 mmol/L)) had higher NT-pro-BNP and were more breathless and congested on assessment. The annual mortality rate for HeFREF and HeFNEF was 12.9% and 9.4% (P=0.001) respectively. Chloride predicted both all-cause mortality (ACM) (hazard ratio (HR) 0.97 (95% confidence interval (CI) 0.95-0.99), P=0.001 for HeFREF and HR 0.97 (95% CI 0.95-0.98), P= < 0.001 for HeFNEF) and the combined end-point of mortality or heart failure hospitalisation (HR 0.97 (95% CI 0.96-0.99), p = 0.006 for HeFREF and HR 0.96 (95% CI 0.95-0.98), P= < 0.001 for HeFNEF) independent of the variables in table 1, loop diuretic use, serum sodium, potassium and bicarbonate, and renal and liver function.
Conclusions: Low serum chloride levels are independently associated with increased all-cause mortality and hospitalisation for heart failure in patients with CHF, regardless of left ventricular ejection fraction.

Patient characteristics			
Variable	HeFREFN=1988	HeFNEFN=2717	p
Average age - years (SD)	71 (11)	75 (10)	< 0.001
Male - %	75	52	< 0.001
NYHA class III/IV - %	35	24	< 0.001
NTproBNP - ng/L (IQR)	1750 (750-3984)	734 (289-1672)	< 0.001

HeFREF - Heart failure with reduced ejection fraction; HeFNEF - Heart failure with normal ejection fraction; SD - standard deviation; NYHA - New York Heart Association; IQR - interquartile range.

P1719

Upgrade of the Barcelona-Bio-HF-calculator: incorporating risk of HF hospitalization and extending risk prediction up to 5 years

J Lupon[1]; M De Antonio[1]; J Vila[2]; I Subirana[2]; A Galan[3]; E Zamora[1]; P Moliner[1]; M Domingo[1]; B Gonzalez[1]; M Boldo[1]; C Rivas[1]; J Barallat[1]; J Santesmases[1]; C Diez-Quevedo[1]; A Bayes-Genis[1]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; [2]Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain; [3]University Hospital Marques de Valdecilla, Santander, Spain

Background: Estimation of the risk of heart failure (HF) hospitalizations has been historically much more difficult than predicting the risk of death. The BCN-Bio-HF-calculator incorporating NTproBNP (marker of myocardial stretch), high-sensitivity cardiac troponin T (marker of myocyte injury), and soluble ST2, (reflective of myocardial fibrosis, remodeling and inflammation) was developed 3 years ago for better estimating the risk of death up to 3 years.
Purpose: The combination of clinical and routine laboratory data with biomarkers reflecting different pathophysiological pathways might also improve the prediction of HF-related hospitalizations.
Methods: Several clinical and treatment variables and extension of prediction to 5-year was performed in order to assess 1-, 2-, 3-, 4- and 5-year risk of all-cause death, HF-related hospitalization and the composite end-point all-cause death/HF-related hospitalization. Model performance was evaluated using discrimination, calibration, and reclassification tools.
Results: The BCN-Bio-HF-calculator was derived from 864 consecutive outpatients (72% men) with mean age 68.2 ± 12 years (65.5%/26.2% NYHA class II/III, LVEF 36%). The follow-up for the present up-graded version was 5 years for the alive patients. During follow-up 363 deaths and 210 HF-related hospitalizations were observed. 430 patients suffered at least one event of the composite end-point. Three new clinical variables (duration of HF in months, number of HF-related hospitalizations in the precedent year, and presence of diabetes mellitus) and 4 new treatments (mineralcorticoid receptor antagonists, angiotensin-2 receptor blocker neprilysin inhibitor [ARNi], cardiac resynchronization therapy and implantable cardiac defibrillator) were added to the previously included variables. Beta-values for ARNi treatment were derived from the benefit observed in the Paradigm Trial. As with the former BCN-Bio-HF-calculator, eight independent models were developed and the calculator may run with the availability of none, one, two, or the three biomarkers. The calculated risk of all-cause death, HF-related hospitalization and the composite end-point significantly improved by additive biomarker data. The average C-statistic for the model with the 3 biomarkers using the 'dxy' Somers rank correlation which incorporates information from censored data (time-to-event outcome) was 0.79 for all-cause death, 0.73 for HF-related hospitalization and 0.76 for the composite end-point, while the AUC at 5 years considering each event as a binary outcome (logistic regression models) were 0.85, 0.75 and 0.84 respectively.
Conclusions: A new version of the BCN-Bio-HF-calculator that incorporates some new clinical variables together with 3 biomarkers reflecting different pathophysiological pathways better allowed individual prediction of all-cause death, HF-related hospitalization and the composite end-point at 1, 2, 3, 4 and 5 years.

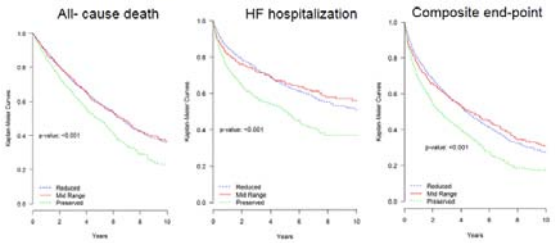
P1720

Clinical characteristics and outcomes of patients with heart failure with mid-range ejection fraction.

N Farre[1]; J Lupon[2]; E Sole-Gonzalez[3]; J Gonzalez-Costello[4]; J Vila[5]; S Perez[5]; M De Antonio[2]; E Roig[3]; C Sanchez-Enrique[4]; C Enjuanes[1]; P Moliner[2]; A Bayes-Genis[2]; D Luiso[6]; S Mirabet[3]; J Comin-Colet[1]
[1]Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; [2]Germans Trias i Pujol Hospital, Department of Cardiology, Badalona (Barcelona), Spain; [3]Hospital de la Santa Creu i Sant Pau, Department of Cardiology, Barcelona, Spain; [4]University Hospital of Bellvitge, Barcelona, Spain; [5]Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain; [6]Hospital del Mar, Department of Cardiology, Barcelona, Spain

Background: Controversy exists as to whether patients with heart failure with mid-range ejection fraction (HFmrEF), defined as ejection fraction (EF 40-49%), represent a distinct heart failure (HF) phenotype.
Purpose: To analyze baseline characteristics and outcome of patients with HFmrEF compared to patients with preserved (HFpEF, EF>50%) and reduced (HFrEF, EF < 40%) ejection fraction.
Methods: Prospective observational study of HF patients followed up at 4 university hospitals with a dedicated Heart Failure Unit. Baseline characteristics and outcomes were recorded.
Results: Fourteen percent (n = 504) of the 3580 patients included had HFmrEF. In this group mean age was 68 ± 13 years (compared with 66 ± 13 years in HFrEF and 74 ± 11 in HFpEF, p < 0.001) and 40% were female (30% in HFrEF and 57% in HRpEF, p < 0.001). Functional class (NYHA III-IV) was similar between HFmrEF and HErEF (34% and 33% of patients, respectively), but worse in HFpEF (44%), p < 0.001. NTproBNP was highest in HFrEF (median 1898 [769-4465] ng/L) and decreased as EF increased (1484 [532-3866] ng/L in HFmrEF and 1320 [635-2818] in HFpEF), p < 0.001. The main etiology for HF was ischemic in HFrEF and HFmrEF (52%) whereas it was hypertension in HFpEF (42%). As expected, use of beta blockers, ACEI and MRA were higher in HFrEF, and its use decreased in HFpEF. Median follow-up was 3.66 [1.69-6.04] years. In the whole cohort, all-cause death, HF hospitalization and the composite end-point were 47%, 35% and 59%, respectively. Outcomes were worse in HFpEF, without differences between HFrEF and HFmrEF (Figure 1). However, after multivariate analysis, no differences in outcomes were seen between the three groups.
Conclusions: Patients with HFmrEF have a clinical profile in between HFpEF and HFrEF. There were no differences in all-cause mortality and HF hospitalization between the three groups.

Figure 1: Kaplan-Meier curves for long-term outcomes divided by ejection fraction.



P1721

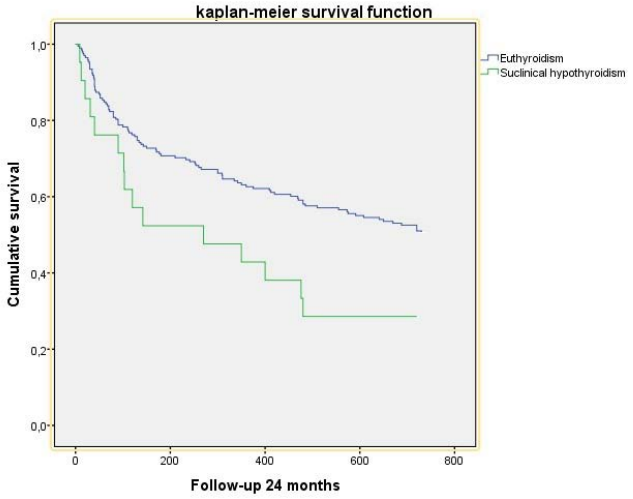
The prognostic impact of subclinical hypothyroidism in heart failure

M L Goncalves[1]; HUGO Antunes[1]; JULIO Gil[1]; LUÍS Abreu[1]; BRUNO Marmelo[1]; M I Pires[1]; ISABEL Cunha[1]; DAVIDE Moreira[1]; INÊS Almeida[1]; COSTA Cabral[1]
[1]Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal

Introduction: The treatment of comorbidities is a key component with a prognostic impact (PI) in heart failure (HF). These include thyroid disorders, which should be accessed in HF. The importance and approach of its subclinical forms is still not well defined.
Objective: To evaluate the PI of suclinical hypotyroidism (SH) in patients (P) with HF.
Methods: Included P hospitalized between 2009-2015 for acute HF (AHF) in a Cardiology ward. Were excluded P without thyroid function (TF) assay on admission, and P receiving amiodarone/ anti thyroid drugs/ thyroid hormones. Division into 2 groups, according to TSH and freeT4 value: Euthyroidism (E) - normal TSH and T4f; SH - elevated TSH [≥5.5mUI / L] and normal T4f. Endpoints: death of any cause, readmission (R) for AHF or combined endpoint (occurrence of one of these events). Follow-up (FU): 2 years. Analysis of association, survival and risk estimation.
Results: Of a total of 1006P hospitalized, 236P were selected. 54.2% male, mean age 76.5 ± 10.4 years, in-hospital death 4.7%. In the FU: death 20.1%; R by AHF 35.6%; Combined endpoint - 50.2%. Groups descriptives are in table. There were no differences in age or other clinical, analytical or echocardiographic characteristics. There is an association between SH and a higher number of R by

AHF at 12M, 18M and 24M (X2 = 6.10 p = 0.013, X2 = 11.22 p = 0.001, X2 = 9.77, p = 0.002 respectively) in relation to the E group. No association between death and SH in FU was found. In Cox regression, high levels of TSH were associated with a higher risk of reaching the combined endpoint (HR: 1.1, IC95: 1.0-1.7, p = 0.05). The survival rate of P with SH was lower than that of P with E (Kaplan-Meier Log-Rank: X2 = 5.33, p = 0.021).
Conclusion: A negative PI of SH was observed in the HF P, which may correspond to a decompensation factor or HF marker of severity. This study emphasizes the importance of dosing TF at all P and the more rigorous follow-up of P with SH. In the future it will be important to evaluate whether the therapeutic intervention in SH has a positive impact on the adverse prognosis of these P.

	Group E	Group SH	
Female %	43,3	66,7	p = 0.05
Sistolic BP admission - mmHg	141,5±31,6	126,7±21,8	P=0.01
BNP admission - pg/ml	748,9±804,1	1785,4±2038,4	p = 0.09
T4f - ng/dL	1,2±0,2	1±0,1	P < 0.001
Previous loop diuretic %	31,3	83,3	P=0.014
PSAP - mmHg	36,5±16.1	58,6±21,2	P=0.006



Kaplan-Meier survival 24Months

P1722

Aldosterone receptor antagonists decrease mortality and CV hospitalizations in CHF with reduced left ventricular ejection fraction(LVEF), but not in CHF with preserved LVEF. A metaanalysis of RCTs

R De Vecchis[1]; C Cantatrione[1]; D Mazzei[1]; C Ariano[1]; N Maurea[2]
[1]Cardiology Unit, Presidio Sanitario Intermedio "Elena d'Aosta", Naples, Italy; *[2]Division of Cardiology,Istituto Nazionale "Fondazione Giovanni Pascale" IRCCS, Naples, Italy*

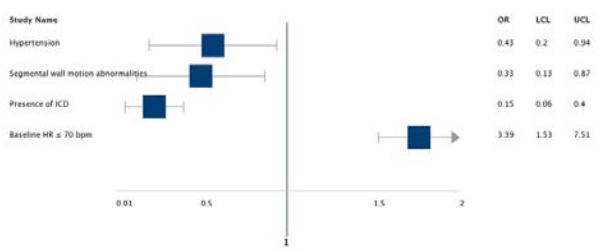
Background Aldosterone receptor antagonists(ARAs) have been associated with improved clinical outcomes in patients with heart failure with reduced left ventricular ejection fraction (HFREF), but not preserved left ventricular ejection fraction(HFpEF). With the aim to study this topic more deeply , we carried out a meta-analysis of selective and nonselective ARAs in HFREF and HFpEF.
Methods: We searched Pubmed and Scopus databases. We decided to incorporate in the metaanalysis only randomized controlled trials(RCTs) of ARAs in patients with CHF if they met the following criteria: experimental groups included patients with CHF treated with ARAs in addition to the conventional therapy ; control groups included patients with CHF receiving conventional therapy without ARAs. Outcomes of interest were all-cause death, hospitalizations from cardiovascular cause, hyperkalemia, or gynecomastia.
Results: We detected 15 studies representing 15671 patients. ARAs were associated with reduced odds of all-cause death(OR=0.79; 95% CI= 0.73-0.87) and hospitalizations from cardiovascular cause (OR= 0.73; 95% CI = 0.61-0.89). However, a subgroup analysis showed that these advantages were limited to HFREF (all- cause death : OR=0.77, 95% CI=0.69-0.84; hospitalizations from cardiovascular cause: OR= 0.66, 95% CI=0.51-0.85), but they did not affect the HFpEF group (all-cause death: OR= 0.91, 95% CI= 0.76-1.1; hospitalizations from cardiovascular cause: OR = 0.85, 95% CI= 0.7-1.09). ARAs increased the risk of hyperkalemia(OR= 2.17; 95% CI= 1.88-2.5). Nonselective ARAs, but not selective ARAs increased the risk of gynecomastia (OR = 8.22; 95% CI=4.9-13.81 vs. OR = 0.74, 95% CI= 0.43-1.27).
Conclusions: ARAs reduced the risk of adverse cardiac events in HFREF but not HFpEF. In particular, ARA use in HFpEF patients is questionable, since in this CHF type no significant improvement in all –cause death and cardiovascular hospitalizations was demonstrated with ARA treatment , in the face of the well-known risks of hyperkalemia and/or gynecomastia that chronic ARA therapy entails. Selective ARAs are equally effective as nonselective ARAs, without a risk of gynecomastia.

P1723

The importance of heart rate as a predictor of cardiac functional recovery in newly diagnosed heart failure

AV Valika[1]; KP Paprokas[1]; DV Villines[1]; M R Maria Rosa Costanzo[1]
[1]Advocate Heart Institute, Cardiology, Naperville, United States of America

Background: Left ventricular ejection fraction (LVEF) predicts outcomes in HF patients. In patients with HF and reduced LVEF, rates of LV recovery (LVR) range between 19% and 50%, but factors predictive of LVR remain unclear.
Methods: Review of the electronic medical record identified between 2006 and 2016 224 consecutive patients aged > 18 years, new HF diagnosis and a LVEF ≤ 35% who received guidelines-directed medical therapy (GDMT) and were followed ≥ 1year. LVR was defined as a rise in LVEF ≥ 40%. Stress-induced cardiomyopathies were excluded. After determination of LVR rates, patients with LVR were compared with those with persistent LV dysfunction (LVD) in terms of clinical characteristics and the composite outcome of death and HF hospitalization using the log-rank test. Multivariate logistic regression analysis was utilized to identify baseline clinical variables predictive of LVR. LVEF was serially measured by echocardiogram. GDMT target doses were per published guidelines.
Results: Population characteristics were: age = 63 ± 13; 38.5 % female; 83.2% Caucasian; 38.1% ischemic HF; baseline LVEF = 23% ± 6%; baseline heart rate = 75 ± 13 bpm. Background GDMT: ACE inhibitors (ACEi) = 74.3%; Angiotensin receptor blockers (ARB) = 19.7%; Beta blocker (BB) = 95.4%; Aldosterone antagonist (AA) = 34.0%; the % of patients achieving target doses of ACEi and BB were, respectively, 33.7 and 40.2. LVR occurred in 154/244 patients (63.1%), and the median time to LVR was 9.0 months (IQR = 4.5-19.0). Average final EF in LVR patients was 49% ± 6%. Compared to LVD, LVR included fewer patients with ischemic HF (54.4% vs. 28.6%, p < 0.001) and CKD (3.9% vs. 11.1%, p = 0.028), and more subjects on ACEi (67.4% vs. 80.3%, p = 0.025), and target BB doses (30.9% vs. 46.1% p = 0.029). By multivariable analysis baseline heart rate < 70 bpm was the only independent predictor of LVR (OR = 3.39, 95% CI = 1.5-7.5, p = 0.003); hypertension, segmental wall motion abnormalities, and ICD were negative predictors of LVR (Fig). Presence or absence of ARB or AA and target doses of ACEi, ARB, or AA did not predict LVR.
Time to HF hospitalization or death was significantly longer in LVR than LVD subjects (105.5 ± 3.8 days vs. 90.6 ± 6.2 days, p = 0.04). This composite endpoint was less frequent in those who achieved target BB doses (5.4% vs. 16.7%, p = 0.027). Time to all-cause mortality was longer for LVR than LVD patients (115.8 ± 2.6 days vs. 96.4 ± 5.5 days, p = 0.001).
Conclusions: LVR rates in contemporary HF patients are higher than previously reported. Whereas hypertension, segmental wall motion abnormalities and ICD decrease the likelihood of LVR, a baseline HR ≤ 70 bpm is the sole independent predictor of LVR. These findings suggest that early modulation of heart rate in de-novo HF patients may facilitate LVR.



Predictors of Left Ventricular Recovery

P1724

Prognostic implication of right and left-sided hemodynamic congestion in patients with heart failure

P Rozentryt[1]; JU Nowak[1]; J Niedziela[1]; B Hudzik[1]; P Leszek[2]; T Rywik[2]; EA Jankowska[3]; W Doehner[4]; S Von Haehling[5]; SD Anker[5]; M Gasior[1]
[1]III Department of Cardiology, Silesian Centre for Heart Diseases, Zabrze, Poland; *[2]National Institute of Cardiology, Warsaw, Poland*; *[3]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; *[4]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany*; *[5]University Medical Center Gottingen (UMG), Department of Innovative Clinical Trials, Gottingen, Germany*

Introduction: Hemodynamic congestion remains a key prognostic factor in heart failure (HF). Recent findings from ESCAPE trial suggest a congestive burden (CB), taken as a sum of right atrial (RA) and pulmonary capillary wedge pressure (PCWP) be of prognostic value in HF. However, the relative association of RA and PCWP with prognosis and with other typical prognosticators remains poorly understood.
Aim: We sought to investigate the separate association of RA and PCWP with prognosis at different levels of global congestion as represented by CB and to compare them with traditional risk factors.
Material & methods: 239 HF patients (age: 52 ± 10 years, female: 14%, NYHA: 2.9 ± 0.9, LVEF: 25 ± 11%) were electively admitted to the hospital for right-sided catheterization as part of heart transplantation work-up. All were on best tolerated medical therapy and received electrical interventions according to current guidelines. Using Swan-Ganz catheter and thermodilution technique we measured right- and left sided pressures. In each patient we have calculated CB and RA/PCWP (Ratio). All patient were allocated to 1 out of 4 groups according to median value of CB (21 mmHg) and RA/PCWP (0.33): 1 – both CB and Ratio bellow medians, 2 – low CB and high Ratio, 3 – High CB and low Ratio, 4 – both CB and Ratio above medians. During 3 years of follow-up 84 (35%) patients died (all-cause). We compared Kaplan-Meir survival curves for each group. Cox method was and used to estimate adjusted relative risk of death for groups taking as a reference the group with best survival on Kaplan-Maier.
Results: Kaplan-Maier analysis showed best survival in group 3 (log rank p = 0.02). The risk of death in groups with high Ratio remained significant after adjustment for powerful prognosticators (Table 1).
Conclusion: The high RA/PCWP is associated with poor prognosis, the reason for elevated ratio may be attributable either to high RA or low PCWP.

Table 1. Hemodynamic characteristics of

	1. Low CBand low Ratio	2. Low CBand high Ratio	3. High CBand low Ratio (reference)	4. High CB and high Ratio
CB [mmHg]	14.4±4.2	13.2±4.4	30.1±8.4	32.9±8.8
RA [mmHg]	2.3±1.1	5.0±1.9	5.3±2.2	11.2±3.8
PCWP [mmHg]	12.1±3.7	8.2±3.2	25.9±7.0	21.7±6.7
Ratio	0.20±0.08	0.74±0.81	0.21±0.06	0.55±0.24
% Death	33	37	26	52
	Hazard ratio ± 95% CI, p-value			
Unadjusted	0.81, (0.37-1.79) p = 0.63	1.48, (0.84-2.63) p = 0.98	1.0	2.41, (1.37-4.25) p = 0.005
Unadjusted forage, gender, NYHA, LVEF, NTproBNP, MVO_2	1.77, (0.82-3.8) p = 0.15	2.13, (1.06-4.26) p = 0.03	1.0	3.27 (1.70-6.27) p = 0.0004

P1725

Prognostic value of presence, amount and location of myocardial fibrosis detected by contrast enhanced cardiac magnetic resonance in patients with idiopathic dilated cardiomyopathy

L Lupi[1]; M Piazzani[1]; D Farina[1]; E Gavazzi[1]; M Bonavita[1]; I Papa[1]; M Metra[1]; M Maroldi[1]; S Savina Nodari[1]
[1]University of Brescia, Brescia, Italy

Background: Myocardial fibrosis detected by contrast-enhanced cardiac magnetic resonance (CE-CMR) has been related to adverse clinical outcomes in patients with idiopathic dilated cardiomyopathy (DCM), but there are few data about the association between the amount and location of myocardial fibrosis and prognosis.
Purpose: the aim of our study was to evaluate the prognostic role of the presence, the amount and the location of late gadolinium enhancement (LGE) in patients with DCM and left ventricular systolic dysfunction.
Methods: We enrolled retrospectively patients suffering from DCM with left ventricular ejection fraction (LVEF) ≤45% underwent CE-CMR followed at our HF Department from January 2012 to December 2015. We evaluated demographic, laboratoristic and imaging parameters (presence of LGE, as indicator of fibrosis, LVEF, right ventricular ejection fraction, ventricular volumes and myocardial mass). The amount of LGE was calculated by manual planimetry at each left ventricle short axis section. We considered the 17-segments model of the American Heart Association to evaluate the localization of fibrosis. The composite endpoint was death from any cause and hospitalization for arrhythmic causes or heart failure.
Results: We enrolled 179 pts (71% male, mean age 55 ± 15 years). 90 pts (90.3%) showed left ventricular LGE. At univariate analysis, atrial fibrillation (p = 0.005), diabetes (p = 0.005), chronic kidney disease (p = 0.005), presence of LGE (<0.0001), LVEF (p = 0.003), right ventricular ejection fraction (p = 0.006) and myocardial mass (p = 0.002) were predictive of events. At multivariate analysis, only the presence of LGE confirmed its prognostic value (HR 4.597; IC 95% 2.167–9.749; p < 0,0001). LGE area and the number of myocardial segments involved by LGE were both associated with the composite endpoint (trend p = 0.03 and 0.05 respectively). Septal localization was significantly associated with hospitalizations for ventricular arrhythmias (p < 0.0001 compared to other localizations), while lateral wall localization was associated with hospitalizations for heart failure (p = 0.001).
Conclusions: Myocardial fibrosis is an independent predictor of death and hospitalization for heart failure and arrhythmias and its negative prognostic value raises with increasing amount of fibrosis. Septal and lateral wall LGE was associated with a significantly worse prognosis compared to other localizations.

P1726

Characteristics of heart failure patients in indonesia

B Karim[1]; R Irwan Muin[1]; LH Makmun[1]; M Yamin[1]; M Arza Putra[2]
[1]Cipto Mangunkusumo Hospital, Cardiology Division, Internal Medicine Department, Jakarta, Indonesia; *[2]Cipto Mangunkusumo Hospital, Cardiac Thoracic Division, Surgery Department, Jakarta, Indonesia*

Introduction: Heart failure remains the major problems worldwide. Most of it caused by coronary artery disease. The more prevalence of metabolic disease, the prevalence of coronary artery disease which ends up with heart failure is increased.
Purpose: To identify characteristics of heart failure patients in Indonesia.
Methods: The descriptive study design was consecutively conducted in 104 patients with heart failure who were admitted to the Hospital from January – April 2016. All clinical data were collected, including gender, age, symptoms, echocardiography, treatment, and device implantations.
Results: All 104 patients during period January-April 2016, predominantly male (52.9%) comparing with female (47.1%). Range of age 56-64 years old was dominated the event of heart failure in Indonesia, 69% patients had average systolic blood pressure 100-140 mmHg, most frequent symptoms was dyspnea on effort (66%), fatigue (35%), orthopnea (33%), dyspnea at rest (21%), decreased exercise tolerance (20%), and peripheral edema (16%). Most of the patients have New York Heart Association (NYHA) class II (53%) with the sign of elevated jugular venous pressure (14.4%). Echocardiography examination on heart failure revealed reduced ejection fraction below 30% (21%) and preserved ejection fraction above 50% (38%). Ischemic heart disease is the main cause (76.9%) of heart failure and most of the patients have comorbid hypertension (59%), diabetes (29%), valvular heart disease (14.4%), and atrial fibrillation (9.6%). Almost all of heart failure patients consume diuretic (95.2%) if there were congestion, followed by a beta blocker (92.3%), ACE inhibitor (59.6%), mineralocorticoid receptor antagonist (59%), and ARB (38%). Device Implantation was conducted in 3.8% eligible patients during January-April 2016.
Conclusions: Characteristics of heart failure patients are varied. Ischemic heart disease is a predominant cause and optimal medical treatment and device implantation, if indicated, are very beneficial to improve symptoms.

P1727

Heart failure : the smart versus the not so smart hearts

S S Iyengar[1]; ANAND Chopda[1]; ROOPA Babu[1]; C Chakrapani[1]; ANAND Shenoy[1]; G Sreedhara[1]; SUBASH Chandra V[1]
[1]Manipal Hospital, Cardiology, Bangalore, India

On behalf of: Department of cardiology, Hospital, Bangalore, India

Background: Heart failure with preserved ejection fraction (HFpEF), as compared to heart failure with reduced ejection fraction(HFrEF) continues to be a challenging entity.
Aim: To compare clinical profile, treatment and outcome between patients of HFpEF and HFrEF.

Methods: It was a prospective,observational study comparing patients of HFpEF (LV EF >40%) with patients of HFrEF (LV EF ≤ 40%).Serum BNP was estimated in all patients.
Results: 204 patients were studied , 101 patients in HFpEF group and 103 in HFrEF group. Female patients, 80 in number more often had HFpEF than HFrEF (53.5% vs 26.2%, p < 0.001). HFpEF patients were older than patients with HFrEF (69.5 years vs 66.2 years, p = 0.038). Hypertension (68.3% vs 41.7%, p < 0.001) and COPD (13.9% vs 3.9%%, p = 0.012) were more common in patients with HFpEF, whereas obesity (36.6% vs 45.7%, p = 0.004) was more common in HFrEF group. Other conditions like coronary artery disease, atrial fibrillation, chronic kidney disease and acute kidney injury were similar in both groups. BNP was significantly higher in HFrEF group (921.4 units vs 1204 units, p = 0.023), and in those who died. Beta blockers (55.4% vs 79.6%, p < 0.001), loop diuretics (53.5% vs 82..5%, p < 0.001) and digoxin (0 vs 14.6%, p < 0.001) were more commonly used in HFrEF patients. Antiplatelets, statins, ACE inhibitors/ARB's ,MRA, nitrates were used equally in both groups. ICD was implanted more commonly in HFrEF. 1% vs 8.7%)
Repeat hospitalisation rates at 6 months were similar between the two groups. There was no significant difference in mortality at 6 months between the two group. (9.9 % in HFpEF and 13.6% in HFrEF p = 0.187).
Conclusion: HFpEF patients were older. HFpEF was more frequently seen in female patients, hypertensives and COPD patients, whereas HFrEF patients were more often male patients. Surprisingly BMI was higher in patients of HFrEF. Serum BNP was significantly higher in HFrEF group than HFpEF group.Higher serum BNP values at diagnosis indicated a poor prognosis. BNP is a useful test at diagnosis but should be used and interpreted in the context clinical background as it is an expensive test. ICD was implanted more commonly in patients with HFrEF. Utilization of device therapy was low probably reflecting the economic constraints in our country. There was no difference in morbidity and mortality in patients with HFpEF and HFrEF.

P1728

Review of 115 cases of chronic heart failure with reduced ejection fraction in Tunisian Public hospital

MERIEM Drissa[1]; SANA Helali[1]; MEHDI Mechri[1]; SAMIRA Kaabachi[1]; MEHDI Cheour[1]; HABIBA Drissa[1]
[1]*La Rabta University Hospital, adults cardiology, Tunis, Tunisia*

Introduction: Heart failure (HF) has been singled out as an epidemic and is a staggering clinical and public health problem, associated with significant mortality, morbidity, and healthcare expenditures. Objective of the aim of our study is to identify clinical and epidemiological characteristics of chronic heart failure with reduced ejection fraction(EF) and to demonstrate whether the data found in western countries are also observed in our country.
Methods and materiels: Retrospective, descriptive study, carried out at department of a cardiology Hospital During the period from October 2013 to the October 2015. We enrolled patients with the diagnosis chronic heart failure with reduced ejection fraction(EF < 40%) based on echographic results. The data were entered and analyzed using the SPSS 22 software. We calculated the simple frequencies and the relative frequencies (percentages) for the qualitative variables. We calculated averages, and standard deviations e for quantitative variables. For comparing averages and percentages, the student's "t" test and the Pearson chi-square test were used, and in all statistical tests the significance level was set to 0.05.
Résults: A total of 115 patients' files were analyzed; the patients' mean age was 53 ± 12 years. The male sex was predominant with a sex ratio of 2.6 in favor of men. Tobacco was the most common risk factor as it was observed in 56 cases (51%) followed by hypertension in 46 cases (41%) , diabetes In 45 patients (40%) and dyslipidemia in 28 cases (25%). The main comorbidities encountered in our patients were atrial fibrillation in 32 patients (29%) ,renal failure in 22 patients (20%) and stroke in 7 patients (7%).
Dyspnea was the main symptom noted in 100% of patients followed by palpitation in 72 patients (65%.). Frenquency of heart rate (FC) was about 91 ± 21 beats / min [50-160]. The blood pressure was around 118 ± 23 mm Hg left heart failure signs were observed in 57% of cases, global heart failure in 39% and cardiogenic shock in 4%. Decompensation factors were a bronchopulmonary infection in 42% of cases and was ischemic coronary events in 22 patients.the main etiology was ischemic heart disease in 49 patients (44%) then valvular etiology in 26 patients (24%) ,idiopathic CMD in 19 patients (17%) and hypertensive etiology in 16 patients (15%). The intra-hospital evolution under medical treatment was marked by 10deaths. The average length of stay in hospital was 12.1 ± 6.6 days.
Conclusion: Our study showed that heart failure concerned population were young ,We are witnessing a decline in rheumatic valvulopathies .Coronary disease is the main cause in patients treated at our Tunisian hospital; the most common risk factors were arterial hypertension and diabetes.

P1729

Exercise tolerance determinants, renal function and disease progression in outpatients over 75 years old with chronic heart failure

B Stanula[1]; JDK Jaroslaw Damian Kasprzak[2]
[1]*E. Szczeklik's Hospital, Tarnow, Poland*; [2]*Medical University of Lodz, Lodz, Poland*

Introduction: Variety of signs and symptoms arising from underlying disease, comorbidities and aging process itself limits possibilities of identifying independent prognostic factors in patients (pts) over 75 years with chronic heart failure (CHF). Aim was to identify factors determining exacerbations of stable, moderate CHF and exercise intolerance in the elderly pts with comparison to younger pts (age 60-75).
Methods: We studied 91 stable, ambulatory CHF pts (mostly with preserved left ventricular(LV) function; mean age 74 ± 6, men 51%, BMI 29 ± 4 kg/m2, LVEF 59 ± 11%) split into Group 1 (Gr.1 - >75yo, N=50) and Group 2 (Gr.2 - age 60-75, N= 41). All pts underwent physical examination, assessment of quality of life by EQ-5D-3L questionnaire with visual analog scale (VAS), echocardiogram, electrocardiogram, and laboratory tests panel including brain natriuretic peptide (BNP),creatinine,eGFR,cystatin C,complete blood count,C- reactive protein (CRP), six-minute walk test distance (6MWT) – at baseline and after 1-yr.
Results: There were no deaths during 1-yr follow-up, but hospitalizations were prevalent (17%), together with NYHA class worsening(13%), paralleled by progression of diastolic dysfunction (35%). These endpoints were not significantly more frequent in the elderly. Hospitalized elderly had higher NYHA class (p = 0.009), younger had greater degree of LV diastolic dysfunction (p = 0.009), lower BNP level (p < 0.001),history of myocardial infarction (p = 0.027). Elderly with NYHA class deterioration at baseline had more diastolic dysfunction (p = 0.043), history of smoking (p = 0.033), while Gr.2 had lower values for: NYHA class (p = 0.018), systolic and diastolic blood pressure-SBP, DBP (p = 0.001 and p = 0.042), IVA septal (p = 0.020) by tissue Doppler. Diastolic dysfunction worsening was predicted in Gr.1 by lower DBP (p = 0.031), lower initial 6MWT(p = 0.002), greater initial LVEF (p = 0.045), greater E/A ratio (p = 0.042), less initial diastolic dysfunction (p = 0.002); atrial fibrillation history was more frequent (p = 0.018),ACEIs/ARBs were less frequently used (p = 0.043). Diastolic deterioration in Gr.2 was predicted by higher e' lateral (p = 0.048), less diastolic dysfunction (p = 0.014), more AF(p = 0.042),used more anticoagulants (p = 0.004).
Conclusions: Predictors of deterioration are different for the elderly patients with stable, moderate CHF as compared with group age 60-75, with efficient multifactorial models difficult to construct. Multifactorial predictors involve conventional and local echo parameters (LVEF,s' lateral, Vp, mitral E/A ratio),clinical data (DBP, smoking history,AF), and exercise tolerance estimate from 6MWT.

P1730

The effect of 6-month therapy with sildenafil on the intracardiac hemodynamic and inflammation markers in pts with right ventricular dilated cardiomyopathy

TA Abdullaev[1]; YR Akhmatov[1]; I A Igor Tsoy[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

The aim. Assess the impact of a 6-month therapy with sildenafil on clinical and functional parameters in pts with dilated cardiomyopathy (DCM) with a primary lesion of the right heart.
Material and methods: blind randomization method were highlighted two: the first (I; n = 12; male / female 10/2; 42,8 ± 12,5goda) and second (II; n = 13; female / male 8/5; 41,6 ± 11.8 years) group. Thus, pts of the second group in addition to standard therapy (PT) obtained CHF sildenafil individually selected dose (from 37.5 to 75 mg / s; average - 45.8 ± 12.5 mg / day). All pts underwent EKG EhoCG, test 6-minute walk test (6MWT) and C-reactive protein in the serum before and after treatment.
Results: of the study. Analysis of spirometry parameters on the background of a 6-month therapy with sildenafil had a positive impact on the parameters of intracardiac hemodynamics. In particular, the peak velocity of early filling (E) na17,1% increased after treatment rate (before treatment - E = 0.63 ± 0.12 m / s, after - E = 0.76 ± 0.13 m / s, p = 0.016), and the contractile function of the right ventricle - on 8.73% (RV EF before - 42,25 ± 3%, after - 4 6,73 ± 73%, p = 0,033). It should be noted that the improvement of inotropic function of the right heart insignificant decrease in LVM contributed 17.7% (up to 143,42 ± 46,38 gr, after - 118,00 ± 33,67gr, p = 0.128) and a decrease in the size of LA on 17.85% (up to - 29,8 ± 2,88 mm after - 24,48 ± 2,63mm, p = 0.045). Namely, the 6-month treatment with sildenafil contributed to the increase in 6MWT on 36.5% (before 173,6 ± 71,34m after -273,6 ± 82,26 m, p = 0.004) and a decrease in respiratory frequency (RF) both at rest and after exercise (BH rest decreased from 22,34 ± 1,76 to 17,8 ± 1,53, and BH heating from 26,35 ± 3,16 up to 21,8 ± 1, 10 p = 0, 1). The level of CRP in the serum during therapy significantly decreased na44,1% (from 8.6 + 1.4 do3,8 ± 0,8 mg / l; p = 0.03).

Conclusions: The additional use of sildenafil for 6 months significantly enhances the EF RV is accompanied by a decrease in the size of the LA and serum levels of CRP, including good tolerance of physical activity

P1731

Insulin resistance evaluation in patients with coronary artery disease and chronic heart failure without evident disorders of carbohydrate metabolism

B Kurmanbekova[1]; G E Osmankulova[1]; M T Duishenalieva[1]; S SH Mamasaidova[1]; A M Noruzbaeva[1]; E Amelin[1]
[1]*National Center of Cardiology and Internal Medicine, Chronic heart failure, Bishkek, Kyrgyzstan*

Background: Insulin resistance (IR) promotes to development of coronary artery disease (CAD), chronic heart failure (CHF) and type 2 diabetes mellitus (T2DM), along with other risk factors. Affiliation of T2DM to CHF impairs prognosis and enhance mortality. Early detection of IR and carbohydrate metabolism disorders (CMD) seems to be relevant.
Study purposes: to evaluate the IR in patients with CAD and CHF without evident CMD. Study methods: we examine 174 patients with CAD and CHF II-IV (NYHA) class without T2DM and glucose-lowering drugs intake in anamnesis, receiving basic for CHF and CAD therapy (statins, ACE inhibitors/angiotensin receptor blockers, beta-blockers, mineralocorticoid receptor antagonists) and define such parameters as: height, weight, body mass index (BMI), systolic and diastolic blood pressure, FINDRISC points, ECG, daily monitor of ECG, echocardiography, fasting and postprandial glucose levels, HbA1C, lipid profile, estimated GFR, daily proteinuria, NT-proBNP, aldosterone and insulin concentrations with assessment of HOMA-IR, standart oral glucose tolerance test (OGTT) was conducted.
Results: Among 174 patients with CAD and CHF II-IV (NYHA) using OGTT, in 50,5% patients was revealed latent CMD: 59 (33,9%) patients had impaired glucose tolerance (IGT), in 29 (16,7%) – T2DM was newly diagnosed, 86 (49,4%) patients were without CMD. The largest number of FINDRISC points was observed in group with newly diagnosed T2DM ($p < 0,000$) compared with patients with IGT and without CMD. Insulin concentrations were increased in each study groups with CAD and CHF, but was significantly higher in patients with CMD compared with patients without CMD ($p < 0,000$). IR was identified in all patients with CAD and CHF, what is more, its level increased with the growth of CMD explicity and was highest in T2DM group compared with IGT and without CMD groups. Elevated levels of NT-proBNP had a linear relationship with CHF severity. Aldosteron levels increased in all patients with CHF regardless of the CMD presence. Correlation analysis determined strong interrelation between IR and: BMI, FINDRISC points, fasting and postprandial glucose levels, HbA1C, insulin concentrations, but not with ejection fraction, NYHA class and CHF duration.
Conclusions: In 50,6% patients latent CMD were determined, from IGT to newly diagnosed T2DM. IR was revealed in all patients, without reference to CMD availability. However, it was direct linear relationship between IR and CMD explicity. Correlation relationship was elicitate between IR and following indicators: BMI, FINDRISC points, fasting and postprandial glucose, HbA1C and insulin concentrations. Thus, early detection of IR and CMD in CAD and CHF patients, with subsequent their correction, may reduce mortality and improve prognosis.

P1732

The role of anti-oxidants in the treatment of congestive heart failure

TH Theodoros Michailidis[1]
[1]*General Hospital of Veria, Department Of Internal Medicine, Veria, Greece*

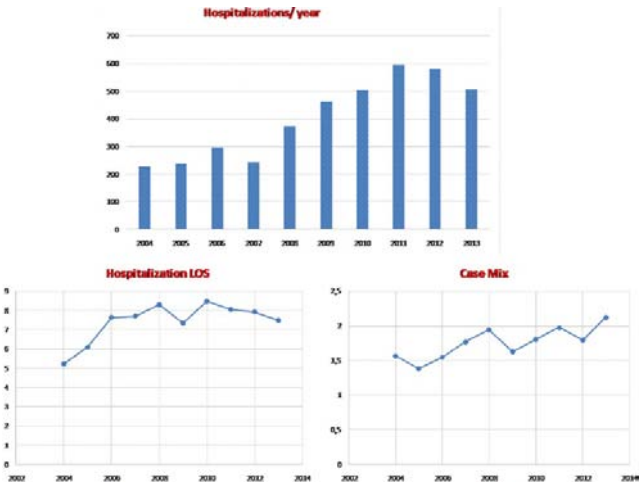
Introduction: Congestive heart failure and oxidative stress are strongly connected, creating a medical "vicious" circle among each other.
Purpose: Our goal was to examine whether the decrease of the oxidative stress levels via use of antioxidants was connected with a subtler presentation of CHF symptoms.
Methods: We studied two groups of men with stage I CHF (65 to 85 years old). All of them were previous smokers (having quitted for at least two years), suffering from CHF and hypertension. None of them suffered from diabetes, COPD or ischemic heart disease. We measured serum malonyl dialdehyde (MDA) levels and serum carbonyl products (CP) in all our patients twice (once at the start of the study and once after a whole year). The difference between the two groups had to do with the addition of vitamin E to their treatment. Group A (consisting of 32 men) patients received ACE or AT inhibitors, statins, calcium channel blockers, beta blockers and a daily intake of 300mg of vitamin E was added to their treatment. On the other hand, group B (31 men) patients received similar treatment without the addition of vitamin E.
Serum MDA and CP were similar in both groups at the start of the study whereas after a year, both oxidative biomarkers were higher in group B ($p < 0,01$ for MDA and CP as well), depicting a much heavier oxidative stress burden in group B (the ones not receiving vitamin E) patients.
Trying to connect this difference between the two groups with the real life quality, we measured the total amount of times that the patients had visited the ER department or were admitted to the Cardiology department due to cardiovascular problems (pulmonary edema, arrhythmias, hypertensive crises etc.).
Results: Group A had the total amount of 83 times, when at the same chronological period of one year group B patients scored a number of 128. Statistical analysis showed an existent but not so strong ($p < 0,05$) difference between the two groups.
Conclusion: The daily intake of antioxidants definitely decreases the oxidative stress in CHF. The positive role of such a decrease in the patient's quality of life needs yet to be furtherly discussed.

P1733

Heart failure hospitalization: a decade-long trend overview in a Tertiary Care Center

G Giuseppe Di Stolfo[1]; S Mastroianno[1]; M Mastroianno[2]; F Giuliani[2]; G De Luca[1]; R Massaro[1]; M Salvatori[1]; DR Potenza[1]; A Russo[1]
[1]*Scientific Institute Casa Sollievo della Sofferenza, Department of Cardiology, San Giovanni Rotondo, Italy*; [2]*Casa Sollievo della Sofferenza Hospital, Information Technology, Innovation and Research Unit, San Giovanni Rotondo, Italy*

Background: Heart failure (HF) is among the most common reasons for hospital admission in the Western World. Investigation of epidemiological tendency represents a fundamental feedback about how we cured in the past to better improve what we would care in the future.
Objectives: This retrospective analysis would focus on decade-long trends in HF hospitalization, length of stay (LOS), in-hospital mortality and Case mix index (CMI) as standard indicator of hospital disease severity in a Tertiary Center Care.
Methods: We retrospectively collected all HF hospitalization in the period 2004-2013, analyzing LOS, CMI, in-hospital-mortality, age and comorbidities as diabetes, hypertension, dyslipidemia, renal disease and atrial fibrillation.
Results: We examined 4026 hospitalizations in a decade-long period. We observed a progressive increase of HF hospitalization prevalence (from 229 to 507 patient/year, $p < 0.01$). There was a significative increasing in LOS (from 5.22 ± 4.61 to 7.49 ± 7.37 days; $p < 0.05$), CMI (from 1.57 ± 1.22 to 2.13 ± 2.17; $p < 0.05$), atrial fibrillation prevalence (from 22.7% to 32.7%; $p < 0.05$) and renal disease prevalence (from 4.4% to 7.3%; $p < 0.05$). There was a slight increase in mean age at admission (from 71.4 ± 12.6 to 74.3 ± 13.3 years) and in-hospital mortality (3.49% to 3.94%). No difference in diabetes, hypertension and dyslipidemia prevalence.
Conclusions: Our retrospective analysis shows an increased burden in heart failure hospitalization, together with a greater case complexity. This finding underlines the urgency to improve health care plan management after discharge with involvement of different clinical care figures sharing a common training and decision process.



HF hospitalization, LOS and CMI

HF Hospitalization epidemiology										
Years	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
N. hospedalization	229	239	296	243	373	462	503	595	579	507
mortality (%)	3,49	2,09	1,35	3,29	2,41	1,95	2,98	2,52	2,59	3,94
age ± SD	71,4± 12,6	71,3 ± 10,7	73 ± 10,8	72,4 ± 13,2	71,3 ± 12,9	72,43 ± 12,14	71,5 ± 12,6	71,8 ± 11,7	71,5 ± 12,05	74,3 ± 13,3
atrial fibrillation (%)	22,71	33,89	32,09	30,86	34,85	27,71	27,44	28,91	28,15	32,74
diabetes (%)	19,21	27,20	22,97	18,52	16,62	24,03	19,09	19,50	20,55	20,51
hypertension (%)	15,28	15,06	15,54	13,99	7,77	8,87	11,13	10,08	11,40	12,82
renal disease (%)	8,73	11,72	11,49	9,05	9,12	12,12	8,75	13,78	17,44	16,37
LOS ± SD	5,21 ± 4,61	6,10 ±3,37	7,66 ± 8.36	7,73 ± 8,03	8,31 ± 9,2	7,36 ± 7,71	8,50 ± 8,96	8,07 ± 8,92	7,94 ± 8,24	7,49 ± 7,37
CMI ± SD	1,56 ± 1,22	1,38 ± 0,8	1,54 ± 1,27	1,77 ± 1,74	1,94 ± 2,09	1,63 ± 1,49	1,80 ± 1,89	1,97 ± 1,97	1,8 ± 1,73	2,13 ± 2,17

P1734

Predictors of non-response to physical rehabilitation in patients with chronic heart failure

VL Galenko[1]; TA Lelyavina[1]; MY Sitnikova[1]
[1]*The North-Western Federal Medical Research Center named after V.A.Almazov, the research laboratory of chronic heart failure , Saint-Petersburg,, Russian Federation*

Introduction: In the world practice physical training is widely used in CHF patients. But in most cases, is not taken into account the influence of the initial clinical status of patients (gender, age, CHFfunctional class, peak oxygen uptake, comorbidity) on the results of physical rehabilitation.
Purpose: To evaluate aerobic physical exercise efficiency, selected on the basis of achievement the lactate threshold during CPET, and to reveal the most significant predictors of inadequate response to physical rehabilitation in CHF patients.
Methods: 77 patients, CHF NYHA II-III were randomized into two groups - primary (aerobic training) and control (standard treatment of CHF). Main group - 64 patients, mean age 54 ± 12,5 years, body mass index (BMI) 26,46 ± 6,4 kg/m2, among them 46 patients (72%) had III CHF functional class and 18 patients (28%) – II CHF functional class. The control group - 13 patients, age 53 ± 17 years, BMI was 25,4 ± 6.8 kg/m2, 12 patients had III CHF functional class, 1 patient – I. The original estimated patient,s initial clinical status. CPET, quality of life (QOL), exercise tolerance (ET) was assessed at baseline and after 1,3,6 months of follow-up. The CPET served on tredmile using hardware "Oxycon Pro", Jaeger, Germany. 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 ± 0.5% and End-diastolic volume decreased by 6 ± 2.0 ml from baseline, QOL was changed by 17.5 ± 8 points (significant regression of symptoms), ET increased by 9 ± 1 points and VO2 peak increased by 4.4 ml/min/kg. In the control group showed an increase EF 4 ± 1,1%, End-diastolic volume decreased by 68 ± 14,8 ml, the change of QOL 14 ± 7,22 points, the increase in ET at 1.5 points, VO2 peak decreased by 1,7 ml/min/kg. Revealed a strong positive correlation between the initial values of VO2 peak and EF (rEF=0,4, p), and between baseline levels of sodium, hemoglobin and the of physical rehabilitation efficiency (rNa= 0,41, p,0,05; rHb = 0,45, p < 0,05). There was a positive impact of the initial content of red blood cells (rEr=0,6, p = 0.03), sodium (rNa=0,4, p = 0.05), LV EF (r=0.5, p = 0.05) and level VE at the peak of exercise load (r=0.5,p = 0.01) on training efficiency. BNP level and a long history of CHF had a negative effect on the result of physical training (rBNP=-0,7, p = 0.05; rCHF=-0,6, p = 0.05). Significant differences in training performance between patients II and III functional class were not received.Conclusion. Aerobic physical exercise in CHF patients, selected on the basis of lactate threshold achievement during the CPET, is effective in improving values of CPET, EchoCG, QOL and increasing exercise tolerance. Age, BNP and uric acid levels can be considered as most significant predictors of inadequate response to physical rehabilitation in CHF patients.

P1735

sST2 and copeptin activity closely associated with E/E' changes during NT-proBNP guided therapy in high risk patients with chronic heart failure after acute decompensation

O Narusov[1]; A Skvortsov[1]; D Koshkina[2]; V Protasov[1]; A Sychov[1]; T Goryunova[1]; V Masenko[1]; S Tereshchenko[1]
[1]*Russian Cardiology Research and Production Complex, Moscow, Russian Federation*; [2]*National Research Center for Preventive Medicine, Moscow, Russian Federation*

Objective: to evaluate the biomarkers activity changes and their association with filling pressure during NT-proBNP guided therapy in CHF patients (pts) at high risk after acute decompensation (ADHF).
Methods: In the prospective single-center trial were included 105 hospitalized pts with ADHF III-IV FC NYHA and LV systolic dysfunction due to coronary artery disease, arterial hypertension and dilated cardiomyopathy. After HF symptoms compensation, at discharge, high risk pts (discharge NT-proBNP 1400 pg/ml) were randomized into group of therapy guided by NT-proBNP (group 1) and standard HF therapy (group 2). Pts in both groups didn't differ by the main clinical characteristics. The goal of treatment was to reduce NT-proBNP concentration of < 1000 pg/ml, or at least 50% of the initial before discharge. At discharge, median NT-proBNP concentration was 3651 (2191,5;6613,0) pg/ml in group 1 and 2862,0 (2015,0;4761,50) pg/ml in group 2, p=0,5. Blood sampling to determine the biomarkers concentrations (NT-proBNP, soluble ST2, copeptin, galectin-3, hsTnT and NGAL) were collected at discharge from the hospital, and 3 and 6 months after. Filling pressure was assessed by E/E'.
Results: At the end of the study all pts in groups 1 and 2 have been treated by recommended combination of iACE/ARB + beta-blocker + MRA (100%), but the mean doses up-titration of iACE/ARB and beta-blockers at the 6 months of treatment were significantly higher in NT-proBNP-guided group, p < 0.05. After 6 months of treatment, median NT-proBNP concentration significantly decreased to 1585,5 (976,5;2612,5) pg/ml(Δ% = -53,1%) in group 1 pts, whereas in group 2 only to 2450,0 (2028,0; 3328,0)pg/ml (Δ% = -11,1%), p = 0.024. The same more pronounced biomarkers activity reduction were found in group 1 pts for sST2 (Δ% = -37,1% vs -10,4%, p = 0,0001) and copeptin concentration (Δ%=-29,9% vs -3,4%, p < 0,001). Concentration of galectin-3, hsTnT and NGAL significantly decreased only in group 1: Δ% = respectively -16,8%, -26,5% and -15,1%, p < 0,01 for all. E/E' significantly decreased only in group 1 from 21,2 ± 4,1 to 14,2 ± 2,8 (Δ% = -30,7%, p < 0,001), vs -11,1% in group 2. In all pts Δ% of sST2 and Δ% of copeptin as Δ % of NT-proBNP concentration very closely correlated with each other, and significantly associated with Δ% E/E' (relatively r=0,63, r=0,7, r=0,67; p < 0.01 for all), compared with other biomarkers.
Conclusion: sST2 and copeptin as NT-proBNP activity are more sensitive and closely associated with E/E' changes during long-term NT-proBNP guided therapy in high risk patients with chronic heart failure after acute decompensation, compared with other biomarkers.

P1737

Galectin-3, longitudinal strain and left ventricular remodelling in patients with aortic stenosis

L Agoston-Coldea[1]; K Bheecarry[1]; T Mocan[1]
[1]*"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania, Cluj-Napoca, Romania*

Background: Aortic stenosis (AS) characterized by a progressive narrowing of the aortic valve triggering left ventricular overload and, consequently, changes in ventricular geometry and in longitudinal myocardial strain. New proinflammatory molecules such as galectin-3 could mediate valve calcification in AS.
Purpose: In the current study, we aimed to assess the relationship between left ventricle remodelling parameters, global longitudinal myocardial strain and new proinflammatory molecules in patients with AS.
Methods: We conducted a prospective study on forty two patients with severe AS (mean age 73 ± 6 years, 23 men) and forty two healthy volunteers matched by age, gender, and body surface areas measuring galectin-3 and NT-proBNP serum levels and specific echocardiographic parameters. Left ventricular remodelling was assessed by left ventricular mass index and relative wall thickness. Peak longitudinal myocardial strain was determined by two-dimensional speckle-tracking imaging.
Results: Most patients with SA had concentric left ventricular remodelling. When compared with healthy volunteers, patients with SA have lower global longitudinal strain (-20.5 ± 0.6 vs. -14.8 ± 3.8%, $p < 0.001$), which is correlated with higher left ventricular mass indexed (r=-0.419, $p = 0.001$), relative wall thickness (r=-0.677, $p < 0.001$), E/E' ratio (r=-0.696, $p < 0.001$), left atrium volume indexed (r=-0.757, $p < 0.0001$), NT-proBNP levels (r=-0.709; $p < 0.001$) and galectin-3 (r=0.718; $p < 0.001$). Relative wall thickness was strongly correlated with levels of galectin-3 (r=0.612, $p < 0.001$) and NT-proBNP (r=0.456, $p = 0.001$). In multivariate linear regression analysis, global longitudinal myocardial strain was associated with lower ejection fraction, increased left atrium volume, E/E' ratio and galectin-3 (R2=0.45, all $p < 0.001$).
Conclusions: In patients with SA, markers of left ventricle remodelling such as increased left ventricular mass indexed and higher relative wall thickness are associated with decreased longitudinal myocardial strain assessed by two-dimensional speckle tracking. Galectin-3 levels were positively correlated with wall thickness and concentric hypertrophy geometry, both of which are crucial indicators of geometric remodelling.

P1738

Trends of heart failure hospitalization during a large period of eleven years.

M L Maria Lucia Fernandez Gasso[1]; D A Pascual Figal[2]; L Hernando Arizatela[3]; J A Palomar Rodriguez[3]; J J Martinez Diaz[1]; J A Giner Caro[1]; J A Castillo Moreno[1]; L Consuegra Sanchez[1]; I Hernandez Fernandez[1]; R M Soto Ruiz[1]; I A Garcia-Escribano Garcia[4]; G Clavel Ruiperez[1]; P Ramos Ruiz[1]; J Garcia Gomez[1]; F Fernandez Montero[5]
[1]*Hospital General Universitario de Santa Lucia, Cardiology, Cartagena, Spain*; [2]*Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain*; [3]*Consejería de Sanidad de la Región de Murcia, Servicio de Planificación Sanitaria, Murcia, Spain*; [4]*Hospital Comarcal del Noroeste, Cardiology, Murcia, Spain*; [5]*Consulta ambulatoria de nefrología, Jaen, Spain*

Background: Heart failure (HF) is a chronic, debilitating, and progressive disease associated with significant mortality and morbidity and represents a burden to the health-care system and it is one of the most important public health problem.
Purpose: To evaluate HF hospitalization during eleven years.
Methods: Study based on the minimum basic hospital discharge data from all hospitals in the Region of Murcia between 2003-2013. Were studied: demographic variables, mortality, length of stay, comorbidities and Elixhauser index.
Results: A total 27.158 HF episodes in 16.827 patients (1,62 cases/person) were identified. Hospital discharge rates were 2,26/1000 people/year, being female gender and elderly (over 75 years) significantly more prevalent. In-hospital average lenght-of-stay was 9.4 days and in-hospital mortality was 9.2%. The Elixhauser index progressive increased from 3.54 in 2003 to 4.37 in 2013. Hypertension, diabetes mellitus, atherosclerosis and dyslipidemia were present in 46.2%, 36.7%, 32.3% and 30.8%.
Conclusions: Between 2003-2013 a change is not observed in terms of length of stay and hospital mortality.The Elixhauser index increased up to one point throughout the period.

Characteristics. Hospitalization for HF

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Hospitalizations	1.641	1.754	1.948	2.253	2.472	2.614	2.592	2.723	2,819	3.019	3.323
Median age	74,4	75,0	75,6	75,8	76,3	77,0	77,2	77,8	77,9	78,0	78,4
Female	58,1	54,9	57,5	56,9	58,0	56,7	56,4	59,3	57,3	57,9	57,2
Age categories (%)											
0-44	1,6	1,6	1,4	1,4	1,5	1,3	1,0	1,2	1,3	1,3	0,4
45-64	12,6	12,5	9,3	10,9	9,7	9,6	8,6	9,0	9,6	9,5	9,5
65-74	29,9	26,5	28,2	26,7	24,1	22,0	22,4	18,8	15,7	16,3	15,6
75-84	41,0	42,9	44,0	43,1	46,5	44,9	46,0	45,2	46,9	44,6	47,7
> 85	15,1	16,5	17,1	17,9	18,2	22,2	22,1	25,9	26,4	28,3	26,8
Length of stay (days)	9,3	9,6	9,6	9,3	10,2	9,7	9,5	9,5	9,0	8,7	9,4
Mortality (%)	10,3	10,2	9,3	7,5	8,5	8,5	10,1	8,4	9,8	9,9	9,3
Elixhauser index	3,54	3,62	3,67	3,73	3,70	3,96	4,05	4,14	4,23	4,23	4,37
Diabetes	42,4	43,7	45,5	46,6	46,8	48,0	45,4	46,1	45,6	47,5	47,7
Atherosclerosis	29,7	32,6	35,7	33,0	30,9	30,1	31,4	31,1	31,6	33,4	34,0
Dylipidemia	21,3	25,9	26,2	27,3	27,9	27,7	30,7	31,4	34,7	36,5	38,5
Hypertension	36,7	41,4	38,4	42,6	42,2	38,9	41,9	41,1	40,8	42,6	42,0
Smoking	18,3	18,3	17,2	21,3	16,7	17,7	18,2	16,8	16,8	15,7	15,4

P1739

6 minute walk distance, NYHA class and hemoglobin levels best predict health related quality of life in chronic stable heart failure patients

T Tara Mannion[1]; L Devaney[1]; S Fall[1]; M Carey[1]; A Jago[1]; S Fay[1]; R Pharithi[1]; V Maher[1]
[1]*Adelaide & Meath Hospital, Dublin, Ireland*

Background: Heart Failure patients experience diminished functional capacity which may impair their quality of life (1, 2). However it is not known which parameter best predicts Quality of Life in the heart failure population and if this differs in patient sub groups.
Purpose: We evaluated if correlations exist between indices of cardiac function and HRQoL in all chronic stable heart failure patients surveyed and in different subgroups. Associations were assessed between health related quality of life (HRQoL) and indices of cardiac function including 6MWT, NYHA, Steps per day, Ejection fraction, LV size, ECG rate and rhythm, BNP, hemoglobin (Hb) and renal function.
Methods: 158 clinically stable heart failure patients, whose weight, condition and medications were stable for the previous 3 months, participated. Functional capacity was evaluated via 6 minute walk testing (6MWT), New York Heart Association (NYHA) class and 3 day-accelerometer measuring daily step count (Fitbit). Other indices of cardiac function were also recorded including ECG (rhythm, rate), Echocardiography (LV size, ejection fraction), and biochemical measures (NT pro BNP, Hb, renal function). HRQol was determined using the Kansas City Cardiomyopathy Questionnaire (KCCQ).
Results: Univariate analysis demonstrated significant correlations between HRQoL and measures of functional capacity; 6MWT (Spearman r= 0.36, $p = < 0.001$), NYHA Class (r= 0.31, $p = < 0.001$), but not with daily step count (Fitbit). In addition, this also revealed significant correlation between HRQoL, and Hb (r= 0.35, $p = < 0.001$). No other statistically significant univariate correlations were revealed in relation to ECG, Echocardiography or biochemical measures and HRQoL. In a multivariate analysis of significant univariate correlants, 6MWT distance ($p = 0.012$), NYHA Classification ($p = 0.037$) & Hb ($p = 0.001$) were revealed to be independent predictors of HRQoL. Independent T-Test and one way analysis of variance revealed statistically significant differences of HRQoL in two patient groups; NYHA Class ($p = 0.001$) and Gender ($p = 0.022$).
Conclusion(s): Improving patients HRQol is essential in HF management. This study highlights that 6MWT, NYHA Class and Hb are the best surrogate markers of HRQOL

compared to other indices of cardiac function. Utilizing 6MWT or NYHA Class in clinical assessments of HF patients may therefore be the best way to tailor medication and/or device therapy, in order to optimize patients HRQoL.

P1740

Xanthine metabolism in patients with chronic heart failure and concomitant chronic kidney disease.

A V Alexandr Bilchenko[1]; MV Kolomietz[1]; AA Bilchenko[1]
[1]Kharkiv Medical Academy for Postgraduate Education , Internal medicine and Nephrology, Kharkiv, Ukraine

Background: Patients with chronic heart failure (CHF) and asymptomatic hyperuricemia have higher rates of cardio-vascular death, and all-cause death or rehospitalization due to worsening heart failure. However, the role of hyperuricemia as a risk factor for both renal and cardiovascular outcomes and in the context of the well-established interrelationship between cardiovascular disease and chronic kidney disease (CKD) is debated.
Purpose: The aim of this study was to examine the association between renal function, serum uric acid level and xanthine oxidase activity (XO) in patients with chronic heart failure and chronic kidney disease.
Methods: The study population consisted of 112 patients (51 men, 61 women) aged (72,5 + 8,6) years. Depending on a presence of concomitant CKD all patients with CHF were divided into 2 groups: with CKD (72 patients) and non-CKD (40) participants. XO activity was determined by a coupled enzyme assay, which results in a colorimetric (570 nm)/fluorometric (lex = 535/lem = 587 nm) product, proportional to the hydrogen peroxide generated. XO activity is reported as nmole/min/mL = milliunit/mL, where one milliunit (mU) of XO is defined as the amount of enzyme that catalyzes the oxidation of xanthine yielding 1.0 mmole of uric acid and hydrogen peroxide per minute at 25°C.
Results: The mean serum uric acid level and XO activity for CHF patients with CKD as compared with non-CKD patients was 7,63 + 0,27 mg/dL (95% confidence interval (CI), 7,09 – 8,160) vs 7,46 + 0,39 mg/dL (95% CI, 6,67 – 8,24; p=0,73) and 7,51 + 1,15 mU/ml (95% CI, 6,03 – 9,99) vs 4,69 + 1,16 mU/ml (95% CI, 2,06 – 5,33; p=0,04), respectively. The mean values of estimated glomerular filtration rate (eGFR) in patients with asymptomatic hyperuricemia and without hyperuricemia were 59,9 + 2,95 mL/min per 1.73 m2 and 76,6 + 6,05 mL/min per 1.73 m2 (p=0,007), respectively. Patients with eGFR ≤ 60 mL/min/1.73 m2 have significantly higher serum uric acid levels and XO activity, compared to those with eGFR > 60 mL/min/1.73 m2 ($p < 0,001$). We find out the significant correlations between eGFR and serum uric acid level (r=-0,3, $p < 0,05$), as well as XO activity (r=-0,5 $p < 0,05$) in CHF patients with CKD. Among patients without CKD significant correlation was observed only between eGFR and XO activity (r=-0,4, $p < 0,05$).
Conclusions: Patients with CHF and concomitant CKD had significantly higher XO activity as compared with CHF patients without CKD. Reduced eGFR in patients with CHF was associated with switching of xanthine metabolism towards oxidase pathway and increased xanthine oxidase activity.

P1741

Prevalence geriatric syndromes among outpatients with and without chronic heart failure

V Valentina Ostapenko[1]; ON Tkacheva[1]; NK Runikhina[1]; YV Kotovskaya[2]; NV Sharashkina[1]; AYU Shchedrina[1]
[1]Pirogov Russian National Research Medical University , Russian Gerontology Clinical Research Center, Moscow, Russian Federation; [2]RUDN University, Moscow, Russian Federation

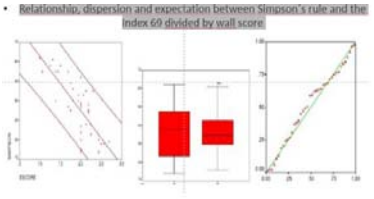
Introduction: The prevalence of heart failure as well as geriatric syndromes increases with age.
Purpose: The aim of our study was to investigate the prevalence of geriatric syndromes in outpatients with and without chronic heart failure (CHF).
Methods: The study includes 356 patients 65-93 years old. Average age was 74.8 ± 6.1 years old, 80.4 % women, 54.8% of them with higher education and 9% still continue to work. Research was conducted in Moscow polyclinic from November 2014 to May 2015. The diagnosis of CHF was determined from medical records. Based on international experience, we have created a 7-item Questionnaire to reveal main geriatric syndromes - weight loss, reduced vision or hearing, causing limitations in daily life, falling, mood disorders, cognitive impairment, urinary incontinence and walking difficulties. For each positive response was given 1 point.
Frailty and pre-frailty was diagnosed by Fried criteria.
Results: One hundred forty-two patients (39,9%) had a diagnosis CHF. The prevalence of frailty and pre-frailty among patients with CHF was higher (frailty 12.4% vs. 6.4%, pre-frailty 66.7% vs. 40.3%, $p < 0.005$). The middle score on the Questionnaire was higher among patients with CHF (3.3 ± 1.5 vs. 2.7 ± 1.5, $p < 0.005$). Significant differences in the responses were obtained for issues about reduced vision or hearing, causing limitations in daily life (66.2% vs. 47.2% $p < 0.005$) and difficulty in movement (59.2% vs. 38.3% $p < 0.005$).
Conclusion: CHF among elderly outpatients is associated with a higher prevalence of geriatric syndromes – frailty and pre-frailty, reduced vision or hearing and walking difficulties.

P1742

Wall motion score index evaluating myocardial performance to assess left ventricular function appropriate to be use at the bedside

CAS Nascimento[1]; B Tura[2]; MG Silva[2]; M Gomes[2]; H Veronesi[2]; APRV Siciliano[2]; AS Silva[2]; A Camarozano[2]; CEV Francisco[2]; MDT Duarte[2]
[1]Oswaldo Cruz Foundation, Evandro Chagas National Institute of Infectious Disease, Rio de Janeiro, Brazil; [2]National Institute of Cardiology, Rio de Janeiro, Brazil

Background: Despite the availability of several, upto date and fast methods to obtain left ventricular ejection fraction (LVEF) values, the subjective impression still the closest one to the physician needing a help number to evaluating their patients tham we show a cardiac formula using the wall score system (WS) to evaluate the LVEF.
Purpose: Evaluate a process to offer to intensivist an archetype number of left ventricular function near to real, because is appropriate to be use in handheld machines at bedside.
Methods: The sample population consisted of 70 hypertensive patients (52.3 ± 10.3 years old , 65% male) with ischemic heart disease with and without failure. We determined the classic wall score system using 17 segments and the LVEF using four different methods (3D, Eyeball, Teichholz and Simpsom Method). 3D measurements were recorded using a GE E9 with V4 transducer and IE33 and portable Phillips CX50 system equipped with a 3.5 MHz transducer and images analyzed by two different observers. The average LVEF was 45 ± 16% by Teichholz and 35 ± 15% by Simpsom Method, Mean Wall Score was 1.7. By regression analysis, we determined a formula that yielded EF calculation using Wall Score system closely resembling the EF obtained by Simpsom rule. The regression equation was Index = 9 0.5 – 27.8 x WS. This formula was further simplified to LVEF = WS divided by 69. Recently we did the same Index in 21(30%) patiens comparing with LVEF obtained by ETT3D with better correlation($P < 0.001$)
Results: In 70% (49 pt)of the patients this last simple formula Index = 9 0.5 – 27.8 x WS or WS divided by 69 yielded a LVEF with very good correlation ($P < 0.02$) with LVEF obtained by, Simpson's rule and the examiner subjective impression (eyeball), and the cardiac performance. LVEF obtained by ETT3D was better correlation($P < 0.001$), increasing the value of the index as it is cheaper and easier to execute.
Conclusions: Calculation of LVEF using wall score is feasible and yields reliable values that can be used in everyday bedside clinical practice with handheld machines without upto date softwares, Another advantage of this method is that we only use the left ventricle segments which are adequately seen.



P1743

Heart failure with mid-range ejection fraction - an echocardiographic finding or a clinical phenotype?

AD Farcas[1]; FP Anton[1]; MA Stoia[1]; CM Goidescu[1]; AF Cocoi[2]; IL Gavrila[2]; LA Vida-Simiti[1]
[1]University of Medicine and Pharmacy, Cardiology Department of County Clinical Emergency Hospital, Cluj Napoca, Romania; [2]Cardiology Department of County Clinical Emergency Hospital, Cluj Napoca, Romania

Background: Clinical data and prognosis for patients with heart failure (HF) with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF) are notably

different. The 2016 ESC Guidelines for HF added a new term – heart failure with mid-range ejection fraction (HFmrEF) to designate patients with EF 40-49% and to bolster the research.
Purpose: The objective of our study is to highlight the features of these patients and to analyze the differences between patients with HFpEF, HFmr EF and HFrEF.
Methods: Our study group included 278 patients (p) with NYHA class II-IV (mean age 66 ± 12y) admitted in the Cardiology Department of CCEH after they signed an informed consent. Clinical exam, echocardiography and lab tests were performed for each patient. Based on the ejection fraction (EF), patients were assigned to three groups: A – 93 p with HFpEF, B – 89 p with HFmrEF and C – 96 p with HFrEF. Study design was approved by the Ethics Committee. Statistical analysis was performed using SPSS 20.
Results: There were no statistically significant differences between groups regarding duration of hospitalization, gender, age and comorbidities (obesity and diabetes). Ischemic heart disease was less frequent (22.4% vs 41%, $p = 0.01$ and 22.4% vs 43.5%, $p = 0.006$) and hypertension was more frequent in group A compared to group B and C (75.1% vs 71.1%, $p = 0.02$ and 75.1% vs 60%, $p = 0.004$). The most frequent cause of decompensation was atrial fibrillation in group B ($p < 0.001$), hypertension in group A ($p < 0.001$) and ischemia in group C ($p < 0.001$). Echocardiography showed that left atrial size (33.9 ± 21.2 vs 25.5 ± 21.3, $p = 0.01$; 33.9 ± 21.2 vs 22.8 ± 19.3, $p = 0.04$), systolic pulmonary artery pressure (43.9 ± 15.1 vs 31.5 ± 12.4, $p = 0.002$; 43.9 ± 15.1 vs 19.4 ± 15.1, $p = 0.02$) and left ventricular diameter (53.7 ± 17.9 vs 36.7 ± 23.1, $p < 0.005$; 53.7 ± 17.9 vs 34.7 ± 21.1, $p = 0.01$) were significantly higher in group C than in group B or A. Beta-blocker doses at discharge were significantly higher in HFpEF patients (32.04 ± 49.95vs 24.16 ± 41.53, $p = 0.02$) and also in HFrEF patients (33.09 ± 37.36 vs 25.93 ± 34.98, $p = 0.019$), but not in those with HFmrEF (31.73 ± 38.57 vs 21.79 ± 31.75, $p = 0.132$). Spironolactone doses were significantly higher at discharge compared to admission in HFpEF (22.39 ± 24.19 vs 15.88 ± 24.36, $p = 0.022$) and HFrEF patients (20.83 ± 23.09 vs 11.25 ± 19.21, $p = 0.001$), but not in those with HFmrEF (18.18 ± 24.42 vs 13.63 ± 25.07, $p = 0.245$). We found no significant difference between ACE-inhibitors/angiotensin-receptor blockers doses at discharge compared to admission.
Conclusions: The treatment strategy for patients with HFmrEF suffered only minor changes during hospitalization compared to those with HFrEF or HFpEF, although they had significant clinical and echocardiographic differences. Future studies involving more patients will provide significant data in this "gray area" regarding phenotype, pathophysiology, prognosis and targeted therapies.

P1744
The frequency of heart failure after acute coronary syndrome in patients with nonobstructive coronary atherosclerosis

S B Gomboeva[1]; A E Baev[1]; Y Rogovskaya[2]; T A Shelkovnikova[1]; W Y Ussov[1]; V V Ryabov[3]
[1]Cardiology Research Institute, Tomsk National Research Medical Centre, Russian Academy of Sciences, Tomsk, Russian Federation; *[2]National Research Tomsk State University, Tomsk, Russian Federation*; *[3]Siberian State Medical University, Tomsk, Russian Federation*

The aim of the study was to evaluate the frequency of heart failure during 6 months after acute coronary syndrome in patients with nonobstructive coronary atherosclerosis.
Material and methods: It is non-randomized open controlled investigation NCT02655718. We present the results of the subanalysis of this study in which included data of patients admitted at the Emergency Department of Cardiology due to ACS in 2015-2016. Inclusion criteria were nonobstructive coronary atherosclerosis (normal coronary arteries / plaques < 50%), confirmed by invasive coronary angiography, age ≥ 18 years at the time of randomization. The exclusion criterion was previous revascularization of the coronary arteries. Twenty two patients were underwent cardiac MRI.
Primary outcomes were hospital mortality, incidence of recurrent ischemia, stroke, and as final diagnosis acute myocardial infarction, unstable angina, Takotsubo syndrome, and myocarditis. Secondary outcomes were death, reccurent myocardial infarction, stroke, the development of heart failure during 6 month after presence of acute coronary syndrome. During 6 months after discharge was hold telephone monitoring for assessment secondary outcomes. Descriptive statistics was used for analysis of data.
Results: Among 913 people who were hospitalized with acute coronary syndrome at the Emergency Department of Cardiology in 2015 - 2016 4.8% (44) patients had nonobstructive coronary atherosclerosis confirmed by coronary angiography. We present the results of subanalysis this investigation including 23 patients. One patient died. Twenty two patients were underwent cardiac MRI. Finally in 13 (56%) cases were diagnosed acute myocardial infarction, in 3(13%) - unstable angina, and a 1/3 of cases had pseudo-coronary scenario of myocarditis. There were 6 (26%) cases of re-hospitalization in 6 months after discharge due to: unstable angina-2 (9%), recurrent myocardial infarction in 1 (4%); noncardiac causes had 3 (13%) patients. The development of heart failure was observed in half patients: NYHA I-1(8%), II-8 (67%), III-3 (25%), NYHA IV-0.
Conclusion: The proportion of patients with nonobstructive coronary artery disease among patients with ACS in 2015-2016 was 4.8%. Heart failure occurred in half patients in 6 months after acute coronary syndrome.

P1745
The impact of a specialised community service on heart failure admissions

E Chua[1]; A Murphy[1]; B Unger-Graeber[2]; S Khan[1]
[1]West Middlesex University Hospital, Cardiology, London, United Kingdom; *[2]Chiswick Health Practice, London, United Kingdom*

Background: Heart failure (HF) admissions are predicted to rise over the next decade, placing increased pressure on healthcare systems. Studies indicate specialised follow up by a multidisciplinary team reduces hospitalization and possibly mortality.
A nurse-led consultant supported community heart failure service commissioned by our local Clinical Commissioning Group was introduced in our hospital's catchment area in 2014. The team receives referrals from general practitioners, hospitals and tertiary centres and has advantages of earlier follow up, satellite clinics and home visits. It serves a diverse local population and allows greater flexibility in management.
Purpose: To evaluate the impact of this service on emergency heart failure admissions, length of stay (LOS) and in-hospital mortality.
Methods: We conducted a retrospective study of emergency admissions to our hospital with a primary diagnosis of heart failure between May 2013 to April 2014 (pre community service, PC group) and May 2015 to April 2016 (after community service, AC group). Our database identified 382 admissions of 271 patients in the PC group and 408 admissions of 319 patients in the AC group.
The AC group was subdivided into those not known to (237 patients) and those under the community team (82 patients). We also stratified patients by New York Heart Association (NYHA) functional classes and ejection fraction (EF) on echocardiogram.
Results: There was a significant reduction in average number of admissions per patient from 1.41 in the PC group to 1.28 in the AC group ($p = 0.01$). Percentage of admissions with codes for complication and comorbidity increased significantly (44.5% to 64.7%, $p < 0.01$). However, there was no significant change in average LOS per patient (19.9 vs 17.3 days) and in-hospital mortality (19 vs 23 patients).
Comparing admissions by NYHA class and EF, there was a significant reduction in average number of admissions per patient only in patients classed as NYHAII (1.52 to 1.19, $p < 0.01$) and patients with severely reduced EF (1.53 to 1.25, $p = 0.03$).
Within the AC group, patients known to the community team had a longer average LOS per patient (22.4 vs 15.6 days, $p < 0.01$). However, these patients had generally more severe disease as reflected by higher percentage classed as NYHAIII and IV.
Conclusions: In conclusion, a nurse-led specialised community heart failure service can be effective in reducing emergency heart failure admission rates, likely more so in patients with less severe disease and fewer comorbidities. This is especially relevant with the increasing demand for inpatient beds. Hence, future studies looking at long term follow up and cost effectiveness of such services would be extremely useful.

ADVANCED HEART FAILURE

P1746
Sarcubitril-valsartan first treatment after inotripic therapy in Stage D Heart failure patients

R Porcile[1]; R L Levin[1]; G Perez Baztarrica[1]; F Salvaggio[1]; R Mayer[1]; L A Botbol[1]; I Vaca Valverde[1]; M T Zuniga Infantas[1]
[1]Universidad Abierta Intericana, Cardiology and Physiology , Universitary Hospital , Buenos aires, Argentina

Purpose: 1)To evaluate clinical utilization of SarcubitrilValsartan (S/V) like first treatment in patients (p) with stage D systolic heart failure after de use of inotropic and diuretics dugs. 2)To evaluate the clinical evolution in 60 days folow up.
Methods: We enrolled p ischemic cardiomyopathy(IC) and ejection fraction(EF) less than 35% admitted for decompensated heart failure between June and October 2016.Inclusion criteria: IC, age18 years, systolic blood pressure >90 mmHg without vasopressors. Were excluded p with infections, renal failure, anemia, cáncer or in mechanical ventilation support. Hemodynamic monitoring was performed using Swan Ganz catheter (SG). All p required intra venous isotropic drugs (ID) and diuretic treatment (DIU). After the suppression of ID and DIU and verifying normal preload and cardiac index by SW (CI>2.2 L/min/m2) and normal volemia (CVP>10,PCOP >15 mmHg) We start an oral dose of S/V of 50 mg each 12 hours. A 6 minutes' walk test was performed 24 hs before and 60 days after hospital discharge checking clinical status, renal function parameters and NT-Probnp.

Results: 9 patients(8men,1women) aged 63 + /-7 year, EF averaged 28.5%. All p received ID average doses 7G/KG/MIN, the starting oral treatment was carvedilol 12.5 day mg,spleronone 25 mg per day and S/V. Average hospitalization time :9.3 days. 8 p performed the 45th day control 1 p received a heart transplant in the 52 day after inclusion. In 2 p we observed symptomatic hypotension that needs doses reduction. No hospital readmission or death during observation period(TABLE)
Conclusions: 1) S/V like first treatment after inotripic therapy in D p is generally well tolerated 2) No hospital readmission or dead and sustained clinical benefit without serious adverse effect during follow up period.3) 60th day Nt-probnp average remain in not congestive range

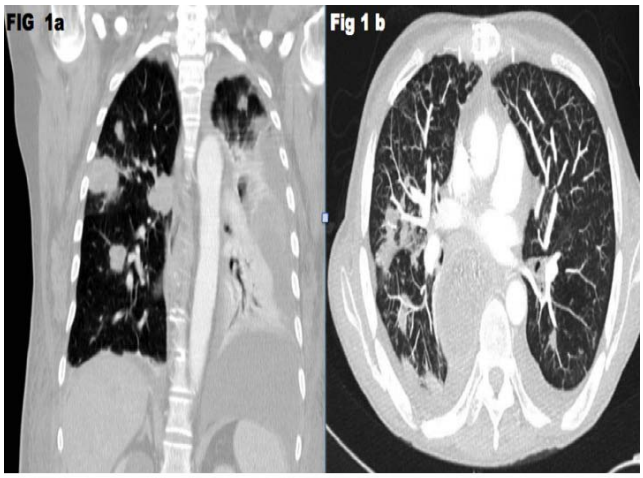
OTHER RESULTS

P	6MWT in hospital	6MWT 2 60 days	SV DOSIS	NYHA CLASS	calculated clearance	NT-probnp 60 days
1	398	401	150	2	86	370
2	427	436	300	1	103	310
3	395	398	300	2	113	298
4	501	505	200	1	110	252
5	298	286	200	3	75	475
6	375	406	400	2	109	360
7	401	397	400	2	68	275
8	310	315	200	1	106	350
Average	388.125	393	268.75	1.75	96.25	336.25

P1747
Invasive pulmonary aspergillosis in heart transplant recipients: is mortality decreasing?

E Flores Umanzor[1]; J Betuel[1]; G Caldentey[1]; G Jimenez-Britez[1]; R San Antonio[1]; P Sanchez-Somonte[1]; G Caixal[1]; M Pujol[1]; M Mimbrero[1]; B Carbonell[1]; S Vazquez[1]; L Tirapu[1]; M Farrero[1]; M Sitges[1]; MA Castel[1]
[1]*Hospital Clinic de Barcelona, Cardiology Department, Barcelona, Spain*

Background: Infection remains a major complication among heart transplant (HT) recipients, causing approximately 20% of deaths within the first year after the transplantation. In this immunosuppressed population, Aspergillus species can produce several clinical presentations including invasive pulmonary aspergillosis (IPA), with a high attributable mortality (53% to 78%).
Aims: To establish the characteristics of IPA infection in HT recipients and their outcomes in our setting.
Methods: Of 328 heart transplants in our center between 1998 and 2016, we identified 5 cases of IPA. Patient records were examined and clinical variables were extracted, including age, sex, primary cardiac diagnosis, date of transplant, immunosuppressant regimen, cytomegalovirus serological status, antifungal prophylaxis, known risk factors for IPA, radiographic features, serum galactomannan level, bronchoscopy and microbiology data. Table 1.
Results: All cases were male patients, with mean age of 62 years. The most common indication for HT was non ischemic dilated cardiomyopathy. Productive cough was reported as the main symptom although two patients were asymptomatic. The most commonly reported radiological abnormality was multiple nodular densities on both chest radiography and chest computed tomography (CT) as shown in Figure 1. Serum galactomannan level was abnormally high in 3 of 5 patients. Bronchoscopy was performed in all patients and Aspergillus fumigatus was isolated in 4 cases on BAL culture. Initial treatment included amphotericin in 4 patients with subsequent change to voriconazole in 3 patients, and posaconazol in 1 patient, with total treatment lasting an average of 12 months. Neutropenia was found just in one patient, renal failure was observed in two patients, and concurrent CMV infection occurred in 3 patients. Only two patients received antifungal prophylaxis since they were in the first 30 days after heart transplantation. All patients survived after a mean follow up of 18 months.
Conclusions: IPA represents a potentially lethal complication after HT. An early diagnosis and a promptly aggressive treatment initiation is the cornerstone for a better survival.



P1748
Global longitudinal strain and cardiopulmonary exercise testing predicts exercise capacity and correlates with previous rejection episodes in heart transplant recipients

BP Dhakal[1]; CM Bianco[1]; SG Al-Kindi[1]; A Bojansky[1]; R Kayatin[1]; M Vest[1]; BD Hoit[1]; GH Oliveira[1]; CA Elamm[1]
[1]*University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, United States of America*

Background: Orthotopic Heart transplant (OHT) is the ultimate treatment option for patients with end-stage heart failure (HF). However, OHT recipients may not reach a normal level of exercise capacity. Exercise capacity data with cardiopulmonary exercise testing (CPET) in OHT recipients and the correlation with echocardiographically-measured left ventricular strain are limited.
Purpose: We hypothesized that speckle-tracking echocardiography (STE) global longitudinal strain (GLS) correlates with exercise capacity measured by CPET in OHT recipients. We also postulated that the number of rejection episodes may have association with GLS.
Methods: Seven OHT recipients following up at our advanced HF clinic 6-18 months after transplantation were recruited into the study. All subjects underwent maximal symptom-limited CPET, STE and RHC with endomyocardial biopsy either simultaneously or within a few days apart. Peak oxygen uptake (VO2), ventilatory efficiency, and other ventilatory parameters were obtained from CPET. Echo measurements included indices of ventricular systolic and diastolic function, systolic tricuspid annular tissue velocity (RVS') and GLS. Medical history and ischemic time of the donors, number and types of rejection episodes of recipients were obtained by chart review. Spearman correlation was used to identify correlation between variables and p value <0.05 was considered statistically significant.
Results: Our patient population consisted of younger males, age 38 ± 12 yrs (mean $\pm$ SD), BMI 27.1 ± 3.8 kg/m^2. The time interval between OHT and echocardiography was 349 ± 94 days. During maximal effort CPET as indicated by peak exercise respiratory exchange ratio ≥ 1.0, OHT subjects had an impairment in their exercise capacity with a mean peak VO2 of 21.1 ± 7.6 ml/kg/min (55 ± 14% of predicted). Peak VO2 correlated with basal right ventricular (RV) dimension (r=0.883, $p=0.02$), mid RV dimension (r=0.829, $p=0.04$) and RVS' (r=-0.828, $p=0.04$). GLS had a strong correlation with the Borg Rating of Perceived Exertion (RPE) (r=-0.894, $p=0.04$) and peak minute ventilation (r=-0.771, $p=0.07$) during CPET. GLS was also significantly associated with resting cardiac output measured by Fick method (r=-0.829, $p=0.04$) and mid RV dimension (r=-0.90, $p=0.037$). There was a trend towards lower GLS and number of prior episodes of low grade acute cellular rejection (ACR, 1R) (r=0.77, $p=0.07$). We did not find any relationship between GLS and ischemic time or cardiopulmonary resuscitation time of the donors. There was no statistically significant correlation between GLS and peak VO2 (r=-0.7, $p=0.11$).
Conclusion: In our pilot study of carefully selected heart transplant patients, GLS "predicts" the peak exercise capacity and is negatively correlated with prior episodes of mild ACR. Indicators of RV parameters are associated with peak

Table P1747

Case	Age/Sex	Days since heart transplant	Radiographic findings/Symptoms	Microbiology/Treatment	Immunosuppression	Known risk factors for IPA	Fungal prophy-laxis
1	59/male	5	Multiple micro-nodular densities/Asymptomatic	Aspergillus fumigatus/ Amphotericin	Prednisone, Cyclosporine + Mycophenolate	Concurrent CMV infection: yes/	Micafungin
2	70/male	12	Multiple micro-nodular densities/ Productive cough	Aspergillus fumigatus/ Voriconazole plus Caspofungin	Prednisone, Tacrolimus + Mycophenolate	Concurrent CMV infection: no	Fluconazole
3	51/male	116	Multiple micro-nodular densities/Productive cough and fever	Aspergillus fumigatus/ Amphotericin + Caspofungin	Prednisone, Tacrolimus + Azathioprine	Concurrent CMV infection: yes	None
4	61/male	189	Multiple micro-nodular densities/Asymptomatic	Aspergillus fumigatus/ Voriconazole + Anidulafungin	Prednisone, Tacrolimus + Mycophenolate	Concurrent CMV infection: no/Neutropenia	None
5	71/male	55	Ground-glass pattern/Chest pain	Aspergillus fumigatus/ Amphotericin	Prednisone, Tacrolimus + Mycophenolate	Concurrent CMV infection: yes	None

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exercise capacity after OHT. Future studies evaluating the association between mild ACR and exercise capacity in OHT recipients are warranted.

P1749
Effectiveness of palliative care in people with persistently symptomatic heart failure: a systematic review

S Datla[1]; A Hoye[2]; M Johnson[2]
[1]*Hull York Medical School, Hull, United Kingdom*; [2]*University of Hull, Hull, United Kingdom*

Background: People with advanced heart failure (HF) are symptomatic, have poor quality of life but, despite recommendations, they have little access to palliative care. The historical lack of evidence for palliative care use in HF patients is a barrier for access to palliative care.
Purpose: To identify the evidence in relation to palliative care for people with persistently symptomatic HF.
Methods: The following databases were searched: Medline, Cochrane database, CINAHL, PsycINFO, HMIC, Care Search Grey Literature. Reference lists, and citations were handsearched and experts contacted. Two independent reviewers screened titles, abstracts and retrieved papers against inclusion criteria. Data were extracted from included papers and studies were critically assessed using the Cochrane risk of bias tool.
Results: Seven phase 3 trials, one phase 2 trial, one quasi-experimental trial, five cohort studies, and one case-control study were included. Studies were heterogeneous in terms of population, intervention, comparator, and outcomes. However, the adequately powered studies, with lower risk of bias, using a multi-disciplinary specialist palliative care intervention showed statistically significant benefit for a variety of patient-reported outcomes such as symptom burden, depression, functional status, and quality of life, as well as resource use and costs of care. Benefit was not seen in studies with a single component/discipline intervention or methodological issues. Possible contamination of controls in some studies may have led to under-estimation of effect. There was no apparent effect on survival.
Conclusion: Results support the use of multi-disciplinary palliative care in managing patients with HF. Across all included studies, findings were inconsistent due to a variety of methodological issues. Further research is needed to identify which patients would benefit most from general and specialist palliative care and the barriers for their access.

P1750
Blood pressure response during cardiopulmonary exercise testing in patients with heart failure predicts failure of medical management

ZJ Zachary II'giovine[1]; N Solomon[2]; AD Devore[2]; D Wojdyla[2]; CB Patel[2]; JG Rogers[2]
[1]*Duke University Medical Center, Medicine, Durham, United States of America*; [2]*Duke Clinical Research Institute, Durham, United States of America*

The prognostic value of peak VO2 and VE-VCO2 slope measured during cardiopulmonary exercise (CPX) testing has been well established in patients with advanced heart failure (HF). Many of these patients also have a blunted blood pressure response (BP) during exercise. This analysis was designed to better understand the prognostic implications of this observation.
We retrospectively studied 166 consecutive ambulatory patients referred to clinic for consideration of advanced HF therapies. Patients underwent cardiopulmonary exercise treadmill testing using either Ekeland or Naughton protocols. Vital sign data was available for 151 patients, which was assessed every 3 minutes during exercise and recovery. Breath-to-breath gas analysis was obtained to measure respiratory exchange ratio (RER), maximal oxygen consumption (peak VO2), and minute ventilation/carbon dioxide production (VE-VCO2).
Patients were stratified into tertiles by change in systolic BP (<13, 13-26, and ≥ 27 mmHg) in response to exercise. Baseline demographics and medications were similar between the groups. Mean exercise time was longer in those with a higher BP response (5.1 vs. 6.0 vs 7.0, respectively, $p = <0.001$). Peak VO2 was lower (10.2 vs. 10.6 vs. 13.6, $p = <0.001$) and VE/VCO2 slope was higher (42.8 vs. 42.1 vs. 36.3, $p = 0.030$) in patients with a lower blood pressure response. Patients with a lower response also had significantly worse survival without transplant or mechanical circulatory support (41% vs. 31 vs. 28%). After multivariate adjustment, an increase in systolic BP up to 20 mmHg was associated with a lower hazard of medical failure (hazard ratio=0.95, $p = <0.0001$ for every 1mmHg increase; failure defined as requirement of left ventricular assist device (LVAD), transplant, or death). When adjusted for an RER >1.05 ($n = 93$), tertiles showed similar progression to death or requirement of LVAD/transplant (42.9% vs. 35.7% vs. 21.4%). Hazard of failure in this subgroup showed a similar but non-significant trend (hazard ratio=0.98, $p = 0.0946$). In conclusion, patients with smaller change in blood pressure in response to exercise were associated with higher rates of death, LVAD, or transplantation.

P1751
Elevated donor C-reactive protein impacts incidence of very early infections following heart transplantation

I Planinc[1]; D Fabijanovic[1]; J Ljubas-Macek[1]; B Skoric[1]; H Jurin[1]; J Samardzic[1]; N Jakus[1]; H Gasparovic[2]; M Cikes[1]; D Milicic[1]
[1]*University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Cardiovascular Diseases, Zagreb, Croatia*; [2]*University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Cardiac Surgery, Zagreb, Croatia*

Purpose: Heart transplantation (HTx) donors frequently have elevated C-reactive protein (CRP) and white blood cell counts (WBCC), predominantly due to systemic inflammatory response to a severe underlying clinical condition, however potentially also influenced by an ongoing infection that may yet not be microbiologically

Table 1.

Donors	Recipients					
CRP quartiles (mg/L)	Very early infection(< 5 days)(n = 12)	Early infection(0-30 days)(n = 61)	Intermediate infection(31-180 days)(n = 37)	Late infection(>181 days)(n = 28)	Treated rejection(n = 24)	Vasculopathy(n = 22)
1. 0.5-37.8(n = 35)	8%	25%	32%	31%	25%	18%
2. 37.9-117.0 (n = 32)	17%	25%	24%	11%	29%	27%
3. 117.1-182.4 (n = 35)	25%	26%	22%	29%	29%	37%
4. 182.5-437.4 (n = 35)	50%*	24%	22%	29%	17%	18%
L quartiles (x10 9)	Very early infection(< 5 days)(n = 15)	Early infection(0-30 days)(n = 67)	Intermediate infection(31-180 days)(n = 40)	Late infection(>181 days)(n = 32)	Treated rejection(n = 24)	Vasculopathy(n = 22)
1. 3.8-10.2(n = 41)	27%	26%	22%	19%	29%	22%
2. 10.3-12.9 (n = 36)	20%	22%	13%	28%	25%	32%
3. 13-17.1(n = 36)	40%	28%	37%	19%	29%	23%
4. 17.2-46.1 (n = 36)	13%	24%	28%	34%	17%	23%

Incidence of observed outcomes in HTx rcps per quartiles of donor inflammatory biomarkers. *p = 0.024

confirmed. We aimed to evaluate the potential consequences of elevated donor WBCC and CRP on recipients (rcp) outcomes.

Methods: We have retrospectively studied pre-explant donor WBCC and CRP for 166 consecutive HTx rcp (117 male, mean age 52 ± 13, median follow-up 31.2 ± 27.4 months) transplanted in our centre between January 2008. and December 2016., and their relation to rcp outcomes (infection, rejection, cardiac allograft vasculopathy, and survival). Per institutional protocol, all patients received meropenem + vancomycin prophylactically for a minimum of 7 days.

Results: Very early infection occurred in 15 rcps (sepsis: 10 pts, pneumonia: 4 pts, UTI: 1 pt), with a significantly higher occurrence in rcps transplanted from donors with higher CRP (Table 1.). Rcps transplanted from donors with CRP in upper quartile tend to have worse survival (not statistically significant). Other studied outcomes were not influenced by CRP values. No significant relation of elevated donor WBCC and incidence of any of studied outcomes was found. Positive donor cultures (urine/tracheal aspirate/sputum/blood culture) did not alter the outcomes.

Conclusion: Donor CRP impacts incidence of very early post-HTx infections, and may influence long term survival, thus warranting cautious donor selection and consideration of appropriate use of prophylactic antibiotics in the very early post-HTx period.

P1752

Ordinal interaction effect of pulmonary vascular resistance and pulmonary arterial wedge pressure on pulmonary RC time

S Sara Moura Ferreira[1]; J Ferreira[2]; R Baptista[2]; MJ Ferreira[2]; A Marinho[3]; S Costa[2]; F Franco[2]; M Pego[2]

[1]Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal; [2]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal; [3]University Hospitals of Coimbra, Paediatric Cardiology, Coimbra, Portugal

Introduction: The pulmonary RC time [the product of pulmonary vascular resistance (PVR) and pulmonary arterial compliance (PCa)] represents the time constant of the mono-exponential pressure decay of pulmonary artery pressure after pulmonic valve closure and has been shown to be useful in the characterization of pulmonary circulation hemodynamics. Exceptions to the steadiness of pulmonary RC time have already been published. We aimed to assess if there is an interaction effect between two factors known to affect pulmonary time constant – pulmonary arterial wedge pressure (PAWP) and PVR.

Methods: This is a retrospective single institution study that included end-stage heart failure patients who underwent a right heart catheterization (RHC) study in the setting of evaluation for heart transplant between 2004 and 2012. RHC was performed via the femoral vein and pressure measurements were obtained using 7F balloon-tipped catheters. All pressure tracings were obtained at end-expiration and were manually reviewed by a heart failure specialist. Cardiac output was determined by the Fick method. PVR was calculated by the following formula: (mean pulmonary artery pressure – mean pulmonary artery wedge pressure) / cardiac output. PCa was calculated as the ratio of stroke volume by the pulmonary artery pulse pressure. Pulmonary RC time was calculated as the product of PVR and PCa.

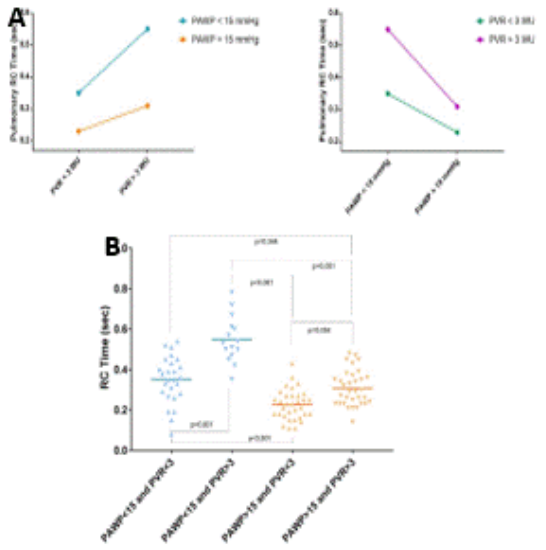


Figure 1. A. Interaction plots showing the mean of pulmonary RC time according to pulmonary vascular resistance (PVR) and pulmonary arterial wedge pressure (PAWP). Non-parallel lines indicate an interaction effect – the effect of one variable on pulmonary RC time is not constant across the second variable. B. Scatter plot of pulmonary RC time according to PAWP and PVR. Each triangle represents a patient; upright triangles – patients with PVR ≤ 3 WU; inverted triangles – patients with PVR > 3 WU; blue triangles – patients with PAWP ≤ 15 mmHg; orange triangles – patients with PAWP > 15 mmHg. Horizontal line – mean of RC time. Statistical significance of the difference of RC time means between each pair is depicted (one way ANOVA followed by Tukey's tests).

Figure 1

Results: 107 patients [83 (78%) men, mean age 51 ± 12 years] were included. The main effect for PAWP yielded a F ratio of F(1, 103) = 90,2, p < 0,001, indicating a significant difference between patients with PAWP ≤ 15 mmHg (RC time 0,42 ± 0,15 s) and patients with a PAWP > 15 mm Hg (RC time 0,27 ± 0,09 s). The main effect

for PVR yielded a F ratio F(1,103) = 54,3, p < 0,001, indicating, also, a significant difference between patients with PVR ≤ 3WU (RC time 0,28 ± 0,11 s) and patients with PVR > 3 WU (RC time 0,38 ± 0,15 s). The interaction effect was significant F(1,103) = 9,3, p = 0,003. This means that the effect of PAWP on pulmonary RC time depends on the level of PVR and vice-versa. The simple effects of PAWP on pulmonary RC time were lower at PVR ≤ 3 WU than at PVR > 3 WU. On the other hand, the simple effects of PVR were lower at PAWP > 15 mmHg than at PAWP ≤ 15 mmHg. Otherwise said, the effects of one variable are not constant across the different levels of the other variable; however, the relative ranking of one variable does not change at different levels of the other, being consistent with an ordinal interaction.

Conclusion: The recognition of an ordinal interaction effect of PVR and PAWP on pulmonary RC time may be important on clinical practice. If pulmonary RC time is used in studies aiming to assess the effect of therapeutic interventions (pharmacological or surgical) on right ventricular afterload, the result may be misleading.

ATRIAL FIBRILLATION

P1753

Catheter ablation of atrial fibrillation in heart failure patients: a first experience.

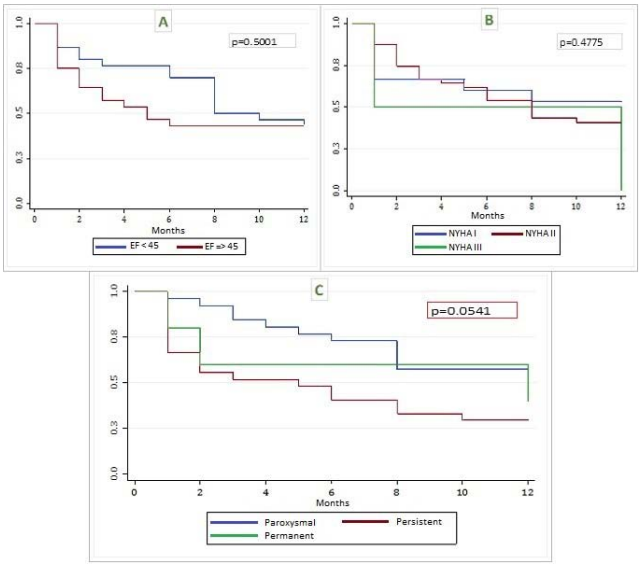
N Nicolas Vecchio[1]; L Ripa[2]; L Tomas[1]; F Cruz[1]; I Mondragon[1]; A Orosco[1]; ML Talavera[1]; A Acosta[1]; S Rivera[1]; G Albina[1]; M Diez[1]; F Scazzuso[1]
[1]Cardiovascular Institute of Buenos Aires (ICBA), Buenos Aires, Argentina; *[2]Central Hospital of Mendoza, Mendoza, Argentina*

Background: Atrial fibrillation (AF) and heart failure (HF) frequently coexist with a significant increase in morbidity and mortality. Rhythm control with pharmacological treatment has failed to keep patients in sinus rhythm (SR).

Purpose: The aim of this study was to assess the efficacy and safety of catheter ablation in patients with AF and HF, and analyze NYHA functional classification (NYHA) and HF hospitalizations during post-procedure follow-up.

Methods: We retrospectively analyzed patients with AF and signs and symptoms of congestive HF or left ventricular ejection fraction (EF) less than 45%, refractory or intolerant to pharmacological treatment, who underwent catheter ablation of AF between July 2009 and March 2016. We excluded patients who did not complete one year of follow-up.

Results: Fifty-eight patients were included. Fifty-five completed at least one year of follow-up. At baseline, mean age was 62.1 ± 10.5 years, 72.4% were men, 67.2% hypertensive and 8.6% diabetics. As a pharmacological treatment, 86.2% were with antiarrhythmics and 55.2% with beta-blockers. Mean EF was 49 ± 13.1% and LA area 26.5 ± 7 cm2. 44.8% had paroxysmal and 46.6% persistent AF. Finally, 70.6% were in NYHA II/III.



Predictors of recurrence at one year

The primary success rate during the procedure was 90.92%. Fifty-five patients were analyzed during follow-up, 33 (60%) had recurrence of AF or atrial flutter after the blanking period. Second catheter ablation was performed in 18 patients and recurrence rate was 44.4%. Therefore, SR rate after two procedures increases to 72.2%. At follow-up, NYHA class in SR group improved significantly more than those in the recurrence group (63.6% vs 36.4%; p = 0.047). No patients in SR had HF hospitalizations, whereas 6 hospitalizations were observed in the recurrence group (0% vs 18.2%, p = 0.07).

Seventy-six ablations were performed between first and second procedures. Eight complications were observed (10.52%), including 3 HF decompensation (3.95%), 2 cardiac tamponade with pericardiocentesis (2.63%), 2 vascular complications (2.63%) and 1 extreme bradycardia (1.32%). No stroke or procedural deaths were observed.

Conclusion: Catheter ablation of atrial fibrillation in heart failure patients refractory or intolerant to antiarrhythmic treatment is a safe procedure with an acceptable success, improving symptoms and decreasing heart failure hospitalizations.

P1754

CHA2DS2VASc score - A strong predictor of new onset atrial fibrillation

G Abreu[1]; P Azevedo[1]; C Rodrigues[1]; I Campos[1]; C Braga[1]; J Martins[1]; C Arantes[1]; M Alvares Pereira[1]; J Marques[1]
[1]Hospital de Braga, Cardiology, Braga, Portugal

Background: The CHA2DS2VASc score is used clinically for stroke risk stratification in atrial fibrillation (AF). Many of the individual risk factors included in this score are also risk factors for atrial fibrillation.

Aim: To examine the CHA2DS2-VASc score performance in predicting new-onset atrial fibrillation in subjects without preexisting diagnosis of atrial fibrillation.

Methods: We analysed 851 patients admitted consecutively in our coronary care unit with a diagnosis of ST segment elevation myocardial infarction in a five-year period. Patients with previous atrial fibrillation (n = 36) or in cardiogenic shock (n = 30) were excluded. CHA2DS2-VASc score was calculated for each patient. The cohort was divided in three groups according to the value obtained: CHA2DS2VASc 0-1 (n = 243, 31%); CHA2DS2VASc 2-3 (n = 334, 42.5%); and CHA2DS2VASc ≥4 (n = 208, 20.5%). For each group we compared clinical and laboratory features, treatment and adverse events. Primary endpoint was the occurrence of new-onset atrial fibrillation after a STEMI.

Results: Patients from CHA2DS2VASc ≥4 group were older (76 ± 9 vs 64 ± 11 vs 55 ± 9 years; p < 0.001). Conventional risk factors were more represented in the higher CHA2DS2VASc score groups: diabetes (51.0% vs 31.1% vs 7.4%; p < 0.001), hypertension (90.9% vs 75.7% vs 37.9%; p < 0.001) and dyslipidaemia (59.6% vs 59.9% vs 42.6%; p < 0.001); except for smoking (8.2% vs 33.2% vs 56.8%; p < 0.001). On admission patients with CHA2DS2VASc ≥4 had more often anaemia (40.1% vs 20.1% vs 12.3%; p < 0.001), renal insufficiency (eGFR < 60 ml/min) (54.6% vs 19.5% vs 3.7%; p < 0.001) and three vessels disease (21.2% vs 17.5% vs 9.1%; p = 0.005). Left systolic ventricular dysfunction was more prevalent (59.1% vs 39.8% vs 34.6%; p < 0.001) in that group. During hospital-stay, patients with CHA2DS2VASc ≥4 developed more frequently heart failure (52.4% vs 24.9% vs 16.9%; p < 0.001), new-onset atrial fibrillation (19.2% vs 11.1% vs 4.1%; p < 0.001); ischemic stroke (2.9% vs 0% vs 0.4%; p = 0.002) and respiratory tract infection (11.1% vs 3.0 vs 5.3%; p < 0.001). In-hospital (8.7% vs 2.4% vs 0.4%; p < 0.001) and 6-month overall mortality (16.7% vs 6.4% vs 2.5%; p < 0.001) were higher in patients with higher CHA2DS2VASc score. In multivariate analysis and after adjusting for different baseline characteristic CHA2DS2VASc score revealed to be an independent predictor of new-onset atrial fibrillation (p = 0.043). Patients with CHA2DS2VASc ≥4 were associated with higher risk of development of new-onset atrial fibrillation [OR 2.90, 95% CI (1.30 – 6.68), p = 0.012]

Conclusion: CHA2DS2VASc score revealed to be a strong predictor of new-onset atrial fibrillation.

P1755

Reduced LA strain predicts atrial fibrillation recurrence after catheter ablation: a systematic review and meta-analysis

G Gani Bajraktari[1]; I Bytyci[1]; MY Henein[2]
[1]University Clinical Centre of Kosova (UCC), Service of Cardiology, Pristina, Kosovo Republic of; *[2]Heart Centre and Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden*

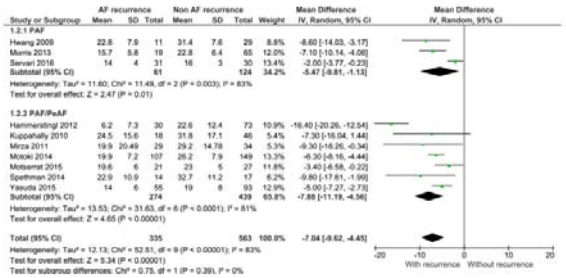
Background and Aim: Despite the improved outcome of patients with atrial fibrillation (AF) who undergo catheter ablation, recurrence of the arrhythmia remains a concern. The aim of this meta-analysis was to assess the potential association between left atrial (LA) strain and AF recurrence after ablation.

Methods: We systematically searched PubMed-Medline, EMBASE, Scopus, Google Scholar and the Cochrane Central Registry, up to December 2016 in order to identify clinical trial and observational studies, which assessed the predictive role of LA strain in AF recurrence after catheter-ablation. The search identified 898 patients form 10 studies, with paroxysmal AF (PAF) and persistent AF (PeAF).

Results: The pooled analysis showed that after a follow-up period of 11.8 ± 8.1 months, patients with AF recurrence had reduced LA strain compared with those

without AF, with a weighted mean difference (WMD) -7.04% ([95% CI -9.62 to -4.45], P < 0.0001). A subgroup analysis showed that LA strain was reduced regardless of AF type; WMD was -5.47% ([95% CI -9.82% to -1.13%], P = 0.003) in PAF and -7.88% ([95% CI -11.19% to -4.56%], P < 0.001) in PAF/PeAF, the difference between these two subgroups was not significant (Chi2=0.75, I2 = 0.0%, p = 0.39). A cut off value of 21% [6% to 30%], was 79% [65-86%] sensitive and 77% [66% to 91%] specific for predicting AF recurrence.

Conclusions: Reduced LA strain significantly predicts recurrence of AF after ablation procedure, irrespective of AF type. This emphasizes the impact of LA wall remodeling on successful ablation.



P1756

Heart failure, left ventricular dimensions and ejection fraction are predictors of thromboembolism in non valvular atrial fibrillation patients treated with direct oral anticoagulants

F Francesco Adamo[1]; N Salvi[1]; R Di Pietro[1]; E Pagliaroli[1]; S Monosilio[1]; I Cardillo[1]; G Benedetti[1]; M Mancone[1]; F Ferrante[1]; F Fedele[1]
[1]*Sapienza University of Rome, Department of Cardiov. & Respiratory Sciences, Nephrology & Geriatrics, Rome, Italy*

Background: The CHA2DS2-VASc score does not always accurately assess the thromboembolic risk in patients with Non Valvular Atrial Fibrillation (NVAF) and, thus, it would be useful to have additional parameters, particularly in patients with CHA2DS2-VASc 1 in whom the need of anticoagulants is debated. We investigated whether the presence of heart failure (HF), left ventricular end-diastolic diameter/BSA (LVEDD/BSA) and left ventricular ejection fraction (EF) both assessed by 2D TTE are predictors of thromboembolic risk in patients suffering from NVAF treated with Direct Oral Anticoagulants (DOACs).

Methods: We evaluated CHA2DS2-VASc, presence of HF clinically assessed, LVEDD/BSA, EF and 1-year incidence of ischemic stroke, TIA or systemic embolism. We used odds ratio (OR), chi-square, linear regression and logistic regression analyses.

Results: Of 273 patients treated with DOACs (129 treated with apixaban, 120 with dabigatran and 24 with rivaroxaban), mean age was 73.1 ± 10.6 years and 152 (55.7%) were males. Mean CHA2DS2-VASc was 3.7 ± 1.7; 81 patients (29.7 %) had HF. Echocardiographic parameters were: LVEDD/BSA 27.6 ± 5.6 mm, EF 48.3 ± 10.6 %. After 1 year of follow up, 6 patients (2.19 %) had a thromboembolic event. Of 6 patients, 5 had HF. A significant association between HF and thromboembolism was found (p = 0.008). The OR of HF patients to have a thromboembolic event was 13.6 (p = 0.008). Linear regression analysis showed significant correlations between CHA2DS2-VASc and both LVEDD/BSA (β = 0.648; 95% CI 0.256 to 1.040) and EF (β = - 2.008; 95% CI -2.727 to -1.289). No significant correlation was found between CHA2DS2-VASc and 1-year incidence of thromboembolism. Logistic regression showed significant associations between LVEDD/BSA, EF and 1-year incidence of ischemic stroke, TIA or systemic embolism (OR 1.15 for each unit increase of LVEDD/BSA; p = 0.001 and OR 0.902 for each unit increase in EF; p = 0.004).

Conclusions: HF and echocardiographic data such as LVEDD/BSA and EF are predictors of thromboembolic risk in patients with NVAF and can be useful parameters in risk stratification, particularly in patients with CHA2DS2-VASc 1 where there is no clear indication to anticoagulation.

P1757

Clinical determinants of B-type natriuretic peptide levels in atrial fibrillation

N Naoki Sato[1]; N Hatori[2]; H Sakai[3]; T Kunishima[4]; Y Hatori[5]
[1]*Nippon Medical School, Tokyo, Japan*; [2]*Kobayashi Hospital, Cardiology, Odawara, Japan*; [3]*Sakai Clinic, Kawasaki, Japan*; [4]*Kunishima Clinic, Kawasaki, Japan*; [5]*Hatori Clinic, Kawasaki, Japan*

On behalf of: the ASSAF-K investigators
Funding Acknowledgements: The Kawasaki Physicians Association

Background: Plasma B-type natriuretic peptide (BNP) levels are elevated not only in atrial fibrillation (AF), but in non-cardiac conditions, e.g., renal dysfunction or obesity. However, it has not been clarified what determine BNP levels in the patients with AF.

Purpose: To examine determinants of BNP levels in AF.

Methods: The ASSAF-K registry, a multicenter, prospective, observational study, was performed to clarify the clinical features of patients with AF in Japan. From this database, 1156 patients were available for the present study. The enrolled subjects were divided two group, i.e., lower and higher BNP groups by the medium level of BNP at 120.8 pg/ml. The association between BNP levels and clinical variables was analyzed using binary logistic regression models.

Results: Clinical features were compared between two groups (table). In multi-variate regression analysis, age (odd ratio (OR) 1.045, 95%CI 1.03-1.06, P < 0.001), persistent AF (OR 2.97, 95%CI 2.20-4.02, P < 0.001), histories of heart failure hospitalization (OR 2.35, 95%CI 1.77-3.13, P < 0.001) and myocardial infarction (OR 1.76, 95%CI 1.03-3.03, P=0.04), hypertrophic cardiomyopathy (OR 5.86, 95%CI 1.97-17.39, P=0.001), and beta-blocker use (OR 2.05, 95%CI 1.54-2.75, P < 0.001) were independent determinants for BNP levels.

Conclusion: Thus, the present study have demonstrated clinical determinants of BNP levels in the patients with AF, suggesting that interestingly the determinants except age are related to cardiac function.

Table

Variables	Lower BNP (N=579)	Higher BNP (N=577)	P-value
Age (yrs)	71.5±10.1	75.5±9.0	< 0.001
Pulse rate (/min)	73.2±13.9	75.7±17.1	0.011
eGFR (ml/min/1.73m2)	62.9±18.7	55.2±18.8	< 0.001
BMI (kg/m2)	23.6±3.7	23.2±3.7	0.062
Persistent AF (%)	54.7	80.2	< 0.001
Heart Failure hospitalization(%)	22.6	49.4	< 0.001
Myocardial infarction(%)	4.7	9.7	0.001
Hypertrophic cardiomyopathy(%)	0.9	5.0	< 0.001
Digitalis(%)	16.4	14.7	0.466
Beta-blocker(%)	28.3	46.3	< 0.001
Calcium channel blocker(%)	9.3	11.6	0.213

Plus minus values:mean ± standard deviation; BNP, B-type natriuretic peptide; eGRF, estimated glomerular filtration ratio; BMI, body mass index; AF, atrial fibrillation.

Comparison of clinical features between lower- and higher-BNP groups

P1758

LA diameter more than 40 mm predicts recurrence of atrial fibrillation after trans-catheter ablation: a systematic review and meta-analysis

G Gani Bajraktari[1]; I Bytyci[1]; MY Henein[2]
[1]*University Clinical Centre of Kosova (UCC), Service of Cardiology, Pristina, Kosovo Republic of*; [2]*Heart Centre and Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden*

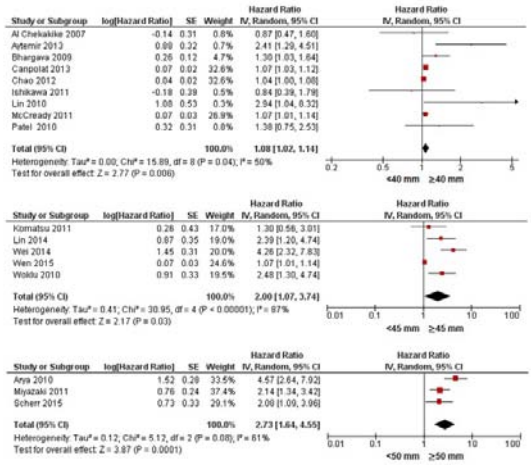
Background and Aim: Left atrial (LA) enlargement is associated with atrial fibrillation (AF) incidence and outcome. Trans-catheter ablation of AF has now become a conventional treatment of AF but its recurrence remains of clinical significance. The predictive role of the LA size in AF treatment is still controversial, hence the aim of this meta-analysis was to analyze the potential association between LA diameter and AF recurrence after ablation.

Methods: We systematically searched PubMed-Medline, EMBASE, Scopus, Google Scholar and the Cochrane Central Registry, up to December 2016 in order to select clinical trial and observational studies, which assessed the predictive role of LA diameter in AF recurrence after catheter-ablation. 13.573 patients from 61 studies with paroxysmal AF (PAF), persistent (PeAF) or longstanding persistent AF (L-PeAF) were included.

Results: The pooled analysis showed that after a follow-up period of 19 ± 7.74 months, patients with AF recurrence had larger LA size compared with those without AF recurrence, with a weighted mean difference (WMD) 0.49 ([95% CI 0.39 to 0.59], P < 0.001), irrespective of the type of AF. A subgroup analysis showed LA diameter to be different; WMD was 2.29 ([95% CI 1.31 to 3.26], P < 0.001) in PAF and 1.51 ([95% CI 1.10 to 1.93], P < 0.001) in PeAF/L-PeAF, the difference between these two subgroups was not significant (Chi2=2.04, I2 = 51.1%, p = 0.15).

LA diameter ≥40 mm predicted AF recurrence HR:1.08 [95% CI 1.03 to 1.14], P=0.006), but the best cut-off value, in all included patients, was ≥50mm HR:2.73 [95% CI 1.64 to 4.55], P < 0.001).

Conclusions: Increased LA diameter significantly predicts recurrence of AF after ablation procedure. While a diameter of 40 mm predicts recurrence, a diameter more than 50 mm is the most accurate predictor.



CARDIOMYOPATHY

P1759

Galectin-3 level and its relationship with clinical status and instrumental parameters in patients with hypertrophic cardiomyopathy

AE Demkina[1]; NS Krylova[1]; NG Poteshkina[1]; EA Kovalevskaya[2]; FM Hashieva[2]
[1]The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation; *[2]City Hospital 52, Moscow, Russian Federation*

Galectin-3 (Gal-3) is a novel marker of cardiac fibrosis and inflammation. The clinical significance of Gal-3 levels is now widely studied. Gal-3 levels in patients with hypertrophic cardiomyopathy (HCM) have been deficiently studied.

Purpose: To assess Gal-3 levels and its relationship with clinical status and instrumental parameters in patients with HCM.

Materials and methods: 30 patients with HCM were examined, (16 men (53.3%), average age 57.0 ± 13.2 years). All patients were treated with bisoprolol (5.5 ± 1.8 mg). In 10 patients (33.3%) obstructive form of the disease was identified. All patients underwent clinical examination, echocardiography with tissue doppler imaging (TDI) and Gal-3 levels evaluation.

Results: Gal-3 level was > 2.28 pg/ml in 17 HCM patients, average mean 4.5 (1.4, 6.9) pg/mL. There was a significant positive correlation between Gal-3 level and following parameters: age (r=0.36, p = 0.05), functional class of chronic heart failure (CHF) by NYHA (r=0.47, p=0.01). There was a negative correlation between Gal-3 level and blood pressure: the history of arterial hypertension (r=0.48, p = 0.01), the maximum values of systolic blood pressure (BP) (r=0.44, p = 0.01) and diastolic BP (r=0.36, p = 0.05) according anamnesis, the level of sistolic BP (r=0.42, p = 0.02) at the office measurement. There was a negative correlation with basal lateral right ventricle (RV) wall s' (r=-0.50, p = 0.05) and medium lateral RV wall s' (r=-0.63, p = 0.009) according to TDI data.

Conclusions: Gal-3 levels was elevated in 56.7% HCM patients. The level of Gal-3 in patients with HCM was assosiated with age, functional class of CHF by NYHA, blood pressure and duration of hypertension anamnesis and RV longitudinal systolic function due to TDI.

P1760

Left atrium characterization in hypertrophic cardiomyopathy: three-dimensional wall-motion tracking technology as a valuable technique

L Marques[1]; N Moreno[1]; H Guedes[1]; R Santos[1]; A Pereira[1]; D Seabra[1]; R Sousa[1]; P Pinto[1]
[1]Centro Hospitalar do Tâmega e Sousa, EPE, Cardiology Department, Penafiel, Portugal

Background: Left atrium (LA) involvement is well established in hypertrophic cardiomyopathy (HCM), with higher volume values and lower deformation parameters being reported. These morphological and functional changes may be the result of secondary pressure overload (due to ventricular diastolic dysfunction, outflow tract obstruction or mitral insufficiency) and/or the result of primary atrial myocardial involvement (pathologically characterized by interstitial fibrosis).

Purpose: Using three-dimensional (3D) wall-motion tracking (3DWMT) echocardiographic technique, we aimed to characterize and compare LA volumes, mass and strain parameters in HCM patients (pts) with healthy controls.

Methods: Thirty-five (35) HCM pts and 27 healthy controls underwent standard bi-dimensional (2D) echocardiography, followed by 3DWMT evaluation. Using Toshiba Artida echocardiography equipment (Toshiba Medical System), global strain values were obtained [global longitudinal strain (GLS), global radial strain (GRS), area tracking (AT)], as well as LA indexed estimated mass, LA indexed end-diastolic volume (EDV), LA indexed end-systolic volume (ESV), LA emptying fraction (LAEF).

Results: We found no age (61.5 ± 10.3 vs 57.5 ± 7.2 years, p = 0.097), gender (p = 0.384) or left ventricular ejection fraction (63 ± 9 vs 65 ± 13%, p = 0.437) differences among HCM and control groups. Regarding volumetric analysis, the HCM group exhibited significant increases in EDV (46.7 ± 14.2 vs 28.0 ± 7.6 ml/m2, p < 0.001) and ESV (32.2 ± 12.0 vs 15.5 ± 5.3 ml/ m2, p < 0.001). In HCM group, LAEF was significantly reduced (31.7 ± 11.4 vs 44.1 ± 12.0%, p < 0.001) and LA estimated mass was significantly higher (17.5 ± 14.5 vs 8.6 ± 1.5 g/ m2, p < 0.001). Regarding strain parameters, we found a significant decrease in GLS of HCM pts (14.0 ± 6.7 vs 24.9 ± 6.3%, p < 0.001).

Conclusion(s): The evaluation of LA by 3DWMT in HCM pts provides detailed information about its volume, mass, function and global deformation parameters. In the analysed cohort, pts with HCM have increased volumes and masses, with a decrease in GLS.

P1761

Comparison between LGE-CMR and histomorphometric quantification of myocardial fibrosis in transplanted hearts for end-stage HCM

G Galati[1]; F Pasquale[2]; O Leone[3]; I Olivotto[4]; F Grigioni[2]; E Pilato[5]; E Biagini[2]; F Cecchi[4]; C Rapezzi[2]
[1]Unit of Cardiology, Cardiovascular Department, IRCCS Policlinico San Donato University Hospital, San Donato Milanese, Milan, Italy; *[2]Institute of Cardiology, Department of Experimental, Diagnostic and Specialty Medicine, S.Orsola-Malpighi University Hospital, Bologna, Italy*; *[3]Division of Pathology, Department of Experimental, Diagnostic and Specialty Medicine, S.Orsola-Malpighi University Hospital, Bologna, Italy*; *[4]Referral Center for Cardiomyopathies, Careggi University Hospital, Florence, Italy*; *[5]Cardiac Surgery, Department of Experimental, Diagnostic and Specialty Medicine, S.Orsola-Malpighi University Hospital, Bologna, Italy*

Background: End-Stage (ES) HCM is one of the main causes of heart failure and represents almost the only indication for heart transplantation in HCM patients. Myocardial fibrosis (MF) and microvascular ischemia are determinant for ES evolution. Recently, our group provided the most accurate histological characterization of extent, distribution, patterns and types of MF in the largest series available in the literature of transplanted ES-HCM patients (n = 30).

Purpose: We conducted a substudy in our cohort with the aim to compare LGE-CMR with histomorphometric quantification of MF in ES-HCM hearts.

Methods: For each heart, a whole midventricular short-axis section (subdivided into 10 samples), 3 samples from basal and 3 from apical level were considered. Histomorphometric MF quantification was performed using a dedicated software and hardware. A 6 SDs threshold exceeding the mean was used to identify LGE areas, which were outlined automatically and artifacts were manually corrected. The total volume was quantified using specific software and expressed as a percentage of LV mass.

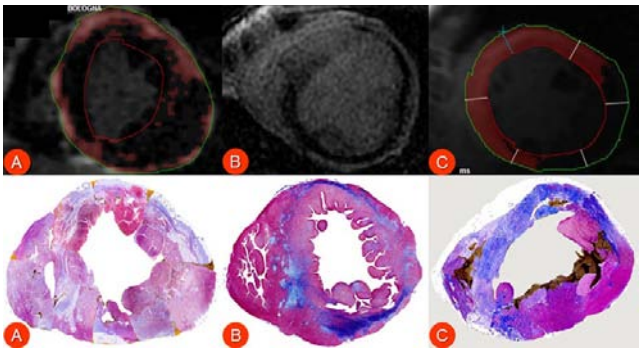
Results: In Table 1 are shown the results for the fibrosis detected in the whole heart (overall fibrosis) comparing the two methods.

Conclusion: We documented a good overlap between LGE-CMR and histological quantification of MF in a group of 4 ES-HCM hearts, in particular when a signal intensity of 6 SDs above reference myocardium was used. However, LGE underestimated fibrosis extent in the patient who had mainly interstitial-perimyocyte MF, showing that this method is unable to detect this fibrosis type. Thus, we confirmed that LGE is able to identify only dense scars but cannot capture more diffuse expansion of the extracellular space, such as that is caused by interstitial fibrosis. Any extent of fibrosis >20% of the whole LV should be regarded as high-risk for ES evolution. To sum up, our study highlighted the necessity to use a comprehensive CMR assessment of MF, using both LGE and the new T1-mapping methods, with the purpose to detect both replacement and interstitial-perimyocyte fibrosis and correctly quantify MF in HCM patients.

T1: LGE vs histological MF quantification

	Overall Fibrosis CMR-LGE 6DS Quantification	Overall Fibrosis Histometric Quantification	Difference LGE-Histology	Replacement Fibrosis	Interstitial-Perimyocyte Fibrosis
Patient 1	48%	48.1%	0.1%		
				+ + +	+
Patient 2	72%	35.5%	36.5%		
				+ + +	+
Patient 3	35%	38.6%	3.6%		
				+ + +	+
Patient 4	30%	35.2%	5.2%		
				+	+ + +
Mean Value	46%	39.4%	11.3%		

Comparison between CMR-LGE and Histometric quantification of MF



Comparison between LGE–CMR and Histology

P1762

Predictors of adverse outcomes and progression of heart failure in patients with hypertrophic cardiomyopathy

EK Kurlianskaya[1]; SM Komissarova[1]; EY Zakharava[1]; TV Ilyina[1]; TV Sevruk[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background.The identification of clinical variants and outcomes in individuals with hypertrophic cardiomyopathy (HCM) with the signs of progressive chronic heart failure (HF) remains a challenge and has not been fully understood. A number of factors have been proposed to identificate subjects with HCM and high risk of CHF progression to a severe stage.
Purpose: The aim of our study is to assess survival rates, outcomes and the influence of factors associated with progressive HF in patients with HCM. Materials and methods. Clinical data of 345 HCM subjects (199 males and 146 females, median age 47 y.o., range 17 - 72 y.o,) treated in RRPC "Cardiology" in the period between 2006 and 2016 have been studied.
Results: Twelve (3,5%) patients with HCM (mean-age 46 ± 12 y.o., 58,3% males) showed signs of Class III-IV NYHA HF accompanied by severe LV myocardial dysfunction. During the follow-up period (median follow-up period 6.7 years), 8 of 12 (67%) patients with Class III-IV NYHA HF showed adverse outcomes: SCD occurred in 1 patient, fatal outcome due to progressive HF occurred in 6 patients , and 1 patient had a fatal stroke. Median uneventful survival was 4.3 years. During the follow-up, 21 (6.1%) patients had progression of HF symptoms from Class II to Class III NYHA. Based on data obtained from a multifactorial analysis, predictors of CHF symptom progression from Class II to Class III NYHA were: LV EF $<56\%$ (OR 4.8; 95% CI 1.6 - 14.5; <0.001), LA size > 47 mm (OR 9.0; 95% CI 3.0-27.6; <0.005), and pseudonormal diastolic dysfunction (OR 9.6; 95% CI 2.8 - 33.4; <0.001). Percentage area of fibrosis with regard to a total myocardial volume based on cardiac MRI was significantly higher in patients with CHF progression (35,8%) than in patients without CHF progression (5,6 %, $p<0.001$). Percentage area of fibrosis with regard to a total myocardial volume based on cardiac MRI allows for an identification of patients with the risk of adverse remodeling with the threshold level > 25%.
Conclusion: Based on the abovementioned data, the discovered predictors allow to identificate patients with adverse remodeling development and risk of end-stage of the disease progression.

P1763

Chronic heart failure in patients with non-obstructive hypertrophic cardiomyopathy: the effect of the angiotensin-converting enzyme inhibitors/angiotensin receptor blockers

AE Demkina[1]; NS Krylova[1]; NG Poteshkina[1]; EA Kovalevskaya[2]; FM Hashieva[1]
[1]*The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation*; [2]*City Hospital 52, Moscow, Russian Federation*

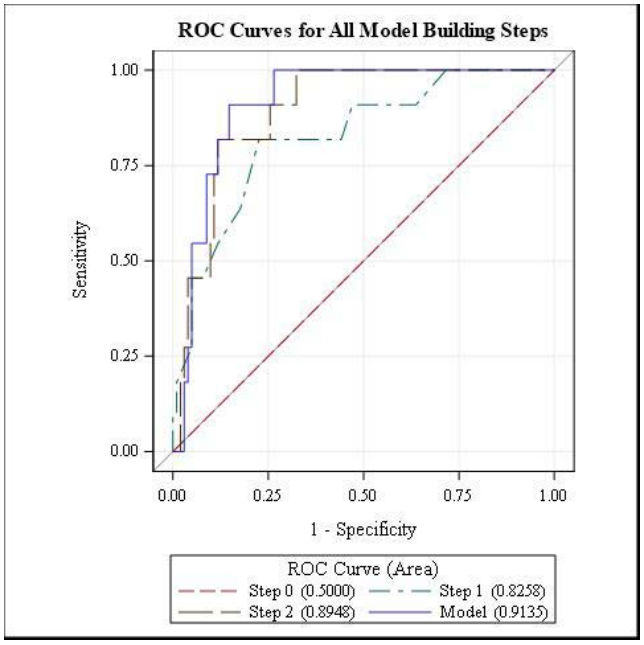
Angiotensin-converting enzyme inhibitors (ACEI) /angiotensin receptor blockers (ARB) is the first-line therapy (IA) in patients with chronic heart failure (CHF). The possibility of their administration in HF with preserved ejection fraction (HFpEF) in patients with nonobstructive hypertrophic cardiomyopathy (HCM) remains debated (IIaC).
Purpose: To asses the effectiveness and safety of ACEI/ARB in HCM patients with HFpEF.
Materials and methods: We examined 40 patients with nonobstructive HCM and CHF II-III NYHA treated with bisoprolol. Patients were randomized into 2 groups: group I - 20 patients, in which perindopril (3.7 ± 1.4 mg, n=14) or losartan (in case of cough 40.0 ± 13.7 mg, n=6) were added to bisoprolol (5.6 ± 1.5 mg) treatment; group II - 20 patients (control group), who continued to receive bisoprolol (5.0 ± 2.0 mg). All patients underwent clinical examination, echocardiography with tissue doppler imaging (TDI) and evaluation of the BNP level before and after 6 months of ACEI/ARB administration.
Results: There were no significant differences in sex, age, clinical – instrumental data and dose of bisoprolol between groups ($p>0.05$). After 6 months of ACEI/ARB therapy in group I there were significantly reduction of BNP level (from 322 ± 18.3 to 154 ± 10.1 pg/ml, p=0.01), thickness of interventricular septum (from 20 ± 1.0 mm to 18 ± 4.0 mm; p=0.001), LV posterior wall (p=0.0001), index of LV mass (from 145.1 ± 15.3 g to 125.1 ± 9.3 g; p=0.04) and right ventricle (RV) wall (p=0.009), decrease of isovolumic relaxation time (IVRT) of transmitral flow ($p=0,0001$), RV (p=0.03) and LV (p=0,007) Tei index. According to the TDI data there was an increase of lateral systolic s' of mitral annulus (MA) ($p=0.01$), a decrease of ivrt' in septal ($p=0.01$), lateral ($p=0.01$), anterior ($p=0.02$) part of the MA. After 6 months of therapy in group II structural and functional parameters didn't change. During the course of ACEI/ARB therapy no adverse event were recorded.
Conclusions: Adding ACEI/ARA to beta-blockers therapy for 6 months in patients with nonobstructive HCM was safely, accompanied by reduction of the myocardial hypertrophy degree with an improvement of diastolic and systolic function of LV and RV and BNP level decrease.

P1764

Early prognostic factors of left ventricular ejection fraction deterioration in Friedreich ataxia

L Legrand[1]; A Diallo[2]; ML Monin[3]; R Isnard[1]; A Durr[3]; F Pousset[1]
[1]*Hospital Pitie-Salpetriere, Assistance Publique-Hôpitaux de Paris, Institut de cardiologie, Paris, France*; [2]*Hospital Lariboisière, Saint Louis, Assistance Publique-Hôpitaux de Paris,, Clinical Research Unit, Paris, France*; [3]*Hospital Pitie-Salpetriere, Assistance Publique -Hôpitaux de Paris, Fédération de Génétique, Paris, France*

Rational: Friedreich ataxia (FRDA) is a progressive neurodegenerative disease associated with scoliosis, diabetes and hypertrophic cardiomyopathy. Progressive decline of Left Ventricular Ejection Fraction (LVEF) is of worse prognosis. There is a need to find early predictors of LVEF deterioration defined as LVEF≤50%.
Methods: 115 FRDA patients with at least two cardiac evaluations were followed during 13 ± 6 years. At baseline and last visit before deterioration, all patients had an initial LVEF > 50%.
Results: 115 patients were included, they were 30 ± 10y (mean ± sd), with a mean neurological onset: 15 ± 8y, age at wheelchair use: 27 ± 11y and a shorter GAA repeat: 620 ± 238 bases pair. Echocardiographic parameters were: LVEF: 68 ± 7%, LV mass index: 102 ± 31 g/m^2, LV diastolic diameter (LVDD): 43 ± 5mm, septal interventricular wall thickness (SIW): 12 ± 3mm. During a follow-up of 13 ± 6 years, 16 patients died and 12 had LVEF deterioration (LVEF < 50%). In multivariate analysis, determinants of LVEF deterioration at baseline were shorter GAA repeat ($p=0.001$) and at last visit: shorter GAA repeat ($p=0, 0001$), SIW ($p=0,005$) and LVEDD ($p=0, 01$). By multivariate logistic regression modelling, optimal time of good prediction is 4 years before LVEF deterioration with a good accuracy: ROC curve with AUC=0, 91, IC95% [0, 85; 0, 97]. Specific cut off points for shorter GAA, SIW or LEDD were respectively 500 pb, 13.3mm and 52,6mm.
Conclusion: Prediction of LVEF deterioration by echocardiography may help physician to manage these young patients, and to initiate early heart failure treatments with improvement of LV remodelling.



ROC curves fo all model buildings steps

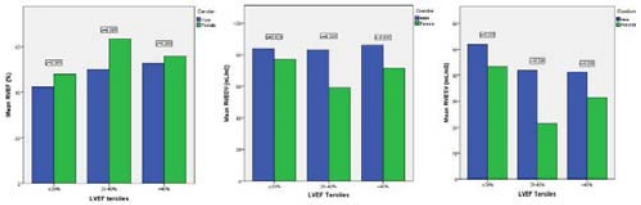
P1765

Gender differences in right ventricular function in dilated cardiomyopathy patients

E Martins[1]; A Sousa[1]; T Pinho[2]; O Azevedo[3]; AR Almeida[4]; S Amorim[2]; B Moura[5]; A Madureira[2]; F Rocha Goncalves[1]; J Silva Cardoso[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; *[2]H. São João, Porto, Portugal*; *[3]Guimares Hospital, Guimaraes, Portugal*; *[4]Garcia de Orta Hospital, Lisbon, Portugal*; *[5]Regional Military Hospital n°1, Porto, Porto, Portugal*

On behalf of: FATIMA investigators
Funding Acknowledgements: PTDC/BIM-MEC/0650/2012

Introduction: Right ventricular (RV) dysfunction has been shown to be an important predictor of worse prognosis in idiopathic dilated cardiomyopathy (DCM).
Purpose: In this work we aimed to evaluate sex-related differences in RV function and volumes, assessed with cardiac magnetic resonance imaging (CMR), in patients with genetic DCM.
Methods: We included 80 consecutive patients diagnosed with idiopathic and familial DCM that underwent a comprehensive CMR with a 3-T scanner, as part of their diagnostic work-up. Ventricular volumes, ejection fraction and mass were measured using dedicated software and were classified as normal or abnormal based on sex and age.
Results: Male and female patients exhibited similar age at diagnosis (36 ± 13 vs 40 ± 14 years, $p = 0.142$), identical proportion of familial cases (55% vs 55%, $p = 0.964$) and positive molecular results (22% vs 26%, $p = 0.730$).
Men and women presented similar mean cardiac index (2.95 ± 0.61vs 2.74 ± 0.83 L/min/m2, $p = 0.0.265$), ventricular mass (78 ± 19 vs 75 ± 24 g/m2, $p = 0.580$), left ventricular (LV) ejection fraction (EF) ($35 \pm 11\%$ vs $32 \pm 11\%$, $p = 0.263$), LV end-diastolic volume (EDV) (126 ± 36 vs 128 ± 38 mL/m2, $p = 0.875$) and LV end-systolic volume (ESV) (83 ± 36 vs 86 ± 38 mL/m2, $p = 0.674$). On the contrary, women presented higher RVEF and lower RVEDV and RVESV ($56 \pm 11\%$ vs $48 \pm 11\%$, $p = 0.008$; 69 ± 21 vs 85 ± 22 mL/m2, $p = 0.006$; 32 ± 20 vs 45 ± 21 mL/m2, $p = 0.012$). The differences in RVEF are particularly significant in the 2nd tercile of LVEF ($29\% \geq$LVEF $< 40\%$) and the differences in volumes, in the 2nd and 3rd tercile of LVEF (Graph: mean right ventricular ejection fraction, mean right ventricular end-diastolic volume and mean right ventricular end-systolic volume according to gender and LVEF terciles).
Conclusions: In patients with DCM, RV functional parameters assessed by CMR are significantly different between genders, particularly in those with LVEF > 29%. These differences might explain the diverse clinical presentations between men and women across the spectrum of LV systolic dysfunction.



Graph

P1766

Prognostic significance of the evolution of non-invasive hemodynamic profile in patients with dilated cardiomyopathy receiving optimal medical treatment

M Merlo[1]; D Stolfo[1]; M Gobbo[1]; G Gabassi[1]; G Barbati[1]; P Naso[1]; G Secoli[1]; F Ramani[1];
B Pinamonti[1]; M Gigli[1]; G Sinagra[1]
[1]University Hospital Riuniti, Cardiovascular department, Trieste, Italy

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Background: Despite the survival improvement of dilated cardiomyopathy (DCM) during the last decades, the prognosis of these patients remains often unpredictable, mostly in the short term after diagnosis.
Aims: To define baseline and short-term "non-invasive hemodynamic" profiles and to assess their possible additive prognostic impacts to clinical and morphological parameters in a large cohort of DCMs.
Methods: We analyzed 385 patients with recently diagnosed DCM (median duration of symptoms: 1 month) from 2005 to May 2015. Baseline and 6-month "non-invasive hemodynamic" profiles were built evaluating the following parameters: significant mitral regurgitation; right ventricular dysfunction; left atrial enlargement (i.e. end-systolic area >13 cm/m2); left ventricular restrictive filling pattern; systolic pulmonary arterial hypertension (i.e. pressure >35 mmHg); E/E' >15. The prognostic values of these models were tested in addition to the clinical and morphological evaluation of patients. The outcome measure of the study was a composite of death or urgent heart transplant
Results: Compared to survivors, patients experiencing death/heart transplant presented a baseline more impaired hemodynamic profile. A rapid significant improvement of all "non-invasive hemodynamic" parameters from baseline to 6-month revaluation was observed. Both baseline and 6-month "non-invasive hemodynamic" models included E/E'>15 and left atrial enlargement as the only independent predictors. Both the baseline and the short-term "non-invasive hemodynamic" models showed an incremental reclassification accuracy vs. the models including only clinical and morphological parameters, mostly in predicting short-term events (event horizon 24 months: baseline models AUC 0.75 vs. 0.41 respectively; $p = 0.002$; 6-month models: AUC 0.90 vs. 0.72 respectively; $p = 0.032$).
Conclusions: E/E' >15 and left atrial enlargement at baseline and their short-term evolution under therapy emerged as the strongest "non-invasive hemodynamic" parameters, significantly improving the prognostic stratification of DCM patients, mostly in the short term.

P1767

Value of electrocardiogram in predicting adverse events in patients with genetic dilated cardiomyopathy

A Sousa[1]; M Campelo[2]; S Amorim[2]; L Lopes[3]; B Moura[4]; O Azevedo[5]; AR Almeida[3]; F Rocha Goncalves[1];
J Silva Cardoso[1]; E Martins[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; *[2]H. São João, Porto, Portugal*; *[3]Garcia de Orta Hospital, Lisbon, Portugal*; *[4]Regional Military Hospital n°1, Porto, Portugal*; *[5]Guimares Hospital, Guimaraes, Portugal*

On behalf of: FATIMA investigators
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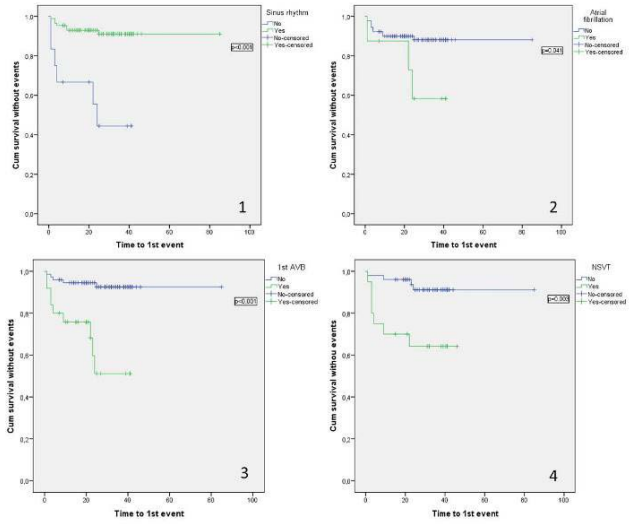
Background: The natural history of patients with dilated cardiomyopathy (DCM) is variable and clinical parameters are poor predictors of clinical outcome.
Purpose: We aimed to determine the prognostic value of electrocardiogram (ECG) in the occurrence of adverse outcomes in patients with idiopathic or familial DCM.
Methods: Multicentric study of consecutive patients with familial DCM ($\geq$ 1 family member with DCM or a first-degree relative with unexplained sudden death $<$35 year) and patients under 50 years with idiopathic DCM, followed at referral centres. Patients underwent extensive clinical evaluation, ECG, 24h-Holter, echocardiogram and cardiac MRI evaluation, when feasible, and molecular analysis. Only patients with follow-up data were included. Assessment of vital status, heart transplantation (HT) and cardiac-related hospitalizations were registered.

Results: We included 99 patients, 59 (60%) male, mean age at diagnosis 38 ± 13 years, mean left ventricle (LV) ejection fraction 34 ± 12% and LV end-diastolic diameter 63 ± 8 mm. Forty-five (46%) patients presented criteria of fDCM (corresponding to 37 families) and 46 (51%) were in NYHA class I. After a median follow-up of 28 (IQR 18) months, 14 (14%) patients experienced adverse events (composite of death, HT and hospitalization from cardiac causes).
Kaplan-Meyer survival analysis showed that sinus rhythm ($p < 0.001$), atrial fibrillation ($p = 0.041$), first-degree atrioventricular block (AVB) ($p < 0.001$) and non-sustained ventricular tachycardia (NSVT) ($p = 0.003$) significantly influenced survival without adverse events (Figure 1-4). Multivariate logistic revealed NSVT as an independent predictor of worse outcome (OR 16.3; 95%CI 1.7-158.3, $p = 0.016$).
Conclusions: In our cohort of DCM patients, 14% experienced an adverse event. Simple ECG data, namely atrial fibrillation, first-degree AVB and NSVT, may help to identify patients at higher risk of worse outcome, whom might beneficiate from a more aggressive clinical vigilance and timely interventions.



Figure

P1768

Incremental prognostic value of cardiopulmonary exercise testing in non-ischemic dilated cardiomyopathy

BP Halliday[1];
K Chiew[1]; S Newsome[2]; R Wassall[1]; A Lota[1]; U Tayal[1]; R Jackson[1]; T Rahneva[1]; AJ Baksi[1]; JG Cleland[3]; SK Prasad[1]
[1]Royal Brompton Hospital, Department of Cardiovascular Magnetic Resonance, London, United Kingdom; [2]London School of Hygiene and Tropical Medicine, London, United Kingdom; [3]Imperial College London, London, United Kingdom

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Introduction: Cardiopulmonary exercise testing (CPET) is commonly used in the follow-up of patients with dilated cardiomyopathy (DCM). CPET variables have been correlated with poor clinical outcomes, however, little is known about their incremental value in addition to other prognostic markers such as brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF) and New York Heart Association (NYHA)symptom class.
Purpose: To investigate the incremental value of CPET in addition to other conventional prognostic markers such as LVEF, BNP and NYHA class.
Methods: We recruited patients with a history of DCM referred for CPET between 2007 and April 2016. CPET was performed using maximal treadmill ergometry. Clinical data contemporary to the CPET were used. The primary end-point was a composite of cardiovascular (CV) death, unplanned CV hospitalisation and cardiac transplantation. The association between the end-point and CPET and clinical variables was examined using proportional hazard modelling.
Results: 126 patients (mean age: 43 years, mean LVEF: 45%, 76 male) were followed up for a median of 2.3 years. 15.9% met the primary end-point. Several CPET and clinical variables were associated with the composite end-point on univariable analysis (table 1). After adjusting for significant non-CPET variables, including BNP, LVEF and NYHA symptom status, exercise time (per minute – HR 0.79; 95% CI 0.67-0.93; $p = 0.005$), minute ventilation - carbon dioxide production relationship (VE/VCO2; per unit – HR 1.1; 95% CI 1.0-1.2; $p = 0.04$), peak oxygen consumption (peak VO2; per ml/kg/min – HR: 0.93; 95% CI 0.87-0.99; $p = 0.03$) and anaerobic threshold (per ml/kg/min – HR 0.89; 95% CI 0.79-0.99; $p = 0.04$) remained predictors of the composite end-point.
Conclusion: Total exercise time, VE/VCO2 slope, peak VO2 and anerobic threshold, as measured by CPET provide incremental prognostic information in addition to BNP, LVEF and symptom status in patients with DCM.

	Total	CV Death or Hospitalisation		Univariable Analysis		
	N=126	No (N=106)	Yes (N=20)	HR	95% CI	P
Exercise HR (bbm)	155.7 (27.7)	158.3 (27.7)	141.2 (23.4)	0.52	0.33, 0.84	0.008
Exercise SBP (mmHg)	150.6 (26.6)	153.6 (26.4)	135.1 (22.3)	0.57	0.35, 0.90	0.017
Exercise DBP (mmHg)	77.1 (12.1)	77.8 (11.9)	73.5 (12.6)	0.74	0.47, 1.15	0.18
Exercise Time (mins)	11.7 (4.3)	12.5 (4.0)	7.9 (3.7)	0.38	0.22, 0.64	<0.001
Peak VO2	27.7 (10.6)	29.1 (10.4)	19.9 (8.3)	0.42	0.23, 0.75	0.004
Predicted VO2	32.0 (8.6)	32.2 (8.3)	30.9 (10.1)	0.92	0.58, 1.46	0.72
AT	20.0 (7.9)	21.0 (7.8)	14.0 (5.6)	0.37	0.18, 0.75	0.006
RER	1.14 (0.13)	1.14 (0.13)	1.13 (0.12)	0.97	0.61, 1.53	0.88
VE/VCO2	30.1 (6.3)	28.9 (4.6)	36.5 (9.4)	1.75	1.28, 2.39	<0.001
Age (Years)	42.8 (15.2)	43.0 (15.3)	41.9 (14.8)	1.02	0.64, 1.65	0.92
Male	76 (60.3)	62 (58.5)	14 (70.0)	1.65	0.63, 4.30	0.31
NYHA II	33 (26.4)	25 (23.8)	8 (40.0)	2.48	0.85, 7.18	0.072
NYHA III / IV	19 (15.2)	13 (12.4)	6 (30.0)	3.63	1.17, 11.32	
LVEF (%)	44.8 (14.8)	47.7 (13.4)	29.5 (12.5)	0.39	0.25, 0.61	<0.0001
BNP (ng/L)	147.7 (270.9)	94.5 (199.7)	422.3 (403.8)	1.87	1.46, 2.40	<0.00001

P1769

Surgical treatment of dilated cardiomyopathy: the reverse remodelling operation and 5-years of follow up

S Sergey Dzemeshkevich[1]; A Dzemeshkevich[1]; YU Frolova[1]; M Malikova[1]; T Voronina[1]
[1]Russian Research Center of Surgery, Dpt of Surgical Treatment of Myocardial Dysfunction, Moscow, Russian Federation

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Background: The shortage of the donor hearts for transplantation leads to the search for new solutions for the surgical treatment of patients with dilated cardiomyopathy and severe heart failure. One of the possible methods could be a reconstructive surgery – the reverse remodelling of the heart.
Purpose: This study aims to review the outcome and 5-years follow up of a surgical reverse remodelling of the heart in cohort of DCM patients.
Patients and methods: We have performed reverse cardiac remodelling in patients with dilated cardiomyopathy. The total number of patients operated with this technique was 24 (19 male and 5 female) patients aged 20–75 (average age – 50,7 ± 2,5).
Results: and discussion. All patients have had a heart failure of the high grade (III FC NYHA – 3, IV FC NYHA – 21 patients). Prior the surgery cardiomegaly was diagnosed by echocardiography in all patients: LVEDP was 7,4 ± 0,9 cm, LVEDV was 277 ± 98 ml, left atrial dimension was 7,2 ± 1,3 cm, LVEF was 29 ± 10%, and PASP was 45 ± 15 mm Hg.
We had no intraoperative mortality. Two patients had died in the early postoperative period after the reverse remodelling. 22 patients were discharged from the hospital. Significant normalization of intracardiac hemodynamics was observed in all 22 patients. Upon hospital discharge all patients had lower heart failure class (I–II FC NYHA) and improvement in the physical exercise tolerance. The comparative analysis of transthoracic echocardiography indicators had revealed the reduction of the heart chambers size and volume, significant decrease of the pulmonary artery systolic pressure, the left ventricular ejection fraction had increased as compared the baseline. In the late period (the follow-up period was 5 years) 5 patients died due to heart failure progression, and 3 patients died suddenly due to fatal cardiac arrhythmias.
Conclusion: The reverse remodelling of the heart could be considered as a promising organ preserving surgical technique for a certain group of DCM patients, allowing us in some cases to postpone or to avoid a heart transplantation.

P1770

Dilated cardiomyopathy: from electrocardiogram to echocardiographic and cardiac magnetic resonance imaging

E Martins[1]; A Sousa[1];
M Campelo[2]; A Madureira[2]; B Moura[3]; L Lopes[4]; O Azevedo[5]; T Pinho[2]; F Rocha Goncalves[1]; J Silva Cardoso[1]
[1]Faculty of Medicine University of Porto, Porto, Portugal; [2]H. São João, Porto, Portugal; [3]Regional Military Hospital n° 1, Porto, Porto, Portugal; [4]Garcia de Orta Hospital, Lisbon, Portugal; [5]Guimares Hospital, Guimaraes, Portugal

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Introduction: Patients with dilated cardiomyopathy (DCM) may present diverse electrocardiogram (ECG) anomalies.
Purpose: We aimed to correlate baseline ECG with left ventricular (LV) and right ventricular (RV) anatomy and function assessed by echocardiogram and cardiac magnetic resonance (CMR).
Methods: Multicentric national study of consecutive patients with idiopathic or familial DCM. Patients underwent extensive clinical evaluation, ECG, Holter, echocardiogram, CMR (in the absence of contra-indications) and molecular study.
Results: We included 111 patients, 48% with familial DCM, 60% males, mean age 47 ± 11 years, with mean age at diagnosis of 39 ± 13 years. Echocardiographic mean LV ejection fraction (LVEF) was 34 ± 11% and LV end-diastolic (LVED) diameter 62 ± 8 mm, CMR mean LVEF was 35 ± 11% and LVED volume 123 ± 30 mL/m2, and 84% presented at least one ECG anomaly.
Patients in atrial fibrillation (10%) presented a higher proportion of RV dysfunction in echocardiogram (46% vs 15%, p = 0.029) and in CMR (100% vs 36%, p = 0.004) and a higher proportion of enlarged RV end-systolic volume (67% vs 24%, p = 0.045). Additionally, patients in sinus rhythm presented higher LVEF in echocardiogram (35 ± 11% vs 30 ± 9%, p = 0.009).
When considering conduction anomalies, 34% and 4% of patients presented left (LBBB) and right bundle branch block (RBBB), respectively, and 28% first-degree atrioventricular block (AVB).
Patients with LBBB presented higher ventricular mass (84 ± 21 vs 72 ± 21 g/m2, p = 0.035) and larger LV volumes (end-diastolic 134 ± 31 vs 117 ± 29 mL/m2, p = 0.025; end-systolic 90 ± 34 vs 74 ± 26 mL/m2, p = 0.036). Curiously, LBBB was associated with better functional RV parameters (RVEF 57 ± 9% vs 50 ± 12%, p = 0.026; RV end-systolic volume 31 ± 10 vs 41 ± 24 mL/m2, p = 0.021).
On the contrary, patients with RBBB presented worse RVEF (42 ± 13% vs 53 ± 11%, p = 0.045) and larger VD (end-diastolic volume 111 ± 34 vs 74 ± 20 mL/m2, p = 0.001). Also, all these patients presented late-gadolinium enhancement (100% vs 34%, p = 0.017).
QRS duration presented a moderate positive correlation with left atrial diameter (r=0.407, p < 0.001).
The presence of first-degree AVB was associated with larger left atrial diameter (47 ± 7 vs 42 ± 8 mm, p = 0.011), worse LVEF (28 ± 11% vs 37 ± 11%, p < 0.001) and a higher proportion of RV dysfunction in echo (43% vs 9%, p < 0.001).
Left atrial anomaly or LV hypertrophy were not associated with any functional LV or RV parameters.
Conclusion: ECG anomalies are frequent in DCM patients. Simple data derived from serial ECG, namely atrial fibrillation, intraventricular conduction delay and first-degree AVB, may be of value in anticipating chamber dimensions and ventricular function evolution, known predictors of outcomes.

P1771

The predictors of the response to cardiac resynchronization therapy in patients with dilated cardiomyopathy

P Manca[1]; S Cossa[2]; GF Tola[1]; A Scalone[1]; B Schintu[1]; A Setzu[1]; S Mameli[1]; N Sanna[1]; A Giardina[1]; L Minerba[3]; G Matta[2]; M Maurizio Porcu[1]
[1]G. Brotzu Hospital, Department of Cardiology, Cagliari, Italy; *[2]G. Brotzu Hospital , Department of Imaging, Cagliari, Italy*; *[3]University of Cagliari, Dipartimento di Sanita' Pubblica, Monserrato, Italy*

Background: Cardiac resynchronization therapy (CRT) reduces mortality and morbidity in patients affected by dilated cardiomyopathy (DCM) and left bundle branch block (LBBB). However, approximately 1/3 of the implanted patients do not show any benefit from this treatment. Aim of the study. To evaluate the clinical, electrical, echocardiographic and cardiac magnetic resonance (CMR) predictors of the response to CRT in patients with DCM.
Methods: We retrospectively analyzed thirty-nine heart failure symptomatic patients (21 M, 18 F, mean age 58 ± 11 yrs, NYHA class II-IV), with a diagnosis of DCM, LBBB and QRS >120ms, who had a complete cardiovascular evaluation including clinical examination, blood parameters, ECG, echocardiography and CMR. All patients underwent coronary angiography to exclude significant (>50%) stenosis. Four patients were in atrial fibrillation (AF) with an adequate rate control and two of them had a biventricular pacing < 90%. All patients were treated with optimal medical therapy for at least 3 months (βb 85%, ACE-I/ATII-A 90%, furosemide 92%, AA 67%). Based on the response to CRT, patients were divided into two groups: Responders = improvement ≥ 1 NYHA functional class and/or improvement >15% in the ejection fraction; Non-Responders = no improvement or even worsening of NYHA functional class and improvement < 15% in the ejection fraction.
Results: At a mean follow up of 38 ± 16 months twenty-four patients (62%) were considered responders, while fifteen (38%) did not show any benefit. At CMR, LV fibrosis was present in only 1/4 of patients, involving < 3% of myocardial mass of the whole population. The predictors of non-response were older age (64 vs 56 years; p = 0,036), higher creatinine level (1,36 vs 0,99 mg/dl; p = 0,036) and a more enlarged left atrium (30 vs 24 cm2; p = 0,012). The four AF patients were all Non-Responders (p = 0,008). No other factors, such as baseline QRS duration and post CRT shortening or LV ejection fraction, showed a prognostic value.
Conclusions: These data confirm that more than 30% of DCM patients do not have any substantial benefit from CRT, independently from the presence of ventricular fibrosis. In our experience, older age, renal impairment, atrial dilatation and AF represent negative prognostic factors.

P1772

Takotsubo cardiomyopathy in diabetic patients - Are there differences?

PM Pedro Azevedo[1]; B Faria[2]; B Marmelo[3]; C Ruivo[4]; R Santos[5]; A Gomes[6]; M Vieira[7]; A Marreiros[1]; L Teles[8]; A Almeida[6]
[1]Faro Hospital, Cardiology, Faro, Portugal; *[2]Hospital Guimaraes, Cardiology, Guimaraes, Portugal*; *[3]Hospital Sao Teotonio, Cardiology, Viseu, Portugal*; *[4]Hospital Santo Andre, Cardiology, Leiria, Portugal*; *[5]Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*; *[6]Hospital Garcia de Orta, Cardiology, Almada, Portugal*; *[7]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[8]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo cardiomyopathy (TC) is an acute and reversible cardiomyopathy that predominantly affects female patients after a precipitating event, namely physical or emotional stress. The catecholamine-driven coronary spasm and myocardial injury have been considered as possible pathophysiologic mechanisms. Some authors state that TC is less prevalent and severe in diabetic patients due to inherent autonomic neuropathy. This study aims to characterize a population with TC and diabetes mellitus (DM) and evaluate the impact of DM in the prognosis of these patients.
Methods: Portuguese multicenter, prospective, descriptive and correlational study, involving 12 hospitals in which all patients with TC since 2004 were included and divided in two groups: diabetic and non-diabetic patients. The baseline demographic characteristics, clinical data, echocardiographic and electrocardiographic parameters, as well as mortality on follow-up were evaluated. We performed univariate and multivariate statistical analysis through SPSS.
Results: 234 patients with TC were included, of which 44 (11,8%) had DM. 90,9% of diabetic patients were female and had a mean age of 73,5 ± 10,2, similarly with non-diabetic patients. Diabetic patients had more frequently hypertension (84,1% vs 64,2%, p = 0,01) and dyslipidemia (70,5% vs 50,5%, p = 0,017) and were less frequently smokers (2,3% vs 16,8%, p = 0,012), On admission, patients with DM were more likely to present with dyspnea (34,1%vs18,9%, p = 0,03) and less likely to have a precipitating factor (43,2% vs 63,2%, p = 0,015). There was a tendency to less episodes of ventricular tachycardia on admission (27,3% vs 43,2%, p = 0.05). There weren't any differences between the groups regarding the type of Takotsubo, the presence of acute heart failure or left ventricular ejection fraction on admission (LVEF).
Diabetic patients had more frequently a LVEF ≤ 40% on discharge (17,5%vs5,9%, p < 0.02) and LVEF ≤ 50% on the first follow-up echocardiogram (12,9%vs1,5%, p < 0,01)
During a mean follow-up time of 33,15 months, there were no significant differences regarding outcomes, namely in-hospital mortality (4,5% in diabetic patients vs 1,6% in non-diabetic, p = 0,23), Takotsubo recurrence (4,5% vs 4,2%, p = 0,9) and mortality on follow-up (9,1% vs 5,8%, p = 0,42).
Conclusion: In this study, the prevalence of DM in patients with TC is relatively low (11,8%), compared with the Portuguese prevalence data for DM (27% in the population over 60 years), suggesting either underdiagnosis due to the more atypical presentation, or a possible protective effect for the development of TC in diabetic patients. There were no differences in outcomes between the two groups and the differences in LVEF probably reflect diabetic cardiomyopathy. Interestingly, there was a tendency for less ventricular tachycardia, which could be due to sympathetic blunting in these patients.

P1773

Comparison of various non-invasive tools for diagnosing AL cardiac amyloidosis

M Martin Nicol[1]; B Assous[1]; M Baudet[1]; R Dautry[1]; A Cescau[1]; A Cohen Solal[1]; B Arnulf[2]; D Logeart[1]
[1]Hospital Lariboisiere, Paris, France; *[2]Hopital Saint-Louis, Paris, France*

Cardiac involvement is the most important cause of death in light chain amyloidosis (AL) and its early diagnosis is a major issue for therapeutic strategy. Gold diagnostic standards are either invasive (cardiac biopsy) or not widely available (cardiac MRI). We aim to compare diagnostic value of various diagnostic tools in this setting.
Methods: Following diagnostic tests were performed after first diagnosis of AL amyloidogenic disorder: clinical examination, blood testing of BNP and troponin I, EKG, echocardiography, 24-hours EKG Holter, cardiac MRI, cardiopulmonary test. Cut-offs were chosen from literature for parameters with continuous values. Final diagnosis of cardiac amyloidois (CA) was done either by MRI if diffuse late

enhancement was present or by an expert consensus (3 clinicians) using all medical files. Diagnostic values of tests as well as their combination were calculated.
Results: Among sixty consecutive patients (64 ± 10 years, 18 with multiple myeloma and 42 with MGUS), final diagnosis of CA was done in 40 patients. Renal, digestive and neurologic AL involvements were present in 45%, 22% and 20% respectively of patients with CA. The table shows diagnostic values of EKG, BNP and echography as well as their combinations. Usefulness of troponin, Holter or stress test was less relevant.
Conclusion: Combining EKG, BNP testing and echocardiography result in nearly optimal diagnosis of CA.

	Se	Sp	NPV	PPV
EKG abnormalities	95%	79%	88%	90%
GLS ≤ - 16%	91%	63%	77%	84%
IVS ≥ 12 mm and GLS ≤ - 16%	91%	81%	81%	91%
EKG abnormalities and IVS ≥ 12 mm and GLS ≤ - 16%	85%	100%	76%	100%
BNP ≥ 100 ng/L and IVS ≥ 12 mm and GLS ≤ - 16 %	89%	76%	76%	89%
BNP ≥ 100 ng/L and EKG abnormalities ans GLS ≤ - 16%	82%	94%	71%	97%
BNP ≥ 100 ng/L and EKG abnormalities and IVS ≥ 12 mm and GLS ≤ - 16%	82%	100%	73%	100%

GLS : global longitudinal strain, IVS : Interventricular septum diastolic thickness, EKG abnormalities : microvoltage and/or pseudo Q wave, Se : sensibility, Sp : specificity, NPV : negative predictive value, PPV : positive predictive value

P1774
The genetics of noncompaction cardiomyopathy

N Shcherbakova[1]; O Kulikova[1]; R Myasnikov[1]; A Zharikova[1]; A Kiseleva[1]; M Kharlap[1]; A Meshkov[1]; E Mershina[2]; V Sinitsyn[2]; S Boytsov[1]
[1]National Research Center for Preventive Medicine, Moscow, Russian Federation; *[2]Federal Center of Treatment and Rehabilitation, Moscow, Russian Federation*

Background: Left ventricular noncompaction cardiomyopathy (LVNC), despite being a relatively rare cardiomyopathy, is a major problem in cardiology, due to its high mortality and the presence of serious complications. Despite significant advances in genetic diagnosis, only a small number of patients with LVNC could be successfully genotyped. Although the use of large panels of genes can increase the impact of genetic testing.
Purpose: In our study we performed exome sequencing of patients with a clinical diagnosis of noncompaction cardiomyopathy and their relatives of 1 and 2 degrees of kinship to detect the genetics causes of the cardiomyopathy.
Methods: In the last few years we formed the cohort of patients with noncompaction cardiomyopathy and their relatives of 1 and 2 degrees of kinship. The enrollment of participants was done by cascade and reverse-cascade methods in the heart failure center. Probands should have met echocardiographic criteria and cardiac MRI criteria for noncompaction. All the participants underwent standart clinical examination which included echocardiography, 24-hours Holter monitoring of ECG, collection of blood, serum and plasma specimens. Molecular testing was performed using exome sequencing for members of 9 families (29 participants). Among them 11 patients fulfilled the criteria of noncompaction cardiomyopathy. The signs of excess trabeculation were found in eight relatives and 10 relatives were negative for any signs of cardiomyopathy. For precise evaluation of pathogenic variants 37 genes earlier associated with noncompaction cardiomyopathy were screened.
Results: We have sequenced specimens of 29 participants. After the primary bioinformatics analysis have been done, all the variants in 37 genes associated with noncompaction cardiomyopathy were annotated and filtered according to population data, data of computational predictive tools (SIFT and PolyPhen2), association to any cardiomyopathy and segregation in family. Likely pathogenic variants were determined in 6 out of 9 families. 3 variants were found in TTN gene, 2 variants in FLNC gene and 1 variant in DMD gene.
Conclusion: The improving accuracy of molecular diagnosis in patients with noncompaction cardiomyopathy would have a solid effect on counseling and screening of members of families. Despite considerable progress in diagnosis and treatment of LVNC in the last decade, the understanding of the pathophysiological processes underlying the disease and the identification of novel genetic, biochemical and immunological markers are topics for further scientific research.

P1775
Ventricular deformation in type 1 diabetes children

R Rim Ben Said[1]; I Zairi[2]; K Mzoughi[2]; F Ben Moussa[2]; S Kammoun[2]; S Fennira[2]; S Kraiem[2]
[1]La Rabta hospital, cardiology, Tunis, Tunisia; *[2]Habib Thameur Hospital, Cardiology, Tunis, Tunisia*

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 24 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. LVEF was preserved with an average of 67,88 ± 1,18%. 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.

P1776
Serum BDNF levels predicts cardiac death in patients with heart failure due to Chagas disease

H Henrique Costa[1]; MMO Lima[2]; PM Martinelli[3]; ERS Camargos[3]; AL Teixeira[4]; AP Ribeiro[1]; MCP Nunes[1]; MOC Rocha[1]
[1]Federal University of Minas Gerais, School of Medicine, Postgraduate Course of Tropical Medicine, Belo Horizonte, Brazil; *[2]Federal University of Jequitinhonha and Mucury Valleys, Diamantina, Brazil*; *[3]Federal University of Minas Gerais, Department of Morphology, Institute of Biological Sciences, Belo Horizonte, Brazil*; *[4]Federal University of Minas Gerais, School of Medicine, Belo Horizonte, Brazil*

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Introduction: Serum brain-derived neurotrophic factor (BDNF) is up-regulated in patients with Chagas disease (ChD) by dysautonomia and chronic inflammatory process. However, the prognostic value of BDNF levels have not been established in patients with heart failure (HF) due to ChD.
Purpose: To verify the prognostic value of serum BDNF in patients with HF due to ChD.
Methods: Forty-nine patients with HF due to ChD (50.1 ± 7.5 years, NYHA II-III, LVEF 35 ± 7%) were evaluated by clinical evaluation, echocardiography and Cardiopulmonary Exercise Testing. Serum BDNF levels were determined by ELISA sandwich in all patients. A receiver-operator curve was constructed to determine the cutoff value of the serum BDNF to predict cardiac death and the value was used in the Kaplan-Meier curve. The prognostic role of BDNF levels was verified by uni and multivariate Cox regression analysis.
Results: After 41 ± 12 months of follow-up, 12 patients died. The concentration of 2.49 ng/mL was the optimal cut point value to predict cardiac death (AUC=0.78) with significant difference between low and high serum BDNF levels (p = 0.006). In the univariate Cox regression, age, gender, body mass index, left ventricular end-diastolic diameter and E/e' ratio were not associated with cardiac death. In the multivariate regression, low (≤2.49 ng/mL) serum BDNF levels (HR 2.6, 95% CI from 2.1 to 3.1, p = 0.001), peak oxygen uptake (HR 1.2, 95% CI from 1.1 to 1.3, p = 0.009) and left ventricular ejection fraction (HR 0.9, 95% CI from 0.7 to 0.9, p = 0.001) and were independent predictors of survival in HF due to ChD patients.
Conclusion: Serum BDNF levels seems to provide useful prognostic information in patients with HF due to ChD.

P1777

Significance of hsTNF-alpha testing in the verification of inflammatory cardiomyopathy.

AY Shchedrina[1]; AA Skvortsov[2]; KA Zykov[2]; OY Narusov[2]; SN Tereschenko[2]
[1]Pirogov Russian National Research Medical University , Russian Gerontology Clinical Research Center, Moscow, Russian Federation; *[2]Russian Cardiological research and productive complex, Moscow, Russian Federation*

Aim: To evaluate the role of hsTNFα in the verification of the inflammatory cardiomyopathy (ICMP).
Methods: 35 patients mean age 40,8 ± 11,3 (21 male, 14 female), I-III Class NYHA, mean LVEF 33,8 ± 6,36%, with symptomatic heart failure for median 2,0 [1,0;3,0] years and suspected inflammatory cardiomyopathy underwent endomyocardial biopsy (EMB). EMB specimens were investigated with histological and molecular-genetic methods with PCR detection of cardiotropic viruses. Diagnosis was based on World Health Organization criteria. Leucocytes and macrophages criteria amount was ≥ 14. Sera were taken for testing hsTNFα.
Results: The total number of EMB patients was 35 (100%). ICMP was diagnosed in 15 cases (42, 8%) [9 cases (25, 7%) were virus-positive and 6 cases (17,1%) were virus-negative]. DCMP without signs of active inflammation was revealed in n=20 (57, 1%). [12 cases (34, 2%) were virus positive and 8 cases (22, 8%) were virus negative]. Mean NYHA FC was 2, 06 ± 0, 77 in ICMP pts group and 2, 17 ± 0, 7 in DCMP pts group (p = 0,6). According to EMB results, in the myocardium of patients with ICMP the median of lymphocytes, expressing CD4 + and CD8 + were 13,5[10,0;20,0] and 10,0 [6,0;11,7] relatively, that was significantly higher compared with group of DCMP without active inflammation: relatively 1,8[0,0;3,2] (p < 0,0001) for CD4 + and 3,1 [1,5;4,2] for CD8 + , (p < 0,0001). Between the groups of ICMP and DCMP without active inflammation there was no significant difference in the level of the hsTNFα 3,1[1,3;9,7] versus 1,9 [0,8;3,9] (p = 0,47) relatively. However, according to the quartiles of infiltrating cells/mm^2 of myocardium, the patients were divided into four groups: 1 group (0-4 cells), 2 group (5-10 cells), 3 group (11-17 cells), 4 group (>17 cells).In pts with more than 17cells/mm^2 was identified the maximum level of hsTNFα 5,1[3,2;10,3] versus 1,3[0,4;3,1] in others groups (0,03). In the group of patients with ICMP there were revealed positive correlations of hsTNFα with the total number of infiltrating cells/mm^2 (r=0,5,p = 0,08), particulary CD68 + /mm^2 of myocardium (r=0,68,p = 0,01), with the stage of hypertrophy (r=0,7; p = 0,002) and cardiosclerosis (r=0,6; p = 0,024). In addition there was a trend to correlation with ESV (r=0,5,p = 0,08).
Conclusions: The level of hsTNFα was significantly higher in patients with the most pronounced inflammatory process and associated with the severity of myocardial infiltration. The level of this cytokine reveals the stage of cardiosclerosis and hypertrophy.

P1778

Diagnostics of wild-type transthyretin cardiomyopathy and its clinical presentation in Czech patients - a single centre experience.

M Milos Kubanek[1]; J Binova[1]; A Krebsova[1]; M Buncova[2];
E Honsova[3]; P Lupinek[1]; J Vrbska[1]; V Melenovsky[1]; J Kautzner[1]
[1]Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic; *[2]Institute for Clinical and Experimental Medicine (IKEM), Radiology, Prague, Czech Republic*; *[3]Institute for Clinical and Experimental Medicine (IKEM), Pathology, Prague, Czech Republic*

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Introduction: Transthyretin cardiomyopathy (TTR-CMP) has been recently recognized as a cause of heart failure with preserved ejection fraction (HFPEF). Availability of non-invasive diagnostics using 99mTc-DPD scintigraphy and emerging modalities of pharmacotherapy have attracted attention of clinicians to this disease. We aimed to analyze our experience with diagnostics and clinical presentation of wild-type TTR-CMP.
Methods: The study group included 16 patients (14 males, 2 females; mean age 80 ± 6 years) diagnosed with wild-type TTR-CMP in our centre from 2010-2016. The diagnosis of TTR-CMP was based on index of maximal myocardial accumulation (IMA) at 99mTcDPD SPECT-CT following administration of 740MBq of 99mTcDPD. IMA was calculated as a ratio of peak myocardial and peak skeletal activity (mean 6.26 ± 2.42; upper limit of normal 1.1 in males and 1.7 in females). In addition, 8 patients (50%) underwent endomyocardial biopsy, which detected transthyretin amyloidosis in all cases.
Results: TTR-CMP was identified in 10 patients (62%) evaluated due to HFPEF. 5 patients (32%) were diagnosed during screening among 80 elderly patients (age > 70 years; 38 males, 42 females) indicated to 99mTcDPD bone scintigraphy due to oncologic diseases (most commonly prostatic and breast cancer). One asymptomatic patient (6%) was diagnosed accidently at echocardiography. 8 patients (50%) had a history of decompensated heart failure, mean NYHA class was 2.2 ± 0.5, median B-type natriuretic peptide BNP 283 ng/l (160-473). Persistent or permanent atrial fibrillation was present in 5 patients (31%), 6 of 11 patients (54%) with sinus rhythm had first-degree atrioventricular block, low QRS voltage was present just in one case. Echocardiography revealed median left ventricular (LV) end-diastolic dimension of 49 mm (45-51), median thickness of interventricular septum of 14 mm (13-16) and median E/Em 13 (8-17). LV ejection fraction was preserved (≥50%) in 13 cases (82%), moderately reduced (40-49%) in 2 cases (12%) and severely depressed (LVEF 35%) in one case (6%).
Conclusion: Diagnosis of TTR-CMP should be considered in elderly patients with echocardiographic signs of myocardial storage disease. Importantly, TTR-CMP can be discovered in almost 6 % of elderly individuals who undergo bone scintigraphy from oncologic reasons.

P1779

EMB-based diagnosis in a large cohort of 2822 consecutive patients with unexplained heart failure : data analysis from 2014-2016

F Felicitas Escher[1]; U Kuhl[1]; U Gross[2]; D Lassner[2]; H-P Schultheiss[2]
[1]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; *[2]Institute of Cardiac Diagnostics and Therapy (IKDT), Berlin, Germany*

Background: The diagnosis of unexplained heart failure is challenging. The current expert consensus statement of the European Society of Cardiology (ESC) maintains that endomyocardial biopsies (EMBs) remain the gold standard for definitive diagnosis of unexplained heart muscle diseases. However, EMB is used infrequently, although histology, immunohistochemical, and molecularbiological analysis of EMB is a prerequisite to make an etiology-driven diagnosis with the aim to identify those patients in whom specific therapy would be appropriate.
Methods and Results: We enrolled n=2822 consecutive patients with unexplained heart failure (2034 men/ 788 women, mean age 51.44 ± 16.04 years) from January 2014 to August 2016, who underwent EMB. The suspected diagnosis had been made by clinicians. EMBs were send to a FDA-proved laboratory (Institute for Cardiac Diagnostic and Therapy Berlin, Germany). Analysis included histology, immunohistochemistry, molecular virology, and gene profiling.
In n=810 patients the suspected diagnosis was acute myocarditis, in 1772 patients myocarditis or inflammatory/dilated cardiomyopathy was suspected. In n=240 patients a storage disorder was suspected.
Based on EMB-results in 58.9% (n = 1664 patients) a specific heart muscle disease could be diagnosed.
In particular, Coxsackie-Adenovirus genomes were present in n=44, Ebstein-Barr-Virus in n=77, Human-herpesvirus 6 (HHV6) in n=426 (including 21 patients with chromosomal integrated (ci) HHV6), and erythrovirus with active viral replication (positive mRNA) in n=649 patients.
Virus-negative intramyocardial inflammation was present in n=810 patients, including a histologically-proven active myocarditis in n=64. Histological proof of giant cells was present in n=20 patients. However, in n=133 patients idiopathic giant cell myocarditis or eosinophilic myocarditis was diagnosed by analysis of myocardial gene expression profile. 116 patients showed evidence of cardiac storage disease.
Conclusions: Based on EMB-results in 58.9% of this large cohort of patients a specific heart muscle disease could be diagnosed. These aetiology-driven diagnoses implicate a specific, causal therapy.
Our data clearly show the necessity of an EMB-based diagnosis, which has a direct clinical consequence regarding a specific therapy in a notable high percentage of patients with unexplained heart failure.

P1780

Evaluation of Th1, Th2, Th17 and Treg cytokines profile in patients with chronic chagas heart disease and systemic arterial hypertension: further studies.

R Bestetti[1]; R Dellalibera-Joviliano[1]; G Lopes[1]; R Furlan-Daniel[1]; K Lopes[2]
[1]University of Ribeirao Preto, Ribeirao Preto, Brazil; *[2]Clinica Sao Rafael, Piumhi, Brazil*

Background: In patients with chronic Chagas cardiomyopathy (CCM), increased plasma cytokines levels have been observed. However, a panel of Th1, Th2, Th17 and Treg cytokines, which encompasses several pro-inflammatory, anti-inflammatory, and regulatory cytokines, has not been determined in patients with this condition. In areas where Chagas disease is endemic, systemic arterial hypertension (SAH) affects 25% of patients with this condition. We have previously observed that a Th1, Th2, and Th17 cytokine panel has been shown to be increased in patients with chronic Chagas disease and SAH. However, this cytokine panel has not yet been determined in patients with CCM and SAH (CCM-SAH).
Purpose: Accordingly, the aim of this study was to evaluate the Th1 (INF-gama, IL-2, IL-12), Th2 (IL-4, IL-10, IL-13, IL-5), Th17 (IL-17, IL-23, IL-6) and Treg (IL-2, TGF-β) cytokines profile in patients with CCM-SAH.

P1781 Cardiomyopathy associated with Shabu

Patient	Shabu consumption pattern	Presentation	Echocardiography	Cardiac Magnetic Resonance	Coronary arteries	
1	41 yearsPhilippineMale	- Chronic.- No consumption last 2 months.	- Acute pulmonary edema.	- LVEF 18%.- Severely dilated left ventricle(LVIDd 74mm).- No improvement in LVEF at 1-year	- Non-ischemic biventricular dilated cardiomyopathy with severe systolic dysfunction.- No LGE.	- CT angiography with no significant coronary lesions.
2	38 yearsPhilippineMale	- Chronic.- Active consumption < 12 hours.	- Heart failure.- Hypertensive crisis.	- LVEF 25%.- Concentric left ventricular hypertrophy (septum 18mm).- Mild ventricular dilatation (LVIDd 60mm).	- Non-ischemic cardiomyopathy with severe systolic dysfunction. Severe left ventricular hypertrophy.- Multiple foci of LGE.	- Coronary angiography with no significant coronary lesions.
3	52 yearsMale	- Chronic.- Active consumption < 12 hours.- Cocaine use.	- Chest pain.- Acute pulmonary edema.	- LVEF 25%.- Concentric left ventricular hypertrophy (septum 15mm).- Mild ventricular dilatation (LVIDd 60mm).	- Non-ischemic cardiomyopathy with severe systolic dysfunction. Moderate concentric hypertrophy.- Foci of LGE in the interventricular union.	- Coronary angiography without lesions.
4	54 yearsPhilippineMale	- Chronic.	- Heart failure.	- LVEF 10-15%.-Severely dilated left ventricle(LVIDd 67 mm).	-Nonischemic biventricular dilated cardiomyopathy with severe systolic dysfunction.- Severe ventricular dilation.- Multiple foci of LGE. Foci of LGE in the interventricular union.	- Coronary angiography without lesions.
5	24 yearsFemale	- Acute consumption < 12 hours.	- Cardiogenic shock.	- LVEF 25%.- Moderate ventricular dilatation (LVIDd 58mm).- LVEF 50% within 30-day.	- Non-ischemic cardiomyopathy.- No LGE.	

CT: Computed tomography; LGE: Late gadolinium enhancement; LVEF: Left ventricular ejection fraction; LVIDd: Left ventricular internal dimension at end-diastole.

Methods: This study focus on 16 patients with CCM, 20 patients with CCM-SAH, and 28 controls. The diagnosis of CCM was based on a positive serology for Chagas disease plus abnormal resting ECG or decreased left ventricular ejection fraction on echocardiogram. The diagnosis of CCM-SAH was done when patients with CCM had a SAH > 140 x 90 mmHg. Quantitative measurements of cytokines were performed on plasma samples using the double-ligand/sandwich enzyme-linked immunosorbent assay (ELISA). The cytokine concentration was expressed in pg/ml by the kit's standard curve.

Results: TNF-alpha levels were 259 ± 1,32 in controls, 412 ± 2,3 in patients with CCM, and 495 ± 3,2 in patients with CCM-SAH ($P < 0.05$). INF-gamma levels were 58 ± 1,57 in controls, 102 in patients with CCM, and 124 ± 2,6 in patients CCM-SAH ($p < 0.05$). IL-1 beta levels were 52 ± 1,33 in controls, 137 ± 3,12 in CCM, and 200 ± 1,56 in patients with CCM-SAH patients ($p < 0.05$). IL-2 levels were 22 ± 1,25 in controls, 45 ± 1,8 in patients with CCM, and 84 ± 2,8 in those with CCM-SAH ($p < 0.05$). IL-6 levels were 77 ± 1,45 in controls, 141 ± 1,8 in patients with CCM, and 195 ± 2,1 in those with CCM-SAH. IL-10 levels were 156 ± 2,8 in controls, 212 ± 2,1 in patients with CCM, and 255 ± in those with CCM-SAH ($p < 0.05$). IL-12 levels were 65 ± 2,1 in controls, 221 ± 2,1 in patients with CCM, and 279 ± 3,2 in those with CCM-SAH ($p < 0.05$). IL-13 levels were 56 ± 1,9 in controls, 84 ± 2,1 in patients with CCM, and 95 ± 2,2 in patients with CCM-SAH ($p < 0.05$). TGF-beta levels were 35 ± 2,2 in controls, 60 ± 2,5 in patients with CCM, and 77 ± 2,3 patients with CCM-SAH ($p < 0.05$). IL-17 were 74 ± 2,5 in controls, 133 ± 2,8 in patients with CCM, and 189 ± 2,7 in those with CCM-SAH ($p < 0.05$). IL-23 levels were 50 ± 2,0 in controls, 144 ± 3,0 in patients with CCM, and 183 ± 3,4 in those with CCM-SAH ($p < 0.05$).

Conclusion: Patients with CCM-SAH have increased plasma levels of pro-inflammatory, anti-inflammatory, and regulatory cytokines in comparison with CCM patients, suggesting a higher level of immunomodulation in patients with CCM-SAH.

P1781

Cardiomyopathy associated with shabu consumption

M Pujol Lopez[1]; L Ortega Paz[1]; EJ Flores Umanzor[1]; M Roque[1]; S Prat Gonzalez[1]; RJ Perea[2]; A Garcia Alvarez[1]; X Bosch[1]

[1]Hospital Clinic de Barcelona, Cardiology Department, Barcelona, Spain; [2]Hospital Clinic de Barcelona, Radiology Department, Barcelona, Spain

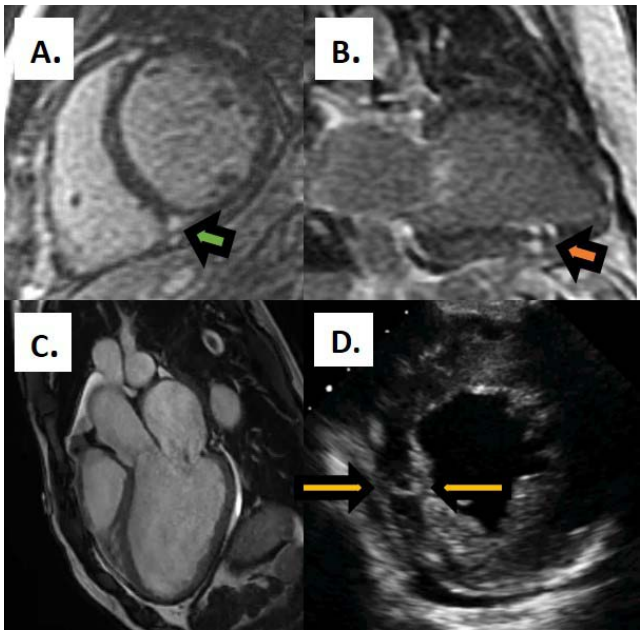
- Shabu is the Philippine name of a high purity methamphetamine also called cristal or ice. Shabu is an emerging drug in Europe with increasing consumption notifications in recent years, especially within Southeast Asian communities (mainly Philippines).

Purpose: To identify the form of presentation and types of cardiopathy associated with the consumption of Shabu in our environment.

Methods: We conducted a prospective inclusion of Shabu consumers who were admitted for heart failure in our hospital during the period from January 2015 to September 2016. We identified five cases of Shabu users with a first episode of heart failure. For diagnosis, an initial urinalysis was performed by immunoassay and confirmed with gas chromatography-mass spectrometry.

Results: The median age of the patients was 42 + 11 years. All patients presented as severe acute heart failure (acute pulmonary edema, cardiogenic shock, or heart failure (NYHA functional class IV)) due to left ventricular dysfunction (mean left ventricular ejection fraction (LVEF) 21 + 5%). Mean left ventricular end-diastolic diameter was 64 + 6 mm. Coronary angiography or computed tomography angiogram excluded obstructive coronary artery disease. Cardiac magnetic resonance imaging identified a non-ischemic cardiomyopathy in all of them with two patterns of late gadolinium enhancement (LGE): foci in the interventricular junction (Fig 1A) or multiple foci of LGE (Fig 1B). All patients presented elevated necrosis biomarkers and QTc interval prolongation (mean QTc 477 + 25 ms). Three types of cardiomyopathy were identified: two patients with dilated (Fig 1C) and two cases with hypertrophic cardiomyopathy (Fig 1D) in chronic consumption and one stress cardiomyopathy in acute consumption.

Conclusions: Shabu related cardiomyopathy presented as severe acute heart failure. All patients presented severe left ventricular dysfunction and QT prolongation. The detection of these five cases of Shabu related cardiomyopathy represents an alert. It should motivate a rapid diagnosis and management of these patients and further, studies on the cardiovascular risk of this drug.



Shabu related cardiomyopathy

P1782

Incidence and predictors of heart failure after acute myocardial infarction in patients without systolic dysfunction and/or history of heart failure

RJ Cobas[1]; B Caneiro[1]; S Raposeiras[1]; E Abu[1]; S Manzano[2]; FE Calvo[1]; M Valdes[2]; A Iniguez[1]

[1]Hospital Álvaro Cunqueiro , Cardiology , Vigo, Spain; [2]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain

Introduction: Heart failure (HF) after myocardial infarction (MI) is common and has been associated with excess mortality. The aim of this study was to provide an evaluation of the factors that predict the development of "the novo" HF in patients after MI with pLVEF.

Methods: A total of 3507 consecutive patients discharged from hospital after AMI between January 2011 and December 2015 in two tertiary hospitals were included. We excluded patients with LVEF < 50%, Killip Class ≥ II and patients with prior or "de novo" HF (n = 1283). The final cohort was made up 2,158 patients. Using a competing risk framework for HF occurrence, accounting for death as a competing episode, predictors of follow-up HF development were assessed by Fine-Gray porportional hazards regression analysis. For the multivariate analysis, we used covariates with $p < 0.05$ in the univariate analysis. The adjusted hazard of HF was expressed as subhazard ratios (sHR) with corresponding 95% confidence intervals (95%CI).

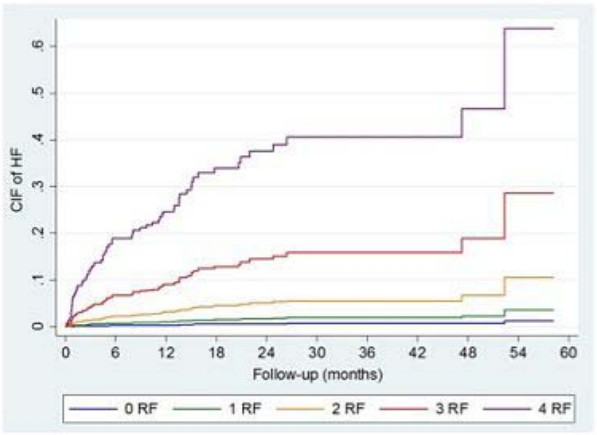
Results: During a follow-up of 20.1 ± 11.8 months, 59 (2.8%) patients developed "de novo" HF. Table 1 shows the uni and multivariate Fine-Gray analysis. Age (as continuous variable, being 70 years the best cut-off to predict HF), hypertension, renal disfunction, and atrial fibrillation were independent predictors for HF development. Basing on the presence or absence of these 4 risk factors, we can stratify the risk of "de novo" HF after MI (Figure 1).

Conclusions: In a contemporary cohort of patients surviving an AMI, the incidence of HF is about 3%, and its occurrence can be easily predicted by 4 previous risk factors.

Table 1. Uni and Multivariate Analysis

Variables	UniV sHR	UniV CI 95%	UniV P value	MultiV sHR	MultiV CI 95%	MultiV P value
Age per 1 year increase	1.08	1.05-1.10	< 0.001	1.04	1.01-1.07	0.07
Female sex, %	2.83	1.69-4.72	< 0.001	1.18	0.59-2.37	0.633
Hypertension, %	4.32	2.05-9.11	< 0.001	3.09	1.05-9.06	0.040
Diabetes Mellitus, %	2.40	1.44-4.00	0.001	1.38	0.75-2.54	0.293
ST-elevation myocardial infarction, %	0.42	0.23-0.77	0.005	0.96	0.50-1.85	0.909
Haemoglobin at admission, g/dL	0.69	0.61-0.78	< 0.001	0.89	0.72-1.10	0.270
CKD EPI-eGFR at admission < 60ml/min/1.73m2	5.12	2.86-9.20	< 0.001	2.30	1.05-5.04	0.037
Atrial fibrillation, %	8.87	5.28-14.90	< 0.001	3.34	1.67-6.66	0.01
Multivessel coronary artery disease, %	2.06	1.03-2.88	0.040	1.33	0.73-2.42	0.356
Complete revascularization, %	0.51	0.29-0.91	0.021	1.01	0.56-1.80	0.984
Statin, %	0.37	0.16-0.85	0.019	0.39	0.13-1.19	0.098

UniV (Univariate Analysis) MultiV (Multivariate Analysis)



Risk stratification based on MV predicto

P1783

Influence of inflammation on the pathogenesis of cardiac ATTR and AL amyloidosis

K Klingel[1]; A Hehn[1]; M Sauter[1]

[1]Department of Molecular Pathology, Tuebingen, Germany

Background: Amyloidosis describes a group of disorders caused by the extracellular deposition of misfolded proteins, which can severely impair the function of the heart. The correct diagnosis of amyloidosis by immunohistological subtyping in endomyocardial biopsies is decisive as it determines the outcome of the disease and the therapy of the patients.

Purpose: In this study we aimed to identify parameters of pathogenicity in cardiac amyloidosis.

Methods and Results: We investigated 5 unselected patients (43 male, 7 female) with Congo red positive endomyocardial biopsies (EMB) by immunohistochemistry in order to classify the forms of cardiac amyloidosis. In 26 patients (52%) we found an ATTR amyloidosis and in 48% an AL amyloidosis with 17 cases of AL-lambda and 7 cases with AL-kappa. Patients with ATTR amyloidosis had a mean age of 78 years and a mean LVEF of 45%, those with AL amyloidosis had 67 years and a LVEF of 47%. As a part of our routine diagnostic program, we also performed immunohistochemical stainings to identify and quantify inflammatory cells in EMB. Astonishingly,

we found in 21/50 (42 %) patients with amyloidoisis a significant cardiac inflammation. In 7/26 (27%) of ATTR amyloidosis and in 12/17 (70%) of AL-lambda and 2/7 (28%) of AL-kappa amyloidosis we found enhanced levels of CD3+ T cells, CD68+ macrophages and MHCII expression. We have shown that lymphoycytic myocarditis is associated with an upregulation of the cytokines IL-1 and IL-6. As a consequence of IL-1 and IL-6 expression, signaling pathways are induced with enhanced ERK1/2 expression being most prominent in EMB of patients with AL-lambda amyloidosis. ERK 1/2 expression is known to be involved in the molecular switch of necrosis to apoptosis. A significant number of apoptotic cardiomyocytes was identified in ATTR as well as in AL amyloidosis by TUNEL assay as well as by electron microscopy. Virus infections were not prominent in amyloidosis patients. Only 1 patient with ATTR amyloidosis and inflammation and 3 patients with AL amyloidosis and inflammation were positive for viral DNA (PVB19 and HHV6) as determined by PCR.
Conclusions: Our results indicate that inflammation in hearts of patients with ATTR and AL amyloidosis is associated with expression of ERK1/2, finally contributing to the emergence of apoptotic myocytes and myocardial damage.

P1784
NEOD001 demonstrates organ biomarker responses in patients with light chain amyloidosis and persistent organ dysfunction independently of previous haematological response

M Michaela Liedtke[1]; RL Comenzo[2]; H Landau[3]; V Sanchorawala[4]; BM Weiss[5]; JA Zonder[6]; J Walling[7]; GG Kinney[8]; M Koller[8]; DB Schenk[8]; SD Guthrie[8]; E Liu[8]; MA Gertz[9]
[1]Stanford University School of Medicine, Stanford, United States of America; *[2]Tufts Medical Center, Boston, United States of America*; *[3]Memorial Sloan Kettering Cancer Center, New York, United States of America*; *[4]Boston University, Boston, United States of America*; *[5]University of Pennsylvania, Philadelphia, United States of America*; *[6]Karmanos Cancer Institute, Detroit, United States of America*; *[7]JW Consulting, Hillsborough, United States of America*; *[8]Prothena Biosciences Inc, South San Francisco, United States of America*; *[9]Mayo Clinic, Rochester, United States of America*

Introduction: Light chain (AL) amyloidosis is a rare and often fatal disease caused by the accumulation of misfolded light chain aggregates (LCs), produced by clonal plasma cells. Current therapies limit LC production; however, ~75% of patients have persistent organ dysfunction. NEOD001 is a novel investigational antibody that targets misfolded LC and is thought to neutralise circulating LC aggregates and clear insoluble deposits. Here we assessed safety and tolerability and analysed organ responses based on consensus criteria and association between organ responses and previous plasma cell–directed (PCD) treatment.
Methods: Inclusion criteria were that patients complete ≥1 PCD treatment before enrolment, attain partial haematological response (HR) or better to any previous therapy and have persistent organ dysfunction. NEOD001 was administered intravenously every 28 days. During the dose-escalation phase, 27 patients received NEOD001 at 0.5, 1, 2, 4, 8, 16 or 24 mg/kg in a 3+3 study design. An additional 42 patients with renal, cardiac or nerve involvement were enrolled and treated (24 mg/kg) in the expansion phase.
Results: In the overall population (N=69) the median age was 61 years (61% male). Median (range) time since diagnosis was 2.9 (0.4-16.0) years, and 45% of patients underwent ≥3 previous PCD regimens. Median time since last PCD treatment to the start of NEOD001 intervention was 5.8 (range, 0.6-85.8) months. Infusions were administered over a mean of 12.8 (range, 2-35) months. NEOD001 treatment was not associated with dose-limiting toxicities, discontinuations, antidrug antibody development or treatment-related serious adverse events. The most frequent TEAEs were fatigue, nausea, upper respiratory tract infection and peripheral oedema. Best response rate indicating organ response was observed in 53% of cardiac-evaluable patients (n=19/36) and 64% of renal-evaluable patients (n=23/36). Time from patients' best HR to previous PCD treatment did not impact the NEOD001 organ response rate (cardiac/renal: 35.6/30.6 [responders] vs 36.6/32.5 [stable] months; P>0.05). Depth of patients' best HR also did not impact the NEOD001 organ response (cardiac/renal: 47.1/68.8% [CR], 66.7/63.6% [VGPR], 42.9/62.5% [PR]; P>0.05). Similarly, time or depth of patients' last HR did not impact the NEOD001 organ response rate (P>0.05). Patients with NEOD001 organ responses were no more likely to have had their last PCD therapy <6 vs ≥6 months from their first NEOD001 dose. Patients' previous treatment type had no impact on the NEOD001 organ response rate (cardiac/renal: 55.6/61.1% [stem cell transplantation], 52.0/68.8% [bortezomib-based therapy], 50.0/57.1% [other chemotherapy]; P>0.05).
Conclusions: These results demonstrate that NEOD001 infusions were safe, well tolerated and associated with organ responses independently of time since previous chemotherapy, depth of haematological response or predominant type of PCD treatment.

P1785
Assessment of left ventricular function in asymptomatic systemic lupus erythematosus ab patients(about 70 cases)

MERIEM Drissa[1]; SANA Helali[1]; SAMIRA Kaabachi[1]; MEHDI Cheour[1]; HABIBA Drissa[1]
[1]La Rabta University Hospital, adults cardiology, Tunis, Tunisia

Introduction and Purpose: Cardiac disease is common among patients with systemic lupus erythematosus (SLE)..The aim of this study is to assess the systolic and diastolic function of the left ventricular (LV) in asymptomatic systemic lupus erythematosus (SLE) patients.
Methods: We included 35 patients without symptoms or signs of heart failure or angina (groupe I) and 35 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),and speckel traking stain rate
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 lupus patients (6.2±0.7cm/vs 9±0.9cm/s,p<0.01) reflecting subclinical LV systolic dysfunction. we notated also a lower speckle tracking derived myocardial deformation (strain and strain rate) in lupus patients (-10% vs-17%) reflecting a systolic dysfunction of left ventricular . 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 patients suffering fromlupus (6± 1.4cm/s vs. 11.5±1.3 cm/s, p<0.01) WITH function. diastolic impaired suggesting p<o,o1). 8±1.7; ±1.8vs (14.1 velocities Ea E of ratio higher
Conclusion: This study shows the presence of systolic and diastolic dysfunction in asymptomatic systemic lupus erythematosus (SLE) patients. Evaluation of left ventricular function by tissue Doppler imaging ,stain rate is useful to detect infraclincal left ventricular dyfunction during systemic lupus.

P1786
Predictors of in-hospital outcome in takotsubo cardiomyopathy, a multicenter study

A L Ana Calvo[1]; O Azevedo[1]; RP Santos[2]; AR Almeida[3]; N Craveiro[4]; B Picarra[5]; R Lima[6]; L Reis[7]; B Marmelo[8]; A Marreiros[9]; N Marques[9]
[1]Alto Ave Hospital Center, Cardiology, Guimaraes, Portugal; *[2]Hospital Centre do Tamega e Sousa, cardiology, Penafiel, Portugal*; *[3]Hospital Garcia de Orta, Almada, Portugal*; *[4]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[5]Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*; *[6]Centro Hospitalar do Alto Minho, Cardiology, Viana do Castelo, Portugal*; *[7]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; *[8]Hospital Sao Teotonio, Cardiology, Viseu, Portugal*; *[9]U.Algarve, Algarve Biomedical Center DCBM , Algarve, Portugal*

Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction in the absence of significant coronary artery disease. The predictors of prognosis of TC are not yet fully established.
Purpose: To identify predictors of outcome in patients (P) diagnosed with TC.
Methods: Multicenter study involving 13 hospital centers that included all patients diagnosed with TC in the last 12 years. We assessed demographic data, precipitating factors and clinical presentation, trying to establish the predictors of after discharge outcomes. We define the occurrence of in-hospital outcome of TC patients as a variable that combine the occurrence of death, stroke/TIA, heart failure, atrial fibrillation, LV thrombus.
Results: We included 234 P diagnosed with TC, predominantly female (89.7%). During hospitalization occurred complications: heart failure (24.4%), atrial fibrillation (9.0%), complete atrioventricular block (2.1%), stroke / TIA (1.7%), LV thrombus (1.3%) and death (2.2%). The combine in-hospital outcome is 32.9%.
We found a significant association of the following variables with the combine in-hospital outcome: (i) history of heart failure (7.8% vs 0.0%, p<0.001); (ii) chronic kidney disease (14.3% vs 2.5%, p=0.001); (iii) precipitant physical stress factor (26.0% vs 14.6%, p=0.036); (iv) presentation with dyspnea (41.6% vs 12.1%, p<0.001); (v) higher Killip Kimball (KK) class at admission (p<0.001); (vi) bifascicular bundle block in EKG (2.6% vs 0.0%, p=0.043); (vii) significant valvopathy (18.2% vs 7.0%, p=0.009); (vii) LV dysfunction (p<0.001).
In the multivariate analysis by CHAID method, the following variables were identified as independent predictors of in-hospital complications: (i) higher KK class in admission (p<0.001); (ii) LV dysfunction (p<0.001).
Conclusion: TC has a high rate of complications in the acute phase. Higher KK class at admission and LV dysfunction were the only independent predictors of in-hospital outcome identified in our study.

P1787

Prognostic impact of QRS duration in patients with Takotsubo cardiomyopathy

H Hugo Antunes[1]; D Bento[2]; M Oliveira[3]; C Ruivo[4]; R Santos[5]; A Gomes[6]; MJ Vieira[7]; L Reis[8]; R Lima[9]; A Marreiros[2]; AR Almeida[6]
[1]Hospital Sao Teotonio, Cardiology, Viseu, Portugal; [2]Faro Hospital, Faro, Portugal; [3]Alto Ave Hospital Center, Guimaraes, Portugal; [4]Hospital Santo Andre, Leiria, Portugal; [5]Hospital Centre do Tamega e Sousa, Penafiel, Portugal; [6]Hospital Garcia de Orta, Almada, Portugal; [7]Hospital of Santarem, Santarem, Portugal; [8]University Hospitals of Coimbra, Coimbra, Portugal; [9]Centro Hospitalar do Alto Minho, Viana do Castelo, Portugal

On behalf of: SUNSHINE

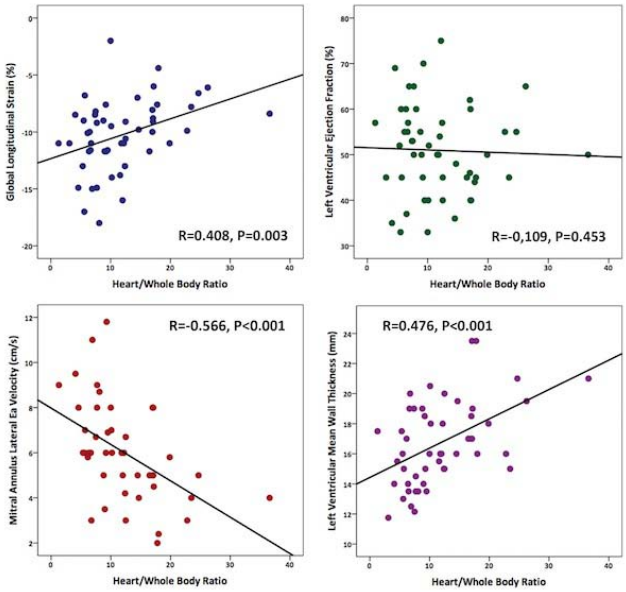
Introduction: Takotsubo cardiomyopathy (TK) is characterized by transient left ventricular dysfunction that may lead to the development of heart failure (HF). The prolongation of the QRS interval on the electrocardiogram (ECG) is a predictor of adverse outcome in patients (P) with HF and acute myocardial infarction. It has not been established whether the same is true for P with TK.
Objective: To evaluate the impact of QRS duration on the outcome of P with TK.
Methods: A multicenter Portuguese study involving 12 hospital centers. Included P hospitalized with diagnosis of TK since 2004. We divided the P in two groups, according to the QRS duration: normal if QRS≤120ms (nQRS) and prolonged if QRS> 120ms (pQRS). Demographic, clinical, electrocardiographic and echocardiographic parameters were evaluated, as well as complications during hospitalization.
Results: We included 234 patients with TK: 89.7% female and mean age 71.6 ± 11.9 years. The nQRS group represents 91% of the sample.
There were no differences between groups regarding the gender, cardiovascular risk factors, history of coronary disease, heart failure, chronic kidney disease or anemia. Upon admission, there was a trend for pQRS to present more frequently with syncope (14.3% vs 4.7%, p = 0.067). In the ECG, the pQRS group included a greater number of P in atrial fibrillation than the nQRS group (43.6% vs. 3.6%, p < 0.001). There were no differences between the groups regarding the presence of ST elevation in the initial ECG. There were no differences in BNP or troponin values at admission or hospitalization.
There were no differences in ejection fraction (EF) at admission or discharge (left ventricular systolic dysfunction in the pQRS group 52.6% vs nQRS 32.6%, p = 0.08).
About the hospitalization complications, there were no differences regarding the evolution to cardiogenic shock. The pQRS group presented more frequently dysrhythmic complications, namely ventricular tachycardia / fibrillation (VT / VF) (9.5% vs 1.9%, p = 0.034), with odds ratio of 5.54.
Conclusion: In this study, the P admitted with TK and pQRS evolved with a higher number of dysrhythmic complications, namely VT / VF risk when compared to P with nQRS. Thus, the pQRS at admission has an impact on the clinical evolution of the P, which implies a need to a closer surveillance during hospitalization.

P1788

Impact of cardiac 99mTc-HMDP uptake on left ventricular function and filling pressure in patients with transthyretin amyloidosis

O Lairez[1]; S Pradel[1]; S Brun[1]; P Pascal[2]; P Fournier[1]; I Berry[2]; J Roncalli[1]; D Carrie[1]; M Galinier[1]
[1]University Hospital of Toulouse - Rangueil Hospital, Department of Cardiology, Toulouse, France; [2]Toulouse Rangueil University Hospital (CHU), Nuclear Medicine, Toulouse, France

Background: Pathophysiology of 99mTc-labeled phosphate agents cardiac uptake by scintigraphy in transthyretin-related (TTR) amyloidosis remains unclear. The aim of this study was to explore the impact of 99mTc-labeled phosphate agents cardiac uptake on left ventricular (LV) functions assessed by echocardiography.
Methods: Fifty patients with TTR cardiac amyloidosis underwent 99mTc-hydroxymethylene-diphosphonate (99mTc-HMDP) scintigraphy and echocardiography with measure of LV morphology, longitudinal strain (LS), systolic and diastolic functions. Cardiac retention by scintigraphy was assessed by visual scoring and the heart/whole body (H/WB) ratio was calculated by dividing counts in the heart by counts in late whole body images.
Results: Mean H/WB ratio was 12 ± 7. Mean LV ejection fraction and global LS were 51 ± 10% and -10 ± 3%, respectively. H/WB ratio was correlated with global LS (R=0.408, P=0.003), Ea (R=-0.566, P < 0.001) and mean left ventricular wall thickness (R=0.476, P < 0.001) but not with LV ejection fraction (R=-0,109, P=0.453, Figure). Segmental myocardial uptake normalized by H/WB ratio was correlated with segmental LS (n = 850 segments, R = 0.162, P < 0.001). H/WB ratio was not correlated with NT-proBNP levels (R=0.219, P=0.148) neither E/Ea ratio (R=0.204, P=0.184).
Conclusion: In patients with TTR cardiac amyloidosis, myocardial uptake by 99mTc-HMDP scintigraphy is correlated with decrease of myocardial LS.



Figure

P1789

Apical sparing pattern of left ventricular myocardial 99mTc-HMDP uptake in patients with transthyretin-related cardiac amyloidosis

A Guellich[1]; A Van Der Gucht[1]; A Galat[1]; A Mukedesi[1]; V Plante-Bordeneuve[1]; E Itti[1]; T Thibaud Damy[2]
[1]GRC-Amyloid Research Institute - APHP - INSERM, Créteil, France; [2]AP-HP - University Hospital Henri Mondor, Creteil, France

On behalf of: GRC Amyloid Research Insitute
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Objective: A decreased longitudinal strain in basal segments with a base-to-apex gradient has been described in patients with cardiac amyloidosis (CA). Aim of the study was to investigate the left ventricular (LV) regional distribution of early-phase 99mTc-Hydroxymethylene diphosphonate (HMDP) uptake in patients with transthyretin-related cardiac amyloidosis (TTR-CA).
Methods: All patients underwent a whole-body planar 99mTc-HMDP scintigraphy acquired at 10 min post-injection (early-phase) followed by a thorax SPECT/CT. The relative segmental uptake % was investigated on AHA 17-segment model and 3-segment model (basal, mid-cavity, apical).
Results: Sixty-one TTR-CA patients were included of whom; 29 were wild-type (wt-TTR-CA) and 32 had hereditary TTR-CA (m-TTR-CA). Early myocardial 99mTc-HMDP uptake occurred in all TTR-CA. In all patients, segmental analysis of the LV myocardial distribution of 99mTc-HMDP uptake showed an increased median uptake (interquartile range) in basal/mid-cavity segments compared to the lowest median uptake of apical segments (respectively 79 [72-86] vs. 72 [64-81]; P < 10-6). This pattern was similar in wt-TTR-CA group (78 [70-84] vs. 70 [61-81]; P < 10-6), in m-TTR-CA group (80 [74-86] vs. 73 [66-82]; P < 10-7) and remains constant independently of the TTR mutation's subtype with P ranging 10-5 to 0.03.
Conclusions: Early-phase myocardial scintigraphy identified regional distribution of 99mTc-HMDP uptake characterized by a base-to-apex gradient, corroborating echocardiographic and cardiac magnetic resonance findings. This relative "apical sparing" pattern was similar across TTR-CA and TTR mutations' subtypes.

P1790

Ability of 99mTc-DPD scintigraphy to predict conduction disorders requiring permanent pacemaker in patients with transthyretin-related cardiac amyloidosis

S Stephanie Brun[1]; S Pradel[1]; D Carrie[1]; M Galinier[1]; P Maury[1]; P Pascal[1]; G Victor[1]; I Berry[1]; P Mondoly[1]; D Ribes[1]; A Duparc[1]; O Lairez[1]
[1]Toulouse Rangueil University Hospital (CHU), 31, Toulouse, France

Background: Transthyretin-related (TTR) amyloidosis is the second most common cardiac amyloidosis. TTR cardiac amyloidosis is a clinical disorder that arises from the cardiac aggregation of insoluble fibrous deposits of misfolded proteins leading

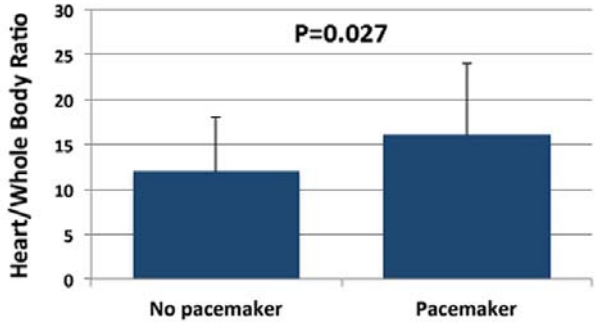
to a high rate of conduction disorders and increased risk of sudden death. TTR cardiac amyloidosis is being increasingly recognized because of the emergence of 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) scintigraphy. 99mTc-DPD scintigraphy has been shown to have excellent results in the diagnosis of TTR cardiac amyloidosis but is value to predict conduction disorders was never described.

Purpose: To evaluate the value of 99mTc-DPD scintigraphy to predict conduction disorders in patients with TTR cardiac amyloidosis.

Method – Fifty patients with positive 99mTc-DPD scintigraphy for TTR cardiac amyloidosis were retrospectively included. Cardiac retention was assessed by visual scoring and the heart/whole body (H/B) ratio was calculated by dividing counts in the heart by counts in late whole body images. Electrocardiograms were reviewed for main conduction system disorders requiring permanent pacemaker.

Results: – Mean age was 80 ± 10 year-old. Nineteen (38%) patients had a pacemaker. There was no difference between patients with or without pacemaker for age (79 ± 9 vs. 80 ± 10 year-old, respectively, P=0.417) or visual score (2.9 ± 0.3 vs. 2.8 ± 0.4, respectively, P=0.589). Patients with pacemaker had a higher H/B ratio than patients without pacemaker (16 ± 8 vs. 12 ± 6, respectively, P=0.027). The area under the ROC curve of H/B ratio to predict presence of pacemaker was 0.688 with a best cut-off value of 12 allowing a sensitivity and a specificity of 79% and 61%, respectively.

Conclusion: – Tracer uptake by 99mTc-DPD scintigraphy assessed by H/R ratio could be a sensitive tool in patients with TTR cardiac amyloidosis to predict conduction disorders requiring permanent pacemaker.



P1791

The role of baseline LVEF towards the recovery of left ventricular function and improvement of left ventricular remodelling in peripartum cardiomyopathy patients: starting position matters

H S Hawani Sasmaya Prameswari[1]; TID Dewi[1]; EM Martanto[1]; AP Purnomowati[1]
[1]*Padjadjaran University, Cardiology, Bandung, Indonesia*

Background: Peripartum Cardiomyopathy (PPCM) has been known to have a unique outcome as compared to other forms of cardiomyopathy. Previous studies have stated that, to a certain extent, there is recovery of left ventricular function observed in PPCM patients. It was postulated that baseline Left Ventricular Ejection Fraction (LVEF) plays a pivotal role in recovery of left ventricular function. To date, the definite role of baseline LVEF in left ventricular function recovery is still shrouded in controversy, whereas its role in improvement of left ventricular remodelling remains to be revealed.

Purpose: This study sought to prospectively evaluate the role of baseline LVEF in recovery of left ventricular function and improvement of left ventricular remodelling in PPCM patients.

Methods: This nested case-control study was part of PPCM prospective cohort registry at Hospital in Indonesia. We enrolled 42 PPCM patients from September 2013 through 6 months follow-up until September 2016. The LVEF and Left Ventricular End Diastolic Volume (LVEDv) index were measured using echocardiography with an application of Simpson's method. The role of baseline LVEF toward recovery of left ventricular function was analysed using multivariate logistic regression whereas its role towards improvement of left ventricular remodelling (delta LVEDV index) was analysed using multivariate linear regression analysis.

Results: Forty-two PPCM patients were enrolled in this study and divided into two groups, the recovery group (n = 21, mean age 31 ± 6 years old), and non-recovery group (n = 21, mean age 33 ± 5 years old). The mean baseline LVEF from the recovery group was 37.5 ± 3.78%, and non-recovery group was 28.2 ± 4.6%. There was a significant role of the baseline LVEF (OR 2.11, CI95%, 1.207-3.691;p 0.009) towards recovery of the left ventricular function after adjusting age, parity, and hypertension in pregnancy. Mean baseline LVEDv index from both groups was 96.6 ± 30.9 ml/m2, with no significant difference (p 0.064) between recovery group (88.1 ± 26.2 ml/m2) versus non-recovery group (105.7 ± 33.3 ml/m2). Mean LVEDv index at 6 months from both groups was 75.8 ± 34.9 with significant difference (< p 0.001) between recovery group (51.3 ± 11.2 ml/m2), and non-recovery group (100.3 ± 3.4 ml/m2), and mean ΔLVEDv index from both groups was 21.06 ± 28.17 ml/m2 with significant difference (p < 0.001) between recovery group (36.8 ± 10.6 ml/m2) and non-recovery group (5.4 ± 4.5 ml/m2). Multivariate linear regression analysis showed significant role of the baseline LVEF towards improvement of left ventricular remodelling (b 2.14; p 0.004) after adjusting age, parity, and hypertension in pregnancy.

Conclusion: Baseline LVEF plays a significant role in recovery of left ventricular function and improvement of left ventricular remodelling in PPCM patients.

P1792

Echographic factors of atrial arrhythmia in patients with arrythmogenic right ventricular dysplasia

R Rim Ben Said[1]; A Zaroui[2]; MF Drissi[3]; H Zargouni[3]; R Mechmeche[3]
[1]*La Rabta hospital, cardiology, Tunis, Tunisia*; [2]*Institut Pasteur, Tunis, Tunisia*; [3]*Clinique Pasteur, tunis, Tunisia*

Background: Consequences of of atrial fibrillation (AF) on patients with arrhythmogenic right ventricular dysplasia (ARVD) is not well studied and predictive factors of these arrhythmias are not well defined. We aims to study transthoracic echocardiography (TTE) to predict AF in these patients

Methods and Results: TTEs of 40 patients diagnosed with definite ARVD (2010 Task Force Criteria) we reanalyzed. Data were compared in patients with AF and all other patients. A total of 10 (40%) patients experienced AF during a median follow-up of 4.5years. Kaplan-Meier analysis revealed, in patients presenting AF, reduced RV fractional area <27% (P < 0.001), larger left atrial volume > 45ml (P=0.001) (apical 4-chamber view), and higher right atrial volume ≥22 ml (P= 0.05) (apical 4-chamber view). 3 patients with AF experienced inappropriate implantable cardioverter-defibrillator (ICD) shocks compared with 4 without AF (36% vs. 9%, P=0.03). AF was more prevalent in the patients who present severe events like heart failure, Ventricular arythmia and death (42% vs. 8%, P=0.02)

Conclusions: Atrial fibrillation in ARVD is associated with worst prognostic like heart failure and cardiac death. Evidence of reduced RV function and atrial dilation are a strong predictors of this complication

P1793

Incidence, characteristics, risk factors and outcomes of supraventricular arrhythmias in Takotsubo cardiomyopathy

O Olivier Auzel[1]; HM Mustafic[2]; RH El Mahmoud[1]; RP Pilliere[1]; OD Dubourg[1]; NM Mansencal[1]
[1]*University Hospital Ambroise Pare, cardiology department, Boulogne-Billancourt, France*; [2]*Geneva University Hospitals, Cardiology, Geneva, Switzerland*

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Background: Takotsubo cardiomyopathy (TTC) is a medical entity mimicking an acute coronary syndrome (ACS). During the acute phase, several complications may occur, even if the prognosis is generally favorable. Only small studies reported a description of supraventricular arrhythmia (SA) in TTC, and little is known about related incidence. We sought to describe the characteristics, incidence, predictive factors and outcomes of SA in patients presenting with TTC.

Methods: Over a twelve-year period, we reviewed all patients (n = 5484) referred to our coronary care unit (CCU) for a suspicion of ACS. All patients presented with a confirmed diagnosis of TTC and a normalization of left ventricular ejection fraction (LEVF) during follow-up. In CCU, all patients were continually monitored by 12-lead ECG to detect the occurrence of SA

Results: TTC was diagnosed in 88 patients according to the Mayo Clinic criteria, in sinus rhythm at the time of diagnosis. Incidence of SA among TTC was 14%. A difference was observed between patients with or without SA occurrence: age, hypertension, systolic pulmonary artery pressure and duration of hospitalization. Of note, patient with SA had significantly more depressed left ventricular ejection fraction at admission (p = 0.006). A large part of patient presenting SA required the use of diuretic for heart failure during hospitalization (p = 0.026). In multivariate analysis, the factors significantly associated with an increased risk of VA were: age (aOR = 1.19, 95% CI: 1.01 – 1.39, p = 0.029) and LEVF (aOR = 0.89, 95% CI: 0.8 – 0.97; p = 0.037). There was no significant difference in mortality rate between patients with or without SA during follow-up.

Conclusions: SA occurred in 14% of patients at the acute phase of TTC and independent predictive factors of SA were age and LEVF. During the acute phase, identification of high-risk SA patients allows better management, with ECG monitoring and therapeutic intervention in the CCU.

COMORBODITIES

P1794

Chemotherapy-induced cardiotoxicity in a Colombian heart failure program

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

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Cardiovascular toxicity of antineoplastic chemotherapeutic agents is a leading cause of premature morbidity and death among cancer survivors.
Objective: To assess the prevalence, clinical features, treatment, and clinical outcomes in a cohort of patients with cardiovascular toxicity induced by chemotherapy in a Colombian heart failure program
Methods: Observational, retrospective study
Results: In 1.358 patients followed by the outpatient heart failure program over a 4 - year period, 23 patients were identified as affected by chemotherapy-induced cardiotoxicity (1.7% of the population) 78.2% were women with a mean age of 57.7 years. The most common cancers treated were breast (60%), lymphoma (21%), and rectal (8.6 %). Type I cardiotoxicity for anthracycline therapy was present in 65% of patients. Other agents identified were cyclophosphamide and traztuzumab Concomitant chemotherapy plus radiotherapy was identified in 73.9% of patients. Pre-chemotherapeutic preventive measures were implemented by oncology service in only 17% of patients. Mean time between chemotherapy and heart failure debut was 5 years. Mean LVEF at acceptance was 27% and 35% during follow-up. Follow-up time was 2.7 years, and LVEF improved in 69% of patients. Electric stimulation therapy was indicated in 26% of patients. Of these, 83% had a CRT-D, and 17% had a ICD. Beta-blockers, renin angiotensin aldosterone system inhibitor made part of the chronic treatment of all patients in our Study. Overall mortality was 17.3%.
Conclusions: In our population, most of our patients were young women with breast cancer that received the standard treatment recommended by ESC guidelines with an improvement in the EF. Heart failure programs are a good strategy for the follow up of patients with cardiotoxicity induced by chemotherapy

P1795

Cardiovascular monitoring and management in cancer patients: a french national survey

L Jovenaux[1]; J Cautela[1]; F Thuny[1]; F Paganelli[1]; F Barlesi[1]
[1]*Hospital Nord of Marseille, Marseille, France*

Background: Cancer treatments can cause serious cardiovascular adverse events consensual guidelines regarding this issue are lacking. The objective was to analyse pratices and knowledge of oncologists about the monitoring of cancer patients under cardiotoxic agents.
Methods: A survey of knowledge and professional practices was conducted among oncologists between august 2015 and august 2016.
Results: A cardiological assessment was almost systematic before the introduction of treatment (96% for anthracyclines and 99% for trastuzumab). However, the per-treatment (respectively 54% and 95%) and post-treatment (49% and 59%) assessments were less frequent and reserved for patients with high cardiovascular risk. The attitude of oncologists in case of left ventricular dysfunction was often heterogenous, whatever the molecules used, particularly for anti-angiogenic. The recommendations of learned societies were not known by 65% of oncologists. Finally, 88% of oncologists thought that the creation of cardio-oncology clinic could improve the management of cardiotoxicity.
Conclusion: The wide variation in practice among oncologists reflects a lack of consensus on the optimal strategy to manage cardiotoxicity. Guidelines exist but are not well known. The making available of tools of good practices among oncologists and cardiologists and a better collaboration between teams should allow equal access for patients to cardio-oncologic care.

P1796

Subgroups analyses of a prospective long-term study in patients with advanced cancer - the prognostic impact of elevated heart rate.

MS Anker[1]; N Ebner[2]; B Hildebrandt[3]; J Springer[2]; H Riess[3]; U Landmesser[1]; AJS Coats[4]; SD Anker[2]; W Haverkamp[5]; SV Haehling[2]
[1]*Charite - Campus Benjamin Franklin, Department of Cardiology, Berlin, Germany*; [2]*University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*; [3]*Charite - Campus Virchow-Klinikum (CVK), Department of Hematology and Oncology, Berlin, Germany*; [4]*University of Warwick, Coventry, United Kingdom*; [5]*Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany*

Introduction: Cardiovascular problems like heart failure are frequently observed in patients with advanced cancer. It is often associated with reduced exercise capacity and quality of life. Nevertheless, the role of the resting heart rate in advanced cancer patients remains unresolved. Previously, we have shown that an elevated heart rate in cancer patients had significant prognostic value. We have now conducted additional subgroup analyses.
Methods: We enrolled 145 patients with histologically confirmed cancer (46% female, age 59 ± 10 yrs, tumour stage I/II/III/IV 11/10/32/46%) from 2005 through to 2010, and 59 healthy controls (46% female, age 60 ± 11 yrs). The cancer group consisted of 36 patients with colorectal, 72 with pancreatic, and 37 with non-small cell lung cancer. A thorough cardiology assessment was performed at baseline including a resting ECG. Patients were followed to January 2017. During a mean follow-up of 34 months for all patients (maximum 126 months), 97 (66%) patients had died (1-year mortality 30% [95%CI 22-38%], 3-year mortality 63% [55-71%]).
Results: As demonstrated before, elevated heart rate ≥75 bpm in cancer patients was associated with an increased mortality also here (HR 1.68 [1.10-2.55], p = 0.017, Cox-proportional hazard analysis). In multivariable analyses this effect remained significant. We now identified four subgroups within this effect was significant as well. A body mass index ≤22.0 kg/m2, i.e. the lowest tertile (n = 49, 34 deaths, HR 2.22 [1.05-4.65], p = 0.036), female gender (n = 64, 41 deaths, HR 2.03 [1.06-3.89], p = 0.033), age < 59 years (n = 69, 46 deaths, HR 2.26 [1.14-4.46], p = 0.019), and without anaemia (haemoglobin ≥12.0 g/dL, n=55, 33 deaths, HR 2.98 [1.33-6.67], p = 0.008) were identified as the subgroups who showed a significantly increased mortality, if the heart rate was ≥75 bpm. Other subgroups of patients (high body mass index, male gender, presence of anaemia and higher age did not show these results (p>0.20), but lack of power may in part be the cause (all HRs: 1.25–1.44).
Conclusion: We have shown that the resting heart rate is an important parameter in predicting the patient's increased mortality. This association is particularly strong in patients with low body mass index, female gender, lower age as well as in those without presence of anaemia.

P1797

The cumulative effect of chemoradiotherapy in the risk of developing cardiotoxicity

AC Ana Catarina Gomes[1]; LR Lopes[1]; AG Ferreira[1]; M Correia[1]; I Rangel[1]; P Fazendas[1]; H Mansinho[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Introduction: Cardiotoxicity is an increasingly recognized side effect of chemotherapy (CT), dependent on the type and dose of drugs used as well as radiotherapy (RT).
Aim: To study the left and right ventricular systolic and diastolic function during CT and the specific effect of CT and RT in the risk of developing cardiotoxicity.
Methods: Prospective study including cancer patients submitted to anthracyclines ± taxanes ± RT ± trastuzumab and referred to echocardiographic monitoring (M-mode and 2D imaging, left ventricle ejection fraction (LVEF) and global longitudinal strain (GLS) evaluated by speckle tracking) at different timepoints during treatment: T0 – before CT, T1 and T2 - during CT, T3 – at the end of CT and T4 - 1 year after the end of CT.
Results: 108 patients, 79.6% females, age 52.47 ± 12.2 years. Breast cancer 69.4%, lymphoma 22.2%, gastric cancer 8.3%. Epirrubicine 52.3% and doxorrubicine 47.7%: cumulative dose 506 ± 222 mg/m2. Docetaxel 57.8% and paclitaxel 2.8%: cumulative dose 511 ± 111 mg/m2. 13.9% under trastuzumab. 50.5% submitted to RT - median 50GY. The LVEF progressively decreased during CT (T0 64.14 ± 4.63%, T1 62.09 ± 4.43%, T2 61.34 ± 4.57%, T3 59.93 ± 4.91% (all p < 0.001) with recover at T4: 62.27 ± 4.69 versus T3 (p = 0.027)). The left ventricle also had the same behaviour (SLG: T0 20.73 ± 2.68%, T1 19.53 ± 2.73%, T2 19.12 ± 2.45%, T3 18.38 ± 2.38%, T4 18.52 ± 2.40% (T0-T1 and T1-T2 p <0.001, T2-T3 p < 0.003, T3-T4 p = 0.242, T0-T4 p = 0.041) as well as the right ventricle (based in TAPSE): T0 22.89 ± 2.89 mm, T1 22.30 ± 3.51 mm, T2 22.20 ± 3.47 mm, T3 21.50 ± 3.18 mm, T4 21.41 ± 2.97 mm (p < 0.001 between T0-T1, T1-T2 and T3-T4; p = 0.019 in T0-T4). There was no difference in LVEF, GLS, TAPSE and tricuspid S' variation in the intervals T0-T3 and T0-T4, between patients with or without trastuzumab and/or RT. The RT was not associated with additional left ventricular systolic dysfunction but was associated to a higher variation of tricuspid S' between T0-T4 (p = 0.015), with comparable baseline values (p = 0.462). This difference was independent of anthracycline type (p = 0.72), tumor side (left versus right) (p = 0.246), age (p = 0.845), body mass index (BMI) (p = 0.91), cumulative dose of anthracyclines (p = 0.925) or taxanes (p = 0.989). The heart rate (HR) gradually increased during treatment: T0 76.82 ± 13.65 beats per minute (bpm), T1 78.96 ± 13.30 bpm, T2 80.91 ± 13.84 bpm, T3 83.70 ± 11.88 bpm

(T0 versus T3, p = 0.033). The HR variation (cutoff of 10 bpm) was not associated with gender (p = 0.669), age (p = 0.557), BMI (p = 0.579), type of cancer (p = 0.91), tumor grade (G1, G2, G3) (p = 0.226), dose of anthracyclines (p = 0.482) and taxanes (p = 0.70) and LVEF variation in T0-T3 (p = 0.106).
Conclusion: CT affects systolic biventricular function. RT with shielding was associated with RV systolic dysfunction but not significant LV systolic function variation. The HR increased during CT and was independent of cancer type, demographics and cumulative dose of anticancer drugs.

P1798
Risk factors for heart failure after epirubicin chemotherapy for breast or colorectal cancer

G Gyorgy Fogarassy[1]; A Vathy-Fogarassy[2]; L Hornyak[3]; T Forster[4]
[1]Balatonfured State Cardiology Hospital, Balatonfured, Hungary; [2]University of Pannonia, Department of Computer Science and System Technology, Veszprem, Hungary; [3]Ferenc Csolnoky Hospital, Oncology Centre, Veszprem, Hungary; [4]University of Szeged, Second Department of Internal Medicine and Cardiology Centre, Szeged, Hungary

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Background: Appearance of dilated cardiomyopathy (DCM) is the most important limiting factor during anthracycline therapy. Incidence of DCM is highly dependent on anthracycline cumulative dose. In a published analysis, epirubicin treatment under dose of 800 mg/ m2 was associated with a low incidence of heart failure (HF). Patients older than 65 years are considered more susceptible for anthracycline-related HF.
Purpose: Our aim was to assess the incidence of HF after epirubicin therapy and to identify the risk factors for HF.
Methods: We conducted a retrospective nation-wide study using the anonymized financial database of the Hungarian National Health Insurance Company. The population and the outcome events were defined with the International Classification of Diseases (ICD) codes. We enrolled all the patients with breast- or colorectal carcinoma by histological confirmation between 1st January 2004 and 31st December 2015. 164 640 patients met enrollment criteria. For eligibility, we specified a chemotherapy-free run-in period of at least 3 years. The patients with assignment of I50 (HF), or I420 (DCM) ICD codes before index chemotherapy were excluded. HF outcome event was established by assignment of I50 ICD code at hospital discharge, or in autopsy report. HF event occurrence was analysed at the subjects with at least 3-year follow-up, or reaching the event earlier. We calculated chi^2 p values for different cumulative doses of concomitant chemotherapies to estimate the dose-dependency of HF. Multivariate binomial stepwise logistic regression was used to calculate odds ratios (OR) for HF.
Results: 8 796 epirubicin-treated patients were eligible for HF analysis. The cumulative incidence of HF was 7.1%. Incidence was highly dependent on epirubicin cumulative dose and age. Epirubicin dose over 709 mg/m2 was proven independent variable with significant association with HF (OR: 1.92, p = 0.007). Risk of HF increased with older age: OR for HF at age 50-59 was 1.84, at age 60-69 was 2.71 and at age over 70 was 5.16, compared to those under 40. The only chemotherapy, besides epirubicin, with cumulative dose-dependency of HF was docetaxel (dose> 510 mg/m2, OR: 1.49, p = 0.034). Other independent variables with significant association with HF (p values ≤0.05) were diabetes mellitus (OR: 1.69), coronary disease (OR: 1.41), capecitabine (OR: 1.45), gemcitabine (OR: 1.73), bevacizumab (OR: 1.49), at paclitaxel a trend to higher HF incidence (OR: 1.23, p = 0.07) was found. Presence of trastuzumab, panitumumab, cetuximab, antifolates, folinic acid, cyclophosphamide, mitomycin, topoisomerase-inhibitors, platinum-containing drugs, vinca alkaloids and dexrazoxane had no significant impact on HF.
Conclusion: We found significant elevation of HF incidence with increasing age, even over 50 years and with epirubicin cumulative dose over 709 mg/m2. The presence of capecitabine, gemcitabine, taxanes and bevacizumab in the treatment was associated with higher risk for HF.

P1799
Improving ventricular function in patients with severe ventricular dysfunction previous to kidney transplantation.

C G Cesar Gerardo Martinez Hernandez[1]; E Toxqui[1]; J Silva[1]; D Ramos[1]; F J Marin[1]; A A Gordillo[1]; F J Rodriguez Quilantan[1]
[1]Mexican Social Security Institute, Internal Medicine - Cardiology, San Luis Potosi, Mexico

Introduction: There is a strong correlation between end stage kidney disease and congestive heart failure associated to severe left ventricular dysfunction. We know now that mortality at three years after hospitalization for congestive heart failure is similar to after acute myocardial infarction. There have been several works evaluating management of left ventricular dysfunction previous to kidney transplantation and an improving of left ventricular function after that is expected. We know that not all the patients improves it and the minor left ventricular function improving, the highest perioperative complications rate and lack of surveillance.
Purpouse: We studied the effect of improving left ventricular function with inotropic agent (levosimendan) previous to kidney transplantation and mobidity/mortality associated to surgery in order to reduce them, and secondary, left ventricular function restoration in order to improve surveillance and life quality.
Methods: We included 6 patients ongoing to kidney transplantation with severe left ventricular dysfunction defined as ejection fraction less than 35%. We practiced a biplanar echocardiography to assess left ventricle ejection fraction pre and post inotropic agent administration. We administered levosimendan with the following scheme: a loading dose of 6mcg/kg/min in a 10 minutes infusion followed by a manteining dose of 0.05mcg/kg/min in a 48 hours infusion. After this, the patients went to a living donor kidney trasnplantation surgery.
Results: The mean ejection fraction was 27.8% pre inotropic agent and the mean ejection fraction post inotropic agent was 51.1%. The morbidity of cardiovascular and all causes was less between those patients with best ventricular function defined by acute pulmonary oedema, cardiogenic shock, miocardial infarction, stroke, acute renal failure or kidney reject. There were no mortality associated to kidney tranplantation. The mean hospitalization days was 7.
Conclusions: Improving ventricular function with inotropic agent before kidney transplantation may reduce morbidity and mortality associated to this one.

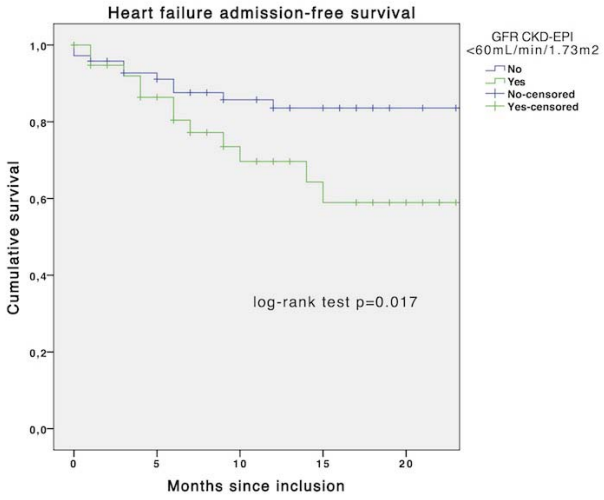
P1801
Different clinical profile in heart failure patients with chronic kidney disease

Z Blazquez Bermejo[1]; D Iglesias Del Valle[1]; E Garcia[1]; J De Juan[1]; E De La Cruz[1]; R Cadenas[1]; V Martinez[1]; E Prieto[1]; R Cano[1]; C Casanova[1]; A Garcia[1]; A Martin[1]; I Plaza[1]
[1]University Hospital Infanta Sofia, Cardiology, Madrid, Spain

Introduction: The prevalence of moderate to severe chronic kidney disease (CKD) in heart failure (HF) is as high as 30-60%. The baseline glomerular filtration rate (GFR) is a predictor of mortality in both acute and chronic HF.
Purpose: The aim of this study was to analyze the different clinical characteristics in HF depending on the GFR.
Methods: 112 patients with HF diagnosis were prospectively included in the HF unit at our institution between May 2014 and December 2016. We identified patients with moderate to severe CKD (GFR with the CKD-EPI equation < 60mL/min/1.73m2) at the time of inclusion. Clinical characteristics and medical treatment were compared among patients with and without CKD. Patients were systematically followed-up in the HF outpatient clinic. All changes in clinical status, admissions or deaths were documented. Kaplan-Meier estimates was used to analyze time to first HF admission or death from any cause.
Results: Mean age was 64.3 ± 13.2 years. 35.2% of patients had CKD at baseline. Clinical characteristics and medical treatment were different in these patients (table). Median follow-up was 13 ± 8.4 months. HF admission-free survival was lower in CKD patients (p = 0.017) (figure).
Conclusions: HF patients with moderate to severe CKD are older, have preserved LVEF more often, have more comorbidity and are less likely to receive optimal medical therapy. CKD patients have worse prognosis; nevertheless, these patients are associated with an increased risk profile, which may partly explain the higher risk.

Clinical characteristics and treatment

	GFR CKD-EPI >60ml/min/ 1.73m2	GFR CKD-EPI < 60ml/min/ 1.73m2	
Age (years)	60.0±12.8	72.0±10.4	p < 0.01
Male (%)	72.2	67.5	p = 0.60
Arterial hypertension (%)	59.7	77.5	p = 0.06
Diabetes mellitus (%)	26.4	55.0	p < 0.01
Significant coronary artery disease (%)	29.2	52.5	p = 0.02
COPD (%)	15.3	20.0	p = 0.52
PAD (%)	4.2	25.0	p < 0.01
Anemia (%)	20.8	40.0	p = 0.03
LVEF < 40% (%)	88.9	72.5	p = 0.03
Beta-blockers (%)	98.6	77.5	p < 0.01
ACE-I or ARB or ARNI (%)	91.7	77.5	p = 0.04
MR antagonist (%)	79.2	62.5	p = 0.06



Heart failure admission-free survival

P1802

Cardiorenohepatic syndrome is common in patients with decompensated heart failure

A Soloveva[1]; S Villevalde[1]; Z Kobalava[1]
[1]RUDN University, Department of Internal Disease Propaedeutics, Moscow, Russian Federation

Objective: Similar factors such as venous congestion and hypoperfusion are thought to underlie both renal and liver injuries in decompensated heart failure (DHF), known as cardiorenal syndrome (CRS) and cardiohepatic syndrome (CHS). The aim of this study was to assess the prevalence and predictors of combination of CRS and CHS in DHF.
Methods: Kidney and liver function was assessed in 322 patients with DHF (190 male, 69.5 ± 10.6 years (M ± SD), arterial hypertension 87%, myocardial infarction 57%, atrial fibrillation 65%, diabetes mellitus 42%, known chronic kidney disease 39%, chronic anemia 29%, left ventricular (LV) ejection fraction (EF) 37.6 ± 12.6%, EF<35% 39.1%). CRS was diagnosed if serum creatinine decreased ≥26.5 μmol/l in first 48 hours of hospitalization. CHS was considered when at least one of liver function tests (LFT) level exceeded upper normal limit on admission. Simultaneous CHS and CRS were considered as cardiorenohepatic syndrome (CRHS). Mann-Whitney test and multivariate logistic regression analysis were performed. $p < 0.05$ was considered statistically significant.
Results: CRS occurred in 60 (18,6%) patients. CHS was diagnosed in 274 (85.1%) patients. Isolated CHS, isolated CRS and CRHS occurred in 78.4, 1.5 and 20.1% patients with hepatic or kidney injury. Patients with versus without CRHS had lower systolic blood pressure (SBP) (130 ± 18 vs 138 ± 19 mmHg, $p < 0.01$), EF (32 ± 10 vs 38 ± 13%, $p < 0.01$), pulse BP (49 ± 16 vs 56 ± 15 mmHg, $p < 0.01$), higher LV mass index (200 ± 50 vs 178 ± 52 g/m^2, $p < 0.01$), LV end diastolic volume (62 ± 6 vs 56 ± 9 mm, $p < 0.001$), higher incidence of severe mitral regurgitation (64.3 vs 39.6%, $p < 0.001$), signs of congestion – jugular venous distension (57.1 vs 39.6%, $p < 0.05$), hepatomegaly (85.7 vs 70.3%, $p < 0.05$), echo-hydropericardium (46.4 vs 22.5%, $p < 0.001$), vasopressor therapy (17.9 vs 6.3%, $p < 0,01$). The independent predictors of CRHS were baseline GFR<45 ml/min/1.73 m^2 (odds ratio (OR) 3.95, 95% confidential interval (CI) 2.15-7.21, $p < 0.01$), SBP<110 mmHg on admission (OR 3.51, CI 1.55-7.94, $p < 0.05$), vasopressor therapy (OR 3.23, CI 1.35-7.73, $p < 0.05$), echo-hydropericardium (OR 2.98, CI 1.62-5.50, $p < 0.01$) and EF<35% (OR 2.96, CI 1.61-5.44, $p < 0.05$).
Conclusions: Isolated CHS, isolated CRS and CRHS occurred in 78.4, 1.5 and 20.1% patients with DHF and hepatic or kidney injury. The independent predictors of CRHS were baseline GFR<45 ml/min/1.73 m^2, SBP<110 mm Hg on admission, echo-hydropericardium and EF<35%.

P1803

Low ferritin reflecting depleted iron stores predicts inspiratory muscle weakness independently of skeletal muscle mass in men with heart failure with reduced ejection fraction

M Michal Tkaczyszyn[1]; M Drozd[1]; K Wegrzynowska-Teodorczyk[2]; I Flinta[3]; M Bolanowski[4]; D Jedrzejuk[4]; W Banasiak[5]; P Ponikowski[1]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland; *[2]University School of Physical Education of Wroclaw, Department of Physiotherapy, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Physiology, Wroclaw, Poland*; *[4]Wroclaw Medical University, Department of Endocrinology, Diabetology and Isotope Therapy, Wroclaw, Poland*; *[5]Military Hospital, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*

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Background: Skeletal and respiratory muscle dysfunction (specific myopathy) constitutes an important pathophysiological feature of heart failure syndrome. We assessed the relationships between respiratory muscle function, skeletal muscle mass, and physical fitness in men with heart failure with reduced ejection fraction (HFrEF), and investigated the hypothesis of whether iron deficiency contributes to respiratory muscle dysfunction in these patients.
Methods: We examined 53 male outpatients with stable HFrEF without asthma or chronic obstructive pulmonary disease (age: 64 ± 10 years; New York Heart Association [NYHA] class I/II/III: 36/51/13%; ischaemic aetiology of HFrEF: 83%; all patients with left ventricular ejection fraction [LVEF] ≤40%) and 10 middle-aged healthy men (control group). We analyzed respiratory muscle strength (maximal inspiratory and expiratory pressure at the mouth [MIP and MEP, respectively]), appendicular lean mass (ALM; reflects appendicular skeletal muscle mass; measured using dual-energy X-ray absorptiometry), physical fitness (components of Functional Fitness Test [FFT] for Older Adults - "Up and go", "Chair stand", and "Arm curl", and 2-minute step test), and parameters of iron status.
Results: MIP, MEP, ALM adjusted for body mass index (ALM/BMI), and MIP adjusted for ALM/BMI were lower in men with HFrEF vs. healthy men (74 ± 23 vs. 106 ± 33 cm H2O, $p < 0.001$; 122 ± 23 vs. 161 ± 28 cm H2O, $p < 0.001$; 81 ± 10 vs. 96 ± 11 100*m^2, $p < 0.001$; and 93 ± 27 vs. 117 ± 40 cm H2O/m^2, $p = 0.04$; respectively). MIP (but not MEP) and MIP adjusted for ALM/BMI (but not ALM/BMI) were lower in men with HFrEF with ID compared with those without ID (67 ± 20 vs. 106 ± 33 cm H2O, $p = 0.02$; and 84 ± 22 vs. 103 ± 28 cm H2O/m^2, $p = 0.02$; respectively). In univariable linear regression analyses MIP was related to (all $p < 0.05$): LVEF (r=0.31), ALM/BMI (r=0.35), N-terminal pro B-type natriuretic peptide (NT-proBNP, r=-0.30), haemoglobin (r=0.35), mean corpuscular haemoglobin (r=0.36), serum ferritin (r=0.41), the presence of ID (r=-0.32), reticulocyte haemoglobin content (r=0.45), and percentage of hypochromic red cells (r=-0.31). In a multivariable linear regression model lower serum ferritin remained an independent predictor of lower MIP when adjusted for ALM/BMI, LVEF, NT-proBNP, and haemoglobin (β=0.36, $p = 0.017$, corrected R^2=34%). Importantly, in multivariable linear regression models, lower MIP was also an independent predictor of worse results in FFT when adjusted for ALM/BMI or relevant clinical variables (NYHA class, estimated glomerular filtration rate, NT-proBNP, and haemoglobin).
Conclusions: In men with HFrEF decreased iron stores (as reflected by low circulating ferritin) predict inspiratory muscle weakness independently of skeletal muscle mass. Importantly, the dysfunction of inspiratory muscles in these patients is associated with worse physical fitness independently of either skeletal muscle mass or disease severity.

P1804

Iron deficiency predicts decreased exercise capacity and physical fitness independently of skeletal muscle mass in men with heart failure with reduced ejection fraction

M Michal Tkaczyszyn[1]; M Drozd[1]; K Wegrzynowska-Teodorczyk[2]; A Czarniawska[3]; R Krajewski[3]; TH Menghis[3]; R Rydzyk[3]; U Szydelko[3]; P Wojcik[3]; W Banasiak[4]; P Ponikowski[1]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland; *[2]University School of Physical Education of Wroclaw, Department of Physiotherapy, Wroclaw, Poland*; *[3]Wroclaw Medical University, Students' Scientific Association, Department of Heart Diseases, Wroclaw, Poland, Wroclaw, Poland*; *[4]Military Hospital, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*

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BACKGROUND: In patients with heart failure concomitant iron deficiency (ID) is associated with decreased exercise capacity. Another important predictor of reduced functional capacity in these patients is skeletal muscle mass loss. We investigated the hypothesis of whether in men with heart failure with reduced left ventricular ejection fraction (HFrEF) ID predicts decreased exercise capacity and physical fitness independently of indices of skeletal muscle mass loss.
Methods: We examined 49 male outpatients with stable HFrEF (age: 65 ± 11 years; New York Heart Association [NYHA] class I/II/III: 39/45/16%; ischaemic aetiology of HFrEF: 86%; all patients with left ventricular ejection fraction [LVEF] ≤40%). We analyzed exercise capacity (6-minute walking test distance - 6MWD), physical fitness

(components of Functional Fitness Test [FFT] for Older Adults - "Up and go", "Chair stand", and "Arm curl" tests, and 2-minute step test [2MST]), indices of skeletal muscle mass (measured using dual-energy X-ray absorptiometry), and parameters of iron status.
Results: Soluble transferrin receptor (sTfR) correlated with 6MWD (r=-0.063, p < 0.001), "Up and go" (r=0.51, p = 0.001), "Chair stand" (-0.56, p < 0.001), "Arm curl" (r=-0.36, p = 0.03), and 2MST (r=-0.45, p = 0.004); serum ferritin - with "Up and go" (r=-0.39, p = 0.008), "Chair stand" (r=0.41, p = 0.005), "Arm curl" (r=0.46, p = 0.002), and 2MST (r=0.39, p = 0.008); and the presence of ID (serum ferritin < 100 μg/L or serum ferritin 100-299 μg/L in combination with transferrin saturation < 20%) - with "Up and go" (r=0.31, p = 0.04), "Chair stand" (r=-0.30, p = 0.046), and "Arm curl" (r=-0.44, p = 0.003). Appendicular lean mass/total lean mass (ALM/TLM) correlated with 6MWD (r=0.44, p = 0.002), "Up and go" (r=-0.34, p = 0.02), "Chair stand" (r=0.37, p = 0.01), and 2MST (r=0.30, p = 0.04); and appendicular lean mass/body mass index (ALM/BMI) with 6MWD (r=0.43, p = 0.003), "Up and go" (r=-0.38, p = 0.009), "Chair stand" (r=0.30, p = 0.04), and 2MST (r=0.34, p = 0.02). In multivariable linear regression models lower serum ferritin was associated with worse results in "Up and go" (β=-0.31, p = 0.045), "Chair stand" (β=0.32, p = 0.04), "Arm curl" (β=0.32, p = 0.03), and 2MST (β=0.42, p = 0.01) independently of skeletal muscle mass (ALM/BMI) and relevant clinical variables (age, haemoglobin, estimated glomerular filtration rate, N-terminal pro-B-type natriuretic peptide, NYHA class). Similarly, higher sTfR was associated with worse results in "Up and go" (β=0.40, p = 0.03) and "Chair stand" test (β=-0.39, p = 0.03), and with shorter 6MWD (β=-0.59, p < 0.001) independently of skeletal muscle mass (ALM/TLM) and aforementioned clinical variables.
Conclusions: In men with HFrEF disordered iron homeostasis is associated with decreased exercise capacity and physical fitness independently of generalized skeletal muscle mass loss.

P1805

Importance of anaemia in a multi-ethnic Asian heart failure population

VJ Goh[1]; J Tromp[2]; THK Teng[3]; WT Tay[3]; P Van Der Meer[2]; LH Ling B Siswanto[4]; CL Hung W Shimizu[5]; S Zhang C Narasimhan[6]; CM Yu S Park[7]; T Ngarmukos H Liew[8]; EB Reyes J Yap[9]; M Macdonald[10]; AM Richards[11]; A Inder[12]; CS Lam[3]
[1]Singapore General Hospital, Singapore, Singapore; *[2]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; *[3]National Heart Centre Singapore, Singapore, Singapore*; *[4]National University Heart Centre, Singapore, Singapore, National Cardiovascular Center Universitas Indonesia, Jakarta, Indonesia*; *[5]Mackay Memorial Hospital, Taipei, Taiwan, National Cardiovascular Centre, Tokyo, Japan*; *[6]Fuwai Hospital, Beijing, The People's Republic of China, CARE Hospital, Hyderabad, India*; *[7]Hong Kong Baptist Hospital, Hong Kong, Korea University Hospital, Seoul, Korea Republic of*; *[8]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, Malaysia QEH2 Clinical research centre, Malaysia*; *[9]Manila Doctors Hospital, Manila, Philippines, National Heart Centre Singapore, Singapore*; *[10]Changi General Hospital, Singapore, Singapore*; *[11]National University Heart Centre, Singapore, Singapore*; *[12]Veterans Affairs Medical Center, Minneapolis, United States of America*

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Background: Anaemia is an important comorbidity in patients with heart failure (HF) in Western populations and is associated with worse outcomes; however data are scarce in multi-ethnic Asian populations.
Aim: To examine the ethnic/geographical variation in prevalence, clinical correlates and prognostic impact of anaemia in Asian patients with HF.
Methods: Asian patients with HF (ejection fraction ≤40%) and anaemia, defined as haemoglobin (Hb) < 13g/dL (men) and < 12g/dL (women) from 11 regions (China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand) enrolled in the ASIAN-HF study were identified. Ethnic groups included Chinese (33.0%), Indian (26.2%), Malay (15.1%), Japanese/Korean (20.2%), and Others (5.6%).
Results: Of the 3886 Asian HF patients (60 ± 13 years, 21% women), 41% were anaemic, with wide variation across ethnicities (32.6-54.4%) (Figure 1A). Indian ethnicity (adjusted OR 3.00; 95% CI 2.17-4.17), age (adjusted OR 1.03; 95% CI 1.02-1.03), presence of diabetes (adjusted OR 1.75; 95% CI 1.47-2.08) and chronic kidney disease (CKD) (adjusted OR 1.71; 95% CI 1.44-2.03) were independently associated with presence of anaemia (all P < 0.001). Ethnicity modified the association of CKD with anaemia (Pinteraction=0.045), with the strongest correlation observed in Japanese/Koreans (adjusted OR 2.86; 95% CI 1.96-4.20; P < 0.001). Anaemic patients had lower Kansas City Cardiomyopathy Questionnaire scores (P < 0.001) and a higher composite endpoint of all-cause mortality and HF hospitalisation at 1 year (25.4% vs. 19.7%, P < 0.001) compared to non-anaemic patients (Figure 1B). The independent association of this composite endpoint with anaemia was modified by ethnicity (Pinteraction=0.02) and was highest in Japanese/Koreans (multivariable HR 1.82; 95% CI 1.14-2.91; P=0.012).
Conclusion(s): This first multi-ethnic Asian HF study shows that anaemia is highly prevalent and adversely impacts quality of life and survival, with striking ethnic differences that deserve further study.

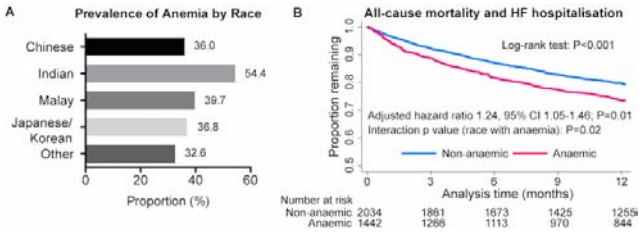

Figure 1

P1806

Iron status in diabetic men with heart failure and reduced ejection fraction

M Drozd[1]; M Kasztura[1]; K Wegrzynowska[2]; P Rozentryt[3]; J Nowak[3]; L Polonski[3]; J Malyszko[4]; E Koc-Zorawska[4]; W Banasiak[5]; P Ponikowski[6]; E Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland; *[2]University School of Physical Education of Wroclaw, Wroclaw, Poland*; *[3]Silesian Center for Heart Diseases (SCHD), Third Department of Cardiology, Zabrze, Poland*; *[4]Medical University of Bialystok, 2nd Department of Nephrology and Hypertension with Dialysis Unit, Bialystok, Poland*; *[5]Military Hospital of Wroclaw, Center of Heart Diseases, Wroclaw, Poland*; *[6]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*

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Both heart failure with reduced ejection fraction (HFrEF) and diabetes mellitus (DM) constitute co-morbidities significantly interfering with iron metabolism. It remains unclear whether and how the concomitance of DM in patients with HFrEF affects iron status.
Methods: We analysed the data of 622 men with stable HFrEF (age: 57 ± 11 years, CAD: 71%, NYHA class III-IV: 41%, LVEF: 27 ± 8%, DM: 30%). ID was defined as serum ferritin <100 μg/L, or serum ferritin 100-299 μg/L with transferrin saturation [TSAT] <20%. Additionally, serum levels of hepcidin and soluble transferrin receptor [sTfR] were assessed as biomarkers of iron status.
Results: Patients with DM as compared with those without DM were older, more obese, had more prevalent CAD, more symptomatic HF, more common hypertension and worse kidney function (all p < 0.05), but with no difference in LVEF, uric acid, hsCRP, NT-proBNP and haemoglobin level between these 2 groups. Regarding iron status, men with HFrEF and DM as compared with those without DM demonstrated a similar prevalence of ID (33% vs 34%, p>.2), and a trend towards a higher prevalence of IDA (13%, vs. 9%, p = 0.08). There were no differences in either serum ferritin or TSAT between DM and non-DM men with HFrEF (p > 0.2), whereas DM was accompanied by reduced sTfR (1.19 (0.96-1.60) vs. 1.31 (1.01-1.83) mg/L, p < 0.05), and a borderline higher hepcidin (65 (33-123) vs. 55 (22-111) ng/mL, p = 0.07). STfR > =1.32 mg/L was found in 50% vs 41% of DM vs non-DM men with HFrEF, respectively (p < 0.05), whereas serum hepcidin <14.5 ng/mL was found in 18% vs 5% of DM vs non-DM men with HFrEF, respectively (p < 0,001). In non-DM men with HFrEF, lower hepcidin was related to younger age, whereas such relationship was not seen in DM subjects. In non-DM men with HFrEF, higher sTfR correlated with lower LVEF, sodium, GFR, and total cholesterol, and higher hs-CRP, NT-proBNP and uric acid (all p < 0.05), whereas in DM subjects sTfR was related only to hs-CRP, NT-proBNP, uric acid and total cholesterol (all p < 0.05).
Conclusions: DM does not differentiate iron status in men with HFrEF based on standard biomarkers (ferritin, TSAT), however the measurements of sTfR and hepcidin suggest the higher prevalence of intracellular ID (reflected by high sTfR) and depleted iron stores (reflected by low hepcidin). Importantly, there are different clinical correlates of novel iron status biomarkers in DM vs non-DM subjects with HFrEF, which might indicate the different pathophysiological mechanisms related to these iron derangements.

P1807

Iron status in patients with heart failure with reduced ejection fraction across different age groups

M Drozd[1]; M Kasztura[1]; M Tkaczyszyn[1]; P Rozentryt[2]; J Nowak[2]; L Polonski[2]; J Malyszko[3]; E Koc-Zorawska[3]; W Banasiak[4]; P Ponikowski[5]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland; *[2]Silesian Center for Heart Diseases (SCHD), Third Department of Cardiology, Zabrze, Poland*; *[3]Medical*

University of Bialystok, 2nd Department of Nephrology and Hypertension with Dialysis Unit, Bialystok, Poland; [4]*Military Hospital of Wroclaw, Center of Heart Diseases, Wroclaw, Poland*; [5]*Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*

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Background: Iron deficiency is a common and ominous co-morbidity in patients with heart failure with reduced ejection fraction [HFrEF]. However, it remains enigmatic whether and how ageing interacts with iron status in this group of patients. The aim of this study was to investigate iron parameters and clinical status in different age groups of patients with HFrEF.
Methods: We analysed the data of 736 stable patients with HFrEF (age: 58 ± 11 years, men: 86%, confirmed coronary artery disease: 71%, New York Heart Association [NYHA] Class III-IV: 44%, LVEF [left ventricular ejection fraction]: 28 ± 8%. ID was defined as serum ferritin < 100 μg/L, or serum ferritin 100-299 μg/L with transferrin saturation [TSAT] < 20%. Additionally, hepcidin and soluble transferrin receptor [sTfR] were assessed in peripheral blood as biomarkers of iron status, reflecting iron stores and intracellular iron status, respectively. All patients were prospectively divided into 4 age groups: < 50 (n = 148), 50-59 (n = 301), 60-69 (n = 174), ≥70 years (n = 113), respectively.
Results: There was a trend towards the higher prevalence of ID in elderly patients with HFrEF (36%, 30%, 40% and 41% - in aforementioned respective age groups, p = 0.07). There were no differences in TSAT, sTfR, MCV, MCH, MCHC, hsCRP and NT-proBNP between patients in different age groups (all p>0.2). The older the patients, the higher prevalence of ID-related anaemia (IDA) (4%, 7%, 16% and 14% - in aforementioned respective age groups, p < 0.01). Elderly patients with HFrEF were characterized by lower haemoglobin (14.5 ± 1.6, 14.2 ± 1.4, 13.8 ± 1.5, 13.2 ± 1.4 g/dL, p < 0.0001), ferritin (199 (98, 310), 170 (106, 296), 167 (89, 277), 144 (72, 241 ng/mL) , p < 0.05) and hepcidin (79 (43, 133), 52 (30, 111), 68 (31, 127), 46 (25, 93 ng/mL) , p < 0.05) and higher eGFR (95 ± 27, 79 ± 22, 70 ± 21, 65 ± 31 mL/min/1.73m2, p < 0.01).
Only among patients with HFrEF aged below 50 years, iron-deficient subjects demonstrated high NT-proBNP and low LVEF as well as high uric acid as compared to those with preserved iron status (all p < 0.05), also in this group sTfR was related with uric acid (r=0.2, p < 0.5) and NT-proBNP (r=0.35, p < 0.001), and Tsat correlated with NT-proBNP (r=0.21, p < 0.05). Only among patients with HFrEF aged below 60 years, iron-deficient subjects demonstrated high hsCRP as compared to those without ID (p < 0.05), which was not seen in older age groups. Also patients with HFrEF and ID aged below 70 years had lower total cholesterol as compared to those with preserved iron status (all p < 0.05).
Conclusions: Elderly patients with HFrEF are prone to develop ID and IDA, and ID is reflected mainly by depleted iron stores (as assessed by low serum levels of both ferritin and hepcidin). There are clinical differences in younger versus older iron-deficient patients with HFrEF, which may presume the diverse pathophysiological background in these separate age groups.

P1808

Anemia in heart failure is associated with higher CA 125, NT-proBNP and hsCRP levels

ME Altinbas[1]; Y Yuksel Cavusoglu[1]; F Mutlu[1]; E Babayigit[1]; K Isgendarov[1]; S Eraslan[1]
[1]*Eskisehir Osmangazi University, Eskisehir, Turkey*

Purpose: Anemia is very common in heart failure (HF). Plasma levels of carbohydrate antigen 125 (CA-125) have been shown to correlate with clinical, hemodynamic, and echocardiographic parameters in HF. Higher level of hsCRP is known to be present in the inflammatory process of HF. NT-proBNP is a well-known biomarker of neurohormonal activation in HF. In this study, we aimed to evaluate the relationship between anemia and plasma levels of CA-125, hsCRP or NT-proBNP levels.
Methods: A total 446 patients with the diagnosis of HF, NYHA II-IV, LVEF < 40% and >18 years of age were included in this study. Plasma levels of CA-125, hsCRP or NT-proBNP levels have been measured from the blood samples. Anemia was defined as hemoglobin levels < 12 gr/dL in females and < 13 gr/dL in males. Patients were classified into two groups: patients with anemia (n = 223) and patients without anemia (n = 223).
Results: Mean age of study population was 67 ± 12 years. Mean EF was 25.4 ± 7.9%. Plasma levels of CA-125 were found to be significantly higher in patients with anemia as compared to those without anemia (56.3 [20.8-130.6] U/mL vs 24.5 [12.5-61.1] U/mL, p < 0.001, respectively). NT-proBNP and hsCRP levels were also found to be significantly higher in patients with anemia as compared to those without anemia (6594 [2535-19250] pg/mL vs 1740 [581-4397] pg/mL, p < 0.001 for NT-proBNP and 18 [8.14-43.04] mg/L vs 8.09 [3.45-21.45] mg/L, p < 0.001 for hsCRP, respectively). Furthermore, a significant positive correlation was found between CA-125 and NT-proBNP (r=538, p < 0.001), and also between CA-125 and hsCRP levels (r=225, p < 0.001).
Conclusions: The results of this study showed that anemia in HF is associated with higher CA-125, NT-proBNP and hsCRP levels, suggesting more severe clinical status of the disease in HF patients with anemia as compared those without anemia.

P1809

Iron stores and prognosis in a cohort of elderly patients with heart failure and preserved ejection fraction

B Nieto Sandoval[1]; J A Jose Satue[1]; A Perez Martin[1]; JC Belinchon Paraiso[1]; S Gonzalo Pascua[1]; J Marrero Frances[1]; A San Martin Prado[1]; C Gutierrez Landaluce[1]; A Zapatero Gaviria[1]
[1]*University Hospital of Fuenlabrada , Fuenlabrada, Spain*

Background: Iron deficiency and anemia are frequent in Heart Failure with reduced ejection fraction (HF-REF) patients, and are related with a worse prognosis, but there are still few data about its prevalence and prognosis in patients with preserved ejection fraction (HF-PEF). The aim of this study is to determine Iron Deficiency and anemia prevalence, and its relationship with prognosis in a cohort of elderly HF-PEF patients.
Patients and methods: All consecutive patients included into our Hospital HF Care Program after having a HF admission from June 2011 to June 2014 were prospectively recruited and followed up in consult and/or by telephone until June 2015. Demographic data, cardiovascular risk factors, Barthel, Lawton and Pfeiffer scores, clinical, biochemical parameters, treatments at discharge (including oral and/or endovenous iron), new admissions and/or death were registered in a specific database integrated in our electronic medical record system. Anemia and iron deficiency were classified following standard ESC criteria.
Results: 173 patients were included during this period. Mean age was 79.8 years (DS 8 years), 113 (65,3%) were women, mean Charlson score was 2.9 and mean Barthel was 84.1%. Ejection fraction (EF) was measured by echocardiography in 170 (98%) patients; 82 % of patients (139) had HF-PEF (EF >50%), HF-PEF patients were slightly younger, usually women, and had statistically significant higher BMI and lower NT-proBNP levels than non-HF-PEF patients. Mean follow-up was 649 days. 48 (27.7%) patients died during follow up, 33 of them having HF-PEF (23.7% of this cohort). 82 patients (48%) had a readmission during first year of follow up. Iron status was registered in 154 patients (89%); anemia was present in 85 (63%) of HF-PEF patiens, iron deficiency in 92 (67%) and absolute iron deficiency in 67 (48%). Anemia was statistically related to male sex and lower iron levels and transferrin saturation, but higher serum ferritin (165 vs 124, p = 0.28 NS) Increased mortality in our HF-PEF patients was statistically related in univariate analysis with age, previous hospital admissions, dependence in Barthel score, low albumin level, high ferritin level and non use of betablockers. Using a composite end-point of heart failure readmission during first year of follow up or death, lower Barthel Score and albumin values, higher NT pro-BNP and ferritin level, and absence of iron deficiency, had an statistically significant worse prognosis. No one of the treatments registered produced any change in this composite outcome, including betablockers, aldosterone antagonist and oral and/or endovenous iron.
Conclusions: Anemia and Iron Deficiency are usual findings in our elderly HF-PEF patients. In contrast of evidence yet published in HF-REF patients, isolated anemia and/or iron deficiency didn't show a worse prognosis in our patients, and higher levels of ferritin were associated with poor outcomes

P1810

Anemia in heart failure - The underdog of risk predictors?

A Alanoud Alsaud[1]; DALIA Ali[1]; DALIA Ali[1]; IYAD Farah[1]; IYAD Farah[1]; M Bdeir[1]; M Bdeir[1]; A Alameen[1]; A Alameen[1]; A Mahmoud[1]; A Mahmoud[1]
[1]*National Guard Hospital, Cardiovascular Disease Management Program, Riyadh, Saudi Arabia*

Background/Aim: Anemia is frequent in chronic heart failure and has shown to reduce survival in heart failure, particularly in patients with reduced ejection fraction. However, there is paucity of such data in a Saudi heart failure population.
Methods: We studied patients enrolled in a dedicated Heart Failure Disease Management Programme (n = 2727, 72% male). Clinical characteristics and mortality data were analysed for the entire cohort and categorized using WHO Classification of anaemia. Categorical variables were presented as percentages, compared by chi-square test and expressed as odds ratio and 95% confidence intervals. Continuous data were summarized as mean ± SD. Relationship between parameters was analysed using regression analysis. Survival analysis was performed using Kaplan Meir curves. Data was analysed using JMP(SAS for Windows and p < 0.05 considered significant.
Result: Some 35% patients had anemia, of which 10% was severe. Some 20% had Hb>15 g/dl. Patients with anemia were older, more likely to be NYHA Class II-III, have renal impairment and reduced ejection fraction (all p < 0.0001). Anemic patients were

less likely to receive ACEI, beta blockers, aldosterone antagonists (all $p < 0.001$) and more likely to be on diuretics, vasodilators and anti-platelets (all $p < 0.001$). Anemic patients had significantly reduced survival (log rank $p < 0.0001$), as shown by Kaplan Meir curve analysis.
Conclusion: Anemia is quite prevalent in a Saudi heart failure population with a significant preponderance in older patients with significant comorbidities. It is also associated with poor survival compared with those with normal haemoglobin levels.

P1811
Clinical benefits of intravenous iron therapy in patients with defibrillator due to heart failure with left ventricular dysfunction.

A Ruiz-Salas[1]; MA Miguel Antonio Lopez Garrido[1]; A Robles-Mezcua[1]; N Gonzalez-Cruces[1]; L Morcillo-Hidalgo[1]; JM Garcia-Pinilla[1]; JJ Gomez-Doblas[1]; E De Teresa-Galvan[1]; J Alzueta-Rodriguez[1]
[1]*University Hospital Virgen de la Victoria , Department of Cardiology, Malaga, Spain*

Background: Iron deficiency is a commonly present comorbidity in patients with advanced heart failure (HF), and contributes to the existence of a higher mortality and worse quality of life. Many of these patients have high energy devices with remote monitoring that transmit arrhythmic episodes and a series of clinical parameters that try to anticipate the cardiac clinical deterioration and improve the prognosis. We conducted this study in order to know the clinical benefits of intravenous iron therapy in this population.
Methods: We studied all the HF patients with NYHA functional class II-III and iron deficiency which were carriers of high-energy devices (ICD and ICD-CRT) with remote monitoring and who received intravenous iron therapy with ferric carboxymaltose in the years 2012-2015. We recorded their clinical characteristics, parameters of remote monitoring and adverse events during 3 months follow-up.
Results: We studied 32 patients (65 years, 30% women). We observed an improvement in NT-proBNP values at three months of intravenous iron treatment (2369 mg/dL vs 1510 mg/dL, $p = 0.01$). Mean heart rate at night was lower after three months of the treatment (73bpm vs 69bpm, $p = 0.024$), without significant differences in mean heart rate during the day (75bmp vs 72 bmp, $p = 0.2$), number of ventricular extrasystoles (138 vs 136, $p = 0.17$), ventricular doublets (54 vs 45, $p = 0.25$), and non-sustained ventricular tachycardia (8.3 vs 0.2, $p = 0.29$), although a reduction of these was observed after the three months of treatment. An increase in the number of hours of physical exercise performed was objetified after the intravenous treatment (2.2 vs 2.6, $p = 0.021$). Comparing the number of HF decompensations in the year prior to treatment with the events in the subsequent follow-up (decompensation of HF and/or death), a statistically significant reduction was observed (51.4% vs 12.9%, $p < 0.001$). There were no complications associated with the infusion and all patients had good treatment tolerance.
Conclusions: 1. We observed a tendency to reduce the mean heart rate and the number of ventricular extrasystoles and non-sustained ventricular tachycardias assessed by remote monitoring at 3 months of the treatment.
2. After the treatment the patients realized more physical activity and had less decompensations of HF.

P1812
Anaemia and iron deficiency in Heart Failure: role of chronic anticoagulant and antiplatelet therapies.

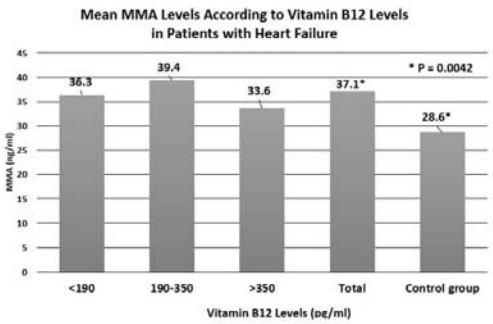
F Nicoli[1]; C Vignati[2]; A Del Torto[1]; N Corrieri[1]; A Bonomi[2]; T Calogero[2]; M Mapelli[2]; D Brusoni[2]; A Apostolo[2]; PG Agostoni[2]
[1]*University of Milan, Milan, Italy*; [2]*Cardiology Center Monzino IRCCS, Milan, Italy*

Introduction: Anaemia and iron deficiency are frequently reported comorbidities of Heart Failure (HF) and adverse prognostic factors associated with an independent risk for HF hospitalization and mortality.
Purpose: It's known the prevalence of anaemia increases with HF severity and other comorbidities (advanced age, female gender, renal disease, diabetes mellitus). We investigated a correlation between anaemia/iron deficiency in HF and chronic anticoagulant and/or antiplatelet therapies, either alone or in combination.
Methods and Results: We retrospectively studied 629 patients hospitalized for HF between Dec 2013 and Aug 2016, 65% men. We collected values of blood count, iron status, creatinine, INR and BNP in different groups based on either anticoagulant or antiplatelet therapy or both: group 1 (no therapy, n=104), group 2 (Vitamin K Antagonists (VKAs), n=194), group 3 (either a VKAs or a Novel Oral Anticoagulant (NOAC), plus antiplatelet therapy, n=65), group 4 (NOACs alone, n=39) and group 5 (antiplatelet therapy alone, n=227). The prevalence of iron deficiency and anaemia were respectively 75.99% (male 73%, female 82%) and 51.35% (male 49.3%, female 55.15%). We found a difference in the prevalence of anemia among HF classes based on LVEF (p 0.0067) and a correlation between the severity of anaemia (moderate anaemia) and female sex (p 0.0114). We found at the multivariate analysis predicting factors of anaemia (age, creatinine and RDW for the presence of anaemia; female sex, RDW and OSAS for the severity) and iron deficiency (RDW alone). Therefore we used Anova analysis corrected by confounding factors to obtain a comparison between all groups' variables, achieving significant differences on INR ($p<0.0001$), as parameter of good accuracy of data collection, but also on ferritin (p 0.015) and transferrin ($p < 0.0001$). In particular we found significant differences in ferritin between group 1 and 2 (p 0.0586) and in transferrin between group1 and 2 (p 0.0013) and between group 2 and 5 ($p < 0.0001$). Haemoglobin had only a typical trend with the highest value in group 4 (adjusted mean 13.3 g/dL, C.I. 95% 12.6-14), which was the same in all the previous sequence analysis.
Conclusion: We analyzed a population with prevalence of iron deficiency and anaemia in perfect line with European data, obtaining predicting factors of them and a different prevalence of anaemia in the HF classification. We demonstrated a correlation between the severity of anaemia and female sex and a significant iron deficiency in VKA patients. Haemoglobin had a typical trend that was maintained in all progressive analysis between groups based on antiplatelet and/or anticoagulant therapies, with the highest value in patients with NOACs therapy alone. The absence of statistical significance may result from the different numeric composition of groups. We expect it will be achieved by increasing the sample size of the population, due to an increasing of NOACs prescription.

P1813
Methylmalonic acid in patients with heart failure

K Polytarchou[1]; D Varvarousis[2]; C Pantziou[3]; C Psachoulia[3]; N Christodoulis[3]; D Oikonomou[4]; G Feredinos[4]; K Manousiadis[4]; K Triantafyllou[4]; N Sakellaris[4]; K Kappos[4]; S Ioannidou[3]; A S Manolis[1]
[1]*Athens University Shool of Medicine, Third Department of Cardiology, Athens, Greece*; [2]*Nikea General Hospital, Second Department of Cardiology, Athens, Greece*; [3]*Evangelismos General Hospital of Athens, Department of Biochemistry, Athens, Greece*; [4]*Evangelismos General Hospital of Athens, First Department of Cardiology, Athens, Greece*

Background: Vitamin B12 deficiency in patients with heart failure (HF) might be underestimated. These patients may have "falsely" normal vitamin B12 serum levels due to coexisting hepatic dysfunction. Methylmalonic acid (MMA) has been identified in several studies as an early indicator of vitamin B12 deficiency. Data regarding vitamin B12 and MMA in patients with HF are scarce.
Aim: To investigate vitamin B12 and MMA serum levels in HF patients.
Methods: 47 consecutive patients admitted to our hospital with symptoms and signs of acute decompensated heart failure were included in the study. Demographic and clinical characteristics as well as echocardiographic parameters were recorded. Blood samples were collected during the first 24 hours of hospitalization and complete blood count, creatinine, vitamin B12, NT-pro BNP and MMA levels were measured. A total of 12 healthy individuals (blood donors) constituted the control group, whereby MMA serum levels were also measured.
Results: Preliminary analysis of data among 47 HF patients (aged 70.5 ± 12.5 years; 50% with ischemic cardiomyopathy) indicated typical systolic dysfunction (redused left ventricular ejection fraction-LVEF $< 40\%$,HFrEF) in the majority (77.7%) of patients, mild systolic dysfunction (mid-range LVEF 40-49%, HFmrEF) in 8.3% and preserved systolic function (preserved LVEF $\geq 50\%$, HFpEF) in 11.1%; right heart failure was present in 57.4%. Mean hematocrit was $38.2 \pm 7.9\%$, creatinine 1.17 ± 0.31 mg/dl, and NT-proBNP levels 4694.4 ± 4260.1 pg/ml. Vitamin B12 levels averaged 358.8 ± 221.8 pg/ml. MMA levels were 37.1 ± 10.1 ng/ml in HF patients and 28.6 ± 2.7 ng/ml in the control group ($p = 0.0042$). In patients with vitamin B12 at lower normal levels (< 350 pg/ml), MMA was high (mean 39.4 ± 9.4 ng/ml) and in patients with higher normal vitamin B12 levels (>351 pg/ml), MMA levels were low (mean 33.6 ± 9.3 ng/ml, $p = 0.08$) , but still higher than control patients (Figure).
Conclusion: Patients with HF may have elevated levels of serum MMA, possibly indicating a subclinical vitamin B12 deficiency state.



Methylmalonic acid (MMA) levels

P1814

Sleep-disordered breathing is linked to peripheral endothelial dysfunction and not to myocardial function in ischemic stroke: A mechanistic link complicating the acute phase

N Nadja Scherbakov[1]; A Sandek[2]; N Ebner[2]; M Valentova[2]; AH Nave[2]; E Jankowska[3]; JC Schefold[4]; S Von Haehling[2]; SD Anker[2]; JB Fiebach[1]; KG Haeusler[1]; W Doehner[1]
[1]Center for Stroke Research CSB, Charite University Medical School, Berlin, Germany; *[2]University Medical Centre Göttingen, Innovative Clinical Trials, Department of Cardiology and Pneumology , Göttingen, Germany*; *[3]Wroclaw Medical University, Wroclaw, Poland*; *[4]Bern University Hospital, Bern, Switzerland*

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Introduction: Sleep-disordered breathing (SDB) after acute ischemic stroke is frequent and may be linked to stroke-induced autonomic imbalance.
Methods: In the present single-center study we assessed SDB by transthoracic impedance records integrated into Holter system. Additionally, peripheral endothelial dysfunction (ED) using reactive hyperemia index [RHI] was assessed using pulse arterial tonometry device in the acute phase of ischemic stroke and one year afterwards in patients without a history of SDB prior the stroke. Cardiac systolic and diastolic function was assessed by transthoracic echocardiography.
Results: SDB was observed in-hospital in 56 (57%) out of 99 patients with acute ischemic stroke (69 ± 11 years, 73% male, median NIHSS 5 [2.25-7.75], BMI 27.8 ± 3.4 kg/m^2). Compared to patients without SDB (68 ± 13 years, 49% males, median NIHSS 3 [2-4], BMI 28.6 ± 5.7 kg/m^2), ED was significantly prevalent in patients with SDB (32%vs. 64%; $p < 0.01$). After adjustment for multiple confounders, presence of SDB remained independently associated with ED (odds ratio 3.38 [CI 1.27-9.01], $p < 0.05$). Forty-one patients underwent repetitive measurements one year after stroke (12.8 ± 0.8 months). The prevalence of SDB decreased from 59% to 14% in this cohort ($p < 0.001$). Compared to patients without SDB, ED remained impaired in stroke patients with persisting SDB ($p < 0.05$). Presence of impaired left ventricular ejection fraction (LVEF) had additional impact on severity of SDB (median AHI 11.3 [IQR 10.75-43.25]) compared to patients with normal LVEF (median AHI 4.7 [2-10]) or preserved LVEF (median AHI 5.1 [7-28], $p < 0.05$). However, no significant difference in prevalence of SDB was observed between all three groups. In addition, LVEF and atrial fibrillation was not associated with presence of SDB in logistic regression analysis.
Conclusions: SDB was highly prevalent in acute stroke. Presence of the SDB was independently associated with peripheral ED but not cardiac function. Peripheral ED improved with the recovery to normal breathing pattern suggesting a mechanistic link of SDB and ED in ischemic stroke.

P1815

Sleep apnea syndrome in patients with chronic heart failure

CC Diaconu[1]; D Berceanu[2]; D Bucur[2]; D Belciu[2]; GN Dediu[3]; MA Iancu[4]; AR Zaki[2]
[1]University of Medicine and Pharmacy Carol Davila, Emergency Clinical Hospital Floreasca, Bucharest, Romania; *[2]Emergency Clinical Hospital Floreasca, Bucharest, Romania*; *[3]University of Medicine and Pharmacy Carol Davila, Emergency Clinical Hospital Sf. Ioan, Bucharest, Romania*; *[4]University of Medicine and Pharmacy Carol Davila, Family Medicine, Bucharest, Romania*

Introduction: Sleep apnea syndrome seems to be a frequent comorbidity in patients with heart failure. The purpose of the study was to analyze the frequency and impact of sleep apnea syndrome in patients with chronic heart failure, hospitalized in the Internal Medicine clinic of a University Clinical Emergency Hospital.
Methods: The study included 980 patients with chronic heart failure, consecutively admitted between January 1st, 2016-November 30, 2016. We have retrospectively and comparatively analyzed the frequency of sleep apnea syndrome and the clinical correlations in patients with chronic heart failure, using SPSS software.
Results: The distribution by sex in the group of study: 49.8% men, 50.2% women. The mean age of the whole group was 74 ± 11.6 years. The distribution of comorbidities in patients with chronic heart failure was: 66,84 % arterial hypertension, 39.9 % atrial fibrillation, 32.85 % coronary heart disease, 31.13 % chronic kidney disease, 28.87 % dyslipidemia, 26.23 % type II diabetes, 24.49 % pulmonary hypertension, 21.94 % obesity, 18.16 % bundle branch blocks, 16.94 % anemia, 7.85 % stroke, 7.14 % chronic obstructive pulmonary disease, 4.49 % sleep apnea, 0.51 % asthma. Sleep apnea syndrome was more frequent in men than women ($p < 0.01$). Heart failure patients with dyslipidemia had a higher frequency of sleep apnea syndrome ($p = 0.018$). A total of 392 patients had atrial fibrillation, of which 25 were also diagnosed with sleep apnea syndrome (6.37 %) vs 568 patients without atrial fibrillation, 20 having a diagnosis of sleep apnea syndrome (3.52 %). This difference was statistically significant ($p = 0.029$). 6 patients out of 656 hipertensive patients presented sleep apnea (0.91%) vs 39 patients with sleep apnea out of 324 normotensive patients ($p = 0.004$). 11 from 70 patients with chronic obstructive pulmonary disease were also diagnosed with sleep apnea vs 34 out of 910 patients without chronic obstructive pulmonary disease (15.72 % vs 3.74 %; $p < 0.001$).
Conclusions: Sleep apnea syndrome is a frequent comorbidity in patients with heart failure. Atrial fibrillation was more frequent in patients with heart failure and SAS than in patients with heart failure without SAS.

P1816

Consequences of obstructive sleep apnoea syndrome and hypertension on left ventricular diastolic function

L Mathe[1]
[1]IVth Medical Hospital, Tirgu-Mures, Romania

Study Objectives: Obstructive sleep apnoea syndrome (OSAS) is a frequent sleep disorder that is known to be an independent risk factor for arterial hypertension (AHT). Age, diabetes mellitus and obesity are considered as independent but additive factors. These factors are also contributors to left ventricular hypertrophy (LVH) and LV diastolic dysfunction (LVDD), which are important causes of cardiovascular morbidity. In this review, we present an overview of how OSAS may promote changes in LV geometry and diastolic dysfunction through its best-known cardiovascular complication, arterial hypertension. We hypothesized that the severity of sleep disordered breathing (SDB) would be associated with LVDD even for subclinical SDB.
Methods: This was a prospective long-term observational study. 56 participants had overnight polysomnography followed by transthoracic echocardiography. OSA was characterized by the apnea-hypopnea index (AHI, events/hour). The LVDD was assessed by echocardiography using combined categories with tissue Doppler imaging and left atrial (LA) volume measurement.
Results: 12 (21,4%) subjects were free sleep apnea (SA) AHI (apnea-hipopnea index ≤5/h), 15 (26,7%) had mild SA (AHI = 5-14/h), 17 (30,3 %) had moderate SA (AHI= 15-30/h) and 12 (21,4 %) had severe SA (AHI≥30/h). Among the participants, 27 patients (48,21 %) had LVDD. The prevalence of LVDD increased with the SDB severity from 8.6 % (normal) to 12.7 % (mild) to 40.0 % (moderate-to-severe SDB) ($p < 0.0001$). In the multivariate logistic regression analysis, the odds ratio of having LVDD in the moderate-to-severe SDB group vs. normal group was 5.96 (95 % CI, $P = 0.006$).
Conclusions: OSA is associated independently with diastolic disfunction. Echocardiographic measures of adverse cardiac remodeling are strongly associated with OSA and AHT, but are confounded by obesity. Hypoxia could be a stimulus for hypertrophy in individuals with OSA.

P1817

Elevated B12 levels in systolic heart failure patients - associations with right heart failure and impaired prognosis

D Ural[1]; O Argan[2]; M Aktas[3]; K Karauzum[4]; IY Karauzum[5]; G Kozdag[5]; AA Agir[5]
[1]Koc University, Istanbul, Turkey; *[2]Kocaeli State Hospital, Department of Cardiology, Kocaeli, Turkey*; *[3]Eregli State Hospital, Department of Cardiology, Zonguldak, Turkey*; *[4]Kocaeli Derince Hospital, Kocaeli, Turkey*; *[5]Kocaeli University, Faculty of Medicine, Department of Cardiology, Kocaeli, Turkey*

Background and Purpose: Unfavorable impact of iron deficiency on the outcome of heart failure (HF) has been well established, but the clinical implications of B12 and folic acid are not clear. The aim of the present study was to investigate clinical correlates and prognostic value of vitamin B12 and folic acid levels in HF patients with reduced ejection fraction HF (HFrEF).
Methods: The study group consisted of 129 chronic stable HFrEF patients with a functional class of NYHA II-IV and 50 controls. Data regarding clinical, echocardiographical and laboratory features with special emphasis on symptoms and signs of right heart failure were recorded for all patients. Vitamin B12 and folic acid levels were estimated by chemiluminescence assay. Primary endpoint of the study was all-cause mortality.
Results: Median ejection fraction of the HFrEF patients was 25% (range 10-45%), and 71 of them (55%) had symptoms or signs of right HF. Median B12 levels in HFrEF patients with were significantly higher compared to controls (270 pg/ml vs. 198 pg/ml; $p = 0.005$), but folic acid was similar between the study groups (7.7 ng/ml vs. 8.5 ng/ml; $p = 0.305$). Univariate correlates of serum B12 were age, ischemic etiology, NT-proBNP, eGFR, uric acid, total cholesterol, direct bilirubin, AST and albumin. In stepwise linear regression analysis, direct bilirubin was the most important independent determinant of serum B12 levels (B 135, 95%CI[B] 93-177; $p < 0.001$) followed by age and ischemic etiology.Patients were followed for a median duration of 16 (13-17) months. Death occurred in 25 patients. B12 levels were significantly higher in deceased patients compared to survivors (379 [274-499] pg/ml vs. 249 [181-399] pg/ml; $p = 0.005$), but folic acid was not different among the two groups. ROC analysis showed that B12 values ≥270 pg/mL had 80% sensitivity and 56% specificity for predicting all-cause mortality (AUC 0.69, 95%CI 0.58-0.80; $p = 0.005$).

In Cox regression analysis, independent determinants of death were age (exp[B] 1.061, 95%CI 1.018-1.107; p = 0.005), presence of abdominojugular reflux (exp[B] 0.291, 95%CI 0.114-0.741; p = 0.010) and severe tricuspid regurgitation (exp[B] 0.068, 95%CI 0.017-0.269; p < 0.000). Despite having a significant univariate association with all-cause mortality, B12 level lost its significance in multivariate analysis.
Conclusions: Increased B12 in HFrEF patients is associated with increased direct bilirubin due to right HF, but neither B12 nor folic acid were independently associated with mortality.

P1818
Chronic kidney disease criteria are common in hospitalized patients arterial hypertension and diabetes mellitus

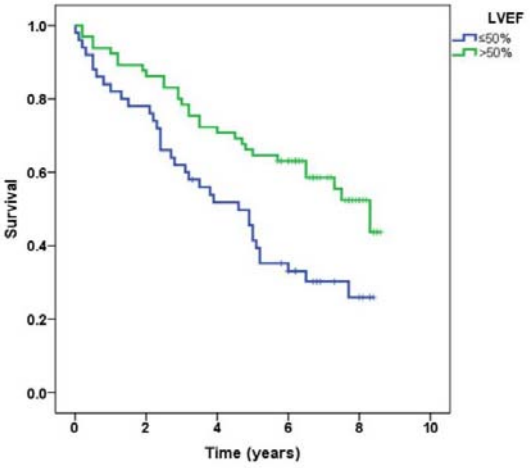
V Kulakov[1]; N Manukhina[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background and aim: Chronic kidney disease (CKD) is accepted as an independent cardiovascular disease (CVD) risk factor. Type 2 diabetes mellitus (T2DM) and arterial hypertension (AH) are leading risk factors for both CVD and CKD. The aim of the study was to assess the prevalence of decreased glomerular filtration rate (GFR) and high/very high albuminuria in patients with AH and T2DM.
Methods: In 319 patients with AH and T2DM admitted in city clinical hospital (37% men, age 65 ± 11 years (M ± SD), body mass index 30 ± 7 kg/m^2, blood pressure 135 ± 16/80 ± 9 mmHg, median AH duration 12 years (interquartile range 10;15), T2DM duration 10 years (4;15), dyslipidemia 70%, chronic heart failure 50%, anemia 28%, atrial fibrillation 20%) GFR was assessed by CKD-EPI equation and albuminuria – by albumin/creatinine ratio (ACR) in spot urine morning sample.
Results: GFR < 60 ml/min/1.73 m^2 was revealed in 127 (39.8%) patients, wherein GFR in the range of 45- < 60, 30- < 45, 15- < 30, < 15 ml/min/1.73 m^2 was found in 18, 17, 5 and 0.6% respectively. ACR>30 mg/g was detected in 123 (39%) of patients, wherein ACR in the range 30- < 300 and >300 mg/g was found in 29 and 10%. CKD criteria (GFR < 60 ml/min/1.73 m^2 and/or ACR>30 mg/g) were detected in 182 (57%) patients. Non-albuminuric CKD (GFR < 60 ml/min/1.73 m^2 without albuminuria) was found in 59 (18.5%) patients, isolated (without GFR decrease < 60 ml/min/1.73 m^2) high/ very high albuminuria - in 55 (17%) patients, combined decreased GFR and high/very high albuminuria – in 68 (22%) patients. Patients with vs without albuminuria were older (67.2 ± 10.8 vs 63.7 ± 10.7 years), more aware of kidney diseases (59 vs 41%), had lower level of hemoglobin (122 ± 23 vs 130 ± 21 g/l), p < 0.05 for all. Patients with vs without CKD criteria were older (67 ± 10 vs 60 ± 11 years), had higher prevalence of anemia (34 vs 10%), heart failure (55 vs 32%).
Conclusions: High prevalence (57%) of CKD criteria was revealed in hospitalized patients with AH and T2DM. GFR < 60 ml/min/1.73 m^2 was found in 39.8% of patients, ACR>30 mg/g – in 39%, combined decreased GFR and high/ very high albuminuria – in 22% of patients.

P1819
Impaired left ventricular function predicts all-cause and cardiovascular mortality in patients with renal failure: a 5-year prospective study

C Chris Kapelios[1]; I Eleftheriadou[1]; A Tentolouris[1]; D Doulgerakis[1]; I Moyssakis[1]; S Chorepsima[1]; S Michail[1]; N Tentolouris[1]
[1]*Laiko University General Hospital, Athens, Greece*

Introduction: Chronic kidney disease (CKD) is a global health problem with major socioeconomic impact. In the last decades intense scientific interest has been dedicated to the increased cardiovascular (CV) mortality of patients with CKD. Numerous studies have attempted to identify risk factors for morbidity and mortality in patients with CKD, especially in patients with renal failure (RF) (estimated glomerular filtration rate [eGFR] < 15 mL/min/1.73 m2). The aim of our study was to prospectively evaluate the prognostic value of indices of LV function in all-cause and CV mortality in patients with RF.
Methods: A total of 133 consecutive patients with RF were included in the study. We recorded a) the baseline characteristics of the patients, including left ventricular function parameters, and b) the long-term outcomes, and used uni- and multi-variate proportional hazards models to identify predictors of all-cause and CV during long-term follow-up. The patients' survival rates were analyzed by the Kaplan-Meier method and compared using the log-rank test. All P values were two-sided and a value < 0.05 was considered statistically significant.
Results: Complete follow-up data was available for 123/133 (92.5%) patients who were included in the final analysis. Mean age of the population was 59.5 ± 14.6 years and 64.2% were males. Diabetes was present in 39% of patients, whereas 58(47.2%) had a history of CVD at baseline. Mean left ventricular ejection fraction (LVEF) was 50.9 ± 6.9% and eGFR was 10.7 ± 1.6 ml/min/1.73m^2. The patients were followed for 4.9 ± 2.6 years (median 5.9 years), A total of 69 deaths were recorded: 36 CV, 21 non-CV and 12 of unknown cause. After adjustment for age, waist circumference, smoking status, history of diabetes mellitus and coronary artery disease, serum glucose and triglycerides, LVEF was identified as an independent predictor of all-cause (HR: 0.950; 95%CI: 0.916-0.985, P=0.006) and CV mortality (HR: 0.935; 95%CI: 0.885-0.988, P=0.018). Based on the mean value of LVEF the study population was divided into two groups. The cumulative survival rates at follow-up were 30% and 55.4% for patients with a LVEF ≤50% vs. >50%, respectively (p = 0.004) [Figure].
Conclusion: LVEF represents an independent risk factor for all-cause and CV mortality in patients with RF. These findings strongly suggest that left ventricular function assessment could be utilized for risk stratification and potential treatment tailoring of patients with RF.



P1820
Cardiac masses in pediatric population

R Rania Hammami[1]; D Abid[1]; B Rekik[1]; F Mroua[1]; F Triki[1]; S Charfeddine[1]; L Abid[1]; S Kammoun[1]
[1]*Hedi Cheker Hospital, Department of Cardiology, Sfax, Tunisia*

Introduction: Infant heart masses are rare. Most are benign tumors. Rhabdomyomas constitute the most common tumor. Malignant tumors are exceptional. Antenatal diagnosis is possible and it requires perinatal monitoring in order to optimize the management and prognosis.
Patients and methods: it was a retrospective study between January 2008 and December 2016, including all patients aged less than 16 years with heart masses diagnosed with transthoracic or fetal echocardiography
Results: Of the 6451 pediatric transthoracic echocardiography and 364 fetal echocardiographs performed during the study period, 12 cardiac masses were identified with an incidence of 0.17%: nine cases of rhabdomyomas, 1 case of intrapericardial immature teratoma,1 case of hydatid cyst and 1 case of cardiac thrombus in a patient with coarctation of the aorta with left ventricular dysfunction. The diagnosis was made in antenatal in 8 cases of rhabdomyoma and in the case of teratoma. Five patients with intraventricle rhabdomyoma showed heart failure symptoms. The evolution was favorable with total or partial regression of all cases of rhabdomyomas, it was fatal in patients with immature teratoma (patient died after tamponade) and with hydatid cyst (patient died following the intracardiac rupture of the cyst). The cardiac thrombus disappeared under anticoagulant treatment and the patient evolved well after surgery of the coarctation.
Conclusion: Clinical presentation, treatment and progression of cardiac tumors are variable. Rhabdomyomas have an excellent prognosis. Fetal echocardiography significantly improved diagnosis and management of such patients.

P1821
Association of genetic polymorphism of TCF7L2 with the severity of cardiac remodeling and adipokines disbalance in comorbidity of essential hypertension and type 2 diabetes

A Shalimova[1]; O Bilovol[1]; L Bobronnikova[1]
[1]*Kharkiv National Medical University, Clinical Pharmacology, Kharkiv, Ukraine*

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. Nowadays one of the worldwide

popular medical studies is the study of the genes responsible for the development of insulin resistance, which is an important part in the formation of DM2. Meanwhile the role of heredity in another pathogenetic link of DM2 – genetic defects in β-cells of the pancreas is still less studied. It is believed that gene polymorphism Transcription Factor 7-Like 2 (TCF7L2) affects the amount and functional activity of the β-cells.

Objective: to establish the association of genetic polymorphism of TCF7L2 with the severity of cardiac remodeling and adipokines disbalance in EH and concomitant DM2 in Ukrainian population.

Design and Method: We examined 320 patients aged from 45 to 60 years old with EH stage II, grade 2 and concomitant DM2, moderate, subcompensated (main study group); 90 patients with EH without DM2 (comparison group) and 31 healthy individuals (control group).

Methods: echocardiography, enzyme immunoassay (determined levels of adiponectin and leptin). Rs7903146 polymorphism of TCF7L2 was assessed by molecular genetic method.

Results: Allele T, which according to some scientists is associated with the development of DM2, occurred in significantly more patients of the main group as compared to the group of patients without DM2 ($p < 0.01$) and the control group ($p < 0.001$): 16.9% of main group patients had homozygous genotype T/T and 47.2% of patients had heterozygous genotype C/T. At the same time C/C genotype was established only in 35.9% of main group patients while in 48.9% of comparison group patients and in 61.3% of control group patients was diagnosed genotype C/C.

It was found that patients with homozygous T/T and heterozygous C/T genotypes had a more pronounced cardiac remodeling than patients with genotype C/C: significantly ($p < 0.05$) lower ratio of the maximum velocity of early and late left ventricle filling (E/A) and significantly ($p < 0.01$) higher ratio of peak e and E on the mitral valve in the spectral and tissue Doppler (E/e). It was also established that patients with genotypes C/T and T/T of TCF7L2 gene had significantly lower levels of adiponectin ($p < 0.001$) and leptin ($p < 0.05$), than carriers of genotype C/C. In comparison group TCF7L2 polymorphism did not affect the severity of cardiac remodeling and adipokines disbalance.

Conclusions: genetic polymorphism of TCF7L2 gene is associated with the development of comorbidity of EH and DM2 in Ukrainian population. Rs7903146 gene polymorphism of TCF7L2 affects the severity of cardiac remodeling and adipokines disbalance in comorbidity of EH and DM2. Patients with EH without DM2 had no significant difference of indicators of cardiac remodeling and adypokines levels depending on polymorphism of TCF7L2 gene.

P1822

Sodium-glucose co-transporter-2 inhibitors as oral antidiabetic in patients wit heart failure

J Jose Morgado[1]; JRG Roa Garrido[1]; PRO Rodriguez Ortega[1]; BMM Martinez Mora[1]; SCF Camacho Freire[1]; TMS Moraleda Salas[1]; ALS Lopez Suarez[1]; JDF Diaz Fernandez[1]

[1]*Hospital Juan Ramon Jimenez, Cardiology, Huelva, Spain*

Background/Introduction: There is a relationship between the prevalence of heart failure (HF) and Diabetes Mellitus Type 2 (T2DM), resulting the most prevalent comorbidity in DM.Furthermore, HF has worse prognosis in patients with T2DM.Recently, a randomized trial with a Co-Transporter-2 Inhibitors(SGLT-2 inhibitors)has reduced cardiovascular mortality and hospitalizations for HF.This class of therapy reduces blood glucose levels,blood pressure,produce an osmotic diuresis and weight loss.

Purposes: Evaluate the efficacy and safety of SGLT-2 inhibitors in patients with T2DM and HF.

We want to assess possible changes of metabolic and HF situation, and check security of this treatment. We quantify: Glycemic control (A1c).

Body mass index (BMI). Improvement in heart failure situation (functional class, value of N-terminal prohormone of brain natriuretic peptide: NTproBNP). Decrease in diuretic dose. Check security of the treatment.

Methods: Prospective, analytical and observational,unicentric study on T2DM patients who do not reach therapeutic objective with oral antidiabetic medications(glycohemoglobin higher 6.5%)and suffer HF(admission for HF in the last 6 months or high level of NTproBNP plus HF symptoms),independent of left ventricular ejection fraction (LVEF). N:11 patients.7 patients received canagliflozine,3 empagliflozine and 1 patient dapagliflozine. We start treatment with SGLT2 inhibitors at stable HF situation, understood as unchanged treatment for heart failure during 3 months. We calculate at beginning and after 90 days next measures: Heart failure situation: NTproBNP, New York Heart Association (NYHA) classification, dose of diuretic.

Metabolic control: A1c, BMI.

Security: hypoglycemia epysodes.

Results: Basal characteristics: Mean age was 66.4 ± 8.6 years, 37 % female, 100% with hypertension. Mean LVEF was 40.4 ± 10%, mean NT-proBNP level was 1430 ± 1243 pg/mL, and the mean of dose of furosemide was 52.7 ± 38.2 mg daily. Mean BMI was 27.9 ± 4.2 kg/m2 and mean A1c 8.45 ± 1.43 %. 73.6% of patients received metformin and 90.9% another oral antidiabetic medication, 63.5% used insulin. Follow-up (90 days): A significant reduction was observed in NT-proBNP values (mean 978 ± 900 pg/mL, $p < 0.05$), BMI (mean 26.7 ± 3.7 kg/m2 , $p < 0.05$), A1c (mean 7.8 ± 0.8 %, $p < 0.05$) and dose of furosemide (mean 53.1 mg ± 37 mg daily, but $p > 0.05$). Furthermore, a significant reduction of rates of admission for Heart Failure was shown (from 1.3 ± 0.8 90 days before to the beginning of SGLT2 inhibitors to 0.01 ± 0.3 90 days after the treatment with SLGT2 inhibitors, $p < 0.05$). It did not show hypoglycaemia epysodes.

Conclusions: This is a pilot study which shows beneficial effects of SGLT-2 inhibitors in patients with Heart Failure and Diabetes Mellitus, improving HF situation and metabolic control. This study has several limitations, specially the short follow-up and small sample size. So, bigger studies, are required to contrast these hypotheses.

P1823

Co-morbidities and fragility are determinants of survival in patients with heart failure and mildly reduced ejection fraction

P Moliner[1]; P Gastelurrutia[1]; J Lupon[1]; X Yang[2]; M De Antonio[1]; M Domingo[1]; S Altimir[1]; B Gonzalez[1]; M Rodriguez[1]; C Rivas[1]; E Fung[2]; E Zamora[1]; J Santesmases[1]; J Woo[2]; A Bayes-Genis[1]

[1]*Germans Trias i Pujol University Hospital, Badalona, Spain*; [2]*The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR People's Republic of China*

Background: Heart failure (HF) is a chronic condition highly prevalent among older people. Due to this fact, fragility and co-morbidities are often present among HF patients. The 2016 Heart Failure (HF) ESC Guidelines boost to investigate the "new" subgroup of patients with HF and left ventricular ejection fraction (EF) mildly reduced (HFmrEF).

Purpose: Our aim was to assess the effect of co-morbidities and fragility on long-term prognosis in ambulatory HFmrEF patients, and to compare it with those observed in HF with reduced (HFrEF) and preserved (HFpEF) EF.

Methods: A score of co-morbidities was created, ranging from 0 to 7, that includes diabetes, hypertension, COPD, renal failure, anemia, peripheral arteriopathy and atrial fibrillation. Fragility was defined as having at least one abnormal evaluation among 4 standardized geriatric scales. Predefined criteria for such scales were: Barthel Index <90; OARS scale <10 in women and <6 in men; Pfeiffer Test >3 (± 1, depending on educational grade); and ≥ 1 positive response for depression on the abbreviated GDS. Median follow-up was 4.9 years [P25–75: 2.5–8.4] for living patients. All-cause death, HF-related hospitalization and the composite end-point of both were assessed.

Results: 169 patients with HFmrEF were evaluated (116 men and 53 women, mean age 67.2 ± 11.8 years, median duration of HF 13 months [Q1-Q3 2–44], ischemic aetiology 58.6%, 104 (61.5%) and 58 (34.3%) in NYHA class II and III respectively) and compared with 999 patients with HFrEF and 146 patients with HFpEF. The number of co-morbidities in HFmrEF patients (2.37 ± 1.6) was similar to that in HFrEF 2.28 ± 1.4 ($p = 0.45$) and significantly lower ($p < 0.001$) than that in HFpEF patients (3.04 ± 1.4). In contrast fragility was more prevalent in HFmrEF (50.3%) than in HFrEF patients (41.5%), $p = 0.03$ and similarly prevalent than in HFpEF (55.5%) patients, $p = 0.36$. During follow-up 78 deaths, 32 HF-related hospitalizations and 85 composite end-points were documented. Co-morbidities and fragility were significantly associated with the 3 end-points: HR 1.56 [1.34–1,82], $p < 0.001$ and HR 2.95 [1.84–4.72], $p < 0.001$ for all-cause death respectively; HR 2.01 [1.58–2.57], $p < 0.001$ and HR 2.27 [1.10–4.67], $p = 0.03$ for HF-related hospitalization respectively; and HR 1.64 [1.41–1.90], $p < 0.001$ and HR 2.80 [1.79–4.39], $p < 0.001$ for the composite end-point respectively. These figures were higher in all the end-points (from 4% to 105%) than that observed in HFrEF and HFpEF patients. In multivariable analysis containing also age, sex NYHA functional class and ischemic aetiology the number co-morbidities remained independently associated with all-cause death ($p = 0.03$), HF-related hospitalization ($p < 0.001$) and the composite end-point ($p < 0.001$) and fragility with all-cause death ($p = 0.01$) and the composite end-point ($p = 0.02$).

Conclusion: Co-morbidities and fragility are determinant of outcome in ambulatory patients with HFmrHF, even more than in HFrEF and HFpEF patients.

P1824

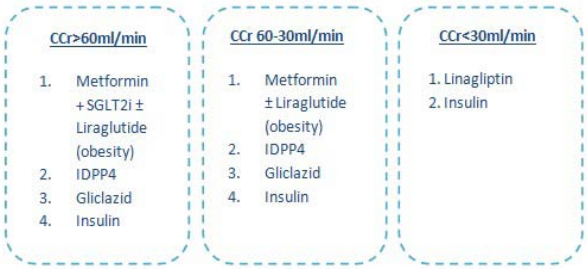
Do we optimize antidiabetic treatment in HF patients?

S Sara Blasco[1]; FJ Camacho[1]; I Lobo[1]; C Collado[1]; P Gonzalez[1]; JA Sanchez-Brotons[1]; I Perez[1]; E Martinez De Morentin[1]; M Iravedra[1]; J Lozano[1]; M Maestre[1]; P Martinez Romero[1]; FJ Morales[1]

[1]*Puerto Real Hospital, Cardiology, Puerto Real, Spain*

Introduction: The latest Heart Failure and Cardiovascular Prevention ESC Guidelines have shown the benefits of empagliflozin in preventing and slowing down the

progression of Heart Failure (HF) and reducing cardiovascular mortality. Our goal is to describe the characteristics of diabetic patients hospitalized in the Cardiology Service, to analyze whether the ESC Guidelines recommendations are being followed, and to suggest new treatment protocols.
Material and Methods: Prospective and descriptive study of type 2 diabetic patients hospitalized in the Cardiology Service from June 15th to December 31st, 2016, comparing patients with chronic HF and de novo HF.
Results: From June 15th to December 31st, out of a total of 121 diabetic patients hospitalized, 33% had chronic HF (due to decompensated heart failure) and 14% were diagnosed with de novo HF. There were no differences found between both groups in regards to age (70 ± 9 vs. 69 ± 14), gender (67% males in chronic HF vs. 50% in de novo HF) nor other cardiovascular risk factors (HTA in 80% patients with chronic HF vs. 77% with de novo HF, 39% of chronic HF patients were or had been smokers vs. 38% with recent HF diagnosis, and nearly 95% of the patients in both groups had IMC ≥ 25). There were significant differences in regards to dyslipidemia (62% with chronic HF vs. 77% with de novo HF), hyperuricemia (42.5% with chronic HF vs. 70% with de novo HF) and creatinine clearance (50% with chronic HF had a creatinine clearance < 60ml/min vs. 38% in de novo HF patients). The average FEVI was 51% ± 13% in chronic HF group vs. 46% ± 17% in patients with de novo HF. Out of the chronic HF patients, 30% had HFrEF, 15% HFmrEF and 55% HFpEF, whereas 27% of the de novo HF patients had HFrEF, 27% HFmrEF and 44% HFpEF. All patients were being properly treated with Beta blockers, ACE inhibitors, and MRA drugs. Still, nearly 50% of the hospitalizations in all Diabetic 2 patients were due to Heart Failure. Regarding previous anti-diabetic drugs, none of the patients were being treated with an SGLT2 inhibitor. 57% of chronic HF patients were under Metformin (15% on its own), 17% sulfonylureas, 15% DPP4 inhibitor and 55% under insulin (15% as single-drug treatment). As for the de novo HF patients, 77% were under Metformin (10% as single-drug treatment), 27% sulfonylureas, 25% DPP4 inhibitor and 33% under insulin. Nevertheless, 40% of the patients with chronic HF and 27% of patients with de novo HF had HbA1c levels out of the target range.
Conclusions: We've detected that ESC guidelines aren't being followed in the use of anti-diabetic drugs in patients with cardiovascular diseases, unlike other cardiovascular risk factors that have well-established treatment protocols. As seen in our study, most of our patients could benefit from the use of the SGLT2 inhibitor to reduce cardiovascular mortality and the development of heart failure. Therefore, we suggest the following treatment protocol.



Anti diabetic treatment protocol

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

P1826
Clinical impact of patients with pure native aortic valve regurgitation undergoing transcatheter aortic valve replacement

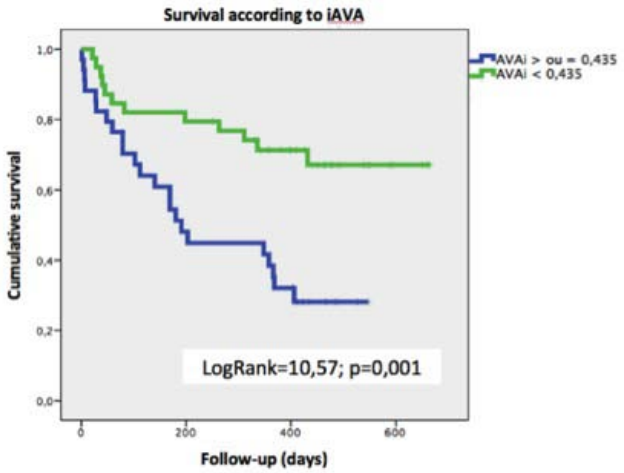
E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; AJ Dominguez-Franco[2]; JM Garcia-Pinilla[2]; L Morcillo-Hidalgo[2]; MF Jimenez-Navarro[2]; JH Alonso-Briales[2]; JM Hernandez-Garcia[2]; E De Teresa-Galvan[2]
[1]Department of Cardiology , Malaga, Spain; [2]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

There are patients with severe aortic regurgitation (AR) 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 clinical outcomes of patients with pure native aortic valve regurgitation undergoing with Transcatheter Aortic Valve Replacement (TAVR) and comparing them with patients with aortic stenosis.
Methods: Between April 2008 and December 2016, 16 consecutive patients with severe pure aortic regurgitation (AR) underwent TAVR with the self-expandable aortic valve prosthesis (CoreValve) and 566 patients with severe aortic stenosis (AS).
Results: The mean age and logistic EuroSCORE were (AR vs. AS) 73.1 ± 17 vs. 79.6 ± 6.2 years, p = 0.001 and 18.2 ± 8.9% vs. 17.49 ± 12, p = 0.818 respectively. There were significant differences in measurement of annulus and ascending aortic size (23.6 ± 2 vs. 22.03 ± 1.8 mm, p < 0.001 and 35.4 ± 5 vs. 31.1 ± 4.6 mm, p = 0.001, respectively). Implantation of prosthesis was performed successfully in all patients with AR and the degree of aortic regurgitation after procedure aortic was: none in 6 patients 37.5%), mild in 5 patients (31.3%), moderate in 3 patients (18.8%) and moderate-severe in two patients (12.6%).
The NYHA functional class improved from 3.37 ± 0.61 (baseline) to 1.37 ± 0.51 (one month) and remained stable at follow-up (1.4 ± 0.54). The mortality at 30 days was 6.3 % in patients with AR compared to 3.4% in patients with AS, p = 0.432 and there was non-significant differences with late mortality (33.3% vs. 33.3%, p = 0.996) after a mean follow-up of 36.5 ± 25 months.
The patients with AR had lower complications after procedure than patients with AS: Occurrence new-onset left bundle branch block 13.3% vs. 50% [OR=0.154 (95% CI 0.034-0.690), p = 0.005], stroke 0% vs. 3.7% [OR=0.971 (95% CI 0.958-0.985) p = 0.433], vascular complications 0% vs. 3.2% [OR=0.972 (95% CI 0.958-0.985) p = 0.468], acute myocardial infarction 0% vs. 1.6% [OR=0.972 (95% CI 0.959-0.986) p = 0.611] respectively.
Conclusions: Patients with pure native aortic regurgitation and and at high or extreme surgical risk might benefit from transcatheter-based therapy. The long-term outcome is favourable compared with patients with aortic stenosis underwent with TAVR.

P1827
Echocardiographic mortality predictors in patients with severe aortic stenosis not submited to valvular intervention

I S S Ines Goncalves[1]; I Ricardo[1]; J Rigueira[1]; JR Agostinho[1]; T Guimaraes[1]; AR Francisco[1]; GL Silva[1]; R Santos[1]; A Ferreira[1]; AG Almeida[1]
[1]Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal

Introduction: Severe aortic stenosis (AS) is one of the pathologies with the highest morbimortality in Cardiology and aortic valvular intervention (AVi) is the only procedure capable of modifying prognosis. The importance of echocardiography in the diagnosis, classification of severity and follow-up is well established. However, it is not clear how the echocardiographic data can allow to assess the risk in AS and, thus, help to guide the therapy.
Purpose: To determine the echocardiographic mortality predictors in patients (pts) with the diagnosis of AS, prior to AVi.
Methods: A retrospective unicentric study was made, with inclusion of consecutive pts with AS (excluding low flow low gradient and paradoxical aortic stenosis), diagnosed during the year of 2015 at a tertiary center, which were not submitted to AVi untill the end of the follow-up period (November 2016). Clinical, laboratory and echocardiographic parameters were collected, and their relationships with mortality were analyzed, using the Cox regression statistical method and Kaplan-Meier survival analysis.
Results: A total of 278 pts were included (54% women, mean age 74 ± 9 years), 86 of which were not submitted to AVi until the end of the follow-up (mean follow-up of 389 ± 186 days). In this subgroup (58.5% women, mean age 80.9 ± 8.7 years, mean NYHA class of 2), using a univariate Cox analysis, were determined as echocardiographic predictors of mortality: the aortic valve area (AVA) and indexed iAVA (p < 0.001), left ventricular ejection fraction (p < 0.001), moderate or severe mitral regurgitation (p = 0.038) and pulmonary systolic artery pressure (p = 0.018). In the multivariate analysis by Cox regression, the only independent predictor of mortality was iAVA (hazard ratio = 3.78; 95% CI 1.55-9.23, p = 0.004). A cut-off value of 0.435 cm2/m2 was determined as the most accurate value for the occurrence of death, as proven with Kaplan-Meier survival analysis (LogRank = 10.57, p = 0.001).
Conclusions: iAVA was an independent predictor of mortality in the natural history of AS. No other echocardiographic parameters, namely transvalvular gradients, exhibited independent prognostic significance. The use of this parameter for individualized prognostic stratification of patients with AS may be especially useful in oligosymptomatic patients in whom the role of valvular intervention and the optimum timing of its performance is not yet established.



Survival according to iAVA

P1828

Long-term results with conventional treatment approach for prosthetic valve endocarditis in patients with prior heart failure

MM Monica Mariana Baluta[1]; E Panaitescu[2]; MM Vintila[3]
[1]Carol Davila University of Medicine-St Pantelimon Clinical Emergency Hospital-Cardiology Department, bucharest, Romania; *[2]Carol Davila University of Medicine and Pharmacy , Medical Informatics and Biostatistics, Marketing, Medical Technology , Bucharest, Romania*; *[3]St. Pantelimon Emergency Hospital, Cardiology, Bucharest, Romania*

Introduction: The initial management strategy in prosthetic valve endocarditis (PVE) patients remains a matter of debate. Evidence based therapeutic strategies are lacking and difficult to be achieved in multicentric manner because prosthetic valve endocarditis (PVE) is a rare condition. The appropriate therapeutic strategies need ultimately to fit the patient.
Purpose: The aim of our work was to analyze if initial conservative intention to treat with antibiotics (AbT) in patients with PVE may influence short- and long-term prognosis and to identify factors for the adverse outcome of this strategy.
Methods: Retrospective analysis of 56 cases of early and late PVE, from 2000 to 2004, 20 women and 36 men, age 54.64 ± 11.34 years, 51.8% with early PVE and 48.2% with late PVE. 44 PVE episodes (78.6%) were treated with antibiotics only (AbG –antibiotic group) and 12 episodes (21.4%) with combined antibiotic and surgery (SurgG-surgery group). The analysis included data of hospital records. Survival at long-term follow up LTFU (12.87 ± 0.97 years) was obtained from National Insurance Database. Patients lost to follow up (n = 10) were excluded from our analysis.
Results: The cure of PVE was obtained with conventional therapy (antibiotics) for 71% of our patients and was independent of the AbT type (multivariate analysis). In the AbG in-hospital death rate was 2% and transfer rate due to complications 27%. 21.4% of patients referred for early surgery due to hemodynamic instability (58.3%), perivalvular extension of infection (75%), embolism (58.3%), and persisting fever (25%) have had a 66.6% survival rate.
Factors related to short-term mortality in this group were: age (p = 0.04), diabetes (p = 0.016), ischemic heart disease (p = 0.07), heart failure (p = 0.07), hemodynamic instability (p = 0.04), persistent fever (p = 0.06), anemia (p = 0.001). The AbT duration overall was 33.55 ± 12.8 days.
Short-term survival rate overall at the end of initial treatment was 90.4%. Long-term follow up survival rate was 44%, very low and relatively homogenous: 42.8 % SurgG, 44.1% AbG. Factors related to long-term mortality were advanced age (p = 0,0009), diabetes (p = 0.038), mid range LV ejection fraction (p = 0.038) and staphylococcus infection (p = 0.053).
Conclusions: In studied patients, there was a very high long-term mortality rates regardless of therapeutic strategy. Nevertheless, in selected patients, without complications, conservative approach could be adequate in the setting of short-term follows up. Younger and hemodynamically stable patients, with non-staphylococcal PVE and with preserved ejection fraction, who are carefully supervised, may be safely treated with antibiotics alone.
Whether the reasons of poor long-term results can be attributed to the lack of early surgery or to the progression of preexistent heart failure remains biased by the limited number of patient, high rate of lost to follow up and by the absence of current concept of "endocarditis team".

P1829

Patent foramen ovale: red flag in radiologically isolated syndrome

E Elisabeta Koci[1]; G Maresca[2]; E Signoriello[3]; G Puoti[3]; G Lus[3]; A Rapacciuolo[1]
[1]Federico II University Hospital, Department of Advanced Biomedical Sciences, Section of Cardiology, Naples, Italy; *[2]Unità Operativa di Interventistica Cardiovascolare, Presidio Ospedaliero Pineta Grande, Castel Voltu, Naples, Italy*; *[3]Second University of Naples, Multiple Sclerosis Center, II Division of Neurology, Department of Clinical and Experimental Medicin, Naples, Italy*

Objectives: To investigate the association of white matter lesions suggestive of demyelinating disease in magnetic resonance imaging (MRI) with patent foramen ovale (PFO) in migraine patients, with and without aura.
Materials: 22 migraine patients, 19 females and 3 males, with MRI evidence of white matter lesions suggestive of demyelinating disease. In 16 patients Barkhof criteria for dissemination in space were respected. For this reason, all the patients practiced further diagnostics including lumbar puncture, autoimmunity panel, thrombophilic evaluation, cardiological evaluation to detect the presence of PFO. Instrumental and clinical follow-up over three years was practiced and MIPAV software was used to analyse MRI imaging.
Results: 13 of 22 patients (59%) had PFO. Significant association was found between PFO and migraine with visual aura (p = 0.03) and thrombophilia (p = 0.04). None of them had oligoclonal bands in csf (p = 0.014). No difference in number, volume and distribution of the lesions between the patients with and without PFO was noticed and 11 out of 16 patients carrying Barkhof criteria for disseminating in space had PFO. The follow up showed a stationary lesion load in all PFO patients, no infratentorial or spinal cord lesions and no enhancement at any time. The presence of PFO didn't affect the lesions localization (periventricular, iuxtacortical, frontal, occipital, temporal or parietal) and corpus callosum lesion was never detected.
Discussion and conclusions: Migraine is often one of the main symptoms leading the patient to perform MRI, discovering, in most of the cases, white matter lesions of unspecific significance and placing always demyelinating diseases in differential diagnosis. Our study underlines the potential pathogenetic role of PFO in generating white matter lesions in migraine patients (59%), particularly in those with visual aura and thrombophilia. On the other side, with the evidence that 11 out of 16 patients carrying Barkhof criteria for disseminating in space had PFO and no clinical and instrumental diagnosis of demyelinating disease, we state that cardiologic evaluation represents a cardinal toll in differential diagnosis of RIS.

P1830

Risk factors, predictors and outcome of patients with complicated infective endocarditis in intensive care unit

F Farook Ahmad[1]; S Cox[2]; ST Chan[3]; E Abdul Rahman[4]; I Zainal Abidin[1]; MA Sadiq[5]
[1]Universiti Malaya Medical Centre, Division of Cardiology, Department of Medicine, Kuala Lumpur, Malaysia; *[2]HeartCare Partners, Department of Cardiology, Brisbane, QLD, 4066, Australia*; *[3]Putrajaya Hospital, Department of Internal Medicine, Pusat Pentadbiran Kerajaan Persekutuan, Presint 7, 62250 Putrajaya,, Malaysia*; *[4]Universiti Teknologi MARA, Department of Cardiology, Selangor, Malaysia*; *[5]Sultan Qaboos University , Cardiology Unit Department of Medicine, Muscat, Oman*

Introduction: Despite improvement in diagnosis and management, infective endocarditis related mortality and morbidity might occur even after successful treatment especially in patients with complicated IE needing medical intensive care unit (MICU) or coronary care unit (CCU) care. However, no previous study has explored the outcomes (for example, heart failure, myocardial infarction and cardiovascular death) in these patients.
Objective: This study investigates the short term, intermediate and long term outcome in patients with complicated IE admitted to MICU/CCU for medical treatment.
Method: A single – centre retrospective analysis was conducted among patients with complicated infective endocarditis requiring admission to MICU/CCU between 2001 and 2016. All patients fulfilled the modified Duke Criteria for definite diagnosis of IE. All patients undergo both transthoracic echocardiography (TTE) and then followed by transesophageal echocardiography (TOE). TTE was performed within 3 days on presentation to the hospital while TOE was performed within 3 days prior to transfer to MICU/CCU or on the day of transfer itself. The patients were identified via the hospital information system.
Results: 65 patients, with a mean age of 47 ± 10 years, were diagnosed with complicated IE, in which, 39 (60.0%) of them were male. IE survivors were defined as patients who survived after being discharged from MICU/CCU and at 6 months follow up with a documented diagnosis of IE. A total of 30 survivors form total patients

of 65 were identified. 50 patients required inotropic support and 41 patients developed multi-organ failure. 22% of the patients developed mobitz type II heart block or complete heart block. 9 patients of the mobitz type II heart block progressed to complete heart block requiring temporary/permanent pacemaker. Microbiology laboratory investigation showed 95% of the patients grew gram-positive cocci in their blood cultures. Surgical intervention was conducted in 30% of the patients and the remaining was medically treated. Biomarkers of acute infection, APACHE III as well as echocardiographic findings were analyzed. Using multivariate analysis, patients who developed acute kidney injury prior transfer to ICU (OR 9 95% CI 1.19–22.00, P = 0.03) or echocardiographic evidence of vegetation size > 15mm (OR 7 95% CI 1.07-17.71 P = 0.03) were identified as predictors for in-patient death.
Conclusion: In contrast to general IE populations, infectious agents and the type of infected impaired valve are not the main predictors of survival in critically ill IE patients. Our study concludes that markers for severity of illness (scores and organ failure) as well as echocardiographic findings of vegetations size >15 mm are independent risk factors for poor prognosis and mortality. In addition, early utilization of TOE to identify large vegetation prompting a more aggressive treatment approach to prevent septic emboli as well as reducing mortality.

P1831

Mitral balloon valvuloplasty: risk factors for lack of success, severe mitral regurgitation and major complications

I P Ivana Picone Borges[1] ; M Nascimento[1] ; ECS Peixoto[1] ; RTS Peixoto[1] ; RTS Peixoto[1]
[1]*Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil*

Background: Mitral balloon valvuloplasty is not always successful and free from complications.
Objectives: To determine the independent risk factors for an unsuccessful procedure, severe mitral regurgitation and major complications in mitral balloon valvuloplasty.
Methods: Longitudinal prospective study of 518 mitral balloon valvuloplasties performed between July 6, 1987 and December 31, 2004, on 429 (82.8%) female patients and 89 (17.2%) male patients with a mean age of 37.5 ± 12.8 years. Major complications were considered to be: perforation with cardiac tamponade, stroke and severe mitral regurgitation per procedure. The continuous variables were transformed in categorical variables and the chi-square or Fisher exact tests to compare the categorical variables, and logistic regression and multiple logistic regression were used to identify independent factors for predicting success, incomplete procedure, severe mitral regurgitation and major complications.
Results: Success was noted in 452 (94.2%) procedures, with major complications occurring in 22 (4.2%) patients, of which ten were severe mitral regurgitation; there were no per-procedure deaths, with four (0.8%) in-hospital deaths. In the multiple logistic regression, lower age predicted success in the procedure; the only variable that predicted an incomplete procedure was the initial period of the procedure, and a score >11 points predicted severe per-procedure mitral regurgitation. There was no independent predictor of major complications in this study.
Conclusions: Success was related to younger patients, an incomplete procedure to the initial period of the procedure and severe per-procedure mitral regurgitation to an echocardiography score >11 points

P1832

Balloon miral valvotomy for patients with mitral stenosis in atrial fibrillation :immediate and long terme prognosis

ALAEDD Jalled[1] ; MAJED Hassine[1] ; MAROUA Mahjoub[1] ; MEJDI Ben Messoud[1] ; HABIB Gamra[1]
[1]*University of Monastir, cardiology A departement, Monastir, Tunisia*

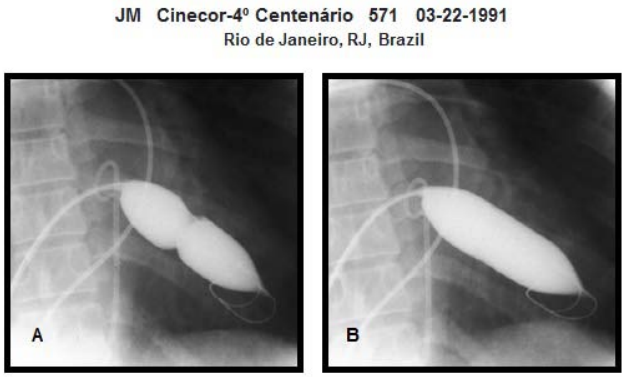
Background: Atrial fibrillation (AF) is a common finding in patients with severe mitral stenosis requiring Ballon Mitral Valvotomy (BMV). Its immediate and long term prognosis remains controversial
Objectivies: We sought to evaluate the effect of AF on immediate and long-term (23years) outcome of patients undergoing BMV
Methods: The immediate procedural and the long-term clinical outcome after BMV of 139 patients with AF were collected and compared with those of 381 patients in normal sinus rhythm (NSR).
Results: patients with AF were older (43.3 vs 29.7 years ; p < 0.001) , had frequently a history of systemic embolisim (9.4% vs 1.6% , p < 0.001) and of mitral commissurotomy (28.1% vs 19.4% , p = 0.035). Symptoms were similar between the tow groups (NYHA>II : 48.9% vs 49.9% , p = 0.648). patients with AF had more frequently a wilkins score >8 (51.4% vs 30.9% , p < 0.001), a larger left atrium (41cm2 vs 32cm2 , p = 0.001) and a lower transmitral gradient (11.1mmhg vs 16.6mmhg ,p < 0.001) BMV was equally successful in the tow groups (90.6% vs 94%, p = 0.187) but resulted in a smaller post BMV areas (2cm2 vs 2.15cm2 , p = 0.012) with a lower mitral valve area gain (0.9cm2 vs 1cm2 , p = 0.015)BMV was not associated with a higher risk of complications (4.3% vs 4.7% , p = 0.844) After a mean follow up of 74 months , patient with AF had the same rate of restenosis (28.3%vs 25.6%, p = 0.96) but required more frequently a mitral valve replacement (16.3% vs 7.7% , p = 0.012) They also experienced higher rates of systemic embolism (3.8% vs 0.6% , p = 0.018) and had a lower rate of event free survival (freedom from death , restenosis and systemic embolism) (52.2% vs 68.8% , p = 0.047). In the group of patients in AF , predictive factors for combined adverse event including death , restenosis , and systemic embolism and mitral valve replacement are : post BMV area < 2cm2 (OR:2.5, 95% CI [1.2; 5.18], p = 0.014) , procedural complication including severe mitral regurgitation and tamponnade (OR:3.95, 95% CI [1.4 ; 11. 13], p = 0.009) and NYHA II ,III during follow up (OR : 3.46 , 95% CI [2.09 ; 5.73], p < 0.001
Conclusion: our data support the fact that patient with AF have worse immediate and long term outcomes after BMV. Post BMV area < 2cm2 , procedural complications and dyspneapredict adverse events during follow up.

P1833

Percutaneous mitral valvuloplasty with balt single balloon and the long-term follow-up. Survival and event free survival

I P Ivana Picone Borges[1] ; ECS Peixoto[1] ; RTS Peixoto[1] ; RTS Peixoto[2] ; AAB Aragao[1] ; ILPB Anjos[3] ; VF Marcolla[1] ; LLB Bandera[3]
[1]*Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil*; [2]*State Institute of Cardiology Aloysio de Castro, Rio de Janeiro, Brazil*; [3]*Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

Introduction: Worwire, mitral ballon valvuloplasty is acknowledged, by cardiology guidelines, as an effective treatment for mitral stenosis. Diferents balloons may be safely used. Single balloon technique is a less expensive technique to perform MBV
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 perfomed, 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 ± 0.30 cm^2. FU was 156 ± 144 months. Multivariate Cox analisys to determine IPS and EFS.
Results: Mean age: 38.0 ± 12.6 (13 to 83) years, 222 (86.7%) female gender, 215 (84.0%) sinus rhythm, echo score (ES) 7.2 ± 1.5 (4 to 14) points and echo mitral valve area (MVA) pre-MBV 0.93 ± 0.21 cm^2. Mean pre and post-MVA (Gorlin): 0.90 ± 0.20 and 2.02 ± 0.37 cm^2, respectively (p < 0.001). Success (MVA ≥1.5 cm^2): 241 (94.1%) procedures. Mean pulmonary artery pressure pre and post-MBV: 27 ± 10 and 20 ± 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 funcional 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 ≤8 points (p < 0.001, HR0.116, 95% IC 0.035-0.384), age ≤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). Independents 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 ≥1.50 cm^2 (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 ≤8 points, age ≤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 ≥1.50 cm^2



P1834

Redo percutaneous mitral commissurotomy interventions for mitral stenosis: immediate and one-year results compared to a primary procedure, a prospective observational study between 2010 and 2015

C Cindy Perron[1]; G Bonnet[1]; JP Mouret[1]; E Salaun[1]; JL Bonnet[1]
[1]*Hospital La Timone of Marseille, Marseille, France*

Introduction: Percutaneous mitral commissurotomy (PMC) has virtually replaced surgery in the treatment of mitral stenosis. However, the indications for PMC in the setting of mitral restenosis remain poorly characterized, and a history of PMC is considered to be an unfavorable anatomic feature in the latest european guidelines. Our study has therefore compared immediate and one-year results of redo versus primary interventions.
Methods: All patients in whom PMC was performed for mitral stenosis between 06/02/2010 and 06/02/2015 in University Hospital were included. Patients have been divided into two groups depending on their status: primary or redo PMC. Clinical, echocardiographic and procedural data have been collected in the medical files. Referring cardiologists were contacted to obtain information at one-year follow-up (restenosis, redo intervention, heart failure, and death).
Results: During the study period, 61 patients underwent PMC for mitral stenosis in our center. It was a redo procedure in 21 cases (33%). Baseline characteristics were comparable in both groups. Initial global success rate, as defined by a post-procedural mitral valve area > 1.5 cm2 without mitral regurgitation > 2/4, was 80%. It didn't significantly differ depending on the status (82.9% for a primary versus 73.7% for a redo intervention; OR=1.717 [0.364; 7.599] ; p = 0.49). One-year overall survival without event was 64.4% (65% versus 63.2% ; OR=1.081 [0.29;3.84] ; p = 0.99). There were no significant differences regarding rates of death (14.6% versus 5.3% ; OR=0.329 [0.006;3.045] ; p = 0.41), heart failure (27.5% versus 15.8% ; OR=0.499 [0.078;2.289] ; p = 0.51), restenosis (15% versus 31.6% ; OR=2.568 [0.573;11.653] ; p = 0.17) or reintervention (5% versus 21% ; OR=4.908 [0.628;59.692] ; p = 0.07).
Conclusion: Redo PMC for mitral stenosis doesn't appear to be a risk factor of immediate and one-year procedural failure. These results should be confirmed or invalidated by a larger study.

DEVICES/CRT/ICD/SURGERY

P1835

Influence of chronic kidney disease on CRT response and clinical outcomes

I Ines Silveira[1]; R B Santos[1]; M Trepa[1]; MJ Sousa[1]; C Roque[1]; A Pinheiro-Vieira[1]; V Lagarto[1]; A Luz[1]; A Hipolito-Reis[1]; S Torres[1]
[1]*Hospital Center of Porto, Cardiology, Porto, Portugal*

Introduction: Chronic Kidney disease (CKD) is common among patients with heart failure (HF) and its presence could have a deleterious impact on outcome. The aim of this study was to evaluate the impact of baseline CKD on cardiac resynchronization therapy (CRT) response and clinical outcomes (composite of global mortality and HF hospitalizations) at 5 years follow up.
Methods: Single-center, retrospective study of patients who underwent CRT implantations between January 2002 and March 2016. A clinical and echocardiographic evaluation were performed previous to CRT and 6-12 months after. CKD was defined as a creatinine clearance ≤ 60 ml/min determined by MDRD formula. CRT response was defined as an increase in LV function ≥5% and an improvement in NYHA class ≥1. Predictors of the composite outcome were determined by logistic regression analysis. Variables with p < 0.1 in univariate analysis were included in multivariate model.
Results: A total of 246 patients were included (mean age 68.8 ± 10.6 years, 63.2% males, 40.7% ischaemic aetiology), with a mean follow-up time of 34.1 ± 21.1 months. CKD was present in 22.4% of patients. Patients with CKD were older (71.7 ± 10.3 vs 67.9 ± 10.6 years p = 0.02), had a higher rate of hypertension (78.3% % vs 65.5% p = 0.022) and had more frequent NYHA class III/IV before CRT implantation (86.8% vs 67.1% p = 0.04), compared to patients without CKD. There were no significant differences regarding gender, cardiomyopathy aetiology, baseline left ventricular ejection fraction or other cardiovascular risk factors. CRT response was similar between groups (43.2 % vs 53.5% p = 0.183). At 5 years follow up, a significant difference was found on composite outcome (44.4% CKD vs 23.0% non-CKD group, p = 0.002). After multivariate analysis, presence of baseline CKD and absence of CRT response were independent predictors of the composite outcome (HR: 2.7; 95% CI 1.3-5.4 p = 0.004 and HR: 0.19; 95% CI 0.06-0.62 p = 0.006, respectively).
Conclusion: Patients with CKD had similar rate of response to CRT but worse prognosis. Presence of baseline CKD was an independent predictor of 5 years HF hospitalizations and global mortality.

P1836

Diastolic function, filling pressures in combination with B-type natriuretic pepetide levels affect cardiac resynchronization therapy response in chronic heart failure patients.

E Hatzinikolaou-Kotsakou[1]; E Reppas[1]; M Kotsakou[1]; G Moschos[1]; P Latsios[1]; G Moschos[1]; TH Beleveslis[1]; M Konstantinidou[1]; A Chantas[1]
[1]*Saint Lukes Private Hospital , Electrophysiology Deparment , Thessaloniki, Greece*

Cardiac resynchronization therapy (CRT) is an established treatment for symptomatic patients (pts) with chronic heart failure (CHF) prolonged QRS duration with Left bundle branch block morphology. Approximately 30% of patients treated with cardiac resynchronization therapy (CRT) do not respond. Identification of 'responders' and 'non-responders' to CRT has attracted considerable attention.
Aim: The aim of the study was to assess and identify if the extent of co-existing diastolic dysfunction and high filing pressures in combination with levels of B -type natriuretic peptide (NT-proBNP) could being best predictors of CRT response.
Methods: A single-center, prospective analysis was conducted in 225 consecutive CRT recipients (CRT-D100%) from January 2007 to October 2015 in a longitudinal CRT database: ischemic cardiomyopathy (n = 128) and DCM (n = .97) Clinical variables and echocardiographic measures were evaluated preimplant and 12 months post implant.All patients underwent conventional 2-dimensional/Doppler echocardiography and Doppler tissue analysis of mitral annular velocities. As a measure of left ventricular filling pressures, the ratio of peak early mitral flow velocity to peak early diastolic mitral annular velocity was derived. NT-proBNP measurements were carried out on a bench-top analyzer. Response to CRT was defined as an absolute increase of >= 5% in left ventricular ejection fraction (LVEF) compared with baseline at 12 months after CRT implantation without heart failure rehospitalization or any cause of death. There were 164 responders (68%) and 61 nonresponders (32%).
Results: Patients responders and non responders did not differ with respect to the cause of CHF or ejection fraction, but in non responders pts deceleration time was shorter (152 +/- 62 vs 218 +/- 88 milliseconds, P = 0. 02) and a restrictive mitral filling pattern was more frequent (35% vs 11%, P = .005). In such patients, the ratio of peak early mitral flow velocity to peak early diastolic mitral annular velocity was higher (16.2 +/- 5.4 vs 11.6 +/- 4.9, P < . 001) and NT-proBNP was elevated 4452 +/- 3825 vs 910 +/- 868 pg/mL, P < 0.012 as compared with responders pts
Conclusions: Severe diastolic dysfuncion, elevated filling pressures associated with higher NT-proBNT levels in pts with CHF could identify responders to CRT. These findings may be used to improve the appropriate use of CRT, to increase the CRT response rate. It is needed our results to be validated on a large prospective multicenter trial.

P1837

Role of global myocardial work in the identification of responders to CRT

E Galli[1]; C Leclercq[1]; A Hubert[1]; A Bernard[2]; O Smiseth[3]; E Samset[3]; E Donal[1]
[1]*University Hospital of Rennes, Cardiology, Rennes, France*; [2]*University Hospital of Tours, Tours, France*; [3]*University of Oslo, Oslo, Norway*

Background: cardiac resynchronization therapy (CRT) has a pivotal role in the management of patients with HF and wide QRS complex, but is affected by still too

many non responders. Aim of the resent study is to evaluate the role cardiac work estimated by pressure-strain loops (PSLs) in predicting CRT response.
Methods: 97 patients with symptomatic heart failure underwent CRT implantation according to current recommendations. Standard 2D and speckle tracking echocardiography were performed before CRTand at 6-month follow-up (FU). PSLs analysis allowed the calculation of global and regional myocardial positive (PosW) and negative work (NegW). A reduction >15% of left ventricular (LV) end-systolic volume at FU defined CRT positive response (CRT+)
Results: at FU, 63 (65%) patients resulted responders to CRT. Global PosW (PosWtot), lateral wall PosW (PosWlat), global NegW (NegWtot), septal NegW (NegWsept) and lateral NegW (NegWlat) were significantly increased in CRT+. At multivariate regression analysis, no regional work parameter emerged as predictor of CRT+, PosWtot >1057 mmHg/% (OR 7.30, p = 0.01) and SF (OR 7.33, p < 0.0001) being the only significant predictors of CRT+. PosWtot was significantly associated to the entity of myocardial remodeling after CRT in both ischemic (r=-0.55, p < 0.0001) and non-ischemic patients (r=-0.65, p < 0.0001).
Conclusions: patients with higher PosWtot, show a favorable response to CRT. These data support the role of residual myocardial contractility in CRT candidates and encourage further studies finalized at the assessment of the myocardial substrate of functional response in CRT candidates

P1838

Level of testosterone as a predictor of response to cardiac resynchronisation therapy

TN Enina[1]; VA Kuznetsov[1]; AM Soldatova[1]; TI Petelina[1]; DV Krinochkin[1]; SM Dyachkov[1]; AY Rychkov[1]; OY Nohrina[1]
[1]Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Tyumen, Russian Federation

Background: Approximately one-third of patients with congestive heart failure (CHF) do not benefit from cardiac resynchronisation therapy (CRT). There is lack information about association of sex hormones, CHF biomarkers levels and response to CRT.
Purpose: To assess the relationship of testosterone level (TES) with effect of CRT in men with CHF.
Methods: In 58 men undergoing CRT (mean age 54.8 ± 9.6 years; 61% ischemic etiology) response to CRT was evaluated as the best decrease of left ventricular end-systolic volume (LVESV) in mean follow-up period 38 [19.0;53.7] months. According to TES level patients were divided into groups: I group (n = 28; 48%) - TES < median (13.82 nmol/L); II group (n = 30; 52%) - TES ≥ median. At baseline, 1, 3 months and each 6 months after implantation echocardiographic parameters, levels of NT-proBNP, interleukin (IL)-1β, IL-6, IL-10, tumor necrosis factor - alpha (TNF-α), matrix metalloproteinase - 9 (MMP-9), tissue inhibitors of MMP 1, 4 (TIMP-1, TIMP-4) were measured. At baseline levels of TES, progesterone (PGN), dehydroepiandrosterone (DHS), estrogen (E2) were evaluated.
Results: The percentage of responders (decrease in LVESV 15-30%) and super-responders (decrease in LVESV ≥30%) was significantly higher in II group (p = 0.05). Increase in left ventricular ejection fraction (p = 0.007) and decrease in LVESV (p = 0.069) were more evident in II group. At baseline levels of IL-1β, IL-10, TNF-α, PGN were higher in II group (all p = 0.05). II group showed decrease of IL-1β level (p = 0.001), IL-6 (p = 0.015), IL-10 (p = 0.001), TNF-α (p = 0.001), TIMP-1 (p = 0.046). In I group only NT-proBNP decreased significantly (p = 0.015). In I group we identified correlations of sex hormones: PGN-IL-10 (r=0.553; p = 0.026), PGN-TIMP-1 (r=0.518; p = 0.048), DHS-NT-proBNP (r=-0.599; p = 0.031), DHS-TIMP-4 (r=-0.671; p = 0.004); in II group: PGN-IL-10 (r=0.710; p < 0.001), PGN-TIMP-1 (r=0.693; p = 0.004), DHS-NT-proBNP (r=-0.566; p = 0.007), DHS-IL-6 (r=-0.543; p = 0.011), E2-IL-6 (r=0.519; p = 0.016). In ROC-analysis level of TES=12.35 nmol/L was identified as a predictor of positive response to CRT with sensitivity of 68.3% and specificity of 52.9% (AUC=0.687; p = 0.026).
Conclusion: Higher level of TES is associated with better effect of CRT and decreased inflammatory activity. Level of TES ≥12.35 nmol/L can be used as a predictor of positive response to CRT. Sex hormones have important physiological role in CHF and response to CRT.

P1839

Multi-biomarkers laboratory strategy for outcome prediction in patients with severe systolic dysfunction submitted to CRT

M Beltrami[1]; A Palazzuoli[2]; A Paoletti Perini[1]; C Tosti Guerra[1]; MG De Gregorio[1]; B Franci[2]; P Pieragnoli[1]; R Nuti[2]; L Padeletti[3]
[1]University of Florence, Cardio-Thoracic and Vascular Department, Florence, Italy; *[2]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy*; *[3]IRCCS Multimedica of Milan, Milan, Italy*

Background: Several biomarkers are studied in order to predict outcome and response to Cardiac resynchronization therapy (CRT). ST-2 is linked to cellular death and fibrosis and it is a new emerging prognostic biomarkers in several Heart Failure (HF) setting, Galectin 3 (Gal-3) is related to myocardial fibrosis and cardiovascular stiffness, and N-terminal portion of the B-type natriuretic peptide (NT-proBNP) represents the more codified biomarker for risk stratification and assessment of the hemodynamic status. Finally, elevated levels of cytokine (IL-6 and TNF-α) have been related to the progression of HF status.
Purpose: 1) to investigate the role of ST-2, Gal3, NT-proBNP IL-6 and TNF-α for outcome prediction in terms of cardiac death, re-hospitalization for HF and sustained ventricular arrhythmias in patients submitted to CRT. 2) to evaluate the impact on renal dysfunction and measured biomarkers on outcome in responders versus non responders.
Methods: We retrospectively evaluated 81 consecutive patients referred for CRT with symptomatic drug-refractory heart failure (NYHA II-IV), left ventricular (LV) systolic dysfunction with ejection fraction (EF) ≤35%, QRS width ≥120 ms. We measured all the aforementioned biomarkers together with creatinine, and estimated the Glomerular Filtration Rate (eGFR) at baseline and after 1 year of CRT. At 1 year an echocardiographic reduction of LV end-systolic volume ≥15% was considered as index of reverse remodeling and used to define a patient as responder to CRT. The outcome was assessed during a mean follow up period of 3 years.
Results: Out of 81 patients submitted to CRT, 51 (63%) were responders. Events rate in responders was 4% respect to 50% in non responders (p < 0.001). None of the studied biomarkers demonstrated a significant difference between responders versus non-responders. Conversely Gal-3 (29.8 + 13.9 ng/mL vs 19.9 + 7.6 ng/mL p = 0.002) and NT-proBNP (5133 + 4300 pg/ml vs 1391 + 1205 pg/ml p < 0.001), together with presence of renal dysfunction (45 + 17 ml/min/1,73 m2 vs 58 + 20 ml/min/1,73 m2 p = 0.008), demonstrated a prognostic significance. Roc curve analyses showed a relation among baseline Gal-3≥23 ng/ml, pro NT-BNP≥1400 and prognosis (AUC 0,65 IC 0,51-0,80 p = 0.04 and AUC 0,69 IC 0,56-0,83 p = 0.01 respectively). The difference between Gal-3 and NT-proBNP from baseline to 12 months was not able to recognize patients with increased risk during 3 years follow up period.
Conclusions: Among patients with HF submitted to CRT the measurement of ST-2 and inflammatory biomarkers do not discern patients with worse outcome. Only baseline Gal-3 and NT-pro BNP may provide additional information for risk stratification.

P1840

Contractile function of the right ventricle as a predictor of the effectiveness of cardiac resynchronization therapy

D Lebedev[1]; S Popov[1]; S Krivolapov[1]; G Savenkova[1]; K Zavadovskij[1]; S Minin[2]
[1]Cardiology Research Institute, Tomsk National Research Medical Center of RAS, Tomsk, Russian Federation; *[2]State Research Institute of Circulation Pathology, Novosibirsk, Russian Federation*

Objective: The objective of the study was to evaluate right ventricular (RV) contractile function in patients with implanted devices for cardiac resynchronization therapy (CRT).
Materials and Methods: The study included 80 patients (49 men) with a diagnosis of dilated cardiomyopathy, mean age of 54 ± 10.5 years, heart failure (HF) functional class (FC) III by NYHA, left ventricular (LV) ejection fraction (EF) of 30.1 ± 3.8%, six-minute walk distance (6MWD) of 290.5 ± 64.3 m, and LV end-diastolic volume (EDV) of 220.7 ± 50.9 mL. Forty five patients had sustained sinus rhythm; 35 patients had chronic drug-resistant atrial fibrillation. All patients had complete blockade of the left bundle branch block; QRS duration ranged from 146 to 240 ms (183 ± 32 ms). CRT devices were implanted to all patients. In patients with persistent atrial fibrillation, complete artificial atrioventricular block was formed. In all patients, LV and RV myocardial contractile functions were assessed using equilibrium radionuclide tomoventriculography prior to CRT and 12 months after CRT device implantation.
Results: Follow-up examination was carried out after 1 year of CRT showing favorable clinical changes: HF FC decreased in all patients from III to II. 69 patients responded to CRT (86.25%); 11 patients (13.75%) did not respond to CRT. The criterion of patient's response to CRT was LV EF increase by 15% or more within 12 months. Responders to CRT showed favorable clinical changes: LV EF increased from 30.1 ± 3.8% to 42.8 ± 4.8% (p ≤ 0.001); LV EDV decreased from 220.7 ± 50.9 mL to 197.9 ± 47.8 mL (p ≤ 0.005). In nonresponders, LV EF did not change significantly (30.1 ± 3.8% vs. 33.8 ± 3.8%, p ≤ 0.001); LV EDV increased from 220.7 ± 50.9 to 227.8 ± 27.8 mL (p ≤ 0.001). All patients were retrospectively divided into two groups: group 1 comprised patients who responded to CRT; group 2 included nonresponders. In patients of group 1, radionuclide tomoventriculography showed that RV peak filling rate (PFR) decreased from 1.8 ± 0.36 to 0.56 ± 0.16 (p ≤ 0.001); mean diastolic filling rate (1/3FR-m) decreased from 0.6 ± 0.2 to 0.36 ± 0.15 (p ≤ 0.001). In patients of group 2, these indices were significantly poorer (by 30% and 60%, respectively). Other parameters did not significantly differ between groups.

Conclusion: CRT in patients with severe HF was significantly more effective in those individuals who had preserved contractility of the right cardiac chambers. The values of RV PFR and RV 1/3FR-m may serve as prognostic criteria for favorable response of patients to CRT.

P1841

Dynamic variation of renal function and novel or old HF biomarkers (ST2, Galectin 3, NT-proBNP) and response to cardiac resynchronization therapy (CRT)

M Matteo Beltrami[1]; A Paoletti Perini[1]; A Palazzuoli[2]; G Ruocco[2]; C Tosti Guerra[1]; P Pieragnoli[1]; G Ricciardi[1]; R Nuti[2]; L Padeletti[1]
[1]University Hospital Careggi, Dipartimento Cuore e Vasi, Università degli Studi di Firenze, Firenze, Italy; *[2]University of Siena, Siena, Italy*

Background: Cardiac resynchronization therapy (CRT) is an established treatment in patients with drug-refractory heart failure (HF), left bundle branch block, and severe left ventricular (LV) dysfunction, although approximately 30% of patients do not respond to such treatment. ST2 is a member of the interleukin-1 family involved in modulating cardiac remodeling and ventricular function. Galectin-3 (Gal-3) is a marker of fibrosis activity and cardiac remodeling. NT-proBNP represents the more codified and measured biomarker for risk stratification and hemodynamic status in HF. However, dynamic changes in the aforementioned biomarkers and structural response to CRT are still poor investigated.
Purpose: To investigate temporal variations of ST-2, Gal-3, NT-proBNP and renal function from baseline to 1-year follow-up, and their interactions with LV reverse remodeling after CRT.
Methods: We retrospectively evaluated 81 consecutive patients referred for CRT according to current Guidelines. We measured ST-2, Gal-3, NT-proBNP, creatinine and estimated Glomerular Filtration Rate (eGFR) at baseline and after 12 months. eGFR was calculated by the CKD-EPI formula. Variations of each marker were calculated as ln(value at 12 months/value at baseline), given the skewed distribution of the data. Echocardiographic response was evaluated at 6 months follow-up, and traditionally defined as reduction of LV end-systolic volume ≥15%.
Results: At baseline, we found significant, mild correlation between Gal-3 and markers of renal function (for eGFR, Spearman's rho -0.348, p = 0.002; for creatinine, rho 0.320, p = 0.004) and with ST-2 levels (rho=0.354, p = 0.001) and stronger correlation with NT-proBNP levels (rho=0.453, p = 0.001). Moreover NT-proBNP showed a mild correlation with eGFR (rho=-0.330, p = 0.003) and creatinine (rho=0.355, p = 0.001). All other correlations were not significant. However, temporal changes from baseline to 12 months for each parameters were not significantly related to each other, except for a very mild correlation between ST-2 and markers of renal function (for eGFR rho=0.236, p = 0.004; for creatinine rho 0.249, p = 0.034). Echocardiographic response was significantly associated with improvement in renal function at 12 months, as compared with baseline (independent sample t-test p = 0.038 for eGFR, p = 0.046 for creatinine), but not with variations in Gal-3 (p = 0.729), ST2 (p = 0.649) and NT-proBNP (0.289). Moreover, percentage changes in eGFR and in creatinine were linearly correlated with percentage changes in LVESV (Spearman's rho 0.229, p = 0.047; rho -0.235, p = 0.041, respectively).
Conclusions: In patients candidates to CRT, markers of renal function, NT-proBNP and Gal-3 are significantly associated before implantation, but their temporal changes at 1-year follow-up are no more correlated. Echocardiographic response to CRT is associated with positive changes in indexes of renal function, but not with changes in NT-proBNP or Gal-3.

P1842

Cardiac resynchronization Therapy pacemaker or defibrillator? Long term follow-upoutcomes

B Belen Alvarez[1]; JR Garcia Seara[1]; RA Abellas Sequeiros[1]; D Iglesias Alvarez[1]; L Gonzalez Melchor[1]; M Rodriguez Manero[1]; XA Fernandez Lopez[1]; I Gomez Otero[1]; JL Martinez Sande[1]; A Martinez Monzonis[1]; JR Gonzalez Juanatey[1]
[1]University Clinical Hospital of Santiago de Compostela, Department of Cardiology, Santiago de Compostela, Spain

Introduction: Cardiac resynchronization therapy (CRT) is a well-established treatment option for patients with advanced HF. The aim of our study is establish wether there were any significant differences in outcomes between CRT-D and CRT-P.

Baseline Characteristics

	CRT-D 172 (52.4%)	CRT-P 156(47.6%)	p-value
Age, y	71±9	70±10	0.326
Sex male, n(%)	127(73.8)	126(80.8)	0.135
Ischemic cardiomyopathy, n(%)	57(33.1)	62(39.7)	0.214
Atrial fibrillation, n(%)	65(37.8)	58(37.2)	0.909
NYHA class II IIIIV	52(30.2) 107(62.2) 13(7.6)	27(17.3) 123(78.8) 6(3.8)	0.004
Betablockers, n(%)	144(83.7)	127(81.4)	0.581
ACEI, n(%)	148(86.0)	135(86.5)	0.897
MRA, n(%)	81(47.1)	73(46.8)	0.957
Amiodarone, n(%)	20(11.6)	21(13.5)	0.616
Glomerular filtration rate	61±24	60±24	0.522
Hemoglobine	13±2	13±2	0.307
QRS duration	165±26	159±26	0.050
LVEF	28±7	26±7	0.063
LVESV	163±62	169±58	0.375

ACEI: angiotensin-converting enzyme inhibitor; CRT-D: Defibrillator with Cardiac Resynchronization Therapy; CRT-P: Pacemaker with Cardiac Resynchronization Therapy; LVEF: left ventricular eyection fraction; LVESV: left ventricular end diastolic volume; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association.

Methods: Our analysis included 328 patientes, who underwent implantation of either a CRT-P (47.6%) or a CRT-D (52.4%) in a single center between August 2001 and April 2015 (follow up 4.7 ± 3.1 year). Patients characteristics and all cause mortality were compared between both groups.
Results: Baseline characteristics are shown in Table 1. The Kaplan- Meier analysis showed no differences of mortality (log Rank p0.425). No-Adjusted all causes of mortality are similar in both groups. (HR 1.14, CI 95% 0.82-1.59, p 0.426), Adjusted all causes of mortality are also similar (HR 0.85, CI 95% 0.58-1.24, p 0.347). Ischaemic cohort did not differences: No-Adjusted all mortality: HR 0.87, CI95%0.52-1.43, p0.571; and Adjusted all mortality: HR 0.79, CI95%0.43-1.43, p0.430
Conclusion: Survival rate was similar with CRT-P and CRT-D, including de the ischemic cohort. No additional impact of ICD were demostrated in our population.

P1843

Predictors of hospitalization for heart failure following cardiac resynchronization therapy

M Maria Trepa[1]; C Gomes[1]; I Silveira[1]; B Brochado[1]; MF Oliveira[1]; R Baggen Santos[1]; VA Dias[1]; C Roque[1]; AP Vieira[1]; H Reis[1]; S Torres[1]
[1]Hospital Center of Porto, Cardiology, Porto, Portugal

Introduction: Cardiac Resynchronization Therapy (CRT) is an established treatment in selected patients with systolic heart failure (HF) and eletrical dyssynchrony. However some patients don't show the expected response and maintain an increased risk for hospitalization for acutely decompensated HF after implantation. The aim of this study was to identify clinical predictors of HF hospitalization after CRT.
Methods: Single-center retrospective observational study including 303 patients who underwent cardiac resynchronization therapy (CRT) between 2002 and 2016. Patients hospitalized for decompensated HF during a 5 year follow-up period were reviewed. The mean follow up time was 34.1 ± 21.1 months. Multivariate models were adjusted for clinical response (improvement in at least 1 NYHA class 6-12 months after CRT), echocardiographic response [improvement of > 5% in left ventricular ejection fraction (LVEF) 6-12 months after CRT], etiology (ischemic vs non-ischemic), chronic kidney disease [(CKD) defined as a creatinine clearance ≤ 60 ml/m2 determined by MDRD formula], diabetes and impaired right heart function after CRT.
Results: During follow-up 57 patients (18.8%) were hospitalized for HF. Regarding baseline characteristics, these patients were more likely to be ischemic (25% vs 14.5%, p = 0.021), diabetic (26% vs 16%, p = 0.05) and have CKD (33% vs 13%, p = 0.01). Age, gender, pré-implantation LVEF, QRS duration and pattern were not statistically different between the groups. Patients who presented worst clinical and echocardiographic response to CRT were at significantly increased risk for hospitalization (respectively: 35.4% vs 15.2%, p < 0.01 and 38.8% vs 7.8%, p < 0.01). Also patients with impaired right heart function after CRT showed more events (28.6%

vs 13.4%). In multivariate analysis absence of echocardiographic response (OR 3.9; p = 0.01) and CKD (OR 3.1; p = 0.03) were independent predictors of HF hospitalization.
Conclusions: Chronic kidney disease and absence of echocardiographic response are independently associated with HF hospitalization. Further studies are needed to assess the usefulness of this findings and its applications.

P1844
Clinical characteristics, predictors, and outcomes of super-responder in cardiac resynchronization therapy of patients with heart failure

J Jaewon Oh[1]; JS Uhm[1]; IC Kim[1]; TH Kim[1]; HN Pak[1]; MH Lee[1]; B Joung[1]; SM Kang[1]
[1]*Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of*

Introduction: Cardiac resynchronization therapy (CRT) can improve cardiac function through reverse left ventricular (LV) remodeling in heart failure (HF) patients with wide QRS duration. Recently, 'super-response' to CRT is known to be associated with improved survival. We assessed clinical characteristics, predictors and outcomes of super-responder in CRT.
Methods: We retrospectively enrolled 76 patients with CRT implantation from January 2010 to October 2015. Pre-defined CRT responders were: responders (decreased LV end systolic volume, LVESV 15-29%), and super-responders (decreased LVESV ≥30%). The response timing before or after 6 months was defined as early or late response, respectively. Clinical outcomes including all-cause mortality and rehospitalizations were assessed during follow-up period (median 555 days)
Results: Mean age, baseline LVEF and QRS duration were 66 ± 11 years, 24.8 ± 6.3% and 164 ± 24ms, respectively. The prevalence of men, LBBB and ischemic origin HF were 46.1%, 69.7% and 14.5%, respectively. At early period, there were 7 (9.2%) responders and 8 (10.5%) super-responders, while 9 (14.3%) responders and 22 (34.9%) supper-responders at late period. There were no mortality cases in early and late overall responders and fewer HF rehospitalization (4.5% vs. 22.2% for responders, p = 0.055) in super-responders. There were not any significant differences between responders and super-responders in terms of the prevalence of men, ischemic origin HF and age, baseline LVEF, QRS duration. However, the follow up QRS duration was significantly narrower (150 ± 20ms vs. 169 ± 21ms, p = 0.037) and the prevalence of LBBB was higher (90.9% vs. 44.4%, p = 0.012) in super-responders than that in responders.
Conclusion: Super-responders of CRT showed favorable clinical outcomes compared to nonresponders or even to responders. The decrease of QRS duration after CRT implantation can be a clinical predictor for super-response to CRT.

P1845
A systematic review of telemonitoring assessment for patients with heart failure

T Farnia[1]; MC Jaulent[1]; O Steichen[2]
[1]*University Pierre & Marie Curie Paris VI, Laboratoire d'Informatique Médicale et Ingénierie des Connaissances en eSanté (LIMICS - UMR_S 1142), Paris, France*; [2]*Hospital Tenon, AP-HP, Sorbonne Universités, UPMC Univ Paris 06, hôpital Tenon, Service de médecine interne, Paris, France*

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Background/Introduction: Telemonitoring (TLM) can improve heart failure (HF) management. However proper assessment of TLM services, and their impact on process and outcomes of care, is required. To the best of our knowledge, there is no standardized evaluation framework for TLM services to comprehensively evaluate the various impacts of TLM. The objectives of this systematic review are to list the criteria used in published evaluations of non-invasive HF TLM services, to describe how they are used and to organise them into a comprehensive evaluation framework.
Methods: The articles were retrieved through Medline, Web of Science and Embase from 1990 to August 2015. Articles were eligible if they were English original reports of a HF TLM evaluation study in English language. Reviews, editorials and position papers and studies implantable devices were excluded.
Results: Overall, 121 articles were selected and reviewed, leading to 52 evaluation criteria that were classified along six dimensions: technical, economical, educational, clinical, organizational and users' perspective. The clinical and economical impacts were evaluated in over 65% of studies whereas the educational, organizational and technical impacts were studied in less than 15%. Users' perspective was the most frequently covered dimension in the development phase of TLM projects, whereas study of the clinical and economical impacts were dominating in the later phases (implementation and integration)(Table 1).
Conclusions: TLM evaluation frameworks should cover all of the six dimensions, appropriately distributed along the TLM project life cycle. Our next goal is to build such a comprehensive evaluation framework for non-invasive HF TLM and to test it on an ongoing TLM project.

Table 1

Dimension	All studies (n = 121)	TLM project phase		
	Development (n = 23)	Implementation (n = 69)	Integration (n = 26)	
Clinical criteria	100 (83%)	11 (48%)	61 (88%)	23 (88%)
Economical criteria	84 (69%)	9 (39%)	50 (72%)	22 (85%)
Users' perspective	52 (43%)	19 (83%)	29 (42%)	12 (46%)
Educational criteria	17 (14%)	3 (13%)	9 (13%)	5 (19%)
Organizational criteria	7 (6%)	1 (4%)	5 (7%)	1 (4%)
Technical criteria	6 (5%)	3 (13%)	3 (4%)	0 (0%)

Coverage of evaluation dimensions across studies and phases of project life cycle

P1846
Implementation of intravenous inotropic protocol in hospitalization unit with telemetry: initial experience

FM Barth[1]; LG Caballero[2]; G Aliti[1]; L Orlandin[1]; LB Silva-Neto[1]; E R Eneida Rejane Rabelo-Silva[3]
[1]*Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil*; [2]*Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*; [3]*Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil*

Background: Intravenous inotropic therapy plays an important role in the management of hospitalized patients with heart failure (HF). In particular, the use of inotropes at lower doses contributed to the potential expansion of its use, with lower rates of complications. Among patients with advanced HF using intravenous inotropic, severe, but stable cases, may be selected to benefit from continued treatment outside the intensive care setting.
Objective: To report the initial experience of the use intravenous inotropes at the ward unit under telemetry monitoring, in stable patients with advanced HF, in a general, public and university hospital.
Methods: Patients with advanced HF, refractory to conventional pharmacological treatment, clinically stable in the Coronary Care Unit for at least 24 hours with an unchanged (low or moderate) intravenous inotropic dose were selected (milrinone/dobutamine).The protocol was prepared by a multidisciplinary team and implemented in an inpatient unit whose staff was adequately trained. Inotrope was infused through a central inserteted peripheral catheter; once the dose was considered stable, the patient was discharged to the ward.
Results: From 09/2015 to 12/2016, 15 patients with advanced HF were followed with the use of inotrope under this protocol (Mean age 54 ± 17 years, 80% male, left ventricular ejection fraction 24 ± 7%, 40% ischemic etiology, 27% familial, 20% idiopathic). Milrinone was used in 13 patients with a median dose of 0.17 (0.27-0.25) μg/kg/min; dobutamine was used in 2 patients with a dose of 5 μg/kg/min. Of the 15 patients, eight were transplanted, two were discharged from hospital, one returned to the intensive care unit due to clinical worsening related to nephrotoxicity secondary to desensitization therapy and four died. There were no adverse events resulting from the use low dose inotropes with protocol.
Conclusions: The use of this low-dose inotrope protocol use in the ward unit with telemetry proved to be feasible and safe, allowing for the prolonged use of this therapy as a bridge for cardiac transplantation, weaning or palliative care support. Learning from the use of low or moderate doses may reconfigure the role of inotropes as transition therapy for management settings.

P1847
Evaluation of e-health tool for heart failure patients

A Blomqvist[1]; K Sjostrom[2]; E Ohman[2]; M Dahlqvist[2]; S Bergenbrant Glas[2]
[1]*CareLigo, Research, Stockholm, Sweden*; [2]*Norrtälje Hospital, Norrtälje, Sweden*

Background: A home-based tool for heart failure (HF) patients exists, which monitors symptoms, titrates diuretics and educates the patient about HF in an interactive manner, in order to promote a better self-care behaviour. If the system detects deterioration in HF status, the patient is advised to seek health care and told who to contact.
Purpose: The tool has previously been shown to improve self-care behaviour, but we wished to assess its impact on HF related in-hospital days, to evaluate the use of the tool from a quality of care perspective.
Methods: We performed an intervention study with a matched control group, with a total of 62 patients. 31 patients in the intervention group (IG) were equipped with the tool and 31 matched controls (CG), were subject to standard care. The patients were followed for 280 days. The groups were well balanced at baseline, with respect to age, gender and diagnosis.
The mean age was 76 ± 10, with 34 % women in the IG and the mean age was 74 ± 10, with 42 % women in the CG. All hospitalisations for the patients were recorded during 280 days.
Results: After 280 days, a multiple regression analysis was performed, resulting in a risk ratio of [RR: 0.64; 95% CI: 0.47-0.87; $p < 0.05$]. There was a statistically significant reduction of HF related in-hospital days by 36 %, corresponding to an average reduction of 1.3 in-hospital days per patient. In total there were 104 HF days registered for the CG and 62 for the IG. There was no significant difference in risk of admission between the two groups (28 % for IG vs 26 % for CG).
Conclusion: Our findings are very similar to what has been published before. The tool appears to help patients to seek care in time when symtoms are worsening, instead of waiting for an acute episode. This is most likely the underlying cause of the reduction of in-hospital days.

P1848

New concepts for remote monitoring and flow control in left ventricular assist device patients - The Medolution project.

N Reiss[1]; T Schmidt[1]; J D Hoffmann[1]; D Willemsen[1]; F Mueller Von Aschwege[2]; J I Roebesaat[2]; J D Schmitto[3]; C Feldmann[3]
[1]Schuechtermann Klinik, Clinical Research, Bad Rothenfelde, Germany; *[2]Clinic Oldenburg, OFFIS, Oldenburg, Germany*; *[3]Hannover Medical School, Hannover, Germany*

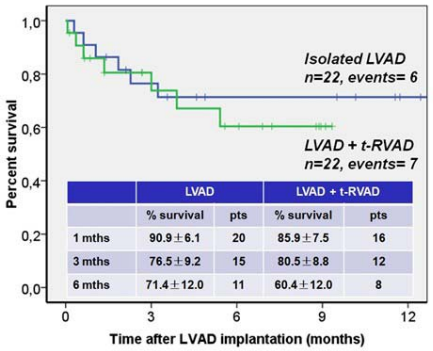
Purpose: An effective outpatient management is the key factor to ensure the long-term success of left ventricular assist device (LVAD) therapy. Ambulatory visits only take place every 3 month so that life-threatening complications (pump thrombosis, driveline infection) can often only be detected and prevented by the patients themselves. In consequence, hospital stays or readmissions are common. Furthermore, flow adaptation during exercise is an unsolved problem in continuous-flow LVAD patients.
It is the intention of the the EU-funded project Medolution, to develop new approaches in order to provide the best possible support for physicians and patients in future.
Methods: Research project: In the meantime, there are different possibilities available for remote monitoring of relevant vital and device parameters in patients with a LVAD. In the future, technical opportunities are increasing. The Medolution project aims to bundle the relevant information (e.g. PAP, INR, thorax-impedance, driveline-pictures, LVAD-data) from different data sources into one platform in order to provide the physician a comprehensive overview of patient situation. In the systems background a big data analysis runs permanently and tries to detect abnormalities and correlations as well. At crucial events, a notification system informs the physician and provides the relevant data via a decision support system. LVAD flow is adapted to the grade of exercise via sensors located in the left atrium.
Results: First results of big data analysis for early detection of pump thrombosis based on LVAD parameters are available. Work on automatic image processing for driveline pictures analysis has started. For experimental tests a mock circulatory loop will be in use to simulate various situations (e.g. hypovolemia or thrombus formation, but also exercise) and to examine sensor connectivity, data transfers, algorithms and notification system.
Currently, both a mobile patient application and an application for the physician are under development.

P1849

Liberal right ventricular assist device extracorporeal membrane oxygenation support for right ventricular failure following implantable left ventricular assist device placement

Q Quentin Fischer[1]; M Kirsch[2]
[1]Hospital Bichat-Claude Bernard, Cardiology, Paris, France; *[2]University Hospital Centre Vaudois (CHUV), Cardiac surgery, Lausanne, Switzerland*

Introduction: Refractory right ventricular failure (RVF) after implantation of left ventricular assist device (LVAD) is a dramatic complication with high morbi-mortality. The addition of right ventricular assist device (RVAD) may help recovery and lead to improve outcomes.
Materials and Methods: From February 2012 to September 2014, 44 patients received a HeartMate II. These patients were retrospectively compared in 2 groups: no t-RVAD group and t-RVAD group according early liberal implantation. Patients in t-RVAD group were treated using extracorporeal membrane oxygenation as a RVAD.
Results: Of the 44 patients, 22 were didn't need RV support (no t-RVAD group), whereas 22 required addition of a temporary RVAD (t-RVAD group). Patients are sicker in the t-RVAD group with higher Michigan risk score (2.61 +/- 2.2 pts vs 1.0 +/- 1.6 pts; $p = 0.013$) and INTERMACs clinical profile (2.1 +/- 0.6 pts vs 3.4 +/- 1.3 pts; $p = 0.0001$). Despite severity of pre-implant conditions in t-RVAD group, clinical outcomes didn't differ in the both groups with similar survival rate at 6 months (60.4 +/- 12 vs 71.4 +/- 9.9 months; $p = 0.585$).
Conclusions: Early and liberal use of temporary RVAD in case of risk factors of RVF allows to improve the prognostic of this pathology with similar survival rate in the both groups.



	LVAD		LVAD + t-RVAD	
	% survival	pts	% survival	pts
1 mths	90.9 ± 6.1	20	85.9 ± 7.5	16
3 mths	76.5 ± 9.2	15	80.5 ± 8.8	12
6 mths	71.4 ± 12.0	11	60.4 ± 12.0	8

Kaplan Meier survival analysis

P1850

Impact of left ventricular assist device implantation on right and left ventricular volumes and functions

C Clement Delmas[1]; P Fournier[1]; S Cazalbou[1]; D Carrie[1]; J Roncalli[1]; M Galinier[1]; O Lairez[2]
[1]Toulouse Rangueil University Hospital (CHU), Cardiology department, Toulouse, France; *[2]Toulouse Rangueil University Hospital, Cardiac Imagery Center, Toulouse, France*

Background: Because the right ventricle is not assisted, its function is a critical determinant of the hemodynamic in patients with left ventricular (LV) assist devices (LVADs) and contributes significantly to postoperative morbidity and mortality. Right ventricular (RV) failure remains a challenge in the area of continuous-flow LVADs. The aim of this study was to evaluate the evolution of RV volumes and function before and after LVAD implantation.
Methods: Ten patients underwent tomographic equilibrium radionuclide ventriculography for the assessment of LV and RV volumes and functions before and after LVAD implantation.
Results: Mean LV and RV ejection fractions before implantation were 20 ± 8 and 46 ± 14%, respectively. LVAD implantation had no impact on RV ejection fraction (46 ± 11% after implantation, P=0.961) but tended to increase LV ejection fraction (31 ± 21% after implantation, P=0.09). LVAD led to a decrease of LV end-diastolic volume (Δ = -136 ± 96 after implantation, P=0.001) and RV end-diastolic volume (Δ=-59 ± 49 after implantation, P=0.004). Conclusion – In patients with preserved RV ejection fraction, LVAD implantation leads to a decrease of RV volumes without impact on RV ejection fraction. The increase of cardiac output induced by the LVAD does not increase RV volumes, which could be explained by the decrease of RV afterload. These results highlight the importance of afterload on the right ventricle in patients with heart failure.

P1851

Allosensitization with new generation left ventricular assist device

M Massimiliano Carrozzini[1]; T Bottio[1]; F Toto[1]; M Comisso[1]; E Manzan[1]; M Cardillo[1]; E Cozzi[1]; V Tarzia[1]; J Bejko[1]; G Gerosa[1]
[1]University Hospital of Padova, Cardiac Surgery Unit, Padua, Italy

Background/Introduction: Impact of HLA-allosensitization in continuous-flow left-ventricular-assist-devices (LVAD) recipients is still under investigation.
Purpose: We sought to assess HLA-allosensitization in patients implanted with Jarvik-2000 or HeartWare as bridge-to-transplantation and compared results in No-VAD patients.
Methods: We included all consecutive patients tested for HLA-allosensitization before heart-transplantation from 2012 to 2016. Tests used were complement-dependent-cytotoxicity on panel-reactive-assay (CDC-PRA) and Luminex.
Results: Included are 119 patients: mean age 51 ± 16 years, 24% female, 62% previously transfused. Forty-one patients entered the VAD group: 26 HeartWare, 15 Jarvik-2000. Seventy-eight patients were No-VAD. Two patients (5%) in the VAD group had a positive CDC-PRA; results in No-VAD group were comparable (8%, p = 0.56). Luminex was positive in 6 VAD patients (15%): HLA-class-I alloantibodies present in 7%, HLA-class-II in 5%, both HLA-class-I and II in 3%. Similar rates were observed in the No-VAD group: 26% positive (p = 0.17), 12% HLA-class-I (p = 0.47), 6% HLA-class-II (p = 0.74), 8% both HLA-class-I and II (p = 0.25). There were no statistical differences both at CDC-PRA (p = 0.25) and Luminex (p = 0.68) between the two LVADs used.
Conclusion(s) Rates of HLA-allosensitization with Jarvik-2000 or HeartWare were lower than those of first-generation LVAD and resulted comparable in No-VAD patients. There were no statistical differences in allosensitization between Jarvik-2000 and HeartWare.

P1852

Success of bridging to transplantation with a continuous- flow left ventricular assist device in a single UK centre

D Brahmbhatt[1]; W Flinn[1]; P Lincoln[1]; A Kydd[1]; C Lewis[1]; J Parameshwar[1]; S Tsui[1]; S Pettit[1]
[1]*Papworth Hospital NHS Trust, Cambridge, United Kingdom*

Background: In the United Kingdom, durable left ventricular assist devices (LVAD) are commissioned for use in patients with advanced heart failure as a bridge to transplantation (BTT) or as a bridge to transplant candidacy (BTC), when elevated pulmonary vascular resistance precludes safe heart transplantation. In 2008, our institution commenced implantation of a single type of continuous-flow LVAD for patients selected by our multi-disciplinary team.
Methods: A prospectively maintained database of all LVAD implants at our institution was interrogated for BTC and BTT continuous-flow LVAD implantation procedures before 1st April 2016 and their follow-up. The data was verified and supplemented by information from medical records. Baseline characteristics including age, aetiology, risk factors, body surface area (BSA) and blood group were recorded. Follow-up was censored at the following events: death, heart transplantation or recovery (LVAD explant). We examined the association between baseline characteristics and success in bridging patients to heart transplantation. T-test was used to compare continuous variable data, and the Chi-squared test was used for categorical data.
Results: During the study period, 64 patients had LVAD implantation, with 41 BTT and 23 BTC. Age ranged from 17 to 66 years old (median 46). 53 patients were male, 11 female. Aetiology was dilated cardiomyopathy (DCM) in 34, ischaemic cardiomyopathy (ICM) in 23, end-stage hypertrophic cardiomyopathy in 6 and restrictive cardiomyopathy in 1. 24 procedures were elective, and 40 were non-elective. The patients had blood groups O (34 patients), A (16), B (10) and AB (4). BSA ranged from 1.45 to 2.47m^2, (mean 1.94). Of 64 implants, one patient had their LVAD decommissioned due to recovery and one patient had their device explanted due to device failure. 54 (84%) patients were listed for transplantation, with 26 (41%) undergoing cardiac transplantation 82 – 1932 days (median 802) after implantation. 22 (34%) patients died during LVAD support 3 – 1598 days (median 171) after implantation. 14 (22%) patients remain on the transplant waiting list, 379 – 2260 days (median 653) after implantation. When comparing baseline characteristics of patients categorised by transplant status, aetiology was the only significant association; patients who were not transplanted were more likely to have an ischaemic cardiomyopathy (47% vs 19%; p < 0.05).
Conclusions: Continuous-flow LVAD may be an effective bridge to heart transplantation in patients with advanced heart failure. Gender, BSA, blood group or indication for LVAD therapy do not appear to impact on the likelihood of successful bridging to transplantation. However, patients with ischaemic cardiomyopathy appear to be less likely to be transplanted compared to other heart failure aetiologies. Further work is needed to investigate complications and adverse events to determine whether they contribute to the differences in transplant rates.

P1853

Percutaneous mechanical circulatory support in cardiogenic shock due to end-stage heart failure and acute myocardial infarction

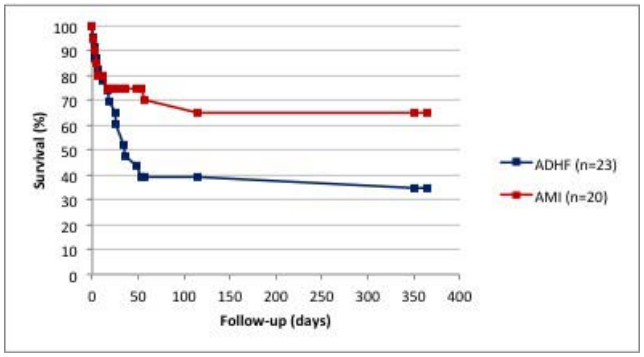
H S Hoong Sern Lim[1]; T Musa[1]; A Ranasinghe[1]; N Howell[1]
[1]*Queen Elizabeth Hospital, Birmingham, United Kingdom*

Background: 'Pump failure' and consequent cardiogenic shock (CS) is a common mode of death in end-stage heart failure (ESHF). However, there are little data on outcomes of percutaneous mechanical circulatory support (PMCS) in CS due to ESHF, unlike acute myocardial infarction (AMI).
Purpose: To describe contemporary outcome of PMCS bridging with veno-arterial extracorporeal membrane oxygenation (ECMO) and/or Impella in patients with CS due to ESHF and AMI.
Methods: Single centre study of consecutive patients with CS due to AMI (n = 20) and ESHF (n = 23) supported with ECMO and/or Impella as the primary PMCS modality.
Results: There was no difference in characteristics between patients with AMI and ESHF, except for lower LVEF [TABLE]. PMCS included 7 Impella, 30 ECMO and 6 Impella + ECMO with no difference between groups. Of the 43 patients, 7 were bridged directly to heart transplantation (4 AMI and 3 ESHF), 4 directly to durable left ventricular assist devices (1 AMI and 3 ESHF), 13 patients underwent further bridging with temporary ventricular assist devices (4 AMI and 9 ESHF) and 24 patients died with/without transplantation or LVAD (7 AMI and 17 ESHF). 1-year survival was 39% and 65% in ESHF and AMI respectively (p = 0.037, log rank test, FIGURE).
Conclusion: Multiple bridging modalities are common in contemporary management of CS. Mortality is higher in patients with CS due to ESHF supported by PMCS compared to AMI.

Baseline characteristics

	ESHF (n = 23)	AMI (n = 20)	P
Age (years)	43±7	46±5	0.536
Males	78%	75%	0.801
Cardiac arrest	26%	35%	0.526
LVEF (%)	13±2	17±2	< 0.001
Mean BP (mmHg)	56±3	58±3	0.426
Heart rate	113±5	120±5	0.062
Cardiac index	1.74±0.08	1.82±0.15	0.227
Lactate	8.2±1.2	8.6±1.2	0.673
Ventilated	61%	80%	0.334
Inotrope score	19.8±2.9	21.5±3.6	0.449
Balloon pump	22%	35%	0.334
Primary PMCS modality			0.526
ImpellaECMOImpella + ECMO	3 (13%)17 (74%)3 (13%)	4 (20%)13 (65%)3 (15%)	

Mean ± standard deviation



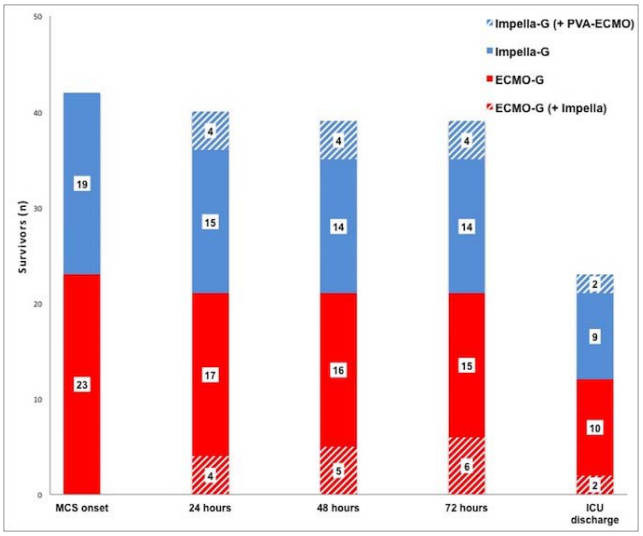
FIGURE

P1854

Circulatory support with ecmo and/or impella for hemodynamic compromise during acute coronary syndrome: a heart team strategy

M Mourad[1]; P Gaudard[1]; P De La Arena[1]; J Eliet[1]; N Zeroual[1]; P Rouviere[1]; F Roubille[1]; B Albat[1]; P Colson[1]
[1]*University Hospital Arnaud de Villeneuve, Montpellier, France*

Objectives: Temporary mechanical circulatory support (TCS) is recommended for patients with acute, profound hemodynamic compromise, including during acute myocardial infarction (AMI). ECMO and Impella are possible TCS devices but the device choice and the timing around the percutaneous coronary intervention (PCI) are not definitely established. We evaluate a heart team strategy based on predefined agreement for the use of TCS in AMI with hemodynamic compromise.
Methods: Our heart team has defined a strategy based on a predefined agreement for the use of ECMO or Impella as TCS in AMI admitted for urgent PCI. The strategy was analyzed retrospectively from a cohort of patients who underwent TCS within 72 hours after admission for PCI in AMI, from January 2009 to April 2015, excluding refractory cardiac arrest.
Results: Among 88 TCS-treated AMI patients, 42 had early TCS: 23 ECMO and 19 Impella. Cardiac management including PCI was similar between the groups but ECMO patients were sicker than Impella patients (higher blood lactate level, p 0.02). Most implantation occurred during PCI (43%) or just after (50%). Change of initial TCS choice was required in 10 cases (24%) for assistance upgrading (4 Impella) or left ventricle unloading (6 ECMO).
Conclusions: A heart team strategy based on predefined agreement for the use of ECMO or Impella as TCS for AMI with hemodynamic compromise seems relevant. ECMO is very effective in case of profound cardiogenic shock. Percutaneous Impella may be more appropriate for less severe hemodynamic compromise, possibly to secure hemodynamics during PCI



Survivors through ICU stay follow-up

P1855

Veno-arterial ECMO/ECLS for cardiogenic shock: short term outcomes

A Antoine Defontaine[1]; E Flecher[1]; S M Rehman[1]; N Nesseler[1]; B Lelong[1]; J-P Verhoye[1]
[1]University Hospital of Rennes, Cardiac and Thoracic Surgery, Rennes, France

Objective: Veno-arterial ECMO (Extracorporeal Membrane Oxygenation) or ECLS (Extracorporeal Life Support) is now widely used to treat severe cardiogenic shock with disparate results. The aim of this study was to present the results at our institution and to identify early prognostic factors.
Methods: Retrospective analysis of prospectively collected data for all patients with cardiogenic shock requiring ECLS at our centre. Post cardiotomy ECLS were excluded.
Results: 159 consecutive patients (122 male – 76.7%), aged 53.9 ± 12.6 years, received ECLS between 2005 and 2016. The etiology of cardiogenic shock was myocardial infarction (100 – 62.9%), dilated cardiomyopathy (27 – 17.0%), ischaemic cardiomyopathy (5 – 3.1%), myocarditis (17 – 10.7%), endocarditis (3 – 1.9%) and rhythmic storm (7 – 4.4%). 31 (19.6%) cases followed external cardiac massage (ECM) and 54 (34.0%) patients were implanted under epinephrine.
84 patients (52.8%) were alive at explant time: 52 (61.9%) were weaned, 16 (19.0%) were transplanted and 12 (14.3%) received long term assist device (other 4 – 4.8%) with a mean duration under ECLS of 10.1 ± 5.8 days. At 6 months follow-up, 63 (39.6%) patients remained alive.
There was no difference in survival between males (74 deaths – 60.7%) and females (22 deaths – 59.5%), p = 0.87. Patients who died at 6 months follow-up were older (56.9 ± 10.4) than survivors (49.4 ± 14.2), p = 0.0025. Patients under ECM at time of setup were less likely to survive (n = 8 – 25.8% vs n=55 – 43.0%, p = 0.0015) as well as patients receiving epinephrine (n = 14 – 25.9% vs n=49 – 46.7%, p = 0.0009).
Creatinine at setup time was lower in the group of survivors (155.9 ± 97.3 µmol/L vs 188.1 ± 99.2 µmol/L, p = 0.0332) as well as lactate (4.1 ± 3.2 mmol/L vs 6.5 ± 4.9 mmol/L, p < 0.0001). Aspartate aminotransferase (AST) was lower in survivors (695.6 ± 1072.4 IU/L vs 1292.0 ± 2890.4 IU/L, p = 0.0021). There was no difference in alanine aminotransferase (ALT) (p = 0.14).
At 24 hours follow-up, creatinine was lower in survivors (133.3 ± 109.0 µmol/L vs 204.3 ± 133.6 µmol/L, p < 0.0001). Lactate was also lower in survivors (2.1 ± 2.3 mmol/L vs 3.5 ± 3.6 mmol/L, p = 0.0027). There was no difference in AST (p = 0.07), ALT (p = 0.25).
Between setup time and 24 hours follow-up, creatinine decreased in survivors (-28.0 ± 65.5 µmol/L) while it increased in the deceased (+17.1 ± 86.7 µmol/L, p < 0.0001). AST also decreased in survivors (-184.8 ± 911.1 IU/L) while it increased in the deceased (+788.2 ± 3552.9 IU/L, p = 0.0034). ALT remained stable in survivors (+2.1 ± 471.1 IU/L) while it increased in the deceased (+431.2 ± 1805.9 IU/L, p = 0.0047). There was no significant difference in lactate (p = 0.82).
Conclusion: ECLS results for patients in acute cardiogenic shock were acceptable at our centre. Younger patients without a requirement of epinephrine or prior ECM at time of setup had improved survival. Furthermore, improvement of creatinine and AST at 24 hours favoured better survival.

P1856

Clinical consequence of new-onset persistent left bundle branch block after transcatheter aortic valve replacement

E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; A Ruiz-Salas[2]; AJ Dominguez-Franco[2]; F Carrasco-Chinchilla[2]; JM Garcia-Pinilla[2]; L Morcillo-Hidalgo[2]; JH Alonso-Briales[2]; JJ Gomez-Doblas[2]; MF Jimenez-Navarro[2]; JM Hernandez-Garcia[2]; E De Teresa-Galvan[2]
[1]Department of Cardiology , Malaga, Spain; [2]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

Background: Cardiac conduction disturbances can develop after transcatheter aortic valve replacement with expandable prosthesis because the conduction system exists adjacent to the aortic valve. However, the clinical consequence of patients with new onset conduction disturbances is not clear.
The aim of this study was to determine the impact of new-onset persistent left bundle branch block (LBBB) on late outcomes after TAVR.
Methods: A total of 368 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 210 patients (57.1%) immediately after TAVI and persisted at hospital discharge.
At a median follow-up of 32 months (range 1 to 78 months), there were no differences in mortality rate between the N-LBBB and no N-LBBB groups (22.9% vs. 27.3%; adjusted-hazard ratio: 0.845 [95% confidence interval (CI): -0.558 to 1280]; p = 0.427. There were no differences between groups regarding cardiovascular mortality HR=-0.511 (95% CI 0.229-1.141),p = 0.102, rehospitalizations for heart failure HR=1.344 (95% CI 0.591-3.058),p = 0.481.
32.9% required PPI in the first month and only 8 patients with N-LBBB required PPI during the follow-up period. There were 3 cases of unexpected (sudden or unknown) death was observed in 2 patients with N-LBBB.
Patients with N-LBBB showed a poorer evolution of left ventricular ejection fraction over time (1 and 3 years) than no N-LBBB group: 61.3 ± 9 vs. 65.1 ± 7,p = 0.011; and 56.2 ± 13 vs. 62.8 ± 7%,p = 0.367, respectively). N-LBBB was also associated with a poorer New York Heart Association functional class at follow-up (1.72 ± 0.7 vs. 1.5 ± 0.5,p = 0.047).
Conclusions: N-LBBB was a frequent complication of transcatheter aortic valve replacement, but it was not associated with any increase in overall or cardiovascular death or rehospitalization for heart failure after a mean follow-up of 2.21 years.

P1857

Predictors of survival and one year outcomes after continuous flow left ventricular assist device implantation

E Nestorovic[1]; N Milic[2]; S Putnik[1]; D Terzic[1]; A Janjic[1]; M Milosevic[1]; D Markovic[3]; J Cumic[3]; A Ristic[4]; D Trifunovic[4]; I Nedeljkovic[4]; M Banovic[4]; S Raspopovic[4]; M Ristic[1]
[1]Clinical Center of Serbia, Department for Heart Transplant, LVAD and ECMO, Hospital for Cardiac surgery, Belgrade, Serbia; [2]Medical Faculty University of Belgrade, Serbia, Department for medical statistics and informatics, Belgrade, Serbia; [3]Clinical Center of Serbia, Belgrade, Center for Anesthesiology and Resuscitation, Belgrade, Serbia; [4] Clinical Center of Serbia, Serbia, Cardiology Clinic, Belgrade, Serbia

Background: The aim of this study was to assess the outcomes of patients with advanced heart failure (HF) treated with continuous flow left ventricular assist devices (CF-LVAD) and to determine factors that may be associated with improved survival, in terms to improve clinical outcomes of CF-LVAD patients.
Methods: This is a prospective study of 47 consecutive patients with advanced HF who received CF- LVAD at our institution. The overall median duration of CF-LVAD support was 13 (9-21) months. In 42 patients CF-LVAD was used as a bridge-to-transplantation (BTT) and in 5 patients as destination therapy (DT). Overall survival and adverse events at 1 year were evaluated. Echocardiographic, functional, renal and liver function outcomes were assessed at 3, 6 and 12 months.
Results: The overall 30 day, 6-months and 1-year survival for both BTT and DT patients were 89%, 85% and 80%, respectively. At 3 months after CF-LVAD implantation, we noticed significantly improvement in dimensions of LV (LVEDD, LVESD), LVEF, BNP, NYHA functional class, blood urea nitrogen and total bilirubin ($p < 0.05$ for all), and they remained normal through all first year of follow-up. Improvements in estimated glomerular filtration rate was significant after 3 months in group of patients with baseline renal dysfunction ($p = 0.004$), with also no further change afterward. Any kind of adverse events were present in 27 (57.4%), with bleeding as the most common complication in 19 (40.4%). In univariate analysis, blood urea nitrogen and renal failure were significant predictors of survival (HR=1.1, $p = 0{,}034$ and HR=14.2, $p < 0{,}001$, respectively). Renal failure was found to be an independent risk factors for the overall survival in multivariate Cox regression analysis (HR= 13.1, $p < 0{,}001$).
Conclusions: CF-LVAD improves functional, cardiac, renal and liver function in patients with advanced HF. As renal dysfunction is common following CF-LVAD implantation and renal failure is an independent risk factor for overall survival, the key of LVAD success is determination of optimal timing of CF-LVAD implantation in order to avoid end-organ dysfunction and achieve better postoperative outcomes.

P1858

Symptoms, physical examination and biomarkers are important determinant of reactions to adaptive servo-ventilation

Y Nishihata[1]; N Komiyama[1]
[1]*St. Luke's International Hospital, Department of Cardiology, Tokyo, Japan*

Background: Adaptive servo-ventilation(ASV) has been reported that it could improve heart failure(HF) condition and prognosis in some small clinical studies. However, a recent large trial showed mortality was increased with ASV. It's not clear what kind of patients should stop or continue ASV.
Purpose: To assesse clinical parameters which could predict the reactions to ASV.
Methods: We investigated 61 HF patients treated with ASV in our hospital between June 2009 and December 2015. We examined patient's background, symptoms, vital sings, laboratory data, cardiac function assessed by echocardiography and clinical responses.
Results: Their mean left ventricular ejection fraction was 37.3± 19.3% and mean NT-proBNP was 8666± 11634 pg/ml. At the time of ASV-initiation, 27 patients felt comfortable (C-group) and 34 felt uncomfortable (UC-group). In C-group, their proportional pulse pressure (PPP) and heart rate (HR) were significantly improved than in UC-group (ΔPPP 6.2± 6.8 vs -0.5± 10.0 mmHg, $p < 0.01$; ΔHR -6.7± 6.4 vs -1.7± 8.2 bpm, $p < 0.01$). Among 32 patients who could continue ASV at least 1 month, patients in C-group showed significant decrease of NT-proBNP than in UC-group ($p < 0.05$). Readmission due to HF under ASV-therapy were observed more frequently in UC-group than in C-group ($p < 0.01$) accompanied by poorer improvement of NT-proBNP ($p < 0.05$). There were 9 patients whose comfortableness became worse and 7 stopped ASV-therapy. The other 2 continued ASV but they were attacked by sudden cardiac death although their NT-proBNP were improved enough. They had might been enough decongested and ASV might worsened their hemodynamics.
Conclusions: Patient's symptoms reflect the hemodynamic responses to ASV, and those could predict the efficacy of ASV-therapy in patients with HF.

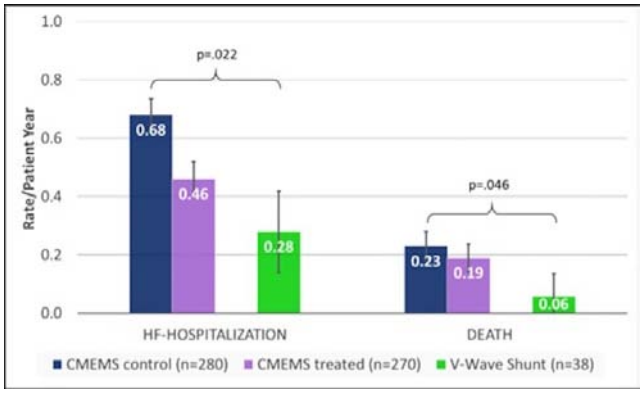
P1859

Impact of interatrial shunting on heart failure morbidity and mortality: comparison to the CardioMems Champion cohort

W T Abraham[1]; J Rodes-Cabau[2]; S Bergeron[2]; M Bernier[2]; I J Amat Santos[3]; T Ben Gal[4]; RAN Kornowski[4]; L Nombela Franco[5]; B Garcia[6]; A Kerner[7]; S D Anker[8]; S Sergio Shkurovich[9]; N L Eigler[9]
[1]*The Ohio State University, Columbus, United States of America*; [2]*Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, Canada*; [3]*University Hospital Clinic of Valladolid, Valladolid, Spain*; [4]*Rabin Medical Center, Petah Tikva, Israel*; [5]*Hospital Clinic San Carlos, Madrid, Spain*; [6]*University Hospital Vall d'Hebron, Barcelona, Spain*; [7]*Rambam Health Care Campus, Haifa, Israel*; [8]*Charité - Universitätsmedizin Berlin, Berlin, Germany*; [9]*V-Wave, Agoura Hills, United States of America*

Funding Acknowledgements: V-Wave, Ltd.

Background: We hypothesized that left atrial decompression with a percutaneously implanted interatrial shunt device would reduce HF hospitalizations and all-cause mortality in patients with advanced HF when compared to a well-matched historic controlled cohort.
Methods: Patients with chronic NYHA Class III/ambulatory Class IV HF, regardless of LVEF, on maximally tolerated guideline directed drug and device therapies, and a prior HF hospitalization or elevated neurohormones were enrolled in a single arm open label study at 6 centers. After transseptal catheterization and implantation of the shunt device across the fossa ovalis, patients were followed for 12 months. Demographics and outcomes were compared to the Champion trial cohort of 550 patients enrolled with similar eligibility criteria. Champion was a prospective, randomized, patient blinded controlled study of implantable pulmonary artery pressure monitoring used to guide HF therapy.



Figure

Results: 38 consecutive patients, 97%/3% Class III/IV, and 21% with LVEF >40%, were successfully shunted. Although shunt patients were generally well-matched to the entire Champion cohort with respect to LV function and usage of drugs and devices, shunt patients were older (66 ± 9 vs. 62 ± 9 years; $p = 0.0083$), were more likely to have an ischemic etiology (76% vs. 60%; $p = 0.041$), have diabetes (68% vs. 49%; $p = 0.020$), have poorer renal function (eGFR 54 ± 20 vs. 61 ± 16 ml/min·1.73m2; $p = 0.0062$) and have higher baseline left atrial pressures (PCWP 20 ± 6 vs. 18 ± 5 mmHg; $p = 0.019$). Shunted patients also had other markers of higher risk including a baseline 6-minute walk distance of 289 ± 112m and NT-proBNP of 2640 ± 2301 pg/ml. During an average follow-up of 11.7 months, shunted patients had 10 hospitalizations for worsening HF and 2 deaths. When compared to the entire Champion cohort there were significant reductions in the annualized rates of heart failure hospitalization and mortality (Figure). Baseline and 6-month doses of renin-angiotensin antagonists and beta-blockers were nearly identical between the shunted and Champion control patient cohorts. Shunted patients were on smaller doses of mineralocorticoid receptor antagonists and larger doses of loop diuretics that remained stable over 6 months ($P < 0.012$ for all comparisons).
Conclusions: Shunt patients with similar eligibility criteria generally had higher risk baseline characteristics than Champion patients. Nonetheless, interatrial shunting was associated with significantly lower rates of HF hospitalization and all-cause mortality than the less ill but otherwise well-matched historical controls. These observations are not explained by different dosing of HF medications and may be indicative of a beneficial device effect. If confirmed in larger prospective randomized controlled studies, interatrial shunt implantation could be an important new approach for treating patients with advanced heart failure.

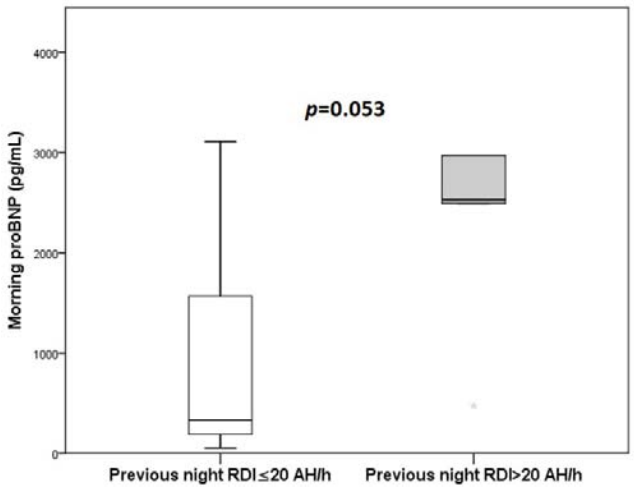
P1860

Antibradycardia pacemaker with sleep apnea monitor: a new tool to evaluate left ventricular filling pressure?

J B Augusto[1]; S Antunes[1]; M Faustino[1]; N Cabanelas[1]; F Madeira[1]; H Vasconcelos[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal*

Background: Sleep apnea (SA) is highly prevalent in pacemaker (PM) patients and it is associated with an increased risk of heart failure. Currently, some conventional antibradycardia pacemakers incorporate a SA monitoring (SAM) function, which enables the detection of severe SA.
Purpose: We aimed to validate a SAM function of antibradycardia pacemakers for the prediction of left ventricular filling pressure, based on the determination of

pulmonary capillary wedge pressure (PCWP) and pro B type natriuretic peptide (proBNP).
Methods: We conducted a prospective study of consecutive patients evaluated in a PM consultation who had a single or dual-chamber antibradycardia PM with an incorporated SAM. SAM detects and reports abnormal breathing events during the night, which can be measured as the number of apnea-hypopneas (AH) per hour: the respiratory disturbance index (RDI). We recorded data regarding: absolute number of apnea-hypopneas and RDI from the night before the consultation (defined as between 00h00 and 05h00) as well as the proportion of nights with RDI>20 AH/h since last device reset. In the morning we assessed both mitral E/e' ratio (using transthoracic echocardiogram) and proBNP. PCWP was calculated using Nagueh's formula (1.24x(E/e') + 1.9mmHg).
Results: A total of 30 patients were included (mean age 78.6 ± 12.0 years, 43.3% male and mean body mass index 26.9 ± 3.9 Kg/m^2). In the preceding night, median RDI was 8.0 AH/h (interquartile range (IQR) 5.0-21.0 AH/h). In the morning, median proBNP was 517pg/mL (IQR 223-2750pg/mL) and median PCWP was 15.9mmHg (IQR 11.8-27.0mmHg). Patients who had a higher proportion of nights with RDI>20 AH/h had significantly higher PCWP and proBNP values (r=0.45 and r=0.61, $p = 0.043$ and $p = 0.004$, respectively). In the preceding night, a higher number of AH as well as a higher RDI were associated with elevated values of proBNP in the morning (r=0.70 and r=0.71, respectively, both $p < 0.001$). There was a trend towards an increased PCWP in patients with higher AH and RDI in the previous night ($p = 0.093$ and $p = 0.068$, respectively). ProBNP also tended to be superior in patients with RDI>20 AH/h in the previous night (median 2529 vs. 330pg/mL, $p = 0.053$) (Figure 1).
Conclusions: Pathologic values obtained in sleep apnea monitors available in conventional antibradycardia pacemakers correlate with elevated proBNP and PCWP values. This new tool might be useful in the evaluation of the risk of heart failure, allowing both assessment and guidance in the management of left ventricular overload.



Morning proBNP according to RDI strata

P1861
Effects of cardiac rehabilitation on exercise capacity and WHO-quality of life undergoing CABG patients- A quasi-randomised controlled trial
J Jamal Uddin[1]
[1]*Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh*

The effect of home-based cardiac rehabilitation following coronary artery bypass graft surgery in a low income country: A controlled trial.
Background: More than 85% of global cardiovascular disease deaths occur in low and middle-income countries with coronary heart disease contributing to more than half of these deaths. Few controlled trials of cardiac rehabilitation (CR) have been conducted in low and middle income countries to date.
Methods: We undertook a quasi-randomized controlled trial design and allocated patients 1:1 to either based CR program in addition to usual care (CR group) or (UC group)usual care alone (UC group) according to their date of surgery. We screened all patients who were admitted to the Department of Cardiac Surgery at Ibrahim Cardiac Hospital & Research Institute (ICHRI) in Bangladesh from July 2012 to July 2013.Male and females patients were included if they were admitted for elective coronary artery bypass graft (CABG) surgery aged 25 to 65 years. Patients allocated to the CR group were offered an initial CR class, and provided with an educational booklet that contained details of home-based exercise programme, and received a monthly telephone call from a member CR team over a 12-month period. Data on exercise capacity as measured by maximal oxygen uptake (VO2max), coronary risk factors, health-related quality of life, and mental health status were collected between 3-12-months follow up. Differences in outcomes were compared between CR and UC groups in patients with complete outcome data.
Results: A total of 142 participants participated in the trial - 71 allocated to CR group and 71 allocated to UC group. At 12 months follow up, 61 (86%) and 40 (56%) patients respectively provided complete outcome data.VO2max at 6-months follow up was higher in the CR compared to UC group (mean difference: 7 ml/kg/min, 95% CI: 2 to 11, $P = 0.005$). Compared to baseline, improvements in overall and domain specific health-related on the WHO-QoL-BREF questionnaire, PHQ-9 assessed mental well-being beingon PHQ-9, and CHD risk factors (body mass index, blood pressure, HbA1C, lipids) were significantly greater ($P < 0.05$) for CR compared to UC group patients.
Conclusions: The addition of a home-based CR programme of an educational booklet supported by healthcare professional telephone calls to usual care following CABG surgery was shown to provide important patient benefits compared to usual care alone. In the context of low or middle

P1862
Staged or combined carotid endarterectomy in patients undergoing coronary artery bypass grafting
R Rustambek Karimov[1]; A Irnazarov[1]; A Yulbarisov[1]; A Djafarov[1]
[1]*Tashkent Medical Academy, Faculty and Hospital Surgery, Tashkent, Uzbekistan*

Background: Ideal surgical approach for patients with hemodynamically significant carotid and coronary disease remains controversial. We analyzed our 4-year experience and compared early and long-term outcome following staged and combined carotid and coronary artery bypass.
Purpose: To compare the short and long-term results as well as the risk factors of both staged and combined carotid and coronary revascularization.
Methods: Overall 260 patients with combined carotid and coronary artery disease undergoing carotid endarterectomy and coronary artery bypass were prospectively involved in the research. First group patients were scheduled for a staged procedure (carotid endarterectomy followed by coronary artery bypass within 1 week). Patients of second group were deemed to a combined procedure (due to the unstable cardiac status). All patient data including immediate perioperative events, 30-day, and long-term outcome, demographics, risk factors were recorded and then analyzed. Patients in both groups were compared for pre- and perioperative data as well as immediate, 30-day, and long-term survival.
Results: First group included 148 patients and second one included 112 patients. Preoperative demographics and clinical data were similar in both groups except that preoperative cerebrovascular events were more common in the latter (31.4% versus 23.4%) and bilateral carotid disease was more common in the first group. The EuroSCORE was higher in the second group patients (2.91 versus 2.65). Carotid surgery techniques were similar; intraluminal shunting was more frequent in the second group than first one (33.33% versus 9.88%). Additional cardiac procedures in addition to coronary surgery was predominant in patients of second group. 30-day neurological adverse event rates, ICU, and hospital stay were significantly higher in the second group. The 30-day mortality was also sigficantly higher in the second group patients (1.96% versus 4.62%).
Conclusion: Staged and combined surgical manners provide truly comparable outcomes. A staged method of treatment may yield a more favorable neurological outcome with noticeably reduced need for intraluminal shunting. However, long-term outcome is similar for both approaches.

P1863
Acute aortic syndromes - What we know and what we don't know
S Alegria[1]; I Rosario Cruz[1]; R Pereira[1]; AI Marques[1]; C Gomes[1]; G Morgado[1]; D Caldeira[1]; O Simoes[1]; AR Almeida[1]; MJ Loureiro[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Introduction: Acute aortic syndromes (AAS) are emergent conditions, with a very high mortality in the first hours. Given this, a timely diagnosis is critical to improve prognosis. However, there are few contemporary epidemiological data.
Objectives: Characterization of a population of patients with AAS admitted to a tertiary hospital without cardiac surgery and identification of predictors of mortality.
Methods: Longitudinal analysis of patients diagnosed with AAS between 2005 and 2016. Cox regression analysis was performed to identify predictors of 30-day mortality.
Results: A total of 39 patients (mean age 68 ± 16 years, 56.4% males) were identified. 79.5% had type A aortic dissection (AD), 15.4% type B and 5.1% were classified as non-A non-B AD. 94.7% had hypertension, 31.4% smoking habits, 24.2% dilation of the aorta and 21.2% previous manipulation of the aorta

by catheterization and/or surgery. The most frequent symptoms at presentation were anterior chest pain (58.8%) and abdominal pain (26.5%). In 13.2% focal neurological signs were observed, and 20.6% had cardiopulmonary arrest. On admission 31.3% were hypotensive and 28.1% hypertensive. The first imaging test performed was transthoracic echocardiogram in 55.3% of the patients and the exam that confirmed the diagnosis was computed tomography in 81.6% and transoesophageal echocardiogram in the remainder. The diagnosis was established less than 4 hours after admission in 53.6%. The main complications were moderate or severe aortic regurgitation in 18.2%, stroke in 13.2%, acute kidney injury in 35.3%, acute myocardial infarction in 10.5%, pericardial effusion in 54.5% and cardiac tamponade in 18.4%. 32.4% of patients required antihypertensive drugs and 12.5% vasopressor support. Pericardiocentesis was performed in 21.6% and emergent surgery in 68.4% (88.5% with type A AD). Among the non-operated patients, 25.0% died before surgery, 16.7% had uncomplicated type B AD, 16.7% were refused, 8.3% had major stroke with poor neurological prognosis, and in 33.3% the reason was unknown. Mortality at 30 days was 33.3%, at 1 year 45.2% and during the total follow-up (849 ± 1196 days) 48.7%. There was a trend towards higher mortality in the non-operated patients (50.0 vs. 25.0%, p = 0.134). Focal neurological deficits (p = 0.022), hypotension at admission (p = 0.021) and the need for vasopressor support (p = 0.039) were identified as predictors of 30-day mortality. The independent predictors were the presence of focal neurological deficits (HR 7.0, 95% CI 1.4-34.1, p = 0.016) and hypotension at admission (HR 4.4, 95% CI 1.1-18, 4, p = 0.041).

Conclusion: AAS present more frequently with chest pain, however there are several forms of presentation, making this a challenging diagnosis. In this study 30-day mortality was high, and focal neurological deficits and hypotension were identified as independent predictors of mortality.

P1864

Effect on long survival of acute myocardial infarction in Killip classes III or IV patients undergoing invasive coronary procedures.

L Laura Sayagues Moreira[1]; RC Vidal Perez[1]; A Lopez Baz[2]; R M Agra Bermejo[1]; U Anido Herranz[1]; JL Allut Garcia[1]; A Lopez Lago[1]; JR Gonzalez-Juanatey[1]; C Galban[1]; J M Garcia Acuna[1]; C Pena Gil[1]

[1]University Hospital of Santiago de Compostela, ICU , Santiago de Compostela, Spain; *[2]HU Princesa, Neurophysiology, Madrid, Spain*

On behalf of: cardioCHUS

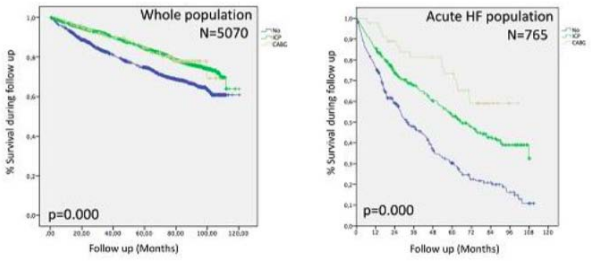
INTRODUCTION. The Killip class classification for heart failure it is used to predict short-term mortality in patients with acute coronary syndrome (ACS)

Objectives: To determine the contemporary long-term prognosis of ACS with acute heart failure graded according to the Killip classification.

Methods: Cohort third level hospital study of consecutive hospitalized patients with ACS diagnosis from 2004 to 2009. Follow-up was done by clinical review or telephone contact and death or cardiovascular events were recorded, as well as the cause of death

Results: 5070 patients were included with a complete follow up after a mean of 5.8 ± 2.6 years. The clinical characteristics were analyzed in relation with Killip class at admission (shown in Table). A stepwise gradient in the adjusted hazard ratio (HR) for mortality was observed with increasing Killip class: class > I HR 4.35 (95% CI 3.81 to 4.97) unexpectedly, in a landmark analysis excluding deaths < 30 days after admission, patients in Killip class IV had a lower adjusted long-term mortality than those in class III (shown in Figure)

Conclusions: The heterogeneity in early versus late risk in patients with Killip class IV that survive at discharge heart failure it is present in our contemporary cohort highlighting the importance of an appropriate early treatment in cardiogenic shock patients



prognosis impact of revascularization

	KILLIP I N:4305 (84.9%)	KILLIP II N:554 (10.9%)	KILLIP III N:146 (2.8%)	KILLIP IV N:65 (1.4%)	P-VALUE
Mean Age (years)	64,5 (SD 13)	72 (SD 13)	77 (SD 7.9)	66.8 (SD 12.9)	0.000
Sex (% male)	3085 (71.7%)	358 (64.6%)	93 (63.7%)	48 (73.8%)	0.001
Hypertension (%)	2373 (55.1%)	345 (62.3%)	102 (69.9%)	26 (40%)	26 (40%) 0.000
Diabetes (%)	1049 (24.4%)	218 (39.4%)	69(47.3%)	17 (26.2%)	0.170
Hyperlipidemia (%)	2054 (47.7%)	237(42.8%)	53 (36.3%)	16 (24.6%)	0.170
ACS with ST elevation(%)	1237 (28.4%)	190 (33.3%)	51 (32%)	51 (69%)	0.000
Prior PCI (%)	370 (8.6%)	40 (7.2%)	9 (6.2%)	2 (3.1%)	0.209
Prior Heart Failure (%)	115 (2.7%)	76 (13.7%)	20 (13.7%)	5 (7.7%)	0.000
Mortality at end follow up (%)	610 (14.1%)	284 (51.3%)	103 (70.5%)	45 (69.5%)	0.000

[Characteristics by Killip Class]

RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONISTS

P1865

Effect of renin-angiotensin antagonist in patients with impaired renal function and heart failure: results from KorAHF registry

SY Se Yong Jang[1]; SC Chae[1]; DH Yang[1]; BH Oh[2]; ES Jeon[3]; JJ Kim[4]; MC Cho[5]; SH Baek[6]; SM Kang[7]; DJ Choi[8]; BS Yoo[9]; KH Kim[10]; HY Park[11]

[1]Kyungpook National University Hospital, Daegu, Korea Republic of; *[2]Seoul National University Hospital, Internal Medicine, Seoul, Korea Republic of*; *[3]Samsung Medical Center, Seoul, Korea Republic of*; *[4]Asan Medical Center, Seoul, Korea Republic of*; *[5]Chungbuk National University Hospital, Chungju, Korea Republic of*; *[6]The Catholic University of Korea, Seoul, Korea Republic of*; *[7]Severance Hospital, Seoul, Korea Republic of*; *[8]Seoul National University Bundang Hospital, Seongnam, Korea Republic of*; *[9]Wonju Severance Christian Hospital, Wonju, Korea Republic of*; *[10]Chonnam National University Hospital, Gwangju, Korea Republic of*; *[11]National Institute of Health, Osong, Korea Republic of*

On behalf of: KorAHF study investigators

Funding Acknowledgements: Korean National Institute of Health

Background: Renin-angiotensin-aldosterone system (RAAS) blockade with angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) is the corner stone in management of patients with heart failure. Some studies proposed the benefit of ACEI/ARB in patients with impaired renal function. However, side effects of those treatment may widely vary depending to the renal replacement therapy. Thus, renal replacement therapy can be important factor in expecting the benefit of ACEI/ARB. We aimed to analyze the different effect of early initiation of ACEI/ARB depending on renal replacement therapy in patients with impaired renal function and heart failure.

Methods: Among 5625 patients from the Korean Acute Heart Failure registry, 426 patients (68.9 ± 13.7 years-old, 253 men) who survived the index hospitalization and had creatinine clearance < 30ml/min/1.73m2 were analyzed. One-year all-cause mortality was used to assess prognosis.

Results: A total of 143 (33.6%) deaths were observed during 1 year follow-up. Among the study cohort, 243 (57.0%) patients with impaired renal function were taking ACEI/ARB at the discharge. Kaplan-Meier survival analysis showed that 1-year mortality was 39.4% and 19.2% for patient with ACEI/ARB and without, respectively (p = 0.0185). ACEI/ARB was significantly related to better prognosis in patients with renal replacement therapy (hazard ratio [HR]=0.462 [0.256-0.835], p = 0.011), whereas it was not in patients without renal replacement therapy (HR 0.756 [0.540-1.421], p = 0.591) in adjusted models (p for interaction=0.045).

Conclusion: Early ACEI/ARB treatment in patients with renal impairment was related to better prognosis especially in patients with renal replacement. Cautions

Table P1866.

Variables	Baseline	6 months	12 months	Groups
LA vol index (mL/m^2)	38.21±2.5338.71±2.64	35.77±1.89*p < 0.0534.80±1.77*	33.23±1.45*p < 0.0532.44±1.62*	R-grE-gr
IVRT, ms	130.54±13.74135.33±18.01	111.43±6.84*p < 0.001106.56±5.67*	100.56±5.31*p < 0.00194.11±5.01*	R-grE-gr
DT, ms	253.03±27.59257.78±33.09	220.35±25.36*p < 0.05212.22±23.73*	192.59±18.61*p < 0.05183.33±14.78*	R-grE-gr
E/A ratio	0.67±0.160.69±0.29	0.76±0.09*p < 0.050.84±0.15*	1.12±0.22*p < 0.0011.21±0.27*	R-grE-gr
E/e ratio	16.54±0.3416.97±0.41	14.66±0.74*p < 0.0513.91±0.53*	11.22±0.81*p < 0.00110.02±0.77*	R-grE-gr
HOMA IR	3.34±0.093.38±0.08	3.20±0.02*p < 0.013.05±0.09*	2.45±0.07*p < 0.0012.21±0.08	R-grE-gr
Mitral inflow patternDelayed relaxation, pts	53 (94.64%)43 (95.56%)	32 (57.14%)*p < 0.00110 (22.22%)	20 (35.71%)*p < 0.0012 (4.44%)	R-grE-gr
Pseudonormalisation	3 (5.376%)2 (4.44%)	2 (3.57%)*p < 0.011 (2.22 %)	--	R-grE-gr
Normal inflow pattern	--	22 (39.29%)*p < 0.00134 (75.56%)	36 (64.29%)*p < 0.00143 (95.56%)	R-grE-gr
	p>0.05			

Note: * - p < 0.001 from baseline

should be needed for initiating ACEI/ARB in patients with renal impairment who are not on renal replacement therapy.

P1866

Influence of long-lasting treatment with ramipril and eprosartan on diastolic dysfunction and insulin resistance

N Nadejda Sapojnic[1]; AP Caraus[1]; A Timbalari[1]; MA Caraus[2]; AN Moiseeva[1]; CD Roibu[3]
[1]Institute of Cardiology , Hypertension, Chisinau, Moldova Republic of; *[2]State University of Medicine and Pharmacy, Chisinau, Moldova Republic of*; *[3]Institute of Neurology and Neurosurgery, Stroke, Chisinau, Moldova Republic of*

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Hypertensive heart disease (HHD) is a hallmark of target organ damages (TOD) in hypertension (HT) and often coexist with insulin resistance (IR). This "satellite conditions"determines reciprocal enhancement on TOD. Pharmacotherapy should aim both HHD and IR and RAAS inhibitors will be of peculiar utility in such conditions.
Methods: 101 hypertensives with HHD (LVH and DD) and IR were randomly assigned to treatment with ramipril (R-gr; n=56, mean dose=15,3mg ± 1,2 mg/daily) or eprosartan (E-gr; n=45, mean dose=850 ± 12,4 mg/daily). Ambulatory blood pressure monitoring (ABPM), transthoracic echocardiography (TE), and HOMAIR were performed at baseline and after 6, 12-months period. Assessment of diastolic function comprised: left atrium (LA) vol index, isovolumetric relaxation time (IRVT), deceleration time (DT), E/A ratio, E/e' ratio. The threshold value for IR (HOMAIR) was considered >2.5.
Results: At baseline, group did not differ statistically with respect to clinic and hemodynamic status (Fig.1). Both therapeutic regimens have gradually improved indices of DD, as well as HOMA-IR values (p < 0.001), but with greater reduction in E-gr (p < 0.001) (Tab.2). To note, at the end of the study significantly decreased the number of patients with pathologic mitral filling patterns with switching to physiologic one in both studied arms but with superiority in E-gr (95.56% subjects in E-gr vs 64.29% in R-gr, p < 0.001) (Tab.2).
Conclusion: The findings showed that both ACEI Ramipril and ARB Eprosartan progressively improve compromised diastolic function and insulin resistance, but with greater efficiency in the Eprosartan-medicated arm, probably due to additional sympatholytic effect of its moiety.

Variables	Ramipril gr (56 pts)	Eprosartan gr (45 pts)	p
Age (yrs)	50.11±0.79	52.04±0.63	p>0.05
History of HT (months)	13.00±1.95	13.41±2.01	
Gender (M)	29 (51.79%)	20 (44.44%)	
SBP (mmHg)	201.31±7.41	203.61±7.84	
DBP (mmHg)	106.25±5.54	107.17±6.02	
HR (bpm)	74.5±5.39	74.33±5.34	
BMI (kg/m^2)	29.35±0.31	29.41±0.21	
HOMA-IR	3.34±0.09	3.38±0.08	
LV remodelling LVMI (g/m^2) RWT	140.42±15.54 0.44±0.06	148,76±10.93 0.45±0.06	

Fig.1 Baseline characteristics of groups

Baseline characteristics of groups

P1867

Real world experience of introducing the new heart failure drug LCZ 696 in ambulatory care setting

L O'connor [1]; J Kelly O' Haire[1]; BF Mcadam[1]
[1]Beaumont Hospital, Department of Cardiology, Dublin, Ireland

Chronic heart failure (CHF) is associated with significant morbidity and mortality. It affects 120,000 people in the Republic of Ireland with the annual estimated cost of €660m to the State. Despite optimal evidence based care, patients continue to experience symptoms and require ambulant IV Frusemide and/or admission for decompensation. The PARADIGM trial reported superiority of LCZ 696 over Enalapril. LCZ 696 is a combined Angiotensin Receptor and Neprilysin Inhibitor (ARNI), reducing the risk of cardiovascular death and hospitalizations with a better tolerability profile. A total of 35 patients were commenced on LCZ 696 (average age 70.6 years, 60% males, 40% females, average EF# 24%, New York Heart Association (NYHA) II-III, NYHA IV (2)) since August 2015 to date. Patients were screened based on criteria from the PARADIGM trial. A standardized protocol for commencement of the ARNI was introduced. A flush out period of 36 hours between the cessation of Angiotensin Converting Enzyme inhibitor and initiation of LCZ696 was initiated. Patients were commenced on the lowest dose 24mg/26mg BD and were followed up closely for any signs of side effects such as hypotension and renal impairment. Of the 35 patients who commenced on LCZ 696, 26 patients tolerated the agent. The average dose was 24mgs/26mgs mg BD, up titration occurred if SBP is > than 100mmHg with only 6 patients reaching the maximum dose of 97mgs/103mgs. The agent was discontinued in 9 patients due to: elevated liver function tests (1), fatigue (2) skin rash (1), symptomatic hypotension (3). Two patients had a significant deterioration in creatinine of over 50%. Three patients died during the time period: 1 due to CHF complicated by an incarcerated hernia, 1 patient died from oesophageal carcinoma, 1 patient died from organ failure and sepsis. Twenty six patients who tolerated LCZ 696 described feeling better and there was a 25% reduction in hospitalizations and need for IV ambulant diuretics for decompensation. One patient on a continuous infusion of Milrinone for the last 6 years was successfully weaned from this infusion following commencement of LCZ 696. There was a significant decrease in natriuretic peptides in patients who tolerated the agent well with 10% of this cohort experiencing a 75 % fall in NT-pro BNP levels, 23% had a 50% drop and 27% had a 25% reduction. A rise in NT pro BNP was observed in reoccurance of atrial fibrillation (1) and decompensation (3). Creatinine levels remained unchanged in 54 % of the patients with 46% having an increase of between 10 and 20%. Summary This is a real world single center experience of the use of ARNI agent in the CHF population. While the patients were selected as per the PARADIGM study, only 6 patients were titrated to the dose achieved in the study. All patients reported feeling better with 5 patients on reduced diuretic doses and most patients maintaining stable renal function with modified responses in natriuretic peptides.

P1868

Changes in hemodynamic parameters and cerebral oximetry during head-up tilt test in heart failure patients: the HARVEST study

H Hannes Holm[1]; E Bachus[1]; V Hamrefors[1]; O Melander[1]; G Taseveska[2]; A Fedorowski[2]; M Magnusson[2]
[1]Skane University Hospital, Department of Clinical Sciences, Lund University, Malmo, Sweden; *[2]Skane University Hospital, Department of Cardiology, Skåne University Hospital, Malmö , Malmo, Sweden*

On behalf of: HARVEST

Aims: Circulatory adaptation to orthostatic stress in congestive heart failure (CHF) has been poorly investigated. We aimed to analyse changes in hemodynamic parameters and cerebral oxygenation in patients with CHF undergoing head-up tilt test (HUT).
Methods: Synchronized non-invasive beat-to-beat hemodynamic monitoring, ECG, peripheral oxygen saturation (SpO2) and near-infrared-spectroscopy (NIRS) were applied to measure hemodynamic changes and absolute frontal cerebral tissue oxygen saturation (SctO2; normal range, 60-80%) during HUT. Forty-seven patients (mean-age: 71 ± 11 years, 79% male) with CHF, New York Heart Association (NYHA) class I–IV (I n=1, II n=16, III=21, IV n=2) and mean ejection fraction (EF) 37 ± 15%, in stable condition were included in the analysis. Twenty-four patients met criteria for heart failure with reduced EF (HFrEF), 9 had heart failure with preserved EF (HFpEF) and 8 had heart failure with mid-range ejection fraction (HFmEF). Differences in continuous variables were compared using Student's t-test
Results: After 3 min of HUT, both systolic (SBP, from 119 ± 28mmHg to 123 ± 23mmHg; p = 0.025), and diastolic blood pressure (DBP, from 64 ± 12mmHg to 69 ± 14mmHg; p < 0.001) significantly increased as also did heart rate (HR, from 70 ± 13bpm to 73 ± 14bpm, p = 0.012). In parallel, SctO2 decreased from 67 ± 5% to 62 ± 5% (p < 0.001). Only 3 patients (7%) met the diagnostic criteria of orthostatic hypotension.
Conclusions: Patients with CHF demonstrated increase in BP and HR paralleled by a significant drop in cerebral saturation during HUT. However, there were no symptoms of orthostatic intolerance reported, which suggests good orthostatic adaptation in patients with stable CHF.

P1869

Prognostic significance of myocardial energy expenditure and myocardial efficiency in patients with heart failure with reduced ejection fraction

MS Cetin[1]; E H Elif Hande Ozcan Cetin[1]; H Sasmaz[1]; A Temizhan[1]; S Aydogdu[1]
[1]*Ankara Turkiye Yuksek Ihtisas Hospital, Department of Cardiology, Ankara, Turkey*

Introduction: In Heart failure (HF) patients, myocardial blood flow (MBF), energy expenditure (MEE), myocardial efficiency has been poorly evaluated because of the necessity of invasive procedures in the determination of these parameters. Transthoracic echocardiography (TTE) can provide reliable data for MEE, MBF (via coronary sinus (CS) flows). Also, myocardial efficiency can be evaluated by the MEE to MBF ratio. We aim to assess MBF, MEE and energy efficiency and the prognostic value of these parameters in HF.

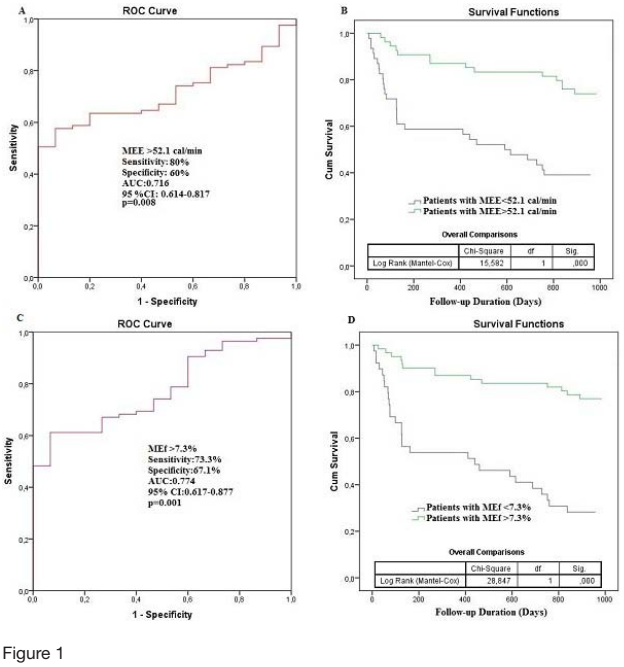


Figure 1

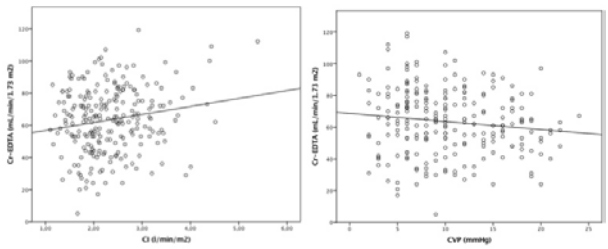
Methods: 80 patients with HF with reduced ejection fraction and 20 healthy subjects were included. Median follow-up duration was 901 ± 361 days. MBF was calculated via coronary sinus blood flow. MEE was measured from circumferential end-systolic stress, stroke volume and left ventricular ejection time. MEE to MBF ratio was determined as MEf.
Results: MEE was lower in HF group than the control group. MBF per minute was higher in HF group whereas MBF per 100 g left ventricular mass was not different. MEf was also lower in HF group. MEE and MEf was significantly correlated with troponin, BNP, uric acid and epicardial fat thickness. In Cox regression analysis, MEE (HR:4.396 (95% CI: 1.230-15.716) and MEf (HR:3.343 (95% CI: 1.025-10.905) were determined as independent predictors of mortality. In ROC analysis for prediction of composite end-point, a cut-off value 52.1 cal/min for MEE had a 80% sensitivity and 60% specificity and a cut-off value 7.3% for MEf had a 73.3% sensitivity and 67.1% specificity.
Discussion: Our study demonstrated that while MEE and MEf diminished in HF, MBF preserved with the symptomatic progression of HF. MEE and MEf were found to be associated with important prognostic markers and independent predictors of mortality in HF. Evaluation of MEE, MBF and MEf with echocardiography may utilize prognostic assessment in HF population.

P1870

Relation between invasive hemodynamics and measured glomerular filtration rate by 51Cr-EDTA clearance in advanced heart failure.

T Tania Deis[1]; L Balling[1]; S Boesgaard[1]; K Rossing[1]; M Schou[2]; F Gustafsson[1]
[1]*Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*;
[2]*Gentofte University Hospital, Gentofte, Denmark*

Background: The interaction between hemodynamics and kidney function in HF is still incompletely understood. In most studies, estimated glomerular filtration rate (eGFR) has been used as a measurement of renal function. Plasma clearance of 51-chromium-labeled ethylenediamine tetra-acetic acid (51Cr-EDTA) is a more accurate measurement of GFR. We investigated the association between invasive hemodynamic parameters and renal function estimated by 51Cr-EDTA in patients with advanced HF. This study tested the hypothesis that patients with reduced 51Cr-EDTA have lower cardiac index (CI) and mean arterial pressure (MAP) as well as higher central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP).
Methods: We retrospectively studied 242 patients with a left ventricular ejection fraction (LVEF) < 45 % treated with contemporary medical HF therapy, who underwent right heart catheterization (RHC) and had renal function estimated by 51Cr-EDTA-clearance.
Results: Univariate analysis demonstrated a significant correlation between mGFR and CI (r2 = 0.030, p = 0.007 and mGFR and CVP (r2 = 0.017, p = 0.049, figure) but no significant correlation was found between mGFR and MAP or mGFR and PCWP. When multivariate analyses were performed, none of the hemodynamic variables remained significantly associated with mGFR.
Conclusions: While CVP and CI were correlated with mGFR the results suggest that hemodynamics only determines renal function in advanced HF to a minor degree challenging the accepted assumption that renal dysfunction in HF mainly is due to renal congestion.



P1871

Impact of percutaneous coronary intervention on microcirculation in patients with myocardial infarction

ROMAN Viskov[1]; ALEX Mitichkin[1]; ANNA Tektova[2]; NINA Kazunina[2]; RAISA Stryuk[2]
[1]*Inozemtsev City Clinical Hospital, Moscow, Russian Federation*; [2]*Moscow State Medical and Dental University, Moscow, Russian Federation*

Research objectives: To assess the impact of percutaneous coronary intervention and coronary artery stenting (PCI) on of microcirculation (MC) in patients with myocardial infarction (MI).
Materials and methods: The study included 92 patients (61 male and 31 female, the median age 62,5 years [25%;75%:55,0;72,0 years] with a diagnosis of myocardial infarction, confirmed by clinical, laboratory and instrumental methods. 22 patients was underwent PCI, 70 patients received standard medical therapy alone.
All patients on the 1st and 7th days were examined using Laser Doppler flowmetry (LDF) with a laser analyzer LAKK-02, The amplitude-frequency spectrum of

oscillations was computed using wavelet transform; contribution of endothelial (ECMT), neurogenic (NCMT) and myogenic components (MCMT) of microvascular tone and efficacy index of microcirculation (EIM) - the ratio of active and passive mechanisms of vascular tone regulation. Statistica version 8.0 was used for all statistical testing, and statistical significance was considered when $p < 0,05$.

Results: In day 1 in patients undergoing PCI (group 1) it was revealed a significant increase in the amplitude of neurogenic and vascular components of vascular tone (NCMT 6,30[4,25;8,57], MCMT 4,96[3,30;6,38], ECMT 5,48[3,65;8,23], while in patients treated conservatively (group 2), these indicators were significantly reduced (NCMT 4,01[2,27;5,67], MCMT 3,10[2,05;4,29], ECMT 3,59[2,25;6,20], pNCMT=0,026, pMCMT=0,060, pECMT=0,012).

The ratio of active and passive mechanisms in both groups were comparable and not significantly different: EIM 1,60 [1,46; 2,14] vs 1,59[1,14;1,90], respectively.

On the 7th day in PCI (group 1) indicators of endothelial, neurogenic and myogenic components of microvascular tone declined slightly: NCMT 5,37[3,98;7,18], MCMT 4,75[3,42;5,73], ECMT 4,59[3,68;7,24]. In group 2 only neurogenic tone was decreased NCMT 3,79[2,79;6,64], myogenic tone was unchanged - MCMT 3,09[1,95;4,26] and endothelial tone was increased - ECMT 3,77[2,48;5,70]. Comparison of MC indices, characterizing vascular tone, showed, that parameters normalized amplitudes in patients 2 group were lower, but significant difference was obtained only for myogenic tone ($p = 0,004$), but EIM in group 1 was significantly higher 1,82[1,50;4,26] vs 1,37[1,11;1,88], ($p = 0,013$).

Conclusion: PCI patients for MI, compared with patients, who were treated conservatively, had more active microvascular state and less pronounced contribution to passive mechanisms (heart rate, respiration) in the processes of regulation of vascular tone at this level.

P1872

Hemodialysis induced alterations in coronary blood flow and cardiac function

D Dawood Sharif[1]; I Abu-Mokh[1]; Y Sharif[2]; A Sharif-Rasslan[3]; S Storch[1]; U Rosenschein[1]

[1]Bnai Zion Medical Center, Haifa, Israel; *[2]Technion, Haifa, Israel*; *[3]The Academic Arab College, Mathematics, Haifa, Israel*

Heart failure develops in 20-25% of patients on chronic dialysis. Coronary flow reserve is reduced even in the absence of obstructive coronary artery disease in dialysis patients. Sampling of coronary artery flow velocities is feasible using trans-thoracic Doppler echocardiography (TTE).

Aim: To test the hypothesis that dialysis reduces coronary flow and alters cardiac function.

Methods: Twenty five patients, age 71 ± 10yrs, 40% with heart failure were studied. TTE was performed before, during and immediately after hemodialysis. Doppler sampling of blood velocities in the left anterior descending coronary artery (LAD) was performed.

Results: No ischemic or other serious event occurred during or after dialysis. During dialysis, left ventricular end-diastolic diameter, and velocities through the mitral and aortic valves decreased significantly. While right ventricular longitudinal function decreased significantly during dialysis, tricuspid and pulmonary valves velocities remained without change. Myocardial performance index did not change significantly. Diastolic blood velocity in the LAD decreased from 38 ± 12 to 31 ± 10 cm/sec, $p < 0.001$. LAD flow indices as well as myocardial oxygen demand indices decreased significantly keeping their ratio unchanged during dialysis. After dialysis, left atrial diameter and left ventricular diameters were smaller than before the procedure. Blood velocity parameters in the LAD were similar in those with and without heart failure. Similar changes in echo-Doppler parameters occurred in both groups during dialysis.

Conclusion: Hemodialysis is associated with reduction in left side cardiac chamber diameters and velocities; coronary flow velocities is reduced but with maintenance of blood supply/ demand ratio and thus without ischemic events.

P1873

Percutaneous transarterial renal angioplasty in renovascular hypertension. immediate results and in-hospital evolution

I P Ivana Picone Borges[1]; ECS Peixoto[1]; RTS Peixoto[1]; RTS Peixoto[2]; ILPB Anjos[3]; LLB Bandeira[3]; CT Santos[3]; TLS Macedo[3]; DM Rebello[3]; AAB Aragao[1]

[1]Policia Militar do Rio de Janeiro, Rio de Janeiro, Brazil; *[2]State Institute of Cardiology Aloysio de Castro, Rio de Janeiro, Brazil*; *[3]Severino Sombra University, School of Medicine, Rio de Janeiro, Brazil*

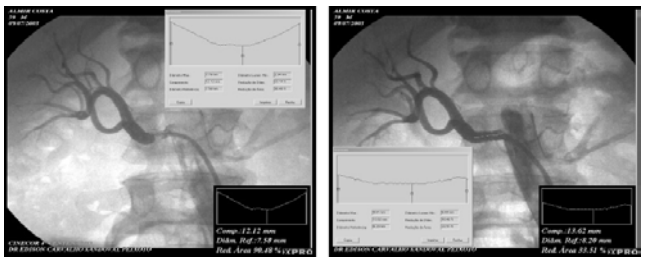
Background: Worldwire, it's not defined the use of stents in all renal vascular hypertension etiologies and the independent variables to predict technical and clinical success.

Objectives: To evaluate percutaneous renal artery intervention outcomes and in-hospital evolution. To identify the independent variables to predict technical and clinical success.

Methods: Eighty eight procedures were analyzed and subdivided into: Group A ($n = 25$), between 1981 and 1992, when the stent was not available; and Group N ($n = 63$), between 1993 and 2006, using balloon and/or stent. The procedures were also grouped by the two principal etiologies: atherosclerosis ($n = 68$) and fibromuscular dysplasia ($n = 11$).

Results: Age and osteal lesion were higher in Group N; Technical success of 98.4% versus 84.0% in N and A group, respectively ($p = 0.0216$), with similar and favorable in-hospital evolution. Pre and post procedure systolic arterial pressures were similar in both groups. Diastolic arterial pressure lower in group N. Whem the atherosclerotic and fibromuscular dysplasia groups were compared: age and osteal lesion were higher in former with similar technical success, in-hospital evolution and pre and post procedure systolic and diastolic arterial pressure in both groups. The systolic and diastolic arterial pressures dropped significantly between pre-procedure and hospital discharge period both etiology, atherosclerotic and fibromuscular dysplasia groups.

Conclusion: Technical success was higher in percutaneous renal artery interventions after the introduction of stents. A balloon angioplasty for fibromuscular dysplasia and, the possibility of implanting a stent for atherosclerotic etiology, constitute efficient renal vascular hypertension treatment



P1874

Association of metabolic syndrome with coronary artery disease extent and severity

A Aferdita Veseli[1]; I Alimehmeti[2]; H Gjergo[3]; J Seiti[1]; E Demiri[4]; S Kabili[5]; B Horjeti[6]; M Lezha[1]

[1]University Hospital Center Mother Theresa, Cardiovascular diseases, Tirana, Albania; *[2]The Faculty of Medicine, Family Medicine and Professional Diseases, Tirana, Albania*; *[3]The Faculty of Medicine, Heart and Vascular Diseases, Tirana, Albania*; *[4]Health Clinic "Neo Style", Tirana, Albania*; *[5]University Hospital "Shefqet Ndroqi", Cardiology, Tirana, Albania*; *[6]American Hospital, Cardiology, Tirana, Albania*

Background: Previous studies have suggested that Metabolic Syndrome (MS) is associated with Coronary Artery Disease (CAD).

Aim: Assessment of the association between MS and angiographic extent and severity of CAD.

Materials and Methods: The study population consisted of 607 consecutive patients who underwent elective coronary angiography in the period November 2011-April 2012. MS was defined according National Cholesterol Education Program (NCEP) Adult Treatment Panel III criteria. Angiographic extent and severity of CAD were quantified employing the modified Gensini score and the percentage of stenosis in the culprit artery.

Statistical Analysis: Data were summarized in the form of mean and percentage for continuous and categorical variables respectively. Linear regression, base and full model, was used to evaluate the correlation of MS and Gensini. Logistic regression, base and full model, was used to evaluate the correlation of MS and CAD. Student's t-test was used for comparing two groups with and without MS.

Results: MS was present in 307 patients (50.6%). Patients with MS consisted of a higher percentage of females (36% vs. 17%, $p < 0.001$), lower prevalence of smoking (44% vs. 56%, $p = 0.017$) and higher prevalence of urban residence (77% vs. 68%, $p = 0.019$). MS patients presented a higher number of diseased coronary arteries (1.5 vs. 1.3, $p = 0.014$) and a higher coronary heart disease Gensini index 9.8 vs 8.4, $p = 0.025$). Logistic regression analysis showed that MS was associated with higher odds of CAD (OR 1.872, 95%CI 1.280-2.737, $p = 0.001$) when adjusted for age and gender. Further adjustment for smoking, socioeconomic and demographic variables slightly increased the association of MS with CAD (OR 1.922, 95%CI 1.301-2.284, $p = 0.001$). Moreover in linear regression, MS proved to be significantly associated with Gensini score both in the basic model (β 2.465, 95%CI 1.246-3.684, $P < 0.001$) and the full model (β 2.344, 95%CI 1.129-3.558, $p < 0.001$).

Conclusion: MS is associated not only with the CAD but also with its extend and severity.

METABOLISM - DIABETES MELLITUS - OBESITY

P1875
Cardiac function in obese pregnant women

K Golinska Grzybala[1]; E Konduracka[1]; J Nessler[1]
[1]*John Paul II Hospital, Department of Coronary Disease and Heart Failure, Krakow, Poland*

Background: During pregnancy cardiovascular system undergoes complex changes including cardiac function and remodelling, left ventricle (LV) hypertrophy, as well as changes in systemic vascular resistance, secondary to growing uteroplacental circulation.
Purpose: The aim of this study was to evaluate the changes in cardiac remodelling, function and systemic vascular resistance throughout gestation in obese pregnant women in comparison to pregnant women with normal weight.
Methods: We conducted a prospective cohort study, which included consecutive 23 obese, pregnant women with singleton pregnancy and 40 pregnant women with normal weight (control group) (mean age 29.1 ± 1.1 vs. 31.1 ± 0.8 respectively, $p = 0.956$). The exclusion criteria were any cardiovascular disease diagnosed before pregnancy, diabetes mellitus, gestational diabetes or gestosis in previous pregnancy, chronic kidney disease, and multiple pregnancy. During pregnancy echocardiography, assessment of blood flow in uterine arteries (pulsatility index (PI) and blood pressure were assessed at two visits (V): V1 between 10 and 14 weeks and V2 between 25 and 30 weeks of gestation.
Results: At V1 we observed higher diastolic blood pressure in obese pregnant women in comparison to control group (82.6 vs. 75.5 mmHg respecticely, $p = 0.016$), as well lower LV cardiac index (LVCI) (2.5 vs. 2.8 l/min/m2, $p = 0.006$) and increased LV mass index (LVMI) (64 vs. 59 g/m2, $p = 0.047$). There was no differences in SVR and PI. At V2 systolic, diastolic and mean arterial pressure were higher than in control group (119 vs. 111 mmHg; $p = 0.017$, 79 vs. 68 mmHg; $p < 0.001$, 92 vs. 82 mmHg; $p < 0.001$, respectively). SVR and PI were increased (1469 vs. 1264 dyns cm-5; $p = 0.015$, 0.68 vs. 0.57; $p = 0.034$, respectively) , LVCI was lower (2.7 vs. 3.0 l/min/m2; $p = 0.033$), in contrast to LVMI (68 vs. 63 g/m2; $p = 0.042$). We observed no differences in LVEF at both visits in study groups, whereas end-systolic meridional wall stress (ESS) (which represents afterload) was significantly increased in obese women at V2 (43 vs. 39, 103 dyn/cm2; $p < 0,001$). What is more, ESS at V2 was positively correlated with LVMI (r=0.423; $p < 0.001$) and PI (r=0.357; $p = 0.001$), also measured at V2.
Conclusions: 1. In obese pregnant women we observed higher blood pressure, systolic vascular resistance and PI in uterine arteries, especially between 25 and 30 weeks of gestation. 2. Myocardial function in these women, expressed by end-systolic wall stress (ESS), LVCI and LVMI is impaired.

P1876
Patterns of left ventricular global longitudinal strain in diabetic patients by speckle tracking imaging.

AHMED Ahmed Elgohary[1]
[1]*research institue of ophthalmology, cardiology, Al Jizah, Egypt*

Introduction: Diabetic patients with normal left ventricular ejection fraction are frequently associated with diastolic dysfunction. Speckle tracking is more sensitive than LVEF in detection subclinical LV systolic dysfunction.
Aim: Detection of different patterns of global longitudinal strain in diabetic patients using global longitudinal strain by speckle tracking.
Methods: fifty two diabetic patients had been referred from internal medicine clinic after they had been tested for HBA1c test and stratified into two groups
Group I: it include26 DM patients with controlled blood sugar.
Group II: it include26 DM patients with uncontrolled blood sugar The two groups had been subjected to the following diagnostic workup: Full medical history, full clinical examination, laboratory assessment , twelve lead resting ECG ,Stress ECG, Echocardiography study, Traditional Tissue Doppler imaging ,Assessment of global longitudinal strain. Patients with IHD, Systolic dysfunction, CHD ,Valvular, Arrhythmia, HOCM ,Pericardial, major systemic disease had been excluded.
Result: there was significant statistical difference in GLS, Age , Diabetic Type ,Diabetic Duration,2HPP Blood sugar level, E/é ratio in controlled DM compared to uncontrolled DM ($p < 0.05$),there was no significant difference in Gender ,FBS. EF, E/A in controlled DM compared to uncontrolled DM.
Conclusion: Diabetic duration was strongly correlated with reduction of global Longitudinal strain. Poor blood glucose control, as indicated by HbA1c>6.5%, leads to reductions in LV global longitudinal systolic strain, which is associated with preclinical LV dysfunction.

P1877
Prevalence and effects of metabolic syndrome in a cardiac rehabilitation program

G Goncalo Neves Pestana[1]; A Rocha[2]; R Pinto[1]; M Tavares-Silva[1]; M Braga[1]; H Nascimento[1]; P Araujo[1]; A Nunes[1]; V Araujo[1]; F Parada[2]; MJ Maciel[1]
[1]*Sao Joao Hospital, Cardiology, Porto, Portugal*; [2]*Sao Joao Hospital, Physical Medicine and Rehabilitation, Porto, Portugal*

Background/Purpose: Cardiac rehabilitation (CR) is an essential tool in the management of patients (pts) after an acute coronary syndrome (ACS), effectively reducing morbidity and mortality. Nevertheless, current data comes from heterogeneous studies and its specific effects in particular subgroups is less clear. Metabolic syndrome (MS) is a pandemic, encompassing a number of cardiovascular risk factors that, together, are associated with a particularly somber prognosis. We looked into the prevalence of MS in a CR population and its effect on response to CR.
Methods: We retrospectively analysed data from a prospective cohort of pts referred to CR within 3 months after ACS and calculated the prevalence of MS as defined by the AHA and related societies in 2009. We then evaluated how this group's response to CR differed from that of pts without MS. Logistic regression and independent samples t-test were used for the statistical analysis.
Results: From a total of 809 pts with available data, 305 (37.7%) met the criteria for MS; these pts were more frequently female (20.3 vs 11.7%, $p = 0.001$) and older (mean age 56 vs 53 years, $p < 0.001$) comparing to pts without MS. Pts with MS were more likely to not complete the CR program, with and odds ratio of 1.74 (95% CI: 1.13-2.67, $p = 0.011$). And while exercise capacity, assessed by treadmill stress test time at baseline and at 3 months follow-up, was also significantly worse in pts with MS, both groups showed significant improvement; indeed, MS pts actually showed a greater relative increase (31 vs 25%, $p = 0.013$). Regarding secondary prevention targets at 1 year of follow-up, according to AHA guidelines, both groups achieved similar proportions of smoking cessation, physical activity, HDL cholesterol, triglycerides and glycaemic control, but blood pressure (86.2 vs 96.5%, $p < 0.001$) and body mass index (BMI, 23.4 vs 52.6%, $p < 0.001$) targets were less frequently attained in MS pts.
Conclusions: Metabolic syndrome is frequent in cardiac rehabilitation patients, but in our cohort they nevertheless showed a greater relative improvement in exercise capacity and similar risk factor profile control compared to those without MS, with the exception of blood pressure and BMI. These findings make it all the more relevant that MS pts seem to abandon the CR program more frequently and they should encourage us to further investigate this association and develop tools to oppose this trend.

P1878
Correlation between glycaemic status and left ventricular diastolic function in type 2 diabetes patients

M M Mohamed Eldeib[1]
[1]*Al-Azhar University, cardiology, Cairo, Egypt*

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 correlation between glycaemic status and left ventricular diastolic function 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 LVEDD,LVESD and LV EF%. 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, mean of DT, mean of IVRT, mean of Em wave, mean of E/Em degree of diastolic dysfunction. 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 for assessment of diastolic function in asymptomatic type 2 diabetic patients and its results are significant correlated with glycemic state.

P1879

Prevalence and characteristics of diabetes mellitus and insulin resistance in heart failure patients across Europe. A report of the 1st Postgraduate Course in Heart Failure of the HFA.

S Paolillo[1]; C Minoia[2]; K Ablasser[3]; G Di Stolfo[4]; M Merlo[5]; A Vachulova[6]; F Ruschitzka[7]; A Mathe[8]

[1]Department of Advanced Biomedical Sciences, Section of Cardiology, Federico II University of Naples , Naples, Italy; *[2]Sant' Antonio Abate Hospital , Cardiology, Gallarate, Italy*; *[3]Medical University of Graz, Department of Cardiology, Graz, Austria*; *[4]Casa Sollievo della Sofferenza Hospital, Cardiovascular Department, San Giovanni Rotondo, Italy*; *[5]University of Trieste, Cardiovascular Department, Azienda Sanitaria Universitaria Integrata, Trieste, Italy*; *[6]The National Institute of Cardiovascular Diseases, Bratislava, Slovak Republic*; *[7]University Heart Center, Department of Cardiology, Zurich, Switzerland*; *[8]University Hospital of South Réunion, Department of Cardiology, Saint-Pierre, Reunion*

On behalf of: 1st Postgraduate Course in Heart Failure of the Heart Failure Association

Introduction: Glucose metabolism abnormalities are common in heart failure with reduced ejection fraction (HFrEF), and adversely influence long-term prognosis. An increasing interest is focused on the recognition of overt diabetes mellitus (DM) and of insulin-resistance (IR) in HFrEF patients to improve therapeutic management and prognosis.
Purpose: Aim of the present report was to analyze the prevalence and characteristics of these conditions in HFrEF patients enrolled across Europe.
Methods: Six HF specialists of 3 European countries (1 from Austria, 1 from France, 2 from North Italy, and 2 from South Italy) were involved in patients' enrollment. In particular, they enrolled consecutive HFrEF patients seen from November 2016 to January 2017 fulfilling the subsequent criteria: 1) age ≥18 years; 2) EF ≤40%; 3) stable clinical conditions; 4) HF diagnosis since at least 6 months; 5) no acute coronary syndrome in the previous 3 months. On the same day patients underwent venous blood sample collection to assess fasting glucose, fasting insulin and glycated hemoglobin. IR was assessed through the evaluation of HOMA-IR, calculated by the formula [fasting Glucose (mmol/L) × fasting Insulin (mIU/L)/22.5], and the presence of IR was defined as HOMA-IR value >2.5.
Results: Two hundred twenty-two HFrEF patients were included in the analysis (72.5% M, mean age 66.5 ± 12.4 yrs, mean EF 30.9 ± 6.7%). The etiology of HF was ischemic in 131 (59%) patients, an idiopathic dilated cardiomyopathy in 75 (33.8%) subjects, and in the remaining cases other causes were identified; 71% of patients were in NYHA class I-II and 29% in NYHA III. Eighty patients (36%) exhibited DM (93.7% type 2 DM, 6.3% type 1 DM) with no significant differences among countries (47 vs. 37 vs. 34% in Austria, France and Italy, respectively; p = ns). Mean fasting glycemia was 141 ± 44 mg/dl, mean HbA1c 7.5 ± 1.7% and mean fasting insulin 20 ± 22 uUI/ml; 34% were on treatment with oral antidiabetics alone, 20% with oral antidiabetic plus insulin, 21% with insulin alone, and the remaining patients were on diet control. HF was of ischemic etiology in 76% of cases, and an adequate, however not optimal HF therapy was prescribed (59% ACE-i or ARBs, 74% beta-blockers, 40% MRAs, 12% LCZ-696). As regards to IR, among non-diabetics the prevalence of IR was 46% with mean HOMA index of 3.1 ± 2.8, mean fasting glycemia of 95 ± 23 mg/dl and mean fasting insulinemia of 12 ± 10 uUI/ml. HF was of ischemic etiology in 55% of cases and HF treatment was not optimal also in this group (65% ACE-i or ARBs, 73% beta-blockers, 30% MRAs, 0% LCZ-696).
Conclusions: Diabetes mellitus and insulin resistance are common comorbidities of European HF patients with similar distribution across countries and still not optimal HF treatment. More efforts are required to prompt recognize glucose metabolism abnormalities in HF and to optimize HF management in these subgroups to improve patients' quality of life and long-term prognosis.

P1880

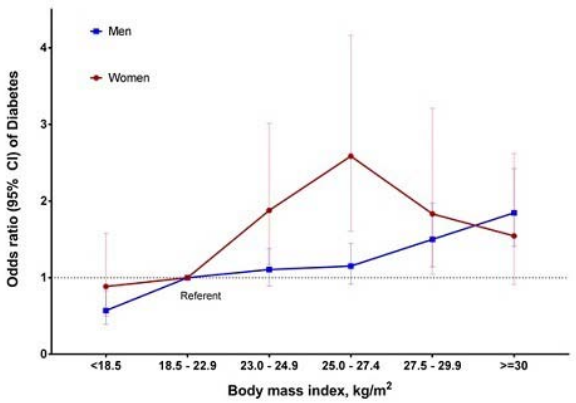
Sex differences in diabetic patients from the ASIAN-HF registry

T-H K Tiew-Hwa Katherine Teng[1]; WT Tay[2]; LM Yan J Tromp[3]; I Anand[4]; AM Richards[5]; SBL Ng G-Sh Lee[2]; JJL Yap[2]; MR Macdonald[6]; LH Ling B Siswanto[5]; HB Liew E-B Reyes[7]; W Shimizu S Zhang[8]; C Narasimhan C-M Yu[9]; SW Park T Ngarmukos[10]; JG Regensteiner[11]; CSP Lam[12]

[1]National Heart Centre Singapore; School of Population Health, University of Western Australia, Singapore, Singapore; *[2]National Heart Centre Singapore, National Heart Research Institute, Singapore, Singapore*; *[3]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; *[4]University of Minnesota, VA Medical Center Minneapolis MN and San Diego, CA, Minneapolis, United States of America*; *[5]National University Health System, Cardiovascular Research Institute, Singapore, Singapore*; *[6]Changi General Hospital, Singapore, Singapore*; *[7]Queen Elizabeth Hospital, Kota Kinabalu, Malaysia*; *[8]Nippon Medical School, Department of Cardiovascular Medicine , Tokyo, Japan*; *[9]CARE Hospital, Islamabad, India*; *[10]Korea University, Department of Cardiology, Seoul, Korea Republic of*; *[11]University of Colorado, School of Medicine, Aurora, United States of America*; *[12]Duke-NUS Graduate Medical School Singapore, National Heart Centre Singapore, Singapore, Singapore*

On behalf of: ASIAN-HF investigators
Funding Acknowledgements: Grants from Boston Scientific Investigator Sponsored Research Program, National Medical Research Council of Singapore, A*STAR and Bayer

Background: Diabetes mellitus (DM) portends a greater risk of heart failure (HF) in women than men. However little is known about sex differences in the association of DM with quality of life (QoL) and outcomes in HF, particularly in Asia.
Aims: To examine sex differences in clinical correlates, QoL and 1-year composite outcome (all-cause mortality or HF hospitalization) in diabetic Asian patients with HF.
Methods: In the ASIAN-HF Registry, a prospective multinational study of symptomatic HF across 11 Asian regions, we compared diabetic women vs men using WHO BMI cut-offs for Asians (lean : BMI <23; obese : BMI ≥27.5 kg/m2) and the Kansas City Cardiomyopathy Questionnaire (higher scores reflecting better QoL).
Results: Among 5255 Asian patients with HF (mean age 59.6 ± 13.1, 78% men), the prevalence of DM was similar in men (43%) and women (42%). Clinical correlates of DM in both men and women were older age and hypertension (in 67% DM ♂ and 68% of DM ♀). When adjusted for age and BMI, the odds of ischaemic aetiology was greater in DM men than women [OR=1.9 (95% CI 1.6-2.4) and OR 2.5 (95% CI 2.0-3.0) in non-DM men vs women respectively; p-interaction = 0.206]. In contrast, the odds of chronic kidney disease (CKD) was higher in DM women than men [OR = 1.6 (95% CI 1.3-2.1) and OR=1.1 (95% CI 0.9-1.4) in non-DM men vs women respectively; p-interaction = 0.019]. Among lean patients, 37% men and 31% women had DM (p = 0.028). Higher BMI was related to increased odds of DM, and this relationship was modified by sex (pinteraction=0.014). Adjusting for age and comorbidities, compared to BMI 18.5-23 kg/m2, the odds of diabetes increased in women above BMI ≥23 kg/m2 and in men above BMI ≥27.5 kg/m2 (Figure). QoL was poorer in diabetic women than men (overall score 60.4 ± 23.0 vs 63.1 ± 23.6, p = 0.045), particularly in the physical limitation domain (61.5 ± 27.3 vs 67.3 ± 25.9, p < 0.001) and self-efficacy (60.3 ± 28.1 vs 66.9 ± 25.8, p < 0.001). Adjusting for age and comorbidities, DM was associated with higher hazards of 1-year composite outcome in women than in men [HR=2.1 (95% CI 1.5-3.1) vs HR=1.4 (95% CI 1.2-1.6) respectively; pinteraction 0.002].
Conclusions: Diabetes is highly prevalent in Asian men and women with HF, even in the absence of obesity, and impacts QoL and 1-year mortality/morbidity outcomes more in Asian women than men.



Odds of diabetes at BMI levels in sexes

HEART FAILURE IMAGING

P1881

Relation between 2-dimensional speckle tracking echocardiography and MPI in diagnosis of coronary artery stenosis and subtle left ventricular dysfunction in stable angina pectoris patients.

M M Moustafa Mohamed Mohamed Eldeib[1]; E Elhefny[1]; A Ibraheem[1]

[1]Al-Azhar University, cardiology, Cairo, Egypt

Background: conventional echocardiography at rest provides little information regarding the presence of coronary artery disease in patients suspected of suffering from stable angina pectoris, Longitudinally orientated myocardial fibers are located subendocardially, the area most susceptible to ischaemia, that is why measurements of longitudinal motion and deformation may be the most sensitive markers of CAD using two-dimensional strain echocardiography (2DSE) The aim of this study was to study the correlation between 2DSE at rest and MPI in diagnosis of CAD in stable angina pectoris patients.
Methods: our study included (80) subjects suspected to be stable angina pectoris patients presented for evaluation of chest pain at Al-Hussein University Hospital – Al-Azhar University – Cairo – Egypt between December 2013 and December 2015
Results: In this study we found there was no correlation between the total number of segments affected in MPI and results of coronary angiography and P value was not significant for the summation of total segments and significant for LAD territory. There was a positive correlation between the number of segments affected in MPI and GLS17, GLS12, GLSr17 and GLSr12; in this study we found there was a positive correlation between the 17 segments in MPI and SLSS and SLSr parameters. In this study we found that strain parameters at BA, BAS, MA, MIS, MAS, AI and AL segments were found to be significant predictor of LAD stenosis and BP and MP were found to be significant predictor of LCX stenosis and BI was found to be predictor of RCA stenosis, also we found that strain rate parameters at BA, MA, MAS, AI, AL and apex segments were found to be significant predictor of LAD stenosis, and BL, BP and ML were found to be significant predictor of LCX stenosis and BI and MI were found to be predictor of RCA stenosis
Conclusion: Using of 2DSE at rest is not inferior to the use of MPI in the non invasive diagnosis of CAD, myocardial deformation imaging based on 2-dimensional longitudinal peak systolic strain analysis may differentiate between ischemic segments and non ischemic segments as compared with SPECT MPI.

P1882
MRI contribution in the diagnosis and left ventricle function evaluation in acute myocarditis

H Henda Neji[1]; M Kilani[1]; M Attia[1]; Z Belhaj[2]; I Kammoun[2]; I Baccouche[1]; S Hantous-Zannad[1]; K Ben Miled-M'rad[1]
[1]Abderrahmen Mami Hospital, Imaging department, Ariana, Tunisia; *[2]Abderrahmen Mami Hospital, Cardiology, Ariana, Tunisia*

Background/Introduction Clinical presentation of acute myocarditis is non-specific. Its diagnosis is challenging because of the overlap with acute myocardial infarction. MRI is nowadays a valuable imaging tool to make an accurate diagnosis of acute myocarditis.
Purpose: The purpose of this work is to describe MRI findings and left ventricle function in acute myocarditis.
Methods: Retrospective review of MRI data of 17 patients referred to imaging department of our institution between June 2015 and December 2016 for high clinical suspicion of acute myocarditis. All exams were performed with a 1.5 T machine. The protocol included STIR, first pass perfusion, early and late enhancement sequences.
The diagnosis of acute myocarditis was made according to Lake Louise consensus Criteria.
Results: Among the 15 patients, 9 (8 men and 1 women) had a positive MRI. Their mean age was 32.2 years. All of them had non-specific chest pain, 7 had a history of recent respiratory tract infection, and 6 had elevated troponins and electric modifications.
Edema presenting as myocardial high signal on STIR sequences was found in 5 patients. Early (on first pass perfusion and/or early enhancement sequence) and late gadolinium enhancement were found in all patients.
All these signs were located to the sub-epicardial myocardium in a linear (7 patients) or patchy (1 patient) presentation. The lateral left ventricle wall was involved in all patients.
Only 2 patients had left ventricle ejection fraction below 50%.
Conclusions: Cardiac MRI is an accurate tool to diagnose acute myocarditis, evaluate the lesions distributions and the left ventricle function.

P1883
Application of Dipirydamole stress Tc99m MIBI SPECT in patients with heart failure and reduced ejection fraction and suspected coronary artery disease

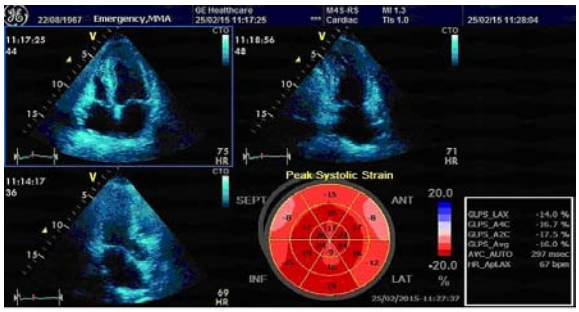
M Kostkiewicz[1]; W Szot[2]; A Lesniak-Sobelga[1]; P Rubis[1]; K Holcman[1]; S Smialek[1]; P Podolec[1]
[1]Institute of Cardiology, Jagiellonian University, John Paul II Hospital, Dpt Cardiovascular Diseases, Krakow, Poland; *[2]John Paul II Hospital, Dept of Nuclear Medicine, Krakow, Poland*

Beckground; Exercise cardiac stress testing in patients with heart failure is generally avoided for safety reasons. Our study aimed to assess overall safety and usefulness of dipirydamole stress myocardial perfusion scintigraphy for detection of possible coronary artery disease and myocardial viability using single-photon emission computed tomography (SPECT) in patients with echocardiographicaly proven heart failure and reduced ejection fraction.
Methods: The study comprised 60 patients with ejection fraction < 35% who underwent a 5-minute dipirydamole infusion (1.5 mg/kg body weight) protocol stress technetium-99m sestamibi SPECT. Visual 17-segment SPECT analysis used a standard five-point scoring system ranging from 0 (normal tracer uptake) to 4 (absent uptake). The SPECT results were considered abnormal if more than two segments had a stress score. All patients underwent coronary angiography procedure. The respective results in the groups were subsequently compared using the U-Mann-Whitney test and Pearson's correlation nonparametric test. Results. Sensitivity in the detection of CAD of gated SPECT study was calculated at the level of 83% , with positive predictive value at 88%. Hemodynamic response during dfipirydamole stress testing demonstrated changes in systolic blood pressure in 30% of patients ,in heart rate in 20% of patients, dyspnea in 25% and incidence of chest pain in 30%. of patients. No serious cardiac events were observed.
Conclusions: Dipirydamole Tc99m MIBI SPECT study was established to be well tolerated, safe and diagnostically accurate in patients with heart failure.

P1884
Two-dimensional speckle tracking echocardiography detects subclinical left ventricular systolic dysfunction among hypertensive patients

I Ivaylo Daskalov[1]; D Stoychev[1]; A Chobanov[1]; M Mladenova[1]; L Demirevska[1]; K Ramshev[1]
[1]MMA, Sofia, Bulgaria

Aim: The aim of this study was to determine a high risk group among hypertensive (HTN) patients on the base of diagnose of subclinical LV systolic dysfunction, defined as reduced global longitudinal strain (GLS) < -19.1%, using two-dimensional speckle tracking echocardiography (2DSTE).
Material and method: Eighty HTN patients were enrolled in the study and compared to 70 healthy volunteers. The participants in both group had preserved EF (>55%).
Results: We did not find significant differences in EF between both investigated groups considering gender and age (p=0.231). The GLS was normal in controls and patients with mild HTN without diastolic dysfunction (DD) (p = 0.897). We found significantly reduced GLS among patients with moderate and severe HTN with DD in different stages (p < 0.01). Multivariate analysis shows that this group has also higher values of BMI (p < 0.01), LVMM (p < 0.001), LAvol (p < 0.001), reduced Sm (p=0.01) and MAPSE (p=0.02).
Conclusion: Two-dimensional STE provides an excellent opportunity for early diagnose of subclinical LV systolic dysfunction among HTN patients. This diagnosis is most common in patients with moderate and severe HTN with DD in different stages when the risk of adverse cardiovascular events is higher, including heart failure. That's the reason to start an early and aggressive treatment as well as strict control of the risk factors.

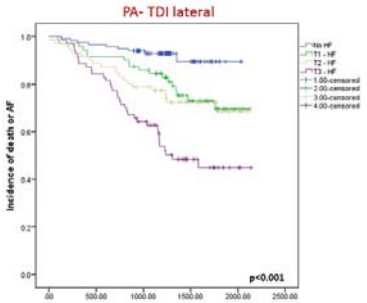


severe HTN, LV hypertrophy,reduced GLS

P1885
Clinical and prognostic association of total atrial conduction time measured by tissue doppler imaging in patients with heart failure. A report from SICA-HF.

V Vincenzo Nuzzi[1]; P Pellicori[2]; T Nikolaidou[2]; A Kallvikbacka-Bennett[2]; C Torromeo[1]; F Barilla'[1]; K Kaur[2]; D Salekin[2]; L Monzo[1]; J Cleland[3]; AL Clark[2]
[1]Sapienza University of Rome, Rome, Italy; *[2]Castle Hill Hospital, Department of Cardiology, Hull York Medical School (University of Hull), Hull, United Kingdom*; *[3]Imperial College Healthcare NHS Trust, London, United Kingdom*

Background: The total atrial conduction time can be measured as the time from the onset of the P wave on the ECG to the peak of the A wave recorded at the mitral annulus using tissue Doppler imaging (A´; P-A´TDI). A long P-A´tdi predicts incident atrial fibrillation (AF) in the general population; however, it has only received little attention in patients with heart failure (HF).
Purpose: We studied the clinical associations and the predictive role of P-A´TDI measured in ambulatory patients with a broad range of HF severity.
Methods: We retrospectively measured P-A´TDI interval in ambulatory patients with HF and sinus rhythm enrolled in the "Studies Investigating Co-morbidities Aggravating Heart Failure" (SICA-HF) programme.
Results: P-A´TDI measured at the lateral mitral annulus was (mean and interquartile range (IQR)) 120 ms (106-135) in 117 controls. It was longer in patients with heart failure with either reduced (LVEF < 50%, N=141; 126 (112-146 ms); P=0.005) or normal left ventricular ejection fraction (LVEF>50% and NTproBNP>125 ng/l, N=71; 128 (108-145) ms; P=0.026). NTproBNP and creatinine correlated positively with P-A´TDI, but only increasing age, left atrial volume and PR interval were independently associated with prolonged P-A´TDI interval.
During a median follow up of 1251 (956 - 1602) days, 73 patients with HF died (N=42) or developed AF (N=31). In univariable analysis, P-A´TDI was associated with increased risk, but only increasing log [NTproBNP], age and more severe symptoms (NYHA III vs I/II) were independently related to an adverse outcome. Patients in whom both P-A´TDI and left atrial (LA) volume were above the median (127 ms and 64 ml, respectively) had the highest incidence of AF (HR: 6.61 95% CI: 2.27-19.31; P < 0.001) compared to those with both P-A´TDI and LA volume below the median.
Conclusions: Measuring P-A´TDI interval identifies ambulatory patients with HF at higher risk of dying or developing AF during follow-up.



	PA-TDI lateral	
	Compared to No HF	Compared to HF – T1
No HF	HR (95% CI); P value	
HF - T1	2.92 (1.31-6.51); 0.009	-
HF - T2	3.42 (1.55-7.53); 0.002	1.17 (0.62-2.22);0.63
HF - T3	7.30 (3.51-15.20); <0.001	2.52 (1.42-4.46);0.002

P1886

The value of stress echocardiography in the prognosis stratification of patients with left ventricular dysfunction

B Bebiana Faria[1]; T Lopes[2]; F Castro[1]; M Oliveira[1]; P Azevedo[3]; M Lourenco[1]; J Portugues[1]; L Calvo[1]; P Von Hafe[1]; O Azevedo[1]; A Lourenco[1]
[1]Hospital Guimaraes, Guimaraes, Portugal; [2]University of Minho - Life and Health Sciences Research Institute (ICVS), Student, Braga, Portugal; [3]Faro Hospital, Cardiology, Faro, Portugal

Introduction: Pharmacological stress echocardiography (SE) is a non invasive imaging method widely used for the evaluation of ischemia. The presence of left ventricular systolic dysfunction (LVSD) on resting echocardiography may limit the impact of SE in the prognosis stratification of patients with suspected or diagnosed coronary artery disease.
Objective: Assess the value of SE in prognosis stratification of patients with suspected or diagnosed coronary artery disease and LVSD.
Methods: Retrospective study including 789 consecutive patients who performed dobutamine or dipyridamole SE between 2010 and 2015. To identify prognosis predictors were collected demographic, clinical, electrocardiographic and echocardiographic data. A combined endpoint of cardiovascular events was defined, consisting of cardiac death, non fatal myocardial infarction and percutaneous or surgical revascularization.
Results: The sample included 789 patients, 65% males, average age 64 ± 11 years. About 71% of the patients performed SE with dobutamine and 29% with dipyridamole.
Patients with LVSD (n = 228; 29.7%) were predominantly males (78%) with a mean age of 65 ± 12 years. Of the patients analyzed 42% had mild left ventricular function depression, 32% moderate and 26% severe, with an average value of fraction ejection of 38%. SE was positive in 17% of patients. The average follow-up time was 30.7 ± 19.7 months, events occurred in 24% of patients, with an average time to the first event of 195 days. SE presented a sensitivity of 38.9% and specificity of 89.9% for prediction of events in patients with LVD, with a positive predictive value of 55.3% and a negative predictive value of 82.2%. Event-free survival in patients with positive SE was significantly lower than patients with negative SE (47 ± 4 months vs. 60 ± 2 months, p = 0.004).
In the univariate analysis, the result of SE was a predictor of events. However, after multivariate analysis only the development of symptoms during SE (p = 0.001) and chronic kidney failure (p = 0.038) were considered independent prognosis predictors in patients with LVSD.
Patients with preserved left ventricular function (LVF) (n = 540, 70.3%) were male in 59.6% of the cases and had a mean age of 65 ± 11 years. The average value of fraction ejection was 62%. SE was positive in 10.7% of the patients. The events occurred in 7.8% of the cases, with an average time to the first event of 312 days. Event-free survival in patients with positive SE was significantly lower than patients with negative result (52 ± 3 months vs. 64 ± 2 months, p < 0.001). In the patients with preserved LVF, a positive result in SE (p < 0.001) and a higher number of modifiable vascular risk factors were identified as independent prognosis predictors (p = 0.043).
Conclusion: The result of SE was identified as independent prognosis predictor in patients with preserved LVF, but not in patients with LSVD.

P1887

Contribution of echocardiographic 2D strain analysis to the long-term follow-up of heart transplant patients

C Goeminne[1]; S Langlet[2]; M Fertin[2]; N Rousse[3]; E Robin[1]; G Leroy[1]; M Moussa[1]; E Hebbar[2]; P De Groote[2]; A Vincentelli[3]
[1]Lille University Hospital, Department of Anaesthesiology and Intensive Care Medicine, Lille, France; [2]Lille University Hospital, Department of Cardiovascular Medicine, Lille, France; [3]Lille University Hospital, Department of Cardiac Surgery, Lille, France

Background: Few studies have evaluated the potential role of 2D strain for the long-term follow-up of heart transplant patients.
Aims: We evaluated the diagnostic and prognostic contribution of echocardiographic 2D strain analysis to the long-term follow-up of heart transplant patients.
Methods: The study population consisted of a cohort of 162 heart transplant patients followed-up at an hospital, France. Donor characteristics, as well as clinical, biological and echocardiographic data were collected. Patients with acute allograft rejection were excluded from the analysis. The 2D strain data was acquired by the same operator in all patients. For statistical analysis, we considered that strain was altered when ≥ -13%, according to the litterature. Cardiovascular events (congestive heart failure, arrhythmias, high-degree conduction disturbances) were assessed in a subgroup analysis.
Results: Data of strain was available in 105 patients. The average strain was -15.8 ± 3.6%, strain was ≥ -13% in 22.8% or the patients. Patients with altered strain were treated with higher dosages of loop diuretics (185 ± 138 mg/day vs. 43 ± 27 mg/day; p = 0.005) and were more frequently dialysed (20 % versus 4 %; p = 0.005). Furthermore, these patients had decreased markers of systolic function such as altered S wave in DTI at the tricuspid ring (8.6 ± 1.9 cm/s versus 9.6 ± 2.0 cm/s, p = 0.038), lower subaortic and subpulmonary velocity time integrals (13.8 ± 3.8 cm/s versus 16.6 ± 3.8 cm/s, p = 0.003 and 13.6 ± 4.4 cm/s versus 15.7 ± 3.6 cm/s, p = 0.041, respectively). Strain was more altered in patients who experienced cardiovascular events (-14.1 ± 4.0 % versus -16.2 ± 3.5 %, p = 0.024).
Conclusion: 2D strain alteration seems to be a marker of chronic cardiac graft dysfunction and may be a useful tool for the management and follow-up of heart transplant patients.

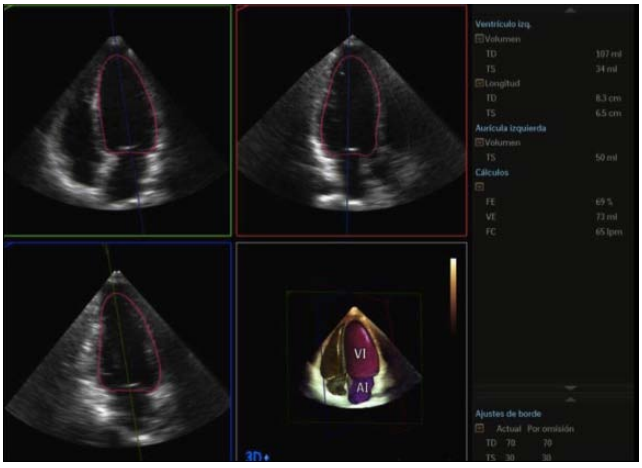
P1888

Automatic 3D echocardiography for left ventricular ejection fraction assessment in daily clinical practice: the present and the future

FJ Francisco Javier Irazusta Cordoba[1]; T Lopez Fernandez[1]; V Rial Baston[1]; P Meras Colunga[1]; O Gonzalez Fernandez[1]; Z Blazquez Bermejo[1]; J Caron Codon[1]; E Refoyo Salicio[1]; R Dalmau Gonzalez-Gallarza[1]; G Guzman Martinez[1]; F Dominguez Melcon[1]; SO Rosillo Rodriguez[1]; M Moreno Yanguela[1]; JL Lopez-Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain

Introduction: The 2D echocardiography (2DE) is the most commonly employed technique for left ventricular ejection fraction (LVEF) quantification. Although the gold-standard in this issue is the cardiac magnetic resonance (CMR). However, its high costs and low availability does not allow becoming the routinary technique for LVEF assessment. Inter and intra-observer variability for LVEF quantification could be improved by new fully automated systems for 3D echocardiography (Auto3DE), and could be an interesting tool for the heart failure outpatient clinic.
Methods: Prospective observational study that analysed 27 patients referred to our institution for LVEF assessment by CMR. In all patients LEVF was also quantified by Auto3DE and 2DE. Simultaneously we evaluated the feasibility of the Auto3DE in other 81 consecutive patients.
Results: Mean age was 49,8 year-old. The most frequent indications for CMR were hypertrophic cardiomyopathy (15,38%), infectious myocarditis (15,38%) and congenital heart disease (23%). The analysis of the left ventricle volume (LVV) and LVEF was 5 times faster by Auto3DE than 2DE, and 10 times faster than CMR (Table 1). Only 35% of the Auto3DE required image edition by a cardiologist during the analysis, compared to the 91% with the 2DE. End-diastolic and end-systolic volumes measured by Auto3DE were significantly closer to CMR measurements than 2DE. Even though LVEF assessment with Auto3DE was lightly overestimated, its correlation with CMR was better (Spearman´s rho: 0,68) than with 2DE (Spearman´s rho: 0,54). Auto3DE was feasible in 70 of the 81 patients (86,5%) and the main limitation was its dependence on acoustic window.
Conclusion: Auto3DE is much faster than other commonly used techniques for LVV and LVEF measurement, with an acceptable accuracy compared with CMR. We could consider it as a useful tool for daily clinical practice.

	CMR	Auto3DE	p	2DE	p
Time (Seconds)	215	22		115	
mean LVEF (%)	58	62	0,08	55	0,05
mean End-Diastolic Vol (mL/m2)	89	77,3	0,1	53,46	0,0001
mean End-Systolic Vol (mL/m2)	40,3	29,68	0,02	21,68	0,0001



P1889

Left ventricular remodeling in normotensive and hypertensive postmenopausal women

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

Aim: To asses changes of left ventricle (LV) structure and function in postmenopausal women depending on hypertension presence and blood pressure (BP) circadian profile type.

Methods: 203 postmenopausal women were included in the investigation: 142 women with surgical menopause (44,3 ± 5,4 years, menopause duration 3,8 ± 2,4 years); and 61 women with natural menopause (46,2 ± 4,7 years, menopause duration 4,3 ± 2,1 years). All patients underwent general clinical examination, ambulatory blood pressure monitoring (Cardiotens-01, Meditech, Hungary) with circadian profile type evaluation, echocardiographic examination with systolic and diastolic left ventricular function assessment. Statistical methods such as Cruskell-Walles criteria and $\chi 2$ test were used.
Results: The prevalence of hypertension in women with natural and surgical menopause was the same: 45,9% (28 pts) and 42,3% (60 pts), respectively (p>0,05). Postmenopausal women, regardless of the presence of hypertension, have different types of circadian BP profile: 100pts were dippers, 51 pts were over-dippers, 52 pts had no nighttime BP reduction (49 pts were non-dippers and 3 pts were night-peakers). Only 39 postmenopausal women (19,2%) had normal LV geometry; 89 pts (43,8%) demonstrated LV concentric hypertrophy, 57 pts (28,1%) – concentric remodeling and 18 women (8,9%) – eccentric hypertrophy. The frequency of LV concentric hypertrophy in hypertensive postmenopausal women was wider than in normotensive ones: 60,2% (53 pts) vs 31,3% (36 pts), 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). The presence of eccentric hypertrophy was the same in both groups.
Nobody of included postmenopausal women had LV systolic function failure. Presence of LV diastolic function disturbance 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.
Maximum prevalence of LV concentric hypertrophy was registered in the group of over-dippers – 52,9% (27 pts); in non-dippers/night peakers it was 28,8% (15 pts), in dippers – 47% (47 pts), p < 0.05. The frequency of concentric remodeling formation was maximal in non-dippers/night peakers (48.1%, 25 pts), which was significantly greater than the specified index in dippers (15%, 15 pts, p < 0,01) and overdippers (33,4%, 17 pts, p < 0,01).
Conclusions: LV remodeling regularities in postmenopausal women depend on BP level and circadian BP profile type. LV diastolic function evolution for the most part depends on LV remodeling type, but not on arterial hypertension presence.

P1890

Orthostatic systolic blood pressure reaction is associated with cardiac remodeling in a heart failure population - The HARVEST study

A Ali[1]; A Fedorowski[2]; J Molvin[3]; E Bachus[2]; H Holm[2]; G Tasevska[3]; A Amra Jujic[2]; M Magnusson[2]
[1]*Skane University Hospital, Department of Medical Imaging and Physiology, Malmo, Sweden*; [2]*Lund University, Malmo University Hospital, Department of Clinical Sciences, Lund, Sweden*; [3]*Malmo University Hospital, Department of Cardiology, Malmo, Sweden*

Background: Orthostatic hypotension (OH) is a sign of autonomic dysfunction and a common comorbidity in patients with heart failure (HF). We aimed to assess relations between orthostatic blood pressure (BP) responses and echocardiographic changes in a series of patients admitted for HF.
Methods: One-hundred-and-forty-nine patients hospitalized for HF (age 74y; 30% women; mean ejection fraction (EF) 40 ± 16%) were examined with conventional echocardiograms and active-standing test. Associations of cardiac remodeling (left and right atrial volume, left ventricular mass) in relation to the difference between supine and standing (after 3 min) systolic/diastolic BP were examined.
Results: In general, systolic and diastolic BP increased by 2 and 1 mmHg respectively on standing. A total of 34 patients (22.8 %; age 77y) met OH criteria. In regression models adjusted for traditional risk factors and EF, decrease in systolic BP upon standing was associated with greater left atrial volume (β=0.062; p = 0.043) and greater left ventricular mass (β=0.081; p = 0.002). No associations were seen for decrease in diastolic BP.
Conclusions: Orthostatic decline in systolic BP among older HF patients is associated with structural cardiac changes, independently of traditional risk factors and HF severity.

Associations in fully adjusted model

	LAV	RAV	LVM			
	β	p	β	p	β	p
Age	-0.002	0.601	-0.002	0.640	-0.004	0.153
Sex	-0.052	0.468	-0.177	0.056	-0.105	0.088
BMI	-0.008	0.233	-0.009	0.323	-0.001	0.880
HT	-0.027	0.688	0.070	0.424	0.103	0.078
LVEF	-0.001	0.519	-0.003	0.203	-0.007	<0.001
Diabetes	-0.011	0.881	0.030	0.757	0.005	0.932
HDL	0.153	0.090	0.052	0.659	0.066	0.396
LDL	-0.120	0.126	-0.247	0.015	0.018	0.790
FPG	-0.188	0.107	-0.421	0.006	0.046	0.644
AF	0.207	0.001	0.185	0.024	0.053	0.332
ΔSBP	0.062	0.043	-0.058	0.133	0.081	0.002

β are unstandardized coefficients. LAV=indexed left atrial volume; RAV=indexed right atrial volume; LVM=indexed left ventricular mass; BMI=body mass index; HT=hypertension; EF=ejection fraction; HDL=high density lipoprotein; LDL=low density lipoprotein; FPG=fasting plasma glucose; AF=atrial fibrillation; ΔSBP=systolic blood pressure reaction

P1891

Characteristic echocardiographic parameters of right ventricular systolic dysfunction in acute dyspnea patients

D Gabartaite[1]; J Bugaite[1]; R Norvilaite[2]; G Ziubryte[2]; A Montvilaite[2]; G Balciunaite[3]; I Alitoit[3]; A Krivickiene[4]; J Motiejunaite[4]; D Zaliaduonyte-Peksiene[4]; R Jurgaitiene[4]; D Zakarkaite[3]; A Mebazaa[5]; A Kavoliuniene[4]; J Celutkiene[3]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; *[2]Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[3]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; *[4]Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; *[5]University Paris Diderot , U942 Inserm, Hospital Lariboisière, Paris, France*

On behalf of: GREAT network
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Introduction: There is still a discussion about the best echocardiographic parameters of acute right ventricular systolic dysfunction (RVSD) in acute settings.
Aim: To estimate the prevalence and to characterize RVSD by novel ultrasound parameters of RV longitudinal function, morphometric right heart parameters, association with left ventricular (LV) systolic function and brain natriuretic peptide (BNP) level in acute dyspnea patients.
Methods: Prospective study enrolled consecutive patients admitted to the emergency department of two university centers with acute dyspnea due to decompensated heart failure (HF) and other reasons. Data of 323 patients (mean age 68.8 ± 12.7 years, 39.3% women) were analysed. Echocardiography focused on RV parameters was performed during the first 48 hours after admission. TAPSE (tricuspid annular plane systolic excursion), RV S' (velocity of the tricuspid annular systolic motion), FAC (fractional area change), right atrial (RA) area, RV basal diameter, RV strain of 3 and 6 segments were measured. Blood sample for BNP level was taken during the first 4 hours. The RVSD was defined by reduced FAC <35%, or, if FAC was not available, by TAPSE <1.7 cm.
Results: Two thirds of patients were diagnosed with chronic left HF (n = 216, 66.9%), reduced LV ejection fraction (LV EF) <40% was measured in 104 patients (32.2%). More than half of study patients (n = 167, 51.7%) had RVSD. Most of them (68%) had a history of chronic left HF (n = 114, 35.3%), LV EF <40% was found in 69 patients (21.4%). In patients with RVSD probability to have LV EF <40% was 48.5% (p < 0.001), and BNP level >1000 ng/l – 47.78% (p = 0.006).
Conclusion: Right ventricular systolic dysfunction was found in more than half of the patients with acute dyspnea, in two thirds of cases it coincided with chronic left heart failure. Patients with right ventricular systolic dysfunction had significantly dilated right chambers and decreased right ventricular longitudinal function assessed by tissue doppler and deformation imaging.

	RV systolic dysfunction group	Normal RV function group	P value
RA area, cm^2	25.59±9.5	22.93±9.48	0.03
RV basal diameter, cm	4.64±0.96	4.28±0.95	0.003
RV S', cm/s	9.46±3.31	11.13±3.55	0.001
RV strain 6 segments, %	-9.98±4.44	-14.24±5.26	0.002
RV strain 3 segments, %	-12.85±5.64	-15.04±8.14	0.006
BNP, ng/l	1403.36±1592.32	936.49±1320.99	0.001

P1892

Ejection fraction of the left atrium in patients with medically controlled arterial hypertension compared to subjects with prehypertension and normotensive healthy controls.

D Dijana Djikic[1]; N Mujovic[2]; B Dejanovic[1]; S Lazic[1]; M Polovina[2]; M Marinkovic[2]; N Jankovic[2]; B Orbovic[2]; A Kocijancic[2]; V Kovacevic[2]; D Simic[2]
[1]University Clinical Center, Pristina, Serbia; *[2]University Clinical Center of Serbia, Cardiology, Belgrade, Serbia*

Very important markers of cardiac dysfunction and predictors of adverse cardiovascular outcome are size and volume of the left atrium (LA).
Objective: To analyze the function of the LA in patients with medically controlled hypertension (HTA) without a history of paroxysmal atrial fibrillation, adults with prehypertension (PHTA) and normotensive healthy controls (NTA).
Subjects and methods: Anteroposterior diameter of LA, maximum and minimum volume of LA (LAVI max, LAVI min.) were quantitated by echocardiography using the biplane area length method on 4-chamber 2D images, and indexed to the body surface area. Left atrial ejection fraction (LAEF) was defined as (LAVI max-LAVI min.) / LAVI max. X 100 in 67 patients with medically controlled arterial hypertension (age 51 ± 9.3), 36 subjects with prehypertension (age 50.6 ± 10.5) and 44 healthy controls (age 53.5 ± 9.8).
Results: There was no difference in the anteroposterior diameter of LA among subjects with PHTA and NTA, both groups differed in relation to the HTA patients (3.2 ± 0.39 vs 3.4 ± 0.27 vs 3.8 ± 0.40, p = 0.110, p <0.001, p <0.001). LAVI max and LAVI min. were significantly higher in HTA patients and PHTA subjects in relation to NTA controls; there was no significant difference between HTA patients and PHTA subjects concerning the LAVI maks, LAVI min. was significantly higher in HTA patients in relation to PHTA subjects (24.7 ± 6.9 vs 28 ± 7.5 vs 40 ± 6.8, p = 0.092, p <0.001, p <0.001; 8.7 ± 2.2 vs 11.3 ± 2.8 vs 17.8 ± 5.2, p = 0.030, p <0.001, p <0.001). HTA patients and PHTA subjects had significantly lower LAEF in relation to NTA controls, LAEF vas significantly lower in HTA patients in relation to PHTA subjects (55.6 ± 7.3 vs 59.8 ± 5.2 vs 64.8 ± 4.4, p = 0.004, p <0.001, p = 0.011). There were no significant differences among groups in LVEF (66.4 ± 3.8 vs. 64.4 ± 9.3 vs. 64.1 ± 8.1, p = 0.523, p = 0.237, p = 0.978).
Conclusion: Our results demonstrate function of the left atrium expressed as EFLP is reduced in patients with arterial hypertension with no history of paroxysmal atrial fibrillation even when the value of TA is medically regulated. Prehypertensive subjects have decreased EF LP in relation to healthy normotensive. LA EF decreased with increasing LA volume.

BIOMARKERS

P1893

Association between in-hospital variation of natriuretic peptides and short term outcomes in patients hospitalised for worsening chronic heart failure (data from FERIC-RO)

I Iulian Cosei[1]; L Antohi[1]; R Radu[1]; SP Collins[2]; C Radulescu[1]; M Chivulescu[1]; P Ponikowski[3]; J Butler[4]; M Gheorghiade[5]; O Chioncel[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania; *[2]Vanderbilt University, Nashville, United States of America*; *[3]Wroclaw Medical University, Wroclaw, Poland*; *[4]Stony Brook University Medical Center, Stony Brook, United States of America*; *[5]Northwestern University, Chicago, United States of America*

On behalf of: FERIC RO investigators

Background: There is a large body of evidence suggesting that variation from admission to discharge of N-terminal prohormone brain natriuretic peptide

(NTproBNP) levels in patients hospitalised for worsening chronic heart failure (HF) is a predictor of future cardiovascular events.
Purpose: The aim of the present analysis was to characterise in hospital trajectory of NTproBNP and to identify the relationship between in-hospital variation of NTproBNP and short term outcomes.
Methods: FERIC-RO study was designed as a prospective, multicentric, national, observational study which enrolled 138 patients hospitalised for worsening chronic HF. NTproBNP has been collected at admission and discharge in all patients. The patients were divided in three groups, stratified by the change from admission to discharge of NTproBNP during hospitalization: group A characterised by reduction of NTproBNP by ≥30%, group B characterised by reduction of NTproBNP <30% and group C consisting of patients with increased levels of NTproBNP. The study outcomes were 3-month all-cause mortality and HF-rehospitalisation.
Results: The demographic and clinical characteristics of patients stratified by in-hospital variation of NT-pro-BNP are shown in the Table 1. The 3-month all-cause mortality rates were 8.9% vs. 10.1% vs. 13.7% (p = 0.008), while the 3-month HF rehospitalisation rates were 13.7% vs. 16.7% vs. 21.5% (p = 0.021), for group A, B and C, respectively.
Conclusion: The present study suggests that the variation of NTproBNP from admission to discharge is a predictor of 3-months all-cause mortality and HF rehospitalisation rates. This finding could be useful to further stratify the patients and to intensify treatment during early post-discharge phase.

Table 1

	Group An=84	Group Bn=39	Group Cn=15	p value
Age (years)	69.4±10	70.2±10	73.4±11	0.067
Gender - female	31%	34%	41%	0.09
Ischemic etiology	59%	63%	63%	0.34
Left ventricular ejection fraction (%)	38±12	36±12	38±10	0.08
Diabetes mellitus	29%	39%	33%	0.11
eGFR(ml/min/1.73m^2)	59±18	55±22	50±17	0.004
Serum sodium (mmol/L)	133±8	133±9	132±8	0.072
Atrial fibrillation	39%	43%	42%	0.50

eGFR=estimated glomerular filtration rate. Values are expressed as mean ± SD or %.

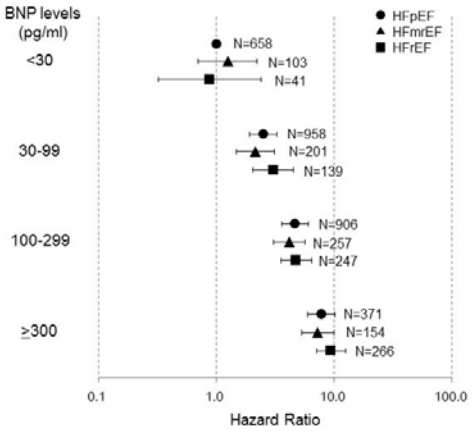
P1894
Comparable prognostic impacts of plasma B-type natriuretic peptide levels among patients with heart failure with preserved, mid-range and reduced left ventricular ejection fraction

S Kasahara[1]; Y Sakata[1]; K Nochioka[1]; K Tsuji[1]; R Abe[1]; T Oikawa[1]; M Sato[1]; T Shiroto[1]; J Takahashi[1]; S Miyata[2]; H Shimokawa[3]
[1]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan; *[2]Tohoku University Graduate School of Medicine, Department of Evidence-based Cardiovascular Medicine, Sendai, Japan*; *[3]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine and Department of Evidence-based Cardiovascular Medicine, Sendai, Japan*

On behalf of: The CHART-2 Study

Background: Although the usefulness of plasma levels of B-type natriuretic peptide (BNP) has been established to estimate the prognosis of patients with heart failure (HF), it remains to be examined whether BNP levels predict the prognosis of HF patients regardless of left ventricular ejection fraction (LVEF). In the past, only one preliminary study showed that, for a given BNP level, the prognosis was comparable between patients with HF with preserved LVEF (HFpEF) and those with HF with reduced LVEF (HFrEF), warranting a further validation study with a large number of patients.
Purpose: To examine the usefulness of plasma BNP levels for long-term risk stratification among HFpEF, HF with mid-range LVEF (HFmrEF), and HFrEF patients.
Methods: The CHART-2 (Chronic Heart Failure Analysis and Registry in the Tohoku District-2) Study is a large-scale prospective observational multicenter cohort study in Japan, in which a total of 10,219 patients with chronic HF or those at high risk for HF were enrolled between 2006 and 2010 and have been prospectively followed up. In the present study, we analyzed the data of 4,301 consecutive Stage C/D HF patients registered in the CHART-2 Study (mean 69 years, male 68%) who were divided into HFpEF (LVEF>50%, N=2,893), HFmrEF (LVEF 40-49%, N=715), and HFrEF (LVEF < 40%, N=693) groups. We performed the Cox proportional hazard models to compare the prognostic impacts of BNP categories among the 3 groups. BNP categories were determined based on the BNP cutoff levels that were indicated to most efficiently discern the mortality risk by the classification and regression trees (CART) analysis.
Results: A total of 1,435 all-cause deaths occurred during the median 6.3-year follow-up. Although median BNP levels were significantly increased from HFpEF to HFmrEF, and then to HFrEF patients (85.3, 127 and 216 pg/ml, respectively, P < 0.001), relationships between log BNP levels and the mortality risk were comparable among the HFpEF, HFmrEF, and HFrEF groups. The CART analysis showed that BNP levels of 28.6, 103, 332 pg/ml were the optimal cut-off levels to discriminate the mortality risk of the patients. Based on these BNP cutoff levels, we divided BNP levels into 4 categories; <30, 30-99, 100-299, and >300 pg/ml. As compared with patients with BNP levels <30 pg/ml in HFpEF (reference), those with BNP levels <30 pg/ml in HFmrEF and HFrEF had comparable mortality risk (hazard ratio (HR) 1.2, P=0.80 and HR 0.87, P=0.45 for HFmrEF and HFrEF, respectively) and those with BNP levels 30-99, 100-299 and >300 pg/ml had comparably increased mortality risks among patients with HFpEF (HR 2.5, 4.7 and 7.8, respectively), HFmrEF (HR 2.1, 4.2 and 7.3, respectively), and HFrEF (HR 3.0, 4.8 and 9.4, respectively) (Figure).
Conclusion: These results indicate that plasma BNP levels have comparable prognostic impacts among patients with HFpEF, HFmrEF and HFrEF.

Figure. Mortality risks among HFpEF, HFmrEF, and HFrEF

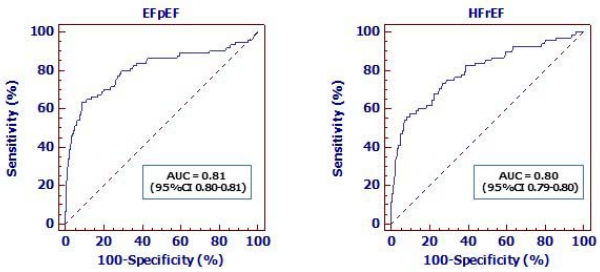


P1895
Plasma B-type natriuretic peptide level is useful to predict incidence for both types of heart failure with and without left ventricular systolic dysfunction in the general population

R Komi[1]; F Tanaka[1]; K Tanno[1]; M Ohsawa[1]; T Onoda[1]; M Ohta[2]; K Ogasawara[1]; A Okayama[3]; M Motoyuki Nakamura[1]
[1]Iwate Medical University, Morioka, Japan; *[2]Iwate Health Service Association, Morioka, Japan*; *[3]Research Institute of Strategy for Prevention, Tokyo, Japan*

On behalf of: Iwate Heart Registry Consortium

Aim: It remains unknown whether the predictive abilities of plasma B-type (BNP) are viable for either heart failure (HF) with preserved ejection fraction (HFpEF) or with reduced ejection fraction (HFrEF) in the general middle-aged and elderly population.
Methods: Participants were recruited from the general population (n = 14,141; mean age=63 years). A Cox regression analysis adjusting for traditional risk factors (age, sex, BMI, hypertension, diabetes, atrial fibrillation, eGFR, smoking) was performed to examine the hazard ratio (HR) of plasma BNP for each type of HF. Moreover, receiver-operating-characteristics (ROC) analysis were used to determine the predictive abilities of plasma BNP for the incidence of two types of HF.
Results: During a median follow-up of 9.0 years, new onset of HF (defined by Framingham criteria) was found in 142 participants (HFpEF, n = 74; HFrEF, n = 68) in the cohort. The HRs for both HF in terms of per one standard deviation (1 SD) increment (as a continuous variable) and values above the 80th percentile (as a categorical variable) of plasma BNP were significantly associated with both types of HF (HFpEF; HR = 3.44 per 1SD, HR = 4.45 at 80th percentile: HFrEF; HR = 7.59 per 1SD, HR = 5.93 at 80th percentile). Moreover, plasm BNP concentration showed optimal predictive abilities for both types of HF (area under curve of ROC analysis: HFpEF= 0.81, HFrEF=0.80) (Figure). In addition, plasma BNP level for the optimal sensitivity and specificity to predict HFpEF or HFpEF was similar (54 pg/ml vs 57 pg/ml).
Conclusion: This study showed that plasma BNP level is a valid predictor for incidence of HF regardless of preserved or reduced left ventricular systolic function in this population.



Area under ROC for HFpEF and HFrEF

P1896

Unbalanced plasma catestatin and norepinephrine predicted adverse outcomes of chronic heart failure

S Songyun Chu[1]; F Peng[1]; L Liu[1]; RX Li[1]; WH Ding[1]
[1]*Peking University First Hospital, Department of Cardiology, Beijing, China People's Republic of*

Background: Catestatin (CST) is a vasopeptide with a broad spectrum of activities in cardiovascular system. The level of plasma CST increased in chronic heart failure patients. And plasma CST increased with NYHA classification escalated with possible protective effect through down-regulation of sympathetic stress. CST might act as a novel biomarker in heart failure. Whether the unbalanced sympathetic status indicated by plasma CST and norepinephrine (NE) related adverse prognosis of heart failure patients, however, is unknown.
Purpose: To investigate the potential predictive ability of ratio of plasma CST and NE on outcomes of heart failure patients.
Methods: We established a chronic heart failure patient cohort of 202 cases who admitted for exacerbation in our center. Plasma CST of these patients was measured with enzyme-linked immune-absorbent assay at admission. After a mean 52.5 months' follow-up, major cardiac adverse events including readmission of heart failure, cardiovascular death and all-cause death were collected. The relationship between ratio of plasma CST and NE level and occurrence of adverse events were analyzed.
Results: There were 117 cases of readmission, 59 cases of all-cause deaths at the end of follow-up, and among them included 49 cases of cardiac deaths. Neither average plasma CST nor NE level was found to have statistical differences between patients with or without readmission. The levels of plasma CST were higher in patients with all-cause death and cardiac death than in survivors (1.06(0.66-1.82) ng/ml vs. 0.75(0.58-1.12) ng/ml, $p = 0.005$ and 1.18(0.69-1.83) ng/ml vs. 0.75(0.58-1.12) ng/ml, $p = 0.002$, respectively). However, there was no significant difference between plasma NE in patients with cardiac or all-cause death and survivors. In univariate Logistic regression, higher plasma CST and NE ratio predicted increased risk of all-cause and cardiac death, the hazard ration (HR) was 1.221 (95% CI, 1.009-1.479, $p = 0.041$) and 1.210 (95% CI, 1.001-1.464, $p = 0.049$), respectively. In multivariate Logistic regression, after adjusted for covariates including age, gender, NYHA function class, eGFR, usage of diuretics, CCB, pulmonary artery pressure, plasma albumin level, CST to NE ratio was not an independent risk factor for cardiac death. For all-cause death, CST to NE ratio was not an independent risk factor, either.
Conclusions: Elevated plasma NE was common in heart failure patients and might indicate for chronic sympathetic activation with little fluctuation. Thus NE alone might not be a good predictor for adverse outcomes. Plasma CST has been known to elevate with the severance of heart failure. And the ratio of CST and NE might be a more sensitive predictor for all-cause and cardiac deaths in heart failure patients and reflect the compensatory mechanisms activated in exacerbation of heart failure. Further studies are needed to understand the effect of CST in heart failure.

P1897

Natriuretic peptides are mainly measured in elderlies, but remain largely underused and sometimes misused: results of big data analysis

M Lescroart[1]; E Sorbets[1];
FX Goudot[1]; N Garnier[2]; N Dubois[3]; G Copin[4]; A Betraoui[2]; M Schwoerer[2]; A Szosteek[2]; V Bonnivard[2]; N Charnaux[5]; C Meune[1]
[1]*Hospital Avicenne of Bobigny, Cardiology, Bobigny, France*; [2]*ProbaYes, Statitistics, Montbonnot, France*; [3]*Clinique de la côte d'émeraude, Biorance Laboratory, Saint-Malo, France*; [4]*Roche Diagnostics, Medical Care, Meylan, France*; [5]*Hospital Avicenne of Bobigny, Biochemistry, Bobigny, France*

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Introduction: Originally limited to acute heart failure diagnosis in the emergency room, natriuretic Peptides (NP) are now considered as prognostic markers in various conditions and are recommended to rule out heart failure in patients presenting with acute or chronic dyspnea. In addition they may be helpful to guide therapy of chronic heart failure patients, although not clearly endorsed by guidelines.
Methods: We examined all biological tests performed in two districts from the west part of France, "the French Brittany", covering 13.653km2 and corresponding to a population of 1.723.653 persons. From February 2010 to august 2015, 22 laboratories (including 6 Hospital/clinic laboratories and 16 non hospital/clinics laboratories) performed 3.606.432 analysis prescriptions in 3.606.432 adult patients>20y. All laboratories are equipped with Roche diagnostics platform and measured NT-proBNP as the NP. We report the settings and conditions of NP measurement.
Results: During the study period, 56.653 (1.6%) measurements of NT-proBNP were performed in 27.527 distinct patients; NT-proBNP measurements gradually increased from 9188 in 2011 to 12938 in 2014 ($p < 0.001$).
The same numbers of measurements were done in men versus women (50.0% each), and 39.828 (70.3%) of measurements have been done in elderly patients ≥ 75y. GP ordered >70% of the measurements and 27.0% were performed in hospital/clinics labs, 10.1% in dedicated emergency labs and the remaining 62.9% in non-hospital/clinic labs.
NT-proBNP was re-measured in 10.167 patients (36.9%) after a median of 60 days [IQR 14-217]. Initial NT-proBNP concentration was 1621 ng/L [IQR 560-3926], and the relative variation between the first and second measurement was 1% [95% CI: -29- + 46].
In combination with NT-proBNP, creatinin was measured only 47.680 times (84.2%); other frequently associated dosages were electrolytes (n = 43165), HbA1C (40074), hemogram (23231), and liver enzymes (17195).
Conclusion: Among a very large cohort, we observed a gradual increase of NP measurements over time but NP measurements only accounted for 1.6% of overall analysis prescriptions. The very large majority of NP measurements was performed in elderly patients, was ordered by GP and 16% of measurements were not performed in combination with creatinin. Big data analysis may offer a unique opportunity to improve our knowledge in current practices.

P1898

Association between NT-proBNP and metabolic status in young healthy adults.

A Anna Alexandrova[1]; I Strazhesko[1]; Y Orlova[1]
[1]*M.V. Lomonosov Moscow State University, Moscow, Russian Federation*

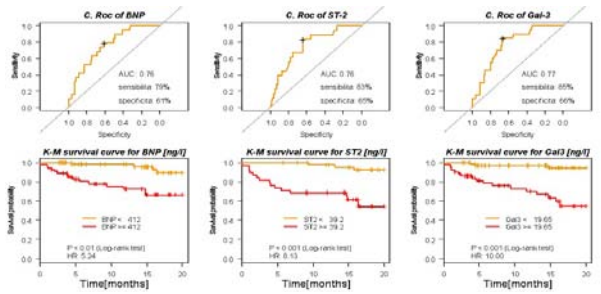
Introduction: The B type natriuretic peptide plays an important role in regulating blood pressure, blood volume, and water and salt balance. The association between N-terminal pro-B type natriuretic peptide (NT-proBNP) and metabolic risk factors is still unclear. It has been suggested that obese individuals have reduced natriuretic peptide levels. The prevalence of obesity and other cardiometabolic disturbances among young adults has increased over the past decade. The aim of this study was to investigate the correlation between NT-proBNP and metabolic risk factors in young apparently healthy adults.
Material and methods: We investigated 282 healthy young adults, mean age 18,5 ± 1,7 years, 47% male. NT-proBNP, waist circumference, body mass index (BMI), fasting plasma glucose, insulin resistance (HOMA-IR) and lipid profile were measured.
Results: NT-proBNP level was 58, 61 + 2,39 pg/ml (M + m). Multivariate regression analysis showed a positive association between NT-proBNP levels and fasting plasma glucose ($p = 0.013$), NT-proBNP and high-density lipoprotein ($p = 0.01$). There was no association between NT-proBNP and body mass index, waist circumference, triglyceride, LDL cholesterol, insulin resistance.
Conclusions: Hyperglycemia is a risk factor most closely associated with a damage to cardiac function. It may be the main target in the prevention of cardiovascular diseases in young adults.

P1899

BNP, Galectine-3and ST-2 cut-off values for long term risk assessment in chronic heart failure patients

CS Vella[1]; F Santini[1]; M Oldani[1]; A Villani[1]; G Malfatto[1]; A Faini[1]; E Makil[1]; G Gianfranco Parati[1]
[1]*University of Milano-Bicocca - Cardiology II, S. Luca Hospital, Milano, Italy*

Background: Data on usefulness of Galectine-3 (gal-3) and ST-2 biomarkers in the prognostic evaluation of patients with chronic heart failure (HF) are less than those for natriuretic peptides.
Objective: aim of this study was to assess the plasma levels of BNP, ST-2 and Gal-3 in HF patients referred to our center, and to estimate their prognostic value in relation to cardiovascular mortality over a 20 month follow-up period.
Methods: From March 2014 to July 2016 we assessed BNP, ST-2, Gal-3 in 124 patients with known diagnosis of HF referred to our clinic and receiving optimal treatment according to ESC guidelines. Patients (68% males, 66% ischemic etiology) were 76.0 ± 9.6 years old, with advanced NYHA class (50% III + IV), high rate of CRT/ICD implantation (53%) and reduced FE (<50% in 77% of cases).
Results: During follow-up (12.2 ± 6.8 month, no data censored), 20 patients died for cardiovascular diseases (16%). We used ROC curves to establish optimal cut-off values in terms of sensibility/specificity for each biomarker, i.e. 412ng/L (79%/61%), 39.2ng/L (83%/65%) and 19.7ng/L (85%/66%) for BNP, ST-2 and Gal-3 respectively. By using these cut-off values, we built Kaplan-Meier survival curves ($p < 0.01$ for all, Log-rank test analysis). Through a Cox regression model the estimated Hazard Ratios (HRs) for cardiovascular mortality were 5.24, 8.13 and 10.00 for BNP ≥412 ng/L, ST-2 ≥39.2 ng/L and Gal-3≥19.65 ng/L, respectively (figure).
Conclusions: Our data indicate possible cut-off values of BNP, ST-2 and Gal-3 for the prognostic stratification of patients with chronic heart failure, and suggest the potential role not only of BNP but also of Gal-3 and ST-2 in the management of HF patients. Our results need to be confirmed in the context of longitudinal studies of larger dimensions.



ROC and K-M curves

P1900

Markers of inflammation are associated with arterial stiffness in young healthy subjects

E Borisov[1]; I Strazhesko[1]; Y Orlova[1]
[1]*M.V. Lomonosov Moscow State University, Moscow, Russian Federation*

Plasma levels of circulating inflammatory molecules, such as high sensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6), fibrinogen (FBG) have been shown to be predictive of future cardiovascular disease (CVD). Chronic inflammation may impair vascular function and lead to an increase of arterial stiffness, an important determinant of cardiovascular risk. The role of arterial stiffness in the development of heart failure was demonstrated recently. There are some studies demonstrated the association between arterial stiffness, measured as increased pulse wave velocity (PWV), increased central blood pressure (BPao), and markers of inflammation in elder people, in subjects with hypertension, rheumatologic diseases. Nowadays there are no enough data about relationship between increased arterial stiffness (early vascular aging) and inflammation in young healthy people.
Material and methods: To explore the relationship between markers of inflammation (hs-CRP, IL-6, FBG) with arterial stiffness, we studied 258 healthy young adults, mean age 18,8 ± 1,6 years, 47% male. PWV and BPao were measured with ambulatory blood pressure monitoring device BPLab Vasotens (BPLab, Russia) and related to plasma levels of inflammatory markers measured by ELISA.
Results: PWV was significantly related to plasma hs-CRP (r=0.14; $P < 0.05$), FBG (r=0.26; $P < 0.001$). There was also a relationship between systolic BPao to hs-CRP (r=0.28; $P < 0.001$), FBG (r=0.25, < 0.001) and diastolic BPao to hs-CRP (r=0.20; $P < 0.001$), FBG (r=0.17, < 0.01). There was no significant association between IL-6 and arterial stiffness. hs-CRP was an independent predictor of PWV and systolic BPao in a multiple stepwise regression model.
Conclusions: Inflammation may be involved in arterial stiffening even in healthy young adults. Anti-inflammatory strategies may, therefore, be of benefit in reducing early vascular aging.

P1901

C reactive protein and procalcitonin elevation are related to NT pro BNP increase, diabetes and lp(a) levels in acute coronary syndromes

L Luciano De Biase[1]; C Miotti[1]; G Gallo[1]; S Burocchi[1]; V Presta[1]; FB Filice[1]; F Simonelli[1]; S Abbolito[1]; F Comito[1]; L Licchelli[1]; G Salerno[2]; M Volpe[1]
[1]*Sapienza University of Rome, Department of Clinical and Molecular Medicine/Cardiology, Rome, Italy*; [2]*Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy*

Introduction: The role of Procalcitonin (PCT) and C Reactive Protein (CRP) in Acute Coronary Syndromes (ACS) is not clear. PCT is an inflammatory molecule released both during infections and other acute inflammatory conditions. CRP is a component of the immunitary system, raising in the circulatory system in pathological events (bacterial infections, ischemic events, multiple trauma and major surgery). As atherosclerosis has an inflammatory component, CRP has been considered an important marker and/or factor of atherosclerosis disease.
Purpose: In order to investigate the relationship between CRP and PCT and NT-proBNP we have studied these proteins in a population of patients with ACS.
Methods: In our prospective study we have analysed 575 patients at admission in our Coronary Intensive Care Unit for ACS confirmed by laboratory analysis, ECG, echocardiogram and a coronary angiography. Patients with infections were excluded. We divided our population into four groups, according to the levels of PCT and CRP at admission: Group 1 PCT + /CRP + , Group 2 PCT-/CRP + ; Group 3 PCT + /CRP-; Group 4 PCT and CRP normal. In particular we evaluated in these groups the distribution of the levels of NT-proBNP, diabetes and Lp(a).
Results: In Group 1 NT-proBNP (845,85 pg/ml) and Lp(a) (30,25 mg/dl) were more elevated, in comparison with Group 2 (521,35 pg/ml NT-proBNP and 25,45 mg/dl Lp(a)), Group 3 (273,70 pg/ml NT-proBNP and 19,70 mg/dl Lp(a) and Group 4 (329 pg/ml NT-proBNP and 19,25 mg/dl Lp(a)). In Group 1 there were 34% diabetics patients, 28% in Group 2, 29% in Group 3, 21% in Group 4.
Conclusions: Our results suggest that PCT and CRP are particularly elevated in patients with a larger ventricular impairment, as measured by NT-proBNP levels. In our population elevated levels of Lp(a) are related to more severe coronary disease. Our data suggest that PCT and CRP can be considered as stress proteins that rise in patients with increased myocardial damage.

P1902

Elevated Levels of urinary 8-oxo-7,8-dihydroguanosin in hospitalized patients with heart failure

H Hua Wang[1]; JF Yang[1]; YY Li[1]; K Chai[1]; JP Cai[2]
[1]*Beijing Hospital,National Center of Gerontology, Beijing, Department of Cardiology, Beijing, China People's Republic of*; [2]*Beijing Hospital,National Center of Gerontology, Beijing , the Key Laboratory of Geriatrics, beijing, China People's Republic of*

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Background: Oxidative stress is known to play a crucial role in the pathogenesis of heart failure. 8-oxo-7,8-dihydroguanosin (8-oxoGsn) is the product of oxidative RNA damage and has high concentration in urine. Recent researches showed that RNA oxidation played an important role in the pathogenesis of many diseases, such as Parkinson, Alzheimer's disease, coronary atherosclerosis and diabetes. However, there is no report on correlation between 8-oxoGsn and heart failure.
Purpose: To investigate whether urinary 8-oxoGsn, a product of oxidative RNA damage, is a clinically useful biomarker for the severity of heart failure and oxidative stress levels in failing hearts.
Methods: We enrolled 149 hospitalized heart failure patients from March 2014 to January 2016,collected clinical data and liquid chromatography tandem mass spectrometry (LC-MS/MS) method established by our laboratory was used to detect the levels of 8-oxoGsn in urine after admission, which was adjusted by creatinine content. Age and sex-matched healthy subjects n=155 were enrolled as the control group. We measured serum NT-proBNP, D-dimer, hemoglobin, interleukin-6 and creatinine, and LVEF were evaluated by echo.
Results: Compared with the control group, the level of 8-oxoGsn in patients with heart failure was significantly increased: [4.68 3.47 6.62 VS. 2.75 2.59 2.85 P = 0.001](Figure 1). We divided the patients with heart failure into two groups at LVEF of 45%, 68 patients with EF≥45% and 74 patients with EF 45%. There was no difference of 8-oxoGsn levels in these two groups[4.02 3.31 5.88 VS. 4.90 3.44 7.67 P=0.082] (Figure1). Correlation analysis showed that 8-oxoGsn level was positively correlated with NT-proBNP and D-dimer and negatively correlated with hemoglobin and creatinine clearance (table 1).

Conclusion: Patients with heart failure had high level 8-oxoGsn in urine, and had independent positive correlation with NT-proBNP, which was an index of ventricular stretch and synthesized in response to wall stress. 8-oxoGsn is a clinically useful biomarker to evaluatethe severity of HF as well as the status of oxidative stress in patients with HFpEF and HFrEF.

Correlation analysis of 8-oxoGsn

Variables	Pearson or Spearman coefficient	Pvalue
NT-proBNP	0.224	0.008
D-dimer	0.333	< 0.001
HGB	-0.187	0.027
eGFR	-0.284	0.001
LVEF	-0.098	0.243

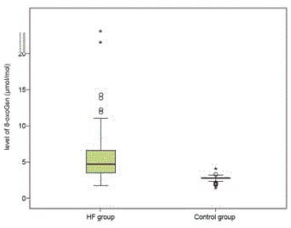


Figure 1.the level of 8-oxoGsn in patients with heart failure group and control group

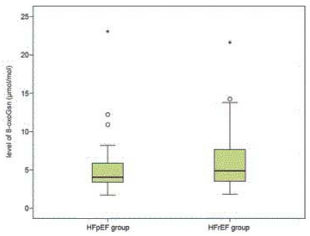


Figure2.the level of 8-oxoGsn in HFpEF(n=68) and HFrEF(n=74)

urinary 8-oxoGsn in heart failure

P1903

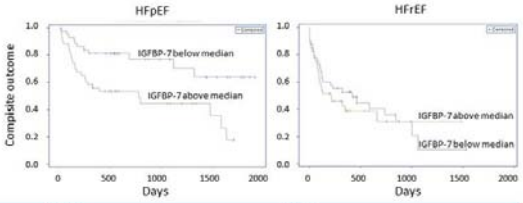
Serum IGFBP-7 is associated with diastolic dysfunction and predicts outcomes in heart failure and preserved ejection fraction

C Camilla Hage[1]; M Bjerre[2]; J Frystyk[2]; H Gu[3]; K Brismar[4]; E Donal[5]; J-C Daubert[5]; C Linde[1]; LH Lund[1]

[1]Karolinska Institutet, Department of Medicine, Cardiology unit, Stockholm, Sweden; *[2]Aarhus University, Department of Clinical Medicine, Medical Research Laboratory, Aarhus, Denmark*; *[3]Karolinska Institute, Department of Clinical Science, Intervention and Technology , Stockholm, Sweden*; *[4]Karolinska Institute, Department of Molecular Medicine and Surgery, Stockholm, Sweden*; *[5]Département de Cardiologie & CIC-IT U 804, Centre Hospitalier Universitaire de Rennes, , Rennes, France*

On behalf of: KaRen group

Purpose: Insulin-like growth factor-binding protein 7 (IGFBP-7), a marker of fibrosis, has been associated with cardiac hypertrophy and diastolic dysfunction in heart failure (HF). We investigated serum IGFBP-7: 1) concentrations in HF with reduced ejection fraction (HFrEF) vs. preserved EF (HFpEF); 2) associations with diastolic dysfunction; 3) and associations with prognosis.
Methods: In the Karolinska Rennes (KaRen) HFpEF biomarker sub-study, consisting of 86 patients with HFpEF (EF ≥45%) and 86 patients with HFrEF, we correlated serum IGFBP-7 with clinical data and diastolic function and assessed associations between IGFBP-7 and the composite outcome of all-cause mortality and HF hospitalization (and in HFrEF transplant or LVAD), using Kaplan-Meier and multivariable Cox regression analyses.
Results: Serum IGFBP-7 (median; IQR) was lower in HFpEF (102; 85-128 ug/L) compared to HFrEF (152; 120-206 ug/L; $p < 0.001$). In both HFpEF and HFrEF, IGFBP-7 correlated with NYHA class (r=0.25; $p = 0.020$ and r=0.25; $p = 0.022$), NT-proBNP (r= 0.53; $p < 0.001$ and r= 0.50; $p < 0.001$), eGFR (r= -0.47; $p < 0.001$ and r= -0.45; $p < 0.001$) and IGFBP-1 (r= 0.30; $p = 0.005$ and r= 0.69; $p < 0.001$). In HFpEF, IGFBP-7 correlated with E/E´ (r=0.31; $p = 0.012$), E/A ratio (r=0.31; $p = 0.011$), and RV end-diastolic area (r=0.27; $p = 0.032$). In HFrEF, but not HFpEF, IGFBP-7 correlated with age (r=0.29; $p = 0.009$) and atrial fibrillation (r=0.34; $p = 0.002$).
Over a median follow-up of 522 (IQR: 238-1089) days in HFpEF and 204 (IQR: 56-415) days in HFrEF, IGFBP-7 predicted the outcome in Kaplan-Meier and multivariable Cox regression in HFpEF, but not in HFrEF (Figure 1).
Conclusions: In HFrEF, serum IGFBP-7 was elevated and associated with HF severity but not prognostic, suggesting a risk marker role. In HFpEF, serum IGFBP-7 was less elevated but independently associated with both severity of HF and prognosis, suggesting that IGFBP-7 may contribute to the progression of HFpEF through oxidative stress and inflammation.



Parameter	HFpEF All-cause mortality or HF hospitalization (n=86)				HFrEF All-cause mortality or HF hospitalization (n=30)			
	n/events	Hazard ratio (per log increase)	95% CI	p-value	n/events	Hazard ratio (per log increase)	95% CI	p-value
IGFBP-7	86/36	4.29	1.44-12.78	0.009	79/50	1.39	0.61-3.14	0.433
IGFBP-7 (adjusted gender, age, eGFR and NT-proBNP)	85/36	4.19	1.01-17.35	0.048	78/49	0.72	0.24-2.14	0.554

Figure 1

P1904

Circulating nitric oxide metabolites predict outcomes of cardiac surgery for heart failure with reduced ejection fraction

S Sergey Mikheev[1]; IA Mandel[2]; VM Shipulin[1]; IV Sukhodolo[3]; YK Podoksenov[1]; Y Svirko[1]; AS Pryakhin[1]; EA Aleksandrova[1]

[1]State Research Institute of Cardiology of Tomsk, Department of cardiovascular surgery, Tomsk, Russian Federation; *[2]Federal Scientific Clinical center of specialized methods medical care and medical technology, Department of anesthesiology and intensive care, Moscow, Russian Federation*; *[3]Siberian State Medical University, Department of morphology and general pathology, Tomsk, Russian Federation*

Introduction: Markers of endothelial function including endothelin-1 (ET-1), nitric oxide (NO) metabolites (nitrate and nitrite) and asymmetric dimethylarginine (ADMA) have been identified as potent predictors of outcome in multiple heart failure models. Cardiac surgery in patient with heart failure with reduced ejection fraction (HFrEF) requires precise evaluation of risks and benefits and is still in need of early predictors of acute heart failure and other complications in postoperative period.
Purpose: We aimed to assess the dynamics of endothelial function markers (NO metabolites, ADMA, ET-1) during coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) in patients with heart failure with reduced ejection fraction to estimate their significance as predictors of acute heart failure and other complications in postoperative period.
Methods: The study included 66 patients subdivided into two groups: patients without heart failure with preserved ejection fraction and normal left ventricle volume, n= 32 (Group I) and HFrEF patients with left ventricle dilation (EF < 35%, left ventricle systolic volume index > 60 mL/m2), n=34 (Group II). All patients had undergone CABG with CPB for multivessel coronary artery disease in 2015-2016. We determined the concentration of ET-1, ADMA and nitric oxide metabolites: total content (NOx.total), nitrite (NO2-) and nitrate (NO3-) in plasma before the surgery, at the end of the surgery and 24 hours after the surgery. The following outcomes were recorded postoperatively: acute heart failure, total ventilation time, neurological disorders, ICU stay length.
Results: The Group II patients presented with significantly lower levels of NOx.total (U=124.4, $p = 0.006$), nitrite (U=102, $p = 0.001$) and nitrate (U=145, $p = 0.23$) at the end of the surgery compared to Group I; there were no differences at the beginning of the surgery and 24 hours after the procedure. No intergroup differences in concentrations of ET-1 and ADMA were found at all control points. In Group II we observed significant decrease of nitrite level by the end of the surgery compared to baseline - 0.57 [0.41; 0.73] vs. 0.89 [0.64; 1.45] μmol/L (Z= -2.48, $p = 0.012$), that returned to initial values 24 h postoperatively - 0.83 [0.61; 1.71] μmol/L (Z= -2.39, $p = 0.016$). Group I demonstrated no significant dynamics of nitrite concentration comparing to baseline values. In Group II end-surgery nitrite level showed a significant negative correlation with cardiopulmonary bypass length ($R = -0.53$; $p = 0.001$), mechanical ventilation time ($R = -0.52$; $p = 0.027$) and ICU stay length ($R = -0.58$; $p = 0.012$). End-surgery nitrite level was independently associated with acute heart failure incidence after surgery (U=32.5; $p = 0.013$).
Conclusion: Decline of nitrite level by the end of the cardiac surgery with CPB may be regarded as an important predictor of complicated course of postoperative period in HFrEF patients.

P1905

HsCRP in patients with heart failure and its associations with outcome

P Pierpaolo Pellicori[1]; A Urbinati[1]; J Zhang[1]; V Nuzzi[1]; P Shah[1]; S Kazmi[1]; AL Clark[1]; JGF Cleland[1]
[1]*University of Hull, Department of Academic Cardiology, Hull, United Kingdom*

Background: Markers of inflammation, including high sensitivity C-reactive protein (hsCRP), are often raised in patients with heart failure (HF); however, little is known about the associations between hsCRP and outcome.
Methods: The prognostic value of hsCRP was studied in consecutive referrals with suspected HF to a specialist clinic serving a local community of ~500,000 people; HF was defined as symptoms or signs with either a reduced left ventricular ejection fraction (LVEF < 45% or left ventricular systolic dysfunction>mild on visual estimate if LVEF could not be calculated) or raised amino-terminal pro-B type natriuretic peptide (NT-proBNP >220 pg/ml).
Results: Of 4463 patients, 3473 fulfilled the criteria for HF. The median (IQR) hsCRP was 4.2 (1.7-9.1) mg/L and 3.9 (1.6-8.8) mg/L in patients with HF and reduced, or preserved LVEF ($p = 0.18$), and 2.9 (1.3-5.3) mg/L in those who did not fulfil criteria for HF ($p < 0.001$). Patients with HF in the highest quartile of hsCRP (range: 9-299 mg/L) were older, had more symptoms and clinical signs of congestion, and higher plasma NTproBNP than those in the lowest quartile (< 0.7 mg/L). LVEF was not an important determinant of plasma hsCRP. During a median follow up of 1490 (IQR: 744-2470) days, 1720 (50%) patients with HF died. In a multivariable Cox model, increasing hsCRP was independently associated with mortality (HR for 10 units change: 1.03 (95% CI: 1.01-1.05), $p = 0.012$). Compared to those in the lowest quartile of hsCRP, those in the highest quartile had a two-fold increase in mortality (HR: 2.23 (95% CI: 1.94-2.55), $P < 0.001$). However, a higher proportion of deaths were non-cardiovascular (CV) in those with elevated hsCRP, regardless of LVEF (At 2 years for hsCRP < 2.5mg/L v >10mg/L; HFrEF - all-cause mortality 11.8% v 34.5%; non-CV 3.0% v 12.4%; HFpEF all-cause mortality 11.8% v 28.3%; non-CV 3.5% v 13.9%).
Conclusions: In patients with HF, higher plasma concentrations of hsCRP are a powerful predictor of mortality, and identify patients with more congestion and higher natriuretic peptides, but who are also more likely to die of non-cardiovascular causes.

P1906

Correlation in biomarkers in patients with chronic heart failure accompanied with depressive disorders.

V Volodymyr Mykhaylov[1]; A Kozhyna[1]
[1]*Kharkiv National Medical University, Kharkiv, Ukraine*

The aim of our research is to study correlation in biomarkers in patients with chronic heart failure (CHF) accompanied with depressive disorders.
For conducting the research 107 CHF patients were involved. The patients were examined with: clinical methods; psycho-diagnostic methods (Hamilton Depression Rating Scale (HDRS), Beck Depression Scale (BDS) State-Trait Anxiety Inventory (STAI), Quality of Life Test); ELISA – to estimate levels of tumor necrosis factor – α (TNF-α) and transforming growth factor -β1 (TGF-β1), levels of serotonin, melatonin, adrenalin, noradrenalin, cortisol. The data were analyzed by descriptive statistical methods.
The results that we got showed that in 47% of CHF patients clinical and psychopathological signs of severe depression and moderate depression were observed. In 10% of CHF patents with severe depression average indicators of HDRS was 28,5 ± 0,7, indicators of BDS – 19,3 ± 0,3, state and trait anxiety indicators of STAI were 46,3 ± 0,3 and 47.5 ± 0,3 respectively. In 37% of CHF patents with moderate depression average indicators of HDRS was 24,5 ± 0,6, indicators of BDS – 16,3 ± 0,3, indicators of STAIT were 32,3 ± 0,3 and 33.5 ± 0,3. In other 53% CHF patients mild depression or absence depression were observed: (HDRS -9,5 ± 0,7, BDS – 10,3 ± 0,4, STAIT - 25,3 ± 0,3 and 28.5 ± 0,3 respectively).
In the CHF accompanied with severe depression levels of serotonin, melatonin, adrenalin were lower than in group of CHF patients with moderate depression and in group of CHF with mild depression or absence depression. Serotonin: 101 ± 8 ng/ml, 112 ± 16 ng/ml, 167 ± 8 ng/ml. Melatonin: 13,6 ± 1,4 ng/ml, 13,9 ± 1,2 ng/ml, 14,6 ± 1,6 ng/ml. Adrenaline: 30,3 ± 7,6 pg/ml, 32,1 ± 8,7 pg/ml, 39,1 ± 8,8 pg/ml respectively. Levels of noradrenalin and cortisol were vice versa higher in groups of SD and MD. Noradrenalin 410 ± 150,2 pg/ml , 363,1 ± 110,3 pg/ml, 210,9 ± 85,8 pg/ml, cortisol: 501 ± 186,1 nmol/l, 473 ± 169,4 nmol/l, 353,7 ± 78,7 nmol/l respectively.
The main levels of TGF-β1 and TNF-α were significantly higher in CHF in patients with severe depression and moderate depression (Severe- 98,71 ± 0,4 pg/ml and 55,45 ± 6,43 pg/ml, Moderate- 78,35 ± 0,4 pg/ml and 44,46 ± 3,23 pg/ml) in comparing with CHF with mild or absence depression (42,3 ± 3,7 pg/ml and 27,2 ± 1,21 pg/ml).
Conclusion: Correlation between biomarker has showed direct dependents between CHF and depression. CHF patients with severe depression and moderate depression characterized by higher indicators of TNF-α and TGF-β1 and leads to more quick development of cardiac hypertrophy and diastolic dysfunction in comparing with CHF patients with mild depression or absence depression.

P1907

Low circulating hepcidin as a measure of iron deficiency in patients with acute and stable heart failure

M Kasztura[1];
M Drozd[1]; P Rozentryt[2]; L Polonski[2]; J Malyszko[3]; E Koc-Zorawska[3]; K Josiak[4]; M Sokolski[4]; J Biegus[4]; R Zymlinski[5]; W Banasiak[5]; P Ponikowski[4]; E A Jankowska[1]
[1]*Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland*; [2]*Silesian Center for Heart Diseases (SCHD), Third Department of Cardiology, Zabrze, Poland*; [3]*Medical University of Bialystok, Department of Nephrology, Bialystok, Poland*; [4]*Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; [5]*Military Hospital of Wroclaw, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*

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Background/Introduction: Hepcidin is a key regulator of systemic iron metabolism. Its elevated level might be involved in pathophysiology of iron deficiency (ID) in some chronic diseases accompanied by inflammation, such as heart failure (HF). There is a scarcity of data on circulating hepcidin level and its relationship with other markers of ID in patients with HF.
Methods: We analyzed data of 291 patients with stable HF (85% men, mean age: 61 ± 11 years, NYHA III-IV: 34%, LVEF: 26 ± 7%) and 165 patients with acute HF (81% men, mean age 65 ± 12 years, NYHA III-IV: 34%, LVEF: 32 ± 7%) and 66 healthy controls (77% men, mean age 60 ± 11 years, LVEF: 64 ± 7%). Sera from all patients were analysed for hepcidin-25 by ELISA validated with a gold standard for hepcidin assessment, liquid chromatography mass spectrometry (LCMS).
Results: Serum hepcidin levels were: 39.6 (27.6 - 61.4) ng/mL (median with lower/upper quartiles) in the control group, 17.7 (4.8 - 45.3) ng/mL, and 57.3 (30.5 – 116.2) ng/mL in all patients in acute and stable HF respectively. In patients with ID as compared to those with optimal iron level hepcidin concentration was significantly lower in acute HF – 11.0 (3.2 – 35.6) ng/mL versus 28.3 (13.3 – 88.7) ng/mL $p < 0.001$, and stable HF – 27.1 (15.6 – 58.4) ng/mL versus 76.2 (42.3 – 131.2) ng/mL, $p < 0.001$. For diagnosis of ID in stable HF group hepcidin ≤31.223 ng/mL had a sensitivity of 58% and specificity of 88% and the area under the receiver operating characteristic (ROC) curve was 0.78 ± 0.03 (95% CI, 0.721-0.839). In acute HF group hepcidin ≤7.998 ng/mL had sensitivity and specificity respectively 48% and 90% and area under ROC curve was 0.703 ± 0.04 (95% CI, 0.623-0.783). Serum hepcidin levels were significantly correlated with ferritin (R=0.55, $p < 0.0001$ for both acute and stable HF) and transferrin saturation (R= 0.26, $p < 0.009$, only for acute HF), and significantly negatively correlated with sTfR level (R=-0.37, $p < 0.0001$ only for acute HF).
Conclusion: Hepcidin concentration is markedly diminished in patients with ID and HF and particularly low in patients with acute HF. Serum hepcidin level might be a useful marker of iron status in patients with HF.

P1908

The role of polymorphism - 634 G/C (rs 2010963) of VEGF-A gene in the carotid intima media thickness changes in chronic heart failure patients

M Maria Iaresko[1]
[1]*L.T.Malaya Institute of Therapy, Kharkiv, Ukraine*

Background: chronic heart failure (CHF) is one of the most common complications of cardiovascular diseases. It is well-known fact that CHF affects various organs and tissues, leads to disruption of their function, that is why it could be in most cases direct cause of death of the patients. It was found that structural changes of the carotid intima media thickness (CIMT) are directly dependent on the level of increasing of endothelin in the blood plasma in CHF patients, which confirms the role of endothelial dysfunction in the development and progression of remodeling processes in the vascular mainstream. One of the major endothelial factors stimulating angiogenesis is a vascular endothelial growth factor (VEGF) – the signal protein produced by the cells to stimulate angiogenesis and vasculogenesis.
Purpose: to examine the effect of genetic polymorphism -634 G/C (rs2010963) of the VEGF-A gene in the development of CIMT changes in patients with CHF.
Materials and Methods: 70 women with CHF in the age from 60 to 65 years were examined. Depending on the genotype, patients were divided into 3 groups: GG - 33 persons, CG - 21 persons, CC - 16 persons. The VEGF concentration was determined by ELISA. The study of the allelic polymorphism -634 G/C (rs 2010963)

VEGF-A gene was performed by polymerase chain reaction with the electrophoretic pattern detection of result. CIMT was assessed sonographically using GE Vivid 7 with 13 MHz.
Results: The study results were showed that in patients with CHF GG genotype polymorphism -634 G/C (rs 2010963) of the VEGF-A gene was dominated. The VEGF level was significantly higher in patients with the GG genotype – 545,2[370,5; 626,4] pg/ml comparing with the genotype CG –232,4[217,5; 394,8] pg/ml and the genotype CC –216,9[137,6; 253,8] pg/ml (p = 0,05). There was no significant differences of the VEGF level among patients with the genotype CG and CC (p>0,05). CIMT assessment has showed that among patients with GG genotype CIMT indicator was significantly higher 1,17 [0,94; 1,25] mm compared with the CC genotype – 0,98 [0,92; 1,04] mm (p = 0,05). There was no significant differences comparing the results of these indicators in CG genotype patients – 1,08 [0,96; 1,11] mm (p-0,05).
Conclusion: it was found that level of VEGF and the CIMT were significantly higher among patients with the GG genotype polymorphism -634 G/C (rs 2010963) of the VEGF-A gene compared with genotypes CG and CC patients. The relationship between the level of VEGF-A, the representatives of GG genotype polymorphism -634G/C (rs 2010963) of the VEGF-A can be regarded as predictors of carotid intima media thickening in patients with CHF.

P1909

5-year prognostic value of different parameters from routine hemogram in patients with idiopathic dilated myocardiopathy and severe systolic disfunction referred to a heart failure unit

JM Sobrino-Marquez[1]; EM Cantero-Perez[1]; E Lage-Galle[1]; D Rangel-Sousa[1]; A Adsuar-Gomez[1]
[1]*University Hospital of Virgen del Rocio, Seville, Spain*

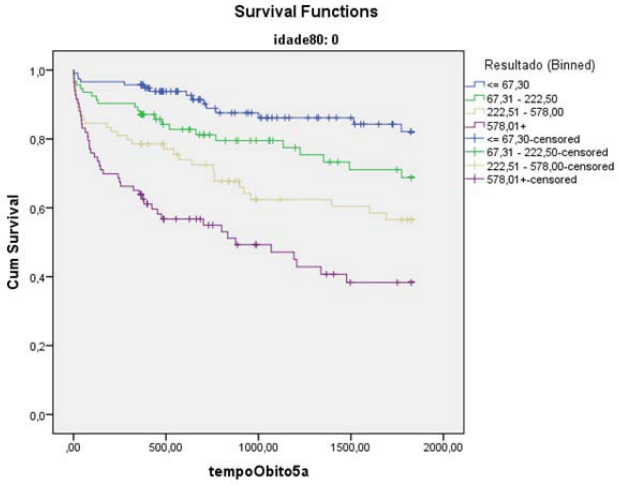
Introduction: We analize the 5-year prognostic value of several parameters from routine hemogram in patients referred for evaluation for non-emergent heart transplantation in our Heart Failure Unit.
Methods: From 2009 to 2011, 87 patients with dilated myocardiopathy and LVEF < 30% were evaluated. Exclusion criteria included coronary artery disease, primary valvulopathies or hipertrophic or restrictive myocardiopathies after echocardiogram, coronariography and cardiac hemodynamics. Evolution after 5 years showed that 49 patients remained in good functional class (group A, 57%), while 38 patients were transplanted or died (group B). We analyzed next parameters from routine hemogram (and indexes derived from them): RDW (red blood cell distribution width), neutrophil count, lymphocite count, neutrophils / lymphocites ratio (NLR) and platelet count. Finally, as part of the BIOSTAT-CHF Scotland Study, NLR and platelet count were chosen for creating the CPNR score, chosing a cut-off value of NLR and platelet count at 3 and 275 respectively. Thus, a patient with both elevated NLR (>3) and platelet count (>275) was allocated a score of 2 (CPNR 2), and a patient shown one or neither was allocated a score of 1 (CPNR 1) or 0 (CPNR 0), respectively.
Results: Median RDW values were 13,9 in group A and 16,3 in group B (p < 0,001). Mean neutrophil count was 5,50 and 6,30, respectively (NS). Mean lymphocite count was 2,22 and 1,64, respectively (p < 0,05) while NLR was 3,33 and 6,06 (p < 0,05). Finally, CPNR didn´t show statistical differences between groups.
Conclusion: In patients with idiopathic dilated myocardiopathy and severe systolic dysfunction referred to a Heart Failure Unit, RDW, lymphocite count and neutrophils / lymphocites ratio show statistically significant differences between patients with good and bad prognosis at a 5-year follow-up.
Discussion: Basic hemogram can be a rapid and available biomarker that could potentially help in risk stratification of CHF patients.

P1910

Applicability of bnp as a biomarker of prognosis for long-term mortality in a comparison between non-elderly, elderly and major-elderly patients in south Brazil.

E Edyuardo Pitthan[1]; HV Hirakata[1]; BJ Barbisan[1]
[1]*Institute of Cardiology of Rio Grande do Sul, Porto Alegre, Brazil*

Introduction: B-type natriuretic peptide (BNP) is used as a short-term biomarker for prognosisin patients with heart failure (HF). The prognostic role for long-term mortality is insufficiently studied.
Objectives: To validate the BNP test as a biomarker of long-term mortality prognosis in patients with suspected HF, comparing the non-elderly < 60 years, elderly (≥60-79 years) with the major-elderly >80 years old.
Methods: The sample consisted of 634 patients with suspected HF, attended at the emergency room between March 2003 and September 2012. The efficacy of BNP to identify patients with heart failure and the association between the level of BNP (POCT Biosite) and long-term prognosis were evaluated. The study was divided into three age groups, Elderly (E) 60-79 (46%) years, major-elderly ≥80years(38%) and Non-Elderly < 60 years old. Cause of death was identified through a search of death certificates in registry offices, informed by the Brazilian Mortality Information System.
Results: Most patients were white (93.1%), female (63.8%), with a mean age of 77.3 (± 8.6) years. HF was diagnosed based on a new gold standard that considered the Framingham and Boston criteria, plus echocardiography and ECG. HF was present in 340 patients (53.5%).Most of these patients (63.5%, n=216) had HF with Preserved Ejection Fraction (HFPEF). In bivariate analysis a BNP> 180pg/ml was associated with a higher risk of mortality. In multivariate analysis BNP> 180pg/ml remained associated with increased risk of mortality,with an HR of 3.4 (CI95%: 1.2 to 9.6;p < 0.02). Survival analysis in 78 months at the end of the study (six years and six months) was performed by Kaplan-Meier curve. The median BNP for the Major Elderly >80 years group with HF was 595pg/ml, with a 27-month mean survival time (MST) and 47% mortality rate. The median BNP for the Elderly between 60-79 years groupwas 369 pg/ml, with a 52-month MST and 38% mortality rate. The Non-Elderly group BNP was 222pg/ml, with an MST >50% and 26% mortality rate.
Conclusion: The BNP level showed association with the mortality index. BNP is an independent prognostic biomarker for long-term mortality in patients with HF in all ages.

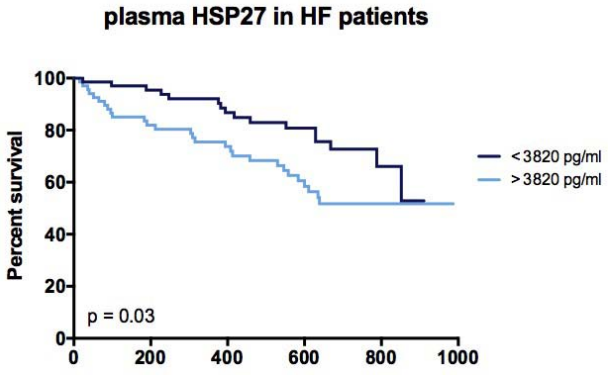


P1911

HSP27 plasma levels as an independent predictor of prognosis in chronic heart failure patients

D Denise Traxler-Weidenauer[1]; M Lainscak[2]; HJ Ankersmit[1]; B Jug[3]
[1]*Medical University of Vienna, Christian Doppler Laboratory for Diagnosis and Regeneration of Cardiac and Thoracic Diseases, Vienna, Austria*; [2]*University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia*; [3]*University of Ljubljana, Division of Vascular Diseases, Department of Internal Medicine, Ljubljana, Slovenia*

Background: Heat-shock proteins (HSP) represent intracellular mechanisms of stress response and are involved in chaperoning and regulating cellular death. However, clinical implications of their overexpression and spill-over into the bloodstream in patients with heart failure (HF) remain elusive, as HSP can represent both protective biological mechanisms as well as biomarkers of disease progression.
Purpose: The aim of this present study was to assess the prognostic impact of HSP27 in chronic HF.
Methods: In outpatients with chronic stable HF (i.e. no change in clinical trajectory for > 3 months) with reduced or preserved left ventricular ejection fraction (LVEF), plasma HSP27 baseline levels were measured using enzyme linked immuno-sorbent assay (ELISA). Patients were followed for a minimum of one year, and multivariate Cox proportional hazards were built for cardiovascular death or HF-associated hospitalisations.
Results: A total of 134 patients with chronic HF (mean age 71 ± 10 years, 34 % female, mean LVEF 36 ± 12 %) were included. During a mean follow-up of 527 ± 260 days, 44 patients (33 %) experienced an event. Mean time to event was 350 ± 236 days. In a Kaplan-Meier survival analysis HSP27 levels above the median (3820.0 pg/ml) indicate a higher risk for an event (p = 0.03). An adjusted Cox proportional hazard model was built using established heart failure parameters (logNTproBNP, LVEF, NYHA classification, age, gender) increased plasma HSP27 levels (HR 2.00, CI 95% 1.02 – 3.90, p = 0.04) emerged as an independent predictor within a multivariate analysis.
Conclusions: HSP27 plasma levels are an independent predictor of prognosis in chronic HF. Our findings suggest that HSP27 may improve risk-stratification in HF beyond known prognostic predictors, such as age, LVEF, NYHA class and natriuretic peptides.



HSP27 Kaplan-Meier survival curve

P1912

Association of microcirculation disturbance with IFR and VEGF-A levels in patients with heart failure

MV Kozhevnikova[1]; EA Zheleznykh[1]; YUA Danilogorskaya[1]; AA Shchendrygina[1]; GA Shakaryants[1]; VYU Kaplunova[1]; AO Yusupova[1]; IS Chekneva[1]; VYU Zektser[1]; EV Privalova[1]; YUN Belenkov[1]
[1]*I.M. Sechenov First Moscow Medical State Universityul. Trubetckay , 8, str. 2, 119992 Moscow, Russia, therapy, Moscow, Russian Federation*

Purpose: to assess the association between IFR and VEGF-A levels, parameters of intracardiac hemodynamic and disturbance of microcirculation in patients with heart failure (HF).
Methods: 52 patients (29 men, age 65,78 ± 8.79, EF 50,96 ± 8.7) with HF and 50 controls (28 men, age 65.31 ± 7.22, EF 59.23 ± 5.06) were included in the study. In HF group included: 27 patients (51,9%) with preserved ejection fraction (HFpEF), 18 (34,6%) patients with mid-range ejection fraction (HFmrEF) and 7 (13,5%) patients with reduced ejection fraction (HFrEF). All patients were investigated according standard cardiac algorithm. We estimated IFR and VEGF-A level, assessed microcirculation (occlusion index (IO) and remodeling of arteriols (index of refraction (RI)) by photoplethysmography.
Results: VEGF-A level was significant higher in patients with HFpEF 123,9 ng/mL (71,33: 176,43) vs HFrEF 217 ng/mL (-41.5:94.17) and HFmrEF patients 217,86 ng/mL (118,55:317.15) (p < 0,005). Decrease of IO in HF group (1,4) vs controls (1,6) p = 0,007 was revealed. A positive correlation between RI level and ejection fraction (r=0,33, p = 0,0037) was determined. IFR level associated with RI (r=0,307; p = 0,0073).
Conclusion: 1. The association between IFR and VEGF-A levels, parameters of microcirculation (IO) and intracardiac hemodynamic parameters (EF) were found in patients with HF. 2. VEGF-A level is differ in patient with HFrEF, HFmrEF and HFrEF. 3. It was determined that IO is decreased in patients with HF.

P1913

SERCA2a as non-invasive biomarker of heart transplant rejection

E Esther Rosello-Lleti[1]; E Tarazon[1]; A Ortega[1]; C Gil-Cayuela[1]; E Sanchez-Lacuesta[2]; P Marin[3]; A Hernandiz[4]; L Martinez-Dolz[1]; M Portoles[1]; M Rivera[1]
[1]*Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain*; [2]*Hospital Universitario y Politécnico La Fe, Hemodynamic Unit, Valencia, Spain*; [3]*Hospital Universitario y Politécnico La Fe, Microscopy Unit, Valencia, Spain*; [4]*Hospital Universitario y Politécnico La Fe, Experimental Cardiology, Valencia, Spain*

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Background: The detection of heart transplant rejection by non-invasive methods represents a challenge since multiple alternatives have been studied but none of them have been able to replace or reduce the number of biopsies in daily clinical practice. Despite of the importance of the study of SERCA2a in the heart, its role as rejection marker in the cardiac rejection has never been analysed.
Purpose: The aim of the study is to analyse if SERCA2a protein could be a marker of cardiac rejection.
Methods: We recruited a total of 127 consecutive endomyocardial biopsies and serum samples from adult patients (>18 years) undergoing cardiac transplantation (49 without allograft rejection and 78 with diagnosis of biopsy allograft rejection: 48 Grade 1 R, 21 Grade 2R, 9 Grade 3R). Serum concentrations of SERCA2a were determined by specific commercial sandwich enzyme-linked immunosorbent assay. We also analysed SERCA2a levels on endomyocardial biopsies by immunofluorescence.
Results: SERCA2a cardiac tissue and serum levels were decreased in patients with acute cardiac rejection. The receiver-operating characteristic analysis showed that SERCA2a strongly discriminated patients with allograft rejection from patients without rejection: normal grafts vs all rejecting grafts (AUC=0.804), normal grafts vs Grade R 1 (AUC=0.751), normal grafts vs Grade R 2 (AUC=0.875), normal grafts vs Grade R 3 (AUC=0.922) p < 0.0001 for all comparisons.
Conclusions: This study demonstrates that a different expression of SERCA2a occurs in rejecting allograft patients, not only at the tissue level but also in the serum, showing their potential role as non-invasive biomarker in heart transplant reject.

P1914

Soluble ST2 in bronchial aspirates of patients with severe respiratory insufficiency and its correlation with acute heart failure

M Navarro Penalver[1]; ME Garcia Garcia[1]; J Sanchez Mas[1]; R Jara Rubio[1]; JJ Santos Mateo[1]; J Sanchez Serna[1]; AM Lax Perez[1]; MC Asensio Lopez[1]; DA Pascual Figal[1]
[1]*Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain*

Background: Recent studies have demonstrated plasma soluble ST2 (sST2)to be a strong predictor of cardiovascular outcomes in acute heart failure (AHF). However, the main sources of sST2 are not completely Known. The aim of this study was to investigate the presence of sST2 in bronchial aspirates of patients with severe acute respiratory insufficiency and its clinical correlates.
Methods: 34 patients (aged 63 ± 16 years, 61% male) with acute respiratory insufficiency (ARI) requiring intubation were included. Bronchial aspirates and blood samples were obtained at the moment of intubation. sST2 levels were measured using an ELISA assay. ARI etiology was classified as cardiogenic (AHF) or non-cardiogenic. Clinical and laboratory data were also recorded.
Results: sST2 was detected in bronchial aspirates (median 6 [Q1-Q3 2.6–72.2]ng/ml). Patients with AHF showed higher bronchial sST2 levels (bsST2) (n = 12, median 29.6 [Q1-Q3 6-142] ng/ml) than those with non-cardiogenic causes of respiratory failure (n = 22, median 3.8 [Q1-Q3 1.9-16.2] ng/ml) (p = 0.02). We found a strong positive correlation between bsST2 and plasma sST2 (rs= 0.41; p = 0.026). bsST2 also correlated with lactate (rs=0.5; p = 0.007), AST (rs=0.44; p = 0.022), troponin T (rs=0.5; p = 0.04) and LDH(rs=0.26; p = 0.004). A negative correlation with LVEF was also found (rs=-0.57; p = 0.024). There was no association between bsST2 levels and the time needing vasoactive support or non invasive mechanical ventilation. bsST2 did not correlate with NT-proBNP levels, renal function or inflammatory parameters like C-reactive protein or procalcitonin.
Conclusion: sST2 is present in bronchial aspirates from patients with severe ARI showing higher levels in those with AHF. bsST2 correlates with cardiac function, metabolic stress and cellular damage.

P1915

Mass spectrometry for detection heart failure with preserved ejection fraction

LK Malinovskaya[1];
A A Bykova[1]; P SH Chomahidze[1]; A L Syrkin[1]; PH YU Kopylov[1]; V B Betelin[2]; YU R Shaltaeva[3]; V S Pershenkov[3]; N N Samotaev[3]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*; [2]*Scientific Research Institute of System Development, Moscow, Russian Federation*; [3]*National Research Nuclear University "MEPhI", Moscow, Russian Federation*

Funding Acknowledgements: This study was supported by Russian Academy of Science

Background: Heart failure (HF) remains the leading cause of poor prognosis and death in developed countries. Early and reliable diagnosis of HF is a relevant and practically significant problem. Numerous prognostic markers of death and HF hospitalization have been identified in patients with HF. However, their clinical applicability is limited and precise risk stratification in HF remains challenging. The diagnosis of HF with preserved ejection fraction (HF-PEF) is still difficult.
Purpose: The purpose of this study was to investigate the correlation between acetone in exhaled breath and N-terminal pro B-type natriuretic peptide concentration in patient with HF-PEF.
Methods: Of 84 patients evaluated between October 2014 and April 2016, 56 patients (HF group) fulfilled inclusion criteria and were compared with healthy subjects (control group, n = 36). Patients with HF were grouped according to ejection fraction (HF-PEF, n = 26; HF with reduced ejection fraction [HF-REF], n = 30) and submitted to exhaled breath collection. Identification of volatile organic compounds

was done by Proton Transfer Reaction – Mass Spectrometry (PTR-MS). All of the patients underwent standart biochemical assessment and biomarkers evaluation (NT-proBNP, Troponin I, Copeptin, Cistatin).
Results: In compare with control group several biomarkers were significantly higher in both HF group. They are acetone, acetic aldehyde, ethanol and propylene. The median (interquartile range) concentration of acetone in HF-PEF group when compared to control group was 1527 ppb [894-2160] vs 1,51 ppb [1,15-1,87], p = 0,001; acetic aldehyde 273 [175-371] vs 2,33 [2,05-2,61], p = 0,001; ethanol 41,9 [13,9-69,9] vs 1,34 [1,23-1,45], p = 0,001; propylene 361 [219-503] vs 2,43 [2,09-2,77], p = 0,001 respectively. Further division into groups with different ejection fraction was analyzed. It has been found that correlation is not significant for HF-REF group (r = 0,12, p = 0,53), while for HF-PEF group is significant correlation (r = 0,54, p = 0,004). The transition to a logarithmic scale, there is a significant relationship between the logarithm of NTproBNP level and the logarithm of acetone in breath (r = 0.294, p = 0.026).
Conclusion: Exaled breath acetone may be a promising noninvasive diagnostic method of HF-PEF, but further investigations are necessary.

P1916

Proteomic biomarker discovery and multiple reaction monitoring assay optimisation to identify diabetic patients with left ventricular diastolic dysfunction

J James O'reilly[1]; C Tonry[1]; E O'connell[1]; AQ Butt[1]; L Murphy[1]; S Pennington[1]; M Ledwidge[2]; K Mcdonald[2]; C Watson[3]; JA Baugh[1]
[1]University College Dublin, Dublin, Ireland; [2]St Vincent's University Hospital, Dublin, Ireland; [3]Queen's University of Belfast, Belfast, United Kingdom

Introduction: The need for biomarkers to identify cardiac dysfunction in patients with diabetes (DM) is becoming increasingly pressing due to the global rise in disease prevalence and reducing healthcare resources to detect and manage these complications. With the risk of heart failure being 2-5 fold greater in those with diabetes, early identification of cardiac dysfunction may facilitate more timely management and reduce or delay future heart failure development.
Methods: Biomarker discovery was carried out in trypsin digested, immuno-depleted human serum on a Q-Exactive mass spectrometer. 200 samples from the Irish STOP-HF cohort were used for the discovery and verification stages. Four pooled age- and gender-matched groups of 50 patients were analysed, with and without DM and with and without asymptomatic left ventricular diastolic dysfunction (LVDD); defined as left atrial volume index ≥34ml/m2 and E' < 10 cm/sec. The subsequent biomarker assay was built on a 6490 multiple reaction monitoring (MRM) mass spectrometer. Proteotypic synthetic peptides (2 per protein), acting as surrogates of the proteins of interest, were pooled and run on an unscheduled method to extrapolate the retention times needed for a scheduled MRM method. Scheduled methods were subsequently run in which collision energies and voltages were analysed. The parameters that resulted in the most reproducibly intense signals while producing the least background were then verified in the original discovery cohort, in the 200 individual samples.
Results: Perseus and MPP software revealed 261 unique proteins from the discovery phase, of which 68 were identified as potential biomarkers for the identification of LVDD in DM. GO-Term enrichment analysis of these 68 proteins revealed the involvement of many inflammatory processes. "Humoral immune response", "complement activation" and "acute inflammatory response" were all significantly over-expressed (q-values: 1.00E-30, 1.00E-30, 1.00E-30 respectively).
The unscheduled run resulted in some peptides being excluded due to poor performance on MRM. Similarly, under the scheduled method some peptides, following optimisation, performed poorly and as such were excluded. At the time of writing, the list stood at 41 proteins of 65 peptides with dot products ≥0.8, consisting of 3 transitions each, all detectable on the same run.
Conclusion: Verification, validation and functional analysis of these protein biomarkers, will lead to the identification of key contributors to pathological processes. Using a biomarker based strategy to identify cardiac dysfunction in patients with diabetes, and the prospect of predicting disease progression has the potential to overcome the cost and access difficulties with cardiac imaging modalities if used as a pre-screen or surrogate for disease.

P1917

Serum ST2 levels are associated with myocardial fibrosis in severe aortic stenosis

R Rafael Sadaba[1]; V Arrieta[2]; V Alvarez[2]; F Olaz[2]; M Ciriza[3]; A Ferandez Celis[4]; J Ibarrola[4]; J De Diego[1]; N Lopez-Andres[4]
[1]Hospital de Navarra, Cardiac Surgery, Pamplona, Spain; [2]Hospital de Navarra, Cardiology, Pamplona, Spain; [3]Hospital de Navarra, Radiology, Pamplona, Spain; [4]Miguel Servet Foundation, Cardiovascular Translational Research, Pamplona, Spain

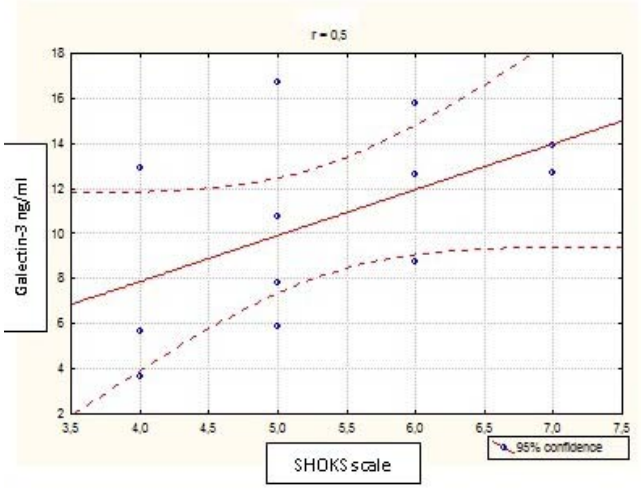
Background/Introduction: Soluble ST2 (sST2) is a biomarker of left ventricular (LV)remodelling, and it has been shown to be a predictor of adverse outcomes in heart failure. Focal myocardial fibrosis (FMF) detected by means of delayed enhancement (DE) cardiac magnetic resonance (CMR) has been proposed as a marker of advanced stage and worse prognosis in patients with severe aortic stenosis (AS).
Purpose: To evaluate the association of sST2 levels and the presence, distribution and severity of FMF in patients with severe AS.
Methods: A consecutive series of 79 patients with symptomatic AS and referred for aortic valve replacement, were prospectively studied with CMR on a 1.5T scanner, obtaining T1 mapping sequences before and 15 minutes after the administration of gadolinium, following a Sh-MOLLI protocol in the ventricular short axis. Blood samples were taken for determination of sST2 levels and other biochemical parameters.
Results: FMF was detected in 42 patients (53%). Patients with FMF showed significantly higher levels of sST2 than patients without FMF (34,6 ± 7,6 vs 17,9 ± 5,6; p < 0,0001). Intramyocardial and subendocardial fibrosis was detected in 23 and 19 patients respectively. Independently of the severity of AS, patients with FMF have higher LV mass (predominantly those with intramyocardial FMF), and LV volume, and less LV ejection fraction (predominantly in those with subendocardial FMF). sST2 levels were higher in patients with intramyocardial FMF. There was a positive correlation between sST2 levels and LV end-diastolic volume (r=0,256; p = 0,041) and LV mass (r=0,28; p 0,0037). Similarly, there was a positive correlation between sST2 levels and FMF mass (r=0,433; p < 0,0001).
Conclusion: In patients with symptomatic AS, there is a relationship between sST2 levels and FMF evaluated by CMR, and between sST2 levels and morphological LV alterations. sST2 may be a prognostic marker of LV remodelling in patients with AS.

P1918

Role of galectin-3 in therapy monitoring of patients with HF

K Karine Gyamdjyan[1]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

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. Plasma levels of galectin-3 and NT-proBNP were assessed at baseline and at the day of discharge, using enzyme-linked immunosorbent assays. The Mann-Whitney U test was used to compare differences between two independent groups. The relationship between galectin-3 levels and other variables of interest was analyzed using Pearson (Spearman for non-parametric data) correlation analysis/ A p < 0,05 was regarded as statistically significant. All patients were assigned to recieve heart failure standard therapy that included ACEI/ARB, BB, loop diuretics and spironolactone.
Results: Galectin-3 plasma levels significantly decreased after holding standard

therapy of heart failure (p < 0,001). Decrease of galectin-3 plasma levels was observed in 84,3% of patients. Changes in galectin-3 levels positively correlated with changes in scale of evaluation of clinical state in CHF (as modified Mareev VY 2000) (r=0,5, p = 0,1). NT-proBNP plasma levels also decreased at the end of the treatment (p < 0,003). Decrease was observed in 84,2% of patients.
Conclusion: in a small cohort of patients palsma galectin-3 and NT-proBNP levels have decreased after holding of standard heart failure therapy. Changes of galectin-3 levels positively correlated with changes in clinical state of CHF.

NT-proBNP and galectin-3 levels dynamics

Biomarkers	Baseline	Before after standard therapy	p
NT-proBNP, pmol/l	121,47 [43,3; 177,88]	82,69 [31,88; 132,66]	0,003
Galectin-3, ng/ml	8,5 (5,21; 15,72)	6,49 [3,36; 12,79]	0,0008

P1919
Regardless of the fibrosis status 12-month kinetics of serum markers of fibrosis are not different in dilated cardiomyopathy patients

P Pawel Rubis[1]; S Wisniowska-Smialek[1]; E Dziewiecka[1]; K Holcman[1]; A Karabinowska[1]; L Khachatryan[1]; P Faltyn[1]; E Wypasek[1]; P Podolec[1]
[1]*Department of Cardiac and Vascular Disease, John Paul II Hospital, Institute of Cardiology, Krakow, Poland*

Funding Acknowledgements: Grant from the Poland National Centre of Science (no. 2013/09/D/NZ5/00252)

Background: Serial assessment of serum markers of fibrosis may provide insight into dynamics of myocardial fibrosis process. It is unknown whether 12-month patterns of markers of fibrosis differ between dilated cardiomyopathy (DCM) patients (pts) with and without fibrosis.
Methods: We included 70 consecutive DCM patients (pts) (48 ± 12.1 years, EF 24.4 ± 7.4%). All pts underwent right ventricular endomyocardial biopsy (EMB) to study cardiac fibrosis. Markers of collagen type I and III synthesis – procollagens type I and III carboxy- and amino-terminal peptides (PICP, PINP, PIIICP, PIIINP), and ECM metabolism controlling factors – tumor growth factor beta-1 (TGF1-β) and connective tissue growth factor (CTGF) were measured in serum at baseline, and 3- and 12-month follow-up.
Results: Based on the EMB results, two groups of pts were identified: without (n = 46, 65.7%) and with (n = 24, 34.3%) fibrosis. Baseline, 3- and 12-month values of PICP, PINP, PIIICP, PIIINP, TGF-β and CTGF did not differ between two groups (Figure 1).
Conclusions: 12-month kinetics of serum markers of fibrosis are similar in DCM pts with and without fibrosis. Regardless of the time point of measurements, reliable differentiation between DCM pts with and without fibrosis, based on serum markers of fibrosis is questionable. These unexpected findings cannot be easily explain and warrant further studies.

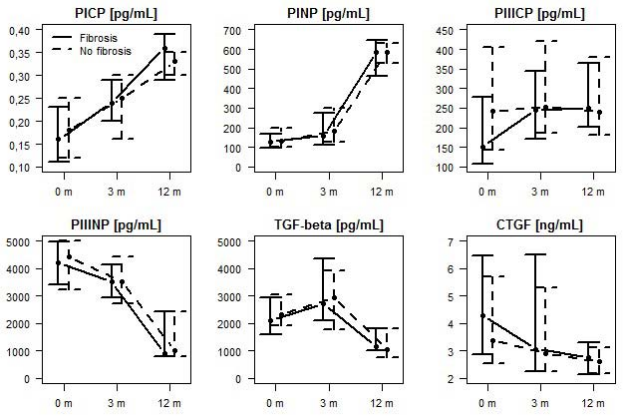


Figure 1

P1920
The use of cardiac multimarker testing in patients with non-obstructive hypertrophic cardiomyopathy

R Radek Pudil[1]; M Vasatova[2]; L Horakova[1]; H Rehulkova[3]; P Rehulka[3]; A Fucikova[3]; V Palicka[2]
[1]*Charles University Prague, Faculty of Medicine in Hradec Kralove, 1st Department of Medicine, Hradec Kralove, Czech Republic*; [2]*University Hospital Hradec Kralove, Institute of Clinical Biochemistry and Diagnostics, Hradec Kralove, Czech Republic*; [3]*Faculty of Military Health Sciences, University of Defence, Department of Molecular Pathology and Biology, Hradec Kralove, Czech Republic*

Introduction: The increase of cardiac markers in patients with hypertrophic cardiomyopathy (HCM) is associated with the severity of left ventricle outflow tract obstruction. However, little is known about the cardiac marker levels in patients with non-obstructive type of HCM.
Purpose: The aim of presented study was to analyze cardiac multimarker testing strategy in detection of the initial structural changes in patients with non-obstructive HCM.
Methods: In the group of 47 patients with non-obstructive HCM (58.4 ± 12.4 years, 12 females), plasma concentrations of creatine kinase MB isoenzyme (CKMB), myoglobin (MYO), glycogenphosphorylase BB isoenzyme (GPBB), and heart type of fatty acid binding protein (FABP) were analyzed with the use of protein biochip system.
Results: Left atrium diameter was 48.2 ± 7.2 mm, and it exceeded reference values in 37 (78%) patients. Right ventricle diameter was 26.1 ± 3.8 mm, and it exceeded reference value in 2 (4%) patients. The end-systolic left ventricle dimension was 31.9 ± 7.1 mm, and it exceeded reference values in 4 (8%) patients. Left ventricle end-diastolic dimension was 47.1 ± 7.3 mm, and it exceeded reference values in 3 (6%) patients. The mean of the interventricular septum thickness was 19.4 ± 4.4 mm, and it exceeded recommended thickness for diagnosis of hypertrophic cardiomyopathy (≥15mm) in all patients. Left ventricle mass was 344.8 ± 129.9 g, and it exceeded reference values for two-dimensional method in all patients. Left ventricle mass index was 171.4 ± 60.2g.m-2, and it exceeded reference values in all patients. The mean of the left ventricle ejection fraction was 67.1 ± 9.9%, and, only in 2 (4%) patients, the LV ejection fraction was below the reference values. Left ventricle fractional shortening was 33.7 ± 8.7, and it exceeded the reference values in 3 (6%) patients. None of the patients had left ventricle outflow tract obstruction. In peripheral circulation, we found increase of hsTnT: [median: 9ng/L (IQR: 5 - 16 ng/L), vs. 7 (5 - 9) ng/L, p 0.03]; CK MB [2 (1.4 - 2.7) μg/L vs. 1.6 (1.1 - 2.2) μg/L, p 0.04]; MYO [46.4 (33.3 - 65.2) μg/L vs. 35.6 (22.8 - 43.7) μg/L, p 0.001]; hFABP [1.8 (1.4 - 3.3) μg/L vs. 1.6 (1.3 - 2.1) μg/L, p 0.05], and GPBB [3.9 (2.5 - 6.3) μg/L vs. 2.3 (1.9 - 4.2) μg/L, p 0.001]. Furthermore, we found significant associations of left ventricle mass index and cardiac markers: hFABP (r 0.41, 95% CI: 0.07-0.66, p 0.01) and with CKMB (r 0.33, 95% CI: 0.11-0.59, p 0.05).
Conclusion: This study indicates potential clinical use of the multimarker testing in diagnosis and screening of the hypertrophic cardiomyopathy even in initial stages.

NURSING

P1921
The impact of educational- supportive self-care package on anxiety, depression and stress in myocardial infarction patients hospitalized in Iran, 2016

N Nader Aghakhani[1]
[1]*Urmia University of Medical Sciences, Urmia, Iran (Islamic Republic of)*

Introduction: Although, Myocardial infarction is one of the most common cardiovascular diseases known which can be controlled, patients are always at risk of physical, and socio–psychological stressors.
Purpose: this study carried out to investigate the impact of educational- supportive self-care package on mean of anxiety, depression and stress in myocardial infarction of an hospital in Iran.
Methods: This pre- and post-quasi-experimental study will carried out on 56 hospitalized patients with heart failure selected from an hospital affiliated with University of Medical Sciences were assessed in 2016. They will assign to two groups of experimental (n = 43) and control (n = 43) groups. They are selected through convenience sampling and divided randomly into two intervention and control groups. Any patient in the experimental group received education after 48 hours of admission and after the disease's acute phase through face to face contact and also a booklet and the questionnaires were completed before the intervention, after the intervention, before discharge from the hospital, and two months after discharge through phone calls or visiting patients in the intervention group if the patients requested. The patients in the control group receive no intervention. At the same time, patients and their relatives were taught about social support in four dimensions of emotional support, tools, information and evaluation. Demographic and DASS questionnaires (anxiety,

stress, depression) were used to collect data. Data were analyzed using statistical software spss version 21.
Results: The findings showed that educational- supportive self-care package can reduce anxiety and depression in experimental group after intervention as a lasting effect. On the other hand, the package does not effect on stress meaningfully decrease among the patients of control group, and only causes the decrease through interaction with the factor "time") p >0.05).
Conclusion: The educational- supportive self-care package can reduce anxiety and depression and a part of stress among patients with myocardial infarction. Thus, it is recommended the results of this study be considered by health and treatment setting managers as a key factoring nursing care programs to decrease of stress, anxiety and depression among patients with myocardial infraction.

P1922
Our network- An hospital acute heart failure unit, an outpatient clinic, a chronic heart failure consultation envolving hospital and primary care

S Susana Quintao[1]; J Campos[1]; C Bastos[1]; I Araujo[1]; F Marques[1]; C Fonseca[1]
[1]Hospital de Sao Francisco Xavier, Day Hospital, Lisbon, Portugal

Heart failure (HF) a disease with growing prevalence requires specialized management. To minimize readmissions and emergency room visits, we implement a HF clinic.
Day Hospital (DH), in partnership with acute HFunit and chronic HFconsultation has a treatment room with 5 monitored seats, two consulting offices for both doctors and nursing, and an area for clinical trials.
The aim of this facility is a reduction in emergency visits and hospital readmissions.
Protocol: patients are discharged to DH for reevaluation within 2 weeks: clinical/analytic reassessment nursing consultation and HF drugs titration. Special attention is payed to education on disease, warning signs, medication, feeding and how to procede when they recognize decompensation and need to come back (ex. IV decongestion treatment up to 3 consecutive days). Direct connection with GPs was implemented. At discharge GP is notified to reevaluate his patient within 2 weeks. GPs may refere back to DH when decompensation, or send to HFconsultation for specialized evaluation/treatment (done within 2 weeks maximum).
Preliminary results showed that inclusion in our HF multidisciplinar management program reduced one year readmissions in 20% (p:0.0017) We have created an efficient network where patients circulate through a close circuit of people well aware of disease willing to improve their quality of life and survival

P1923
Nursing consultation pre-cardiac catheterization in a university hospital: a retrospective study

VF De Freitas Marcolla[1]; E Ferreira[1]; DC Albuquerque[1]; CBOC Naves[1]; AL Viana[1]; IPB Aragao[2]; GP Lima[1]; CAR Cruz[1]; TJF Oliveira[1]; MB Fernandez[1]; SML Costa[1]; MN Leal[1]; SRF Chaves[1]
[1]Rio de Janeiro State University (UERJ), Rio de Janeiro, Brazil; [2]Governo do Estado do Rio de Janeiro, Rio de Janeiro, Brazil

In a report published by the World Health Organization, in 2015, cardiovascular disease remains responsible for most of the deaths attributed to noncommunicable diseases, resulting in the loss of 17 million lives annually. The anamnesis of patients undergoing cardiac catheterization is a necessary condition for the examination because it has the purpose of preventing intercurrences related to the conditions prior to the examination that may undergo some intervention for modification.
Objective: To evaluate the effectiveness of the nursing consultation to improve the quality of care provided.
Methods: Retrospective study of the nursing consultation records, conducted in the biennium 2015-2016, in a university hospital in Brazil. 1990 examinations were planned, with 1377 performed. Of these, only 35.3% were suspended due to lack of patient; 0.7% due to absence of companion; 25.9% because they did not present laboratory tests; 9.4% for having used hypoglycemic medication; 0.7% for having used anti-coagulant medication; 4.7% because they presented laboratory tests with alterations; 3% due to allergy without desensitization; 6.6% had a clinical condition that made the examination impossible; 6.3% due to lack of space; 10% due to lack of material; And 12% for other reasons, including technical problems with haemodynamic equipment.
Conclusion: Nursing pre-cardiac catheterization allowed nurses to plan care for these clients, decreasing the incidence of cancellation of Cardiac Catheterization procedures on the day of the examination, lack of appropriate preparation orientation, previous evaluation of laboratory test data , Evaluation of the access route, and adequacy in the scheduling of priorities, such as the need for femoral access, hemodialysis, and previous hydration.

POPULATION STUDIES - EPIDEMIOLOGY

P1924
Do patients with midterm HF have profile like HFrEF or HFpEF or they have their individual profile. Data from Russian national register 2012

V Y Mareev[1]; E M Seredenina[1]; Y V Mareev[2]; E N Borisov[1]; Y L Begrambegova[1]; M E Tchaikovsky[3]
[1]Medical Scientific Educational Center of M V Lomonosov Moscow State University, Moscow, Russian Federation; [2]Royal Brompton & Harefield Hospitals, Imperial College, London, United Kingdom; [3]Russian Society of Heart Failure Specialists , Moscow, Russian Federation

Background: In the new ESC guidelines for diagnosis and treatment of acute and chronic heart failure (HF) the new classification of heart failure was proposed which include the new type of heart failure – HF with mid-range LVEF (HFmrEF). At this moment, there is a lack prevalence and epidemiology of these patients.
Methods: we used data from Russian National Register 2012. For this analysis, patients were divided into three groups related to their LVEF: < 40%, HFrEF; 40-49% HFmrEF, ≥ 50% HFpEF.
Results: 2055 patients with heart failure were included in this analysis: 542 had HFrEF, 568 HFmrEF, and 945 HFpEF. Patients with HFmrEF were slightly older than patients with HFrEF and slightly younger than patients with HFpEF (mean 64; 61; 66, $p < 0.01$). The number of men was highest in HFrEF (69%) lower in HFmrEF (60%), and lowest in HFpEF (38%), $p < 0.01$. The rate of myocardial infarction in these patients with was slightly lower than in HFrEF (56 vs. 63%, $p < 0.01$) and dramatically higher than HFpEF (24%, $p < 0.01$). However, the prevalence of hypertension in HFmrEF was close to HFpEF (93% vs 96%, $p < 0.01$) and higher than in HFrEF (83%, $p < 0.01$). The prevalence of VT in patients with HFmrEF (7%) was dramatically lower than in HFrEF (21%, $P < 0.01$) and substantially higher than in HFpEF (2%, $P < 0.01$). Patients with HFrEF and HFmrEF have a higher prevalence of smoking and alcohol abuse, which could reflect the fact that there was the greater prevalence of infarctions and higher proportions of men in these groups.
Conclusion: Results of the work showed that patients with HFmrEF have some difference from both HFrEF and HFpEF and we need study which would find the best treatment for this patients.

P1925
Does heart failure influence the clinical characteristics of admitted patients with atrial fibrillation?

A Kartas[1]; I Doundoulakis[1]; D Vasdeki[1]; A Samaras[1]; E Kotsi[1]; E Forozidou[1]; P Tsoukra[1]; T Panagiotidis[1]; H Karvounis[1]; A Tzikas[1]; G George Giannakoulas[1]
[1]AHEPA General Hospital, Thessaloniki, Greece

On behalf of: MISOAC Investigators

Background: Heart failure (HF), which was trichotomized by recent guidelines into HF with reduced ejection fraction (HFrEF), HF with mid-range ejection fraction (HFmrEF) and HF with preserved ejection fraction (HFpEF), frequently coexists with atrial fibrillation (AF). Studies regarding the epidemiologic consequences of this co-occurrence, under the scope of the new classification, are lacking.
Purpose: To determine the effect of HF and its subtypes on the epidemiologic profile of patients with a history of AF who were admitted to a cardiology ward.
Methods: We assessed the prevalence of HF in consecutive patients, who were admitted to the Cardiology Department with any diagnosis, and had a history of AF. Subjects with HF were stratified to HFrEF, HFmrEF, and HFpEF categories, according to their LVEF. Baseline characteristics were calculated [age, main symptom on admission (dyspnea, angina, palpitations, dizziness, fatigue), number of comorbidities (coronary artery disease, stroke/TIA, chronic obstructive pulmonary disease, chronic kidney disease, diabetes mellitus, hypertension, dyslipidemia, vascular, hepatic, gastrointestinal, endocrine, rheumatic, other disease), CHA2DS2-Vasc and HAS-BLED scores]. Comparisons were made between groups with and without HF, and within HF subgroups (t-test, one-way ANOVA, chi-square).
Results: A total of 510 patients (mean age: 73.3 ± 10.9 years) were enrolled. A history of HF (HFpEF:63%, HFrEF:21%, HFmrEF:16%) was present in 45.5% of admitted patients with AF, of which 54.4% had permanent AF. Patients with AF were more likely to present with dyspnea (36%), with higher frequency in HF versus no HF (41% vs 31%, $p = 0.02$), while there was no difference between HF subtypes. Patients with a history of HF (versus no HF) had more comorbidities (3.9 vs 3.3, mean difference (MD) 95% CI: 0.2- 0.9), higher CHA2DS2-Vasc (5 vs 3.7, MD 95% CI: 0.9-1.7) and higher HAS-BLED (2.9 vs 2.5, MD 95% CI: 0.2-0.7), while there were no significant differences between HF subtypes.

Conclusion: Almost half of admitted patients with AF have a history of HF, with permanent AF and HFpEF being the most common phenotype. Patients with AF in the setting of HF had more prevalent dyspnea, a heavier multimorbidity burden, and a higher thrombotic and hemorrhagic risk, irrespective of HF subtype.

P1926

Incidence and healthcare pathways in patients hospitalized for new onset heart failure in a region of northern italy

D Pavan[1]; E Clagnan[1]; F Valent[1]; G Lardieri[1]; V Moretti[1]; L Massa[1]; C Fresco[1]; A Di Chiara[1]; P Pierluigi Lesizza[1]; L Zanier[1]; A Di Lenarda[1]
[1]*Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy*

Background: Our Regional Social and Health Information System (SISSR) provides reliable information on epidemiology, health care pathways and prognosis of cardiovascular diseases (CV). The objective of our analysis was to describe the admission rate for new onset heart failure (HF) and analyze the provided health care among residents in our region in 2009-10.
Methods: The analyses were made by querying the SISSR using SAS Enterprise Guide 7.1. The new cases of HF in 2009-2010 were identified from the Hospital Discharge Diagnosis Codes of the residents in our region with first ICD-9-CM codes 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0-4 , 428.9. For the analyses, SISSR was linked with regional databases of healthcare services and procedures and drug distribution system.
Results: In 2009-2010 there were 5963 admissions for new onset HF (average rate of 2.41 per 1000 person-years; range in 5 Regional Health Authorities 2.14 to 2.72). Hospital admission involved in 86% subjects ≥70 years. Males were prevalent in pts < 80 years, females ≥ 80 years. 82% of the pts were discharged from Medicine, 11% from Cardiology. Comparing the pts of 2009-2010 with those of 2015, prescription of exams (ECG, echocardiogram, chest x-ray, natriuretic peptides) increased from 72% in the 5 years prior to admission to 75% in the 5 years after discharge. The number of pts in CV therapy during the same period increased from 89% to 94%. Comparing the 2009-2010 cohort with 2015, the number of first hospitalizations for HF was reduced by 12%, with a large variability in 5 regional Health Authorities (range -30% - + 3%). The rate x 10,000 pts of age ≥70 years decreased from 117.0 (range 126.2 to 104.8) to 97.4 (range 92.0 to 101.4) while the average stay remained stable (10 days). Among the 5457 who were discharged alive, in 1713 (31%; 28-36%) the home nursing care was active after admission (new activation in 473, 27.6%). Among 1042 GPs working in FVG, 909 (87%) were following at least one patient with HF (39% 1-5 pts; 38% 6-10 pts; 11% >10 pts (average 5.5 pts with HF for each GP, range 0 -22).
Conclusions: The regional data warehouse of our region provides useful information to plan educational activities and improvement of quality of care and clinical pathways. The trend of new admissions for HF is highly variable in the 5 regional Health Authorities, as well as it is clear a lot of room for improvement of post-discharge pathways and care.

P1927

Pharmacotherapy for heart failure in elderly patients with atrial septal defect: Results from CHALLENGE registry

D Ntiloudi[1]; G George Giannakoulas[1]; K Vasiliadis[2]; A Frogoudaki[3]; C Ntellos[4]; A Tzifa[5]; S Brili[6]; A Manginas[7]; D Parcharidou[1]; M Papaphylactou[8]; A Vlahos[9]; S Apostolopoulou[8]; H Karvounis[1]; K Tsioufis[10]; S Rammos[8]
[1]*AHEPA General Hospital, Thessaloniki, Greece*; [2]*General Hospital G. Papanikolaou, Cardiology Department, Thessaloniki, Greece*; [3]*Attikon University Hospital, Cardiology Department, Athens, Greece*; [4]*Tzaneio General Hospital of Piraeus, Cardiology Department, Athens, Greece*; [5]*Mitera General Hospital, Department of Congenital Heart Disease, Athens, Greece*; [6]*Hippokration General Hospital , Cardiology Department, Athens, Greece*; [7]*Mediterraneo Hospital, Department of Cardiology, Athens, Greece*; [8]*Onassis Cardiac Surgery Center, Department of Congenital Heart Disease, Athens, Greece*; [9]*University Hospital of Ioannina, Department of Congenital Heart Disease, Ioannina, Greece*; [10]*Hellenic Cardiological Society (HCS), Athens, Greece*

On behalf of: the CHALLENGE investigators
Funding Acknowledgements: Hellenic Cardiological Society

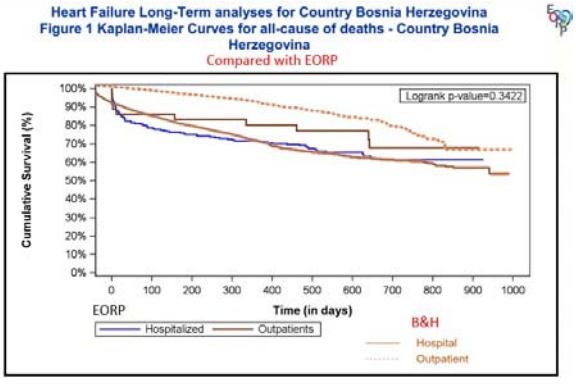
Introduction: As patients with atrial septal defect (ASD) age, prevalence of heart failure (HF) rises.
Purpose: To study the clinical characteristics of elderly (> 60 years) patients with ASD who are under medical therapy for HF and to highlight the predictive factors for prescribing HF pharmacotherapy in this population.
Methods: Data from February 2012 until November 2016 were collected from the national registry of adult congenital heart disease (ACHD) in Greece (CHALLENGE).
Results: A total of 2085 ACHD patients were included, of which 228 (10.9%) were older than 60 years old (63.6% women). ASD was the most prevalent diagnosis (n = 137, 60.1% of elderly patients, mean age 70.4 years, 63.5% women). Percutaneous ASD closure was performed in 27%, surgical repair in 25%, while 48% patients had not undergone any procedure at all. Of elderly ASD patients, 57 (41.6%) were under HF medical treatment. Physicians were more likely to prescribe HF pharmacotherapy in older patients (73.1 vs 69.4 years, $p < 0.001$), in heavily symptomatic patients (76.9% of NYHA III/IV patients vs 33.3% of NYHA I/II, $p < 0.001$), in those who received antiarrhythmic drugs ($p < 0.001$) and in patients with an open defect or surgical ASD closure ($p = 0.001$). Gender did not predict the administration of HF pharmacotherapy. On multivariable analysis, $\nu\nu\eta\alpha$ class III/IV, use of antiarrhythmic drugs and presence of an open defect or history of surgical ASD repair were independent predictive factors for HF pharmacotherapy.
Conclusion: In our national registry, almost 40% of elderly patients with ASD were under HF medical treatment. Advanced functional class and history of arrhythmias were predictors of administration of HF pharmacotherapy, while percutaneous ASD closure was a preventive factor.

P1928

EORP Registar of Bosnia and Herzegovina, comparative differences with other regions included in EORP

E Emir Fazlibegovic[1]; D Pravdic[1]; O Manov[1]; D Zelenika[1]; M Cesko[1]
[1]*Clinical Center Mostar, Mostar, Bosnia and Herzegovina*

Objective: A major goal of EURObservational Research Programme (EORP) is to record and evaluate medical practice in Europe and around the world, based on the collect of real-life data in different countries.
Methods: We did a statistical analysis and comparison of individual patient characteristics in EORP registry of B&H and other countries involved in EORP.
Results: There is a significant difference in the one-year follow-up of patients dying in B&H in relation to the other countries included in EORP in cardiovascular death (93.2%; $p < 0.0001$) between B&H and other countries in the region (51.7% in total and 48.7%). An LVEF in patients in B&H was significantly higher as compared to other countries in the region ($p < 0.0001$) with median EF 51.5%: 37% and the number of patients with an LVEF> 45% was higher in B&H in relation to other countries (59%: 31.6%). Comorbidities have been significantly greater in our patients in relation to other countries with $p < 0.0001$ for the disease: hepatic dysfunction (24.3%: 7.5%), COPD (55.3%: 18. 4%), suffered ICV or TIA (37.3%: 11.7%), peripheral vascular disease (48.6%: 12.3%). Ischemic heart disease was significantly more prevalent ($p < 0.0001$) as a cause of heart failure in 71.4% compared to 53.1% of respondents from other countries. Smoking as a risk factor for CVD were present significant ($p < 0.0001$) with 68.2% of B&H respondents in the registry compared to 50.7% in subjects from other countries. The anemia with hemoglobin < = 12 g / dL (28.3%: 40.6%) was significantly lower in patients B&H in relation to other countries. Intra hospital mortality was significantly represented ($p < 0.0001$) in patients register of B&H 15.3% compared to 4.4% in other countries of the region. Pulmonary edema as a form of hospital presentation was found in 7.5%, while in other countries it was 12.9% ($p < 0.0001$). Significantly ($p < 0.0001$) less application equipment to support heart rate (PM and ICD) in B&H patients in the registry 95.2% compared to 84.8% in other countries. There is significant difference ($p < 0.0001$) in the application of certain pharmaceuticals in the treatment of patients with HF in B&H and other countries, especially diuretics (71.8%: 82%), and inotropic compound (30.2%: 10.6%), especially digitalis (15.3%: 26.4%). One-year survival of patients in the registry EORP and B & H is significantly different as can be seen in the Kaplan-Meier survival curves.(Figure 1)
Conclusions: Education of physicians is necessary to improve treatment and application of modern drugs. In long-term monitoring, we can come up with new knowledge on implementation of specific treatments of the ESC Guidelines for AHF/CHF.



Kaplan Mejer courve of survival

P1929

Predictors of six-month mortality after discharge in patients hospitalized with decompensated chronic heart failure

S Galochkin[1]; S Padaryan[1]; L Babaeva[1]; E Shavarova[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: To evaluate the rate and predictors of mortality in patients hospitalized with decompensated chronic heart failure (DHF).
Material and methods: hospital-based, prospective, observational study using the data from the HF Registry. All patients admitted for two Moscow city clinical hospitals with DHF from January to May 2015 were included into the registry (n = 484). Clinical, demographic, laboratory and instrumental characteristics and medical treatment were evaluated. After 6-month follow up data on mortality are collected by telephone contact with patients or relatives using structured questionary (n = 265).
Results: The median age was 73 years (39, 95); men – 45%. 97% of patients had HF II- IV (NYHA), among them 26% - HF II, 64% - HF III, 10% - HF IV (NYHA). Echocardiography was done in 100% patients with HF. EF < 40% was found in 44% of patients. Uncontrolled arterial hypertension was the main reason for decompensation of chronic HF in 47%, atrial fibrillation - 46%, treatment non-compliance – 36%, coronary artery disease progression – 16%, respiratory infections – 14%, alcohol abuse - 6%, uncontrolled intake of nonsteroidal anti-inflammatory drugs - 2%. 6-month mortality rate was 18,8%. There was no significant difference in mortality rate between groups due to EF (19.1% in HFrEF vs 18.3% in HFpEF). Death due to HF decompensation was the most often reason (53%), among others – 10% - acute coronary syndrome, terminal chronic kidney disease – 5%, advanced cancer - 4%, sudden cardiac death – 4%, not known – 24%. Significant factors for six-month mortality were the following: hemoglobin (Hb) level at admission (p = 0.003), high dose of loop diuretics (p = 0.005), alcohol abuse (p = 0.01). Hb was significantly lower in died pts to compare with survived pts [109 (103; 105) vs 134 (122; 142)] g/l, respectively, p = 0,016). Regression analysis showed association between Hb level and lethal outcomes [OR 1,05; 95% CI 1,01-1,10; p = 0,016] and after adjustment for age, LV EF [adjusted OR 1,05; 95% CI 1,01-1,09; p = 0,027].
Conclusion: in patients hospitalized with decompensated heart failure six-month mortality rate higher in presense of anemia and using of high dose of loop diuretics.

P1930

Admissions to intensive cardiac care units in france in 2014: a cross-sectional, nationwide population-based study.

G Gregoire Mercier[1]; A Riondel[1]; C Delmas[2]; S Manzo-Silberman[3]; G Leurent[4]; M Elbaz[2]; E Bonnefoy-Cudraz[5]; P Henry[3]; F Roubille[1]
[1]*University Hospital of Montpellier, Montpellier, France*; [2]*Toulouse Rangueil University Hospital (CHU), Cardiology department, Toulouse, France*; [3]*Hospital Lariboisiere, Department of cardiology, Paris, France*; [4]*University Hospital of Rennes, Cardiology department, Rennes, France*; [5]*Civils Hospices of Lyon, Cardiology department, Lyon, France*

Background: Intensive Cardiac Care Units (ICCU) are managing patients admitted for heterogeneous and complex pathologies. The available evidence suggests considerable variation in ICCU admission rates within countries. Although a better understanding of this variation would be helpful to cardiologists and policy-makers, its drivers remain largely unknown.
Aim: To explain the geographic variation in the rate of ICCU admission for Heart Failure (HF) in France in 2014.
Methods: This is a nationwide, observational, population-based study based on the French hospital discharge database for the year 2014. All acute inpatient stays for HF with at least one ICCU admission were included. Age- and sex-standardized admission rates were calculated at the departement level and modelled using epidemiological, access and socio-economic variables.
Results: 27,828 stays were included. At the departement level (n = 94), the standardized ICCU admission rate varied between 0.04 and 1.24 per year per 1,000 population. It was positively associated with diabetes prevalence, and negatively associated with the proportion of the population aged 75 years or more and with the driving time to ICCU.
Conclusions: This study sheds light on considerable geographic variation in the ICCU admission rates for HF in France. This variation is explained not only by disease patterns, but by access to ICCU, too. This suggests inequalities of access to highly specialized cardiologic care.

P1931

The proportion of heart failure patients with reduced, mid-range and preserved ejection fraction in a real-life heart failure population

M Szabo[1]; M Dekany[1]; B Muk[1]; D Vagany[1]; T Borsanyi[1]; ZS Majoros[1]; RG Kiss[1]; N Nyolczas[1]
[1]*Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary*

Background: The new ESC guideline for heart failure, published in 2016, introduced the terminology of heart failure with mid-range ejection fraction (HFmrEF) (40%≤LVEF<50%) in addition to the well-known definition of heart failure with reduced (HFrEF) (LVEF<40%) and preserved (HFpEF) (LVEF≥50%) ejection fraction. The diagnostic criteria are the typical clinical signs and symptoms and specific values of left ventricular ejection fraction (LVEF) in every case. In HFmrEF and HFpEF the elevated level of natriuretic peptides and at least one additional criterion of left ventricular hypertrophy and/or left atrial enlargement and/or diastolic dysfunction are necessary.
Purpose: The aim of the study was to identify the proportion of the HFrEF, HFmrEF and HFpEF according to the new ESC guideline in patients with heart failure signs and symptoms, who were not treated for heart failure previously and referred to our heart failure outpatient department.
Patients and methods: We assessed the data of 367 patients (mean age: 63.2 ± 11.8 years, proportion of men: 65.4 %, LVEF: 42.4 ± 12.9 %, NYHA: 2.17 ± 0.35, ischaemic aetiology: 58.3 %, NTproBNP: 2839.6 ± 2935.2 pg/ml) with heart failure signs and symptoms who were not treated for heart failure previously and referred to our heart failure outpatient department between 01.12.2013. and 30.11.2015. HFmrEF and HFpEF were defined if beyond the LVEF criteria NTproBNP>125pg/ml and left atrial enlargement and/or left ventricular hypertrophy exist.
Results: LVEF was under 40% in the case of 173 patients (47.1%), in 52 patients (14.2%) LVEF was between 40% and 50%, and in the case of 142 patients (38.7%) was the LVEF≥50%. In 44 of 52 patients with mid-range ejection fraction NT-proBNP level was elevated, and in 41 cases left atrial enlargement and/or left ventricular hypertrophy were revealed, so in 41 patients HFmrEF was proved. In 104 of 142 patients with preserved ejection fraction NT-proBNP level was elevated, and in 87 cases left atrial enlargement and/or left ventricular hypertrophy were found, so 87 patients were diagnosed as HFpEF. 301 (82.0%) of 367 studied patients were proved to have heart failure and 57.5% of them was HFrEF, 13.6% HFmrEF, and 28.9% HFpEF. In 21.2% of the patients with mid-range ejection fraction and in 38.7% of the patients with preserved ejection fraction heart failure was not verified according to the new ESC guideline criteria.
Conclusion: According to our study, in a real-life heart failure population, the proportion of the patients with HFmrEF is half of HFpEF, and quarter of HFrEF patients. If NT-proBNP and echocardiography criteria are concerned beyond signs and symptoms and LVEF at the diagnosis of HFpEF, the real proportion of the HFpEF patients becomes much lower than it was in the majority of the epidemiological trials.

P1932

Differences between men and women in a our population with heart failure

I Irene Rilo Miranda[1]; JR Beramendi Calero[1]; S Garcia Gutierrez[2]; ANE Anton Ladislao[2]; L Quintas Ovejero[3]; C Goena Vives[3]; M Morillas Bueno[2]; F De La Cuesta Arzamendi[1]
[1]*Hospital Donostia, San Sebastian, Spain*; [2]*Hospital Galdakao-Usansolo, Bilbao, Spain*; [3]*Hospital Comarcal de Mendaro, Cardiology, Mendaro, Spain*

Introduction: This study aims to determine the differential characteristics between men and women among patients with acute heart failure admitted to the Emergency Services 3 hospitals in our 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. 48% (886) were male and 51% (938) female. Females were older at the diagnosis time 81,72 years vs 77,38 (p < 0.0001) and among female was more frequent Arterial Hypertension (86% vs 80 % (p = 0,0014) and therefore heart failure with preserved ejection fraction was more prevalent: 62,72 % vs 38,94 % (p < 0,0001).Moreover, Diabetes Mellitus was more prevalent in males (35 % vs 31 % p0,0565 and the degree of chronic kidney disease was higher in males 7,34 % vs 4,585 % and the rate of ischemic cardiomiopathy is significantly higher in men 40,74 % vs 25,59 % (p < 0,0001). Despite these data in our study we found no significant differences in short-term mortality (4,80 % in women and 3,73 % in men p = 0,2598) and mortality at 3 months (9,18 vs 9,25 % p = 0.96)
Conclusions: Women were older at the diagnosis and had higher prevalence of arterial hypertension. The rate of heart failure with preserved ejection fraction was higher among females. Men presented a higher percentage of ischemic cardiomyopathy, chronic kidney disease and diabetes mellitus.

Despite the differences between sexes in our study we found no significant differences in short-term mortality and mortality at 3 months

P1933

Determination of level of knowledge of cardiovascular disease risk factors among university students.

S Oguz[1]; G Gulsah Camci[1]; B Bayrak[1]; B Erguvan[1]; G Unal[1]
[1]*Marmara University, Health Science Faculty, Nursing Departmant, Istanbul, Turkey*

Background: If we know cardiovascular disease risk factors in our life and take necessary measures, cardiovascular disease can be reduced.
Purpose: This study was planned as cross-sectional and descriptive in order to determine level of knowledge of cardiovascular disease risk factors among university students.
Methods: This research was carried out among the students who are studying in the University, Faculty of Law and Faculty of Health Sciences, Nursing Department between the February - April 2016 dates. The study was attended by 650 students. Data were collected by a Questionnaire" and "Cardiovascular Disease Risk Factors Knowledge Level scale" (KARRİF-BD). Data was analyzed by using frequency, percentage, mean, t-test and one-way ANOVA
Results: The average age of the students was 20.1 ± 3.9, 71.8% were female, 43.5% studied in the nursing department and 56.5% studied in the law deparment. The average body mass index of students was 21.8 ± 8.4. It was determined that the students who participated in the study; there was no chronic disease in 91.7%, 51.4% didn't know the blood pressure value, 96.4% from the absence of heart disease, there was heart disease 30.9% of student's family, 87.2% of them didn't smoke, 68% of them exercised. The mean score of students to KARRIF-BD scale was 19.5 ± 4.6 (min-max: 2-28). It had moderate knowledge level of the students. There was significant difference between mean scores KARRİF-BD and the section of students ($p < .000$), gender ($p < .003$), who know the blood pressure value ($p < .000$). Nursing students and female students had higher information about the cardiovascular disease risk factors ($p < .000$) and the result of changes in risky behavior ($p < .003$) in category of the scale.
Conclusions: When looking at the average scale scores of KARRIF-BD in nursing and law students, the knowledege of nursing students was higher than the law students. The knowledge of female students was higher than male students.

P1934

Prevalence of subclinical atherosclerosis in persons of working age

NA Koriagina[1]; LM Vasilets[1]; AA Shadrin[1]; OB Melekhova[1]; DV Mikhnevich[1]
[1]*Medical Academy, Perm, Russian Federation*

Objective: To evaluate the frequency of occurrence of subclinical atherosclerosis and atherosclerosis risk factors in people of working age with low cardiovascular risk.
Methods: The study included people of working age from 25 to 50 years, had no complaints on the part of the cardiovascular system. All performed: measurement of office blood pressure (BP), evaluation of anthropometric data, the study of risk factors (RF) of atherosclerosis. For verification of subclinical atherosclerosis (CA) carried ultrasound of brachiocephalic arteries (BCA) and multislice computed tomography (MSCT) with the assessment of coronary calcium.
Results: A total of 100 persons of working age, the average age was 46.5 years, 65% of them women. According to the survey: 40% of patients smoking, hypertension was detected in 36% of the SHA heredity burdened with 28%. CA was detected in 42% of patients. The average values of thickness of intima media complex (IMT) does not exceed normal parameters: IMT right - 0.89 mm, IMT left - 0.81 mm (N < 0,9 mm, depending on age). In 43% of patients with AS compared with healthy individuals were determined by atherosclerotic plaques (ASB) in the carotid arteries with stenosis hemodynamically insignificant. Calcification of the coronary arteries was diagnosed in 12.5% of patients. Abdominal obesity was observed in 30 patients with asymptomatic atherosclerosis, representing 58.8%, while in the group of healthy individuals only three persons. In the group with asymptomatic atherosclerosis revealed significant negative correlations of BMI and waist circumference (OT) with HDL-C ($r = -0,66$; $r = -0,71$, $p < 0.05$).
Conclusions: Thus, in 42% of healthy individuals of working age is revealed subclinical atherosclerosis, which involves the need for the introduction into clinical practice algorithms for early diagnosis and prevention of atherosclerosis.

P1935

Prevalence of prehypertension in young adults students technical high school and college. Related variables.

ILPB Anjos[1]; IP Borges[1]; LLB Bandeira[1]; CS Souza[2]; RTS Peixoto[2]; RTS Peixoto[2]; AAB Aragao[3]; VF Marcolla[3]; SA Simoes[3]; ECS Peixoto[2]
[1]*Severino Sombra University, Vassouras, Brazil*; [2]*Fluminense Federal University, SENAI/CETIQT, Niteroi, Brazil*; [3]*Rio de Janeiro State Government, Rio de Janeiro, Brazil*

Background: Worldwide, several studies have been conducted about the association between hypertension in childhood and adolescence and socio-demographic factors: lifestyle, family history and anthropometry.
Objective: This study aims to identify the prevalence of prehypertension and related variables in young adults.
Methods: Cohort study. The variables were collected by questionnaire or measures. Univariate analysis was performed using the chi square and it was performed five multiple logistic regression models for the variables with $p < 0.10$ in the univariate analysis. The students were from three courses, either college as vocational school, were evaluated: gender, age, course, skin color, income, education, lifestyle, history of hypertension, weight, waist circumference and prehypertension defined as VII Joint National Committee: systolic 120-139 and diastolic 80-89 mmHg.
Results: A total of 394 students were evaluated. There were 309 (78,43%) in the normal group (NG) and 85 (21,57%) in prehypertension group (PH) of students. It was found in NG and PG, respectively: females 254 (85.2%) and 44 (14.8%) ($p < 0.001$); males 55 (57,3%) and 41 (42,7%) ($p \leq 0.001$); age (three age ranges: until 19 years, 20-25 and 25-30) more frequent in older ($p = 0.001$); ethnicity (self declared) black 16 (5.2%) and 11 (12.9%) ($p < 0.001$); 62 mother´s hypertension (20.1%) and 28 (32.9%) ($p = 0.024$); overweight 34 (11.0%) and 17 (20.0%) ($p = 0.045$); obese 3 (1.0%) and 10 (11.8%) ($p < 0.001$); increased abdominal circumference 37 (12.0%) and 19 (22.3%) ($p = 0.024$). At least one of five multiple logistic regression models were associated with absence or presence of prehypertension (OR, 95% CI): females (4,026, 2.373 to 6.828), age (1.081, 1.004 to 1.164), hypertensive mother (1.838, 1.027 to 3.289) and greater waist circumference (1.067, 1.035 to 1.100).
Conclusion: About a fifth of the students were considered to be in prehypertension group. Factors associated with prehypertension this study: male, older, mother with hypertension and increased waist circumference

total studants 394 (100%)	normal group 309 (78,43%)	pre-hypertension group 85 (21,57%)	p
female gender male gender	254 (85,2%) 55 (57,3%)	44 (14,8%) 41 (42,7%)	≤ 0,001
ethnicity (self declared) black	16 (5,2%)	11 (12,9%)	< 0,001
mother´s hypertension	62 (20,1%)	28 (32,9%)	0,024
overweight	34 (11,0%)	17 (20,0%)	0,045
obese	3 (1,0%)	10 (11,8%)	< 0,001
increased abdominal circumference	37 (12,0%)	19 (22,3%)	0,024
age (three age ranges: until 19 years, 20-25 and 25-30)	lower ranger	older ranger	0,001

Risk stratification table

PSYCHOSOCIAL - ETHICAL CONCEPTS - EDUCATION

P1936

Professional or personal experience increases the awareness of heart failure in the european population

V Vintila[1]; A Vintila[2]; A Cotoban[1]; S Stork[3]; M Lainscak[4]; D Vinereanu[1]
[1]*University of Medicine and Pharmacy Carol Davila, University and Emergency Hospital Bucharest, Cardiology Department, Bucharest, Romania*; [2]*University of Medicine and Pharmacy Carol Davila, Coltea Clinical Hospital, Internal Medicine Department, Bucharest, Romania*; [3]*Comprehensive Heart Failure Center (CHFC), University of Wurzburg, Wurzburg, Germany*; [4]*Faculty of Medicine, University of Ljubljana, , General Hospital Murska Sobota, Murska Sobota, Slovenia*

On behalf of: Heart Failure Awareness Day Initiative

Background: Heart failure (HF) is a common pathological condition. HF Awarness Day represents an European annual event, with the objective to increase the knowledge of the general population regarding HF symptoms and management.
Aim: To demonstrate that working in the medical field or having a previous exposure to HF would increase the HF awareness.
Method: We analysed 3 annual sets of consecutive data, obtained from questionaires filled in by the general population from various European countries, during Heart Failure Awarness Day campaign (from 2013 to 2015). A score was computed from the correct answers. A cut-off of 6 points was considered to prove HF awareness. Two specific subgroups were defined: group A, with professional experience (present or former employment in the medical field); and group B, with personal experience (patients with HF or their relatives with HF).

Results: A total of 7947 subjects were enroled: 1777, 3685, and 2485 subjects, corresponding to the 3 annual sets, with a similar median score of 7.3 ± 4.4, 7.3 ± 4.4 and 7.0 ± 4.4, respectively. High scoring (above 6) was more frequent in both group A and B, for all 3 annual sets (Table).
Conclusion: Professional or personal experience, achieved either through learning or exposure increases awareness of heart failure in the studied European population.

Professional and personal experience

	2013	2014	2015	TOTAL
Group A score > 6	148(74%)	448(77%)	272(75%)	868*
No Group A score > 6	897(60%)	1739(59%)	1143(58%)	3779*
p value	< 0.001	< 0.001	< 0.001	
Group B score >6	659(71%)	1245(67%)	718(67%)	2622*
No Group B score >6	301(50%)	582(58%)	484(60%)	1367*
p value	< 0.001	< 0.001	< 0.001	
* valid answers				

Group A = professional experience No Group A = no professional experience Group B = personal experience No Group B = no personal experience

P1937

The impact of congestive heart failure on health-related quality of life among patients with cardiac-involved light chain amyloidosis

KL Kristen Mccausland[1]; M Yokota[1]; TP Quock[2]; SD Guthrie[2]; MK White[1]; M Bayliss[1]
[1]Optum, Lincoln, Rhode Island, United States of America; *[2]Prothena Biosciences, Inc., South San Francisco, California, United States of America*

Background: Light chain (AL) amyloidosis is a heterogeneous, rare disease characterised by misfolded protein deposits in tissues and vital organs. While any organ can be affected, cardiac involvement is one of the most common and severe forms of the disease. These patients are at risk for developing serious complications including arrhythmias and congestive heart failure (CHF). Deficits in health-related quality of life (HRQoL) have been documented among cardiac-involved patients, but the incremental impact of CHF on HRQoL among AL amyloidosis patients has not been documented.
Purpose: To compare clinical characteristics and HRQoL of patients with cardiac-involved AL amyloidosis by self-reported history of CHF.
Methods: A non-interventional, online study was conducted among patients with AL amyloidosis (N=341) to assess demographics, disease and treatment history and HRQoL, including the Kansas City Cardiomyopathy Questionnaire–Short Form (KCCQ-12), a validated HRQoL measure specific to heart failure. KCCQ-12 items were used to derive a total summary score and the following subscale scores: symptom frequency, physical limitations, social limitations and quality of life. Characteristics of cardiac-involved patients with self-reported CHF (n = 82) and without CHF (n = 85) were compared using chi square and independent samples t-tests. Differences in HRQoL were examined using multivariable generalised linear models.
Results: Approximately 49% of patients with cardiac involvement reported a history of CHF. Patients with and without CHF were similar in demographics, time to diagnosis and duration of disease. In terms of initial symptom burden, a greater proportion of CHF patients reported numbness in their arms and legs as compared to non-CHF patients (53.8% vs. 30.1%, respectively; p = 0.01); however, the prevalence of other commonly reported symptoms was comparable. The prevalence of having complete hematological response (HR) was significantly lower among patients with CHF as compared to those without (42% vs. 62%, respectively; p < 0.01). Among patients with HR, HRQoL did not differ significantly by CHF status; however, KCCQ-12 scores among patients who had not achieved HR were approximately 30% lower among CHF versus non-CHF patients (p < 0.05 for all). The average total KCCQ-12 score among non-CHF, non-HR patients was 55.7, which corresponds to scores previously observed in patients with New York Heart Association (NYHA) functional class II symptoms. In contrast, scores among CHF, non-HR patients (mean=38.6) were equivalent to scores from patients with NYHA functional class III symptoms.
Conclusion(s): Previous research has documented significant HRQoL burden in AL amyloidosis patients with cardiac involvement. These findings indicate that the impact is even worse among patients with CHF. However, differences are attenuated if HR is achieved.

P1938

Caregiver health behaviors of patients with cardiorespiratory failure

B Bernardo Robles-Uribe[1]; V Pelaez-Hernandez[2]; A Orea-Tejeda[2]; D Gonzalez-Islas[2]; R Sanchez-Santillan[2]; GK Perez-Cortes[2]; S Torres-Montiel[2]; A Figueroa-Herrera[2]; L Verdeja-Vendrell[2]; E Perez-Cabanas[2]; A Navarrate-Penaloza[2]; A Jimenez-Cepeda[2]
[1]National Autonomous University of Mexico, Mexico City, Mexico; *[2]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosio Villegas", Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico*

Background: The vulnerability of caregivers is continuously related to the disease process of patients with cardiorespiratory failure (CRF). The disadvantages of the care provided by the caregivers include the lack of support equipment, the amount of time invested and the physical effort. This affects the normal development of the physical, psychic and social areas of the caregivers, making it worn and dysfunctional.
Purpose: To describe the caregivers health behaviors of the patients with CRF
Method: 19 caregivers of patients with CFR (mean age 56.79 ± 2.89, 78.9% women) participated. The caregiver's health survey was used to identify the psychosocial characteristics of the caregiver. It consists of 30 items, of which 18 were selected for health care behaviors. Descriptive statistics were performed, using the statistical package SPSS version 23.
Results: Regarding the care provided by the caregivers, 52% of caregivers are children of patients and 36.6% are spouses. 84.2% of the caregivers share the same house and only take care of one person. As to their activities, caring for their patients (36.8%), house chores (31.6%) work (21.1%) occupy most of their time. With regard to his / her owns health care behaviors, 73.1% have not had any medical examination done in the last 6 months. 47% of caregivers go to the doctor immediately when they feel bad, 26.3% only when they feel "very sick". 78.9% of the caregivers came to the doctor, dentist or nutritionist in the last 6 months at least once. In contrast to mental health care, 84.2% did not go to the psychologist, therapist or psychiatrist in the last 6 months. 63.2% do some physical activity, 94.7% do not smoke, 73.7% do not consume alcoholic beverages and 57.9% do not report a dietary regimen. Despite the fact that 57.9% of the caregivers reported have the same symptoms as their patients in any occasion. The main reasons that they prevented them to take care of their health, are: lack of time (26.3%), having no one to leave their patient (15.8%), lack of money (15.8%), no reason (15.8%), the distance from the hospital / clinic (5.3%). Likewise, the caregivers has not received information or training from the health professionals about the care of their patient (57.9%), about what it is to be a caregiver and what it implies (78.9%) or about taking care of their own health (63.2%).
Conclusion: These characteristics show an inattention to caregivers that can lead to deterioration of the different areas of their life (physical, psychic, social) and to be a risk factor for cardiorespiratory diseases. Permanent attention to the patient causes exhaustion and self-neglects to generate deterioration in their health, which is reflected in the perception of the same symptoms as their patient's symptoms.

P1939

Endothelial dysfunction, skin temperature, and vulnerability to psychological stress in patients with heart and respiratory failure. Preliminary data

E Perez Cabanas[1]; V Pelaez-Hernandez[1]; A Figueroa-Herrera[1]; A Orea-Tejeda[1]; B Dominguez-Trejo[2]; S Torres-Montiel[1]; B Robles-Uribe[1]; D Gonzalez-Islas[1]; GK Perez- Cortes[1]; AG Navarrete-Penalosa[1]; L Verdeja-Vendrell[1]; A Jimenez-Cepeda[1]; RN Sanchez-Santillan[1]
[1]National Institute of Repiratory Diseases, Heart Failure and Respiratory Distress Clinic, Ciudad de Mexico, Mexico; *[2]National Autonomous University of Mexico, Mexico City, Mexico*

Background: A chronic state of psychological stress impacts the endothelial function by increasing the atherosclerotic and pro- inflammatory process of the cardiorespiratory disease, reducing the skin temperature variability (STV) during psychological stress, and also promotes less vasodilatation, which is a prognostic indicator of re-hospitalizations.
Purpose: To investigate the relationship between bilateral STV during psychological stress and endothelial function in patients with heart and respiratory failure.
Method: 11 patients with heart and respiratory failure (mean age of 70.09 ± 12.80 years, 55.5% males and right-handed dominance) participated in this study. Bilateral STV was assessed during a psychophysiological stress profile of three phases of five minutes each (baseline, arithmetic stressor and recovery), while the patients underwent a stress test, considering these indicators for STV: symmetry (difference between both hands in °C), dominance (the highest temperature in the dominate hand), synchrony (difference between both hands at the end of each phase) and gain (increase of the temperature from the beginning to the end of each phase); more than18 points in the total sum of all indicators was considered low vulnerability to

psychological stress. Function endothelial was assessed using photoplethysmography, which consisted of: baseline, ischemia by five minutes and reactive hyperemia. Maximum Amplitude Time / Total Time index (MAT/TT) was taken at 30, 60, 90, 120 seconds after ischemia. Due to the size of sample, we carried out a non-parametric test (U de Mann-Whitney).
Results: The group with high vulnerability (n = 5; mean age of 74.4 ± 10.69 years, 60% females) presented higher MAT/TT index than those with low vulnerability (n = 6; 66.5 ± 14.22 years 66.7% males), at 60(0.41 ± 0.08 vs 0.40 ± 0.04), 90(0.45 ± 0.07 vs 0.37 ± 0.07), and 120 seconds after ischemia (0.41 ± 0.05 vs 0.39 ± 0.07); however these differences were not statistically significant. On the other hand, differences in symmetry throughout psychophysiological stress profile ($p < 0.05$), and gain during baseline ($p < 0.05$) were statistically significant. Patients with high vulnerability to psychological stress were less symmetrical among both hands and they had less temperature gain.
Conclusion: Patients with more vulnerability to psychological stress showed greater endothelial dysfunction and peripheral vasoconstriction, less symmetry and temperature gain, which is related to worse prognosis. However these are preliminary data, and we will continue increasing the sample size.

P1940
Differences in blood pressure levels during psychological stress among patients with cardiopulmonary disease with internal or external expression of anger

F Figueroa-Herrera[1]; E Perez-Cabanas[2]; V Pelaez-Hernandez[2]; B Robles-Uribe[2]; S Torres-Montiel[2]; A Orea-Tejeda[2]; B Dominguez-Trejo[1]; D Gonzalez-Islas[2]; L Verdeja-Vendrell[2]; RN Sanchez-Santillan[2]; A Jimenez-Cepeda[2]; AG Navarrete-Penaloza[2]; KG Perez-Cortes[2]
[1]National Autonomous University of Mexico, Mexico City, Mexico; *[2]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosio Villegas", Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico*

Background: Anger is a psychosocial risk factor for developing cardiovascular disease. The chronic manifestation of anger produces psychological stress that impacts on the heart and reactivity to psychological stress. Two possible forms of anger management are: 1) Internal Expression, in which anger is suppressed; and 2) External Expression, which involves manifesting anger toward people and objects. On one hand chronic suppression of anger has been associated with increased blood pressure and carotid artery stiffness and on the other hand, the expression of anger has positive health outcomes. However, it is unknown how the type of anger expression influences blood pressure in the face of psychological stress.
Objective: To compare systolic and diastolic blood pressure in the presence of psychological stress among patients with cardiopulmonary disease (CD) with internal or external anger expression.
Method: Twenty-six patients with CD participated. The type of anger expression was evaluated with the State-Trait Anger Expression Inventory (STAXI-2). According to the results, the patients were divided into two groups: 1) internal expression (IAE, n = 11 mean age 72.18 ± 17.14, 63.63% women) and 2) external (EAE, n = 15 mean age 67.67 ± 10.17, 53.33% women). A psychophysiological stress profile of 15 min was applied, divided in three phases of 5 min each 1) Baseline (BL), 2) Arithmetic stressor (AS) and 3) Recovery (R). Mean blood pressure was taking from three measurements made during each phase of the profile. A Mann-Whitney U test was tested to determine differences in systolic blood pressure (SBP) and diastolic (DBP) between the types of anger expression.
Results: There were statistically significant differences in DBP in the three phases of the profile between patients with IAE and EAE. It is found that patients with EAE have a higher SBP and DBP compared to those classified in IAE at all stages.
SBPBL: IAE: 119.51 ± 19.18; EAE: 132.31 ± 24.29 ($z = -1.532$, $p > 0.05$)
DBPBL: IAE: 67.51 ± 9.01; EAE: 78.35 ± 10.74 ($z = -2.336$, $p < 0.05$)
SBPAS: IAE: 121.30 ± 18.19; EAE: 132.58 ± 19.18 ($z = -1.636$, $p > 0.05$)
DBPAS: IAE: 70.06 ± 10.71; EAE: 82.42 ± 12.10 ($z = -2.544$, $p < 0.05$)
SBPR: IAE: 118.03 ± 18.19; EAE: 128.26 ± 22.11 ($z = -1.272$, $p > 0.05$)
DBPR: IAE: 66.33 ± 9.20; EAE: 77.95 ± 9.78 ($z = -2.751$, $p < 0.05$)
Conclusion: SBP and DBP are higher in patients classified with EAE than IAE, which is contradictory to what has been reported in other studies. However within the research is not taken into account if the expression of anger is overreacted, which has an effect on blood pressure. Therefore, the results obtained might suggest that patients in this sample overreacted their anger. For the future, it will be considered the intensity of anger expression.

EXERCICE TESTING AND TRAINING

P1941
Reduced cardiac reserve contributes to exercise tolerance in adult patients with sickle cell anemia

A Ceccaldi[1]; S Hatem[1]; K Stankovic-Stojanovic[2]; P Guedeney[1]; F Nicolas-Jilwan[2]; JP Haymann[2]; G Montalescot[1]; F Lionnet[2]; R Isnard[1]; N Hammoudi[1]
[1]Hospital Pitie-Salpetriere, Cardiology, Paris, France; *[2]Hospital Tenon, Paris, France*

Background: Sickle cell anemia (SCA) is associated with marked exercise intolerance. However, mechanisms underlying this functional limitation remain incompletely characterized. We hypothesized that abnormal cardiovascular reserve is an important determinant of SCA exercise capacity.
Objectives: To investigate the cardiac response to exercise in a contemporary adult SCA population.
Methods: We compared 60 SCA patients (median age, 31 years, 60% women) to 20 controls matched for age and gender. All subjects prospectively underwent a symptom-limited cardiopulmonary exercise testing with combined echocardiography. The oxygen uptake (VO2) and cardiac index (Ci) were simultaneously measured. The difference between arterial and venous oxygen content (C(a-v)O2) was calculated using Fick principle. The left ventricular (LV) function was comprehensively studied at rest and during exercise.
Results: Compared to controls, the SCA patients had severe exercise intolerance (median peak VO2, 19.7 versus 34.3 ml/min/kg, $p < 0.0001$). In SCA population the increase in Ci from rest to peak exercise was widely scattered and correlated closely with peak VO2 ($r = 0.71$, $p < 0.0001$); in contrast, the C(a-v)O2 reserve was homogenously reduced and did not correlate with exercise capacity ($r = 0.18$, $p = 0.16$). Compared to controls, SCA patients had chronotropic incompetence, blunted LV preload reserve and higher LV filling pressures. The SCA patients were classified in tertiles according to peak VO2. While hemoglobin level and C(a-v)O2 were similar, SCA patients in the lower VO2 tertile were characterized by an alteration of cardiovascular reserve related to ageing and to left atrial function deterioration (table).
Conclusion: The ability of cardiovascular system to increase Ci is an important determinant of SCA exercise capacity.

	Lower VO2 tertile (n = 20)	Other VO2 tertiles (n = 40)	p
Age(years)	40 [34-48]	27 [22-34]	0.0002
Hemoglobin(g/dl)	8.1 [7.5-9.5]	8.5 [8.1-9.7]	0.09
Peak VO2(ml/min/kg)	15.1 [14.4-16.8]	21.8 [19.7-23.4]	< 0.0001
Rest Cardiac index(l/min/m^2)	4.2 [3.5-5.1]	3.9 [3.4-4.6]	0.33
Peak Cardiac index(l/min/m^2)	9.0 [8.5-9.5]	10.5 [9.2-12.1]	0.0004
Peak Ca-vO2(ml/dl)	6.6 [6.0 - 7.3]	7.3 [6.2-8.0]	0.11
LV ejection fraction at peak(%)	70 [68-74]	71 [67-74]	0.88
Left atrial volume index at rest(ml/m^2)	57 [40-68]	45 [37-52]	0.02
Left atrial longitudinal strain at rest(%)	31 [28-32]	40 [34-43]	< 0.0001

P1942
Haemodynamic effects of a novel, personalised, home-based physical activity intervention for chronic heart failure

NC Okwose[1]; S Cassidy[1]; K Bailey[2]; J Skinner[2]; GA Macgowan[3]; D Jakovljevic[1]
[1]Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom; *[2]Royal Victoria Infirmary, Cardiology, Newcastle upon Tyne, United Kingdom*; *[3]Freeman Hospital, The Cardiothoracic Centre, Newcastle upon Tyne, United Kingdom*

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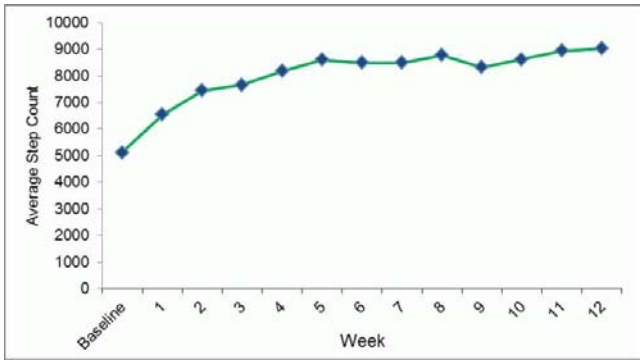
Background/Aim: Exercise-based cardiac rehabilitation programmes are safe and recommended to improve symptoms and outcomes in chronic heart failure (CHF).

However <10% of CHF patients in the UK participate in cardiac rehabilitation programmes due to lack of resources and absence of HF in local commissioning agreements. An effective home-based physical activity intervention may improve current clinical practice and benefit patients. The aim of the present study was to evaluate safety, compliance, and physiological effects of a novel, personalised, home based physical activity intervention in CHF.

Methods: A single-centre pilot study recruited 20 patients (mean age 68±7 years) with stable CHF due to left ventricular systolic dysfunction (LVEF=31±8). At baseline patients underwent maximal graded cardiopulmonary exercise testing with non-invasive bioreactance cardiac output monitoring, assessment of quality of life (Minnesota Living with Heart Failure Questionnaire, MLHFQ), NTproBNP and physical activity level over a 7-day period using pedometers. Following initial assessments, patients were asked to increase and maintain their daily physical activity level by at least 2000 steps per day from baseline for 12 weeks, as this increment has been shown to be associated with a significant 10% reduction in cardiovascular events in high risk patients. All patients were monitored weekly via telephone calls and daily activity levels were recorded using diaries. During the follow-up visit, all assessment performed at baseline were repeated.

Results: Seventeen patients (85%) completed the study, achieved and maintained targeted physical activity level (Figure 1). Number of steps increased significantly from baseline to 3 weeks by 2546 (5108±3064 to 7654±3849 steps/day, p=0.03), and was maintained until week 12 (9022±3942 steps/day). No adverse reactions to increased activity level were reported. On average MLHFQ score decreased by 4 points following intervention (26±18 vs. 22±19, p=0.50), suggesting improvement in quality of life. There was no clinically relevant change in NTproBNP (856±1106 vs 833±1164 ng/L, p=0.95), and O2 consumption at peak exercise (16.8±3.8 vs. 17.6±4.2 ml/kg/min, p=0.54), whereas peak exercise workload and cardiac index increased by 10% and 11% (82±10 vs. 91±19 watts, p=0.21; and 6.8±1.5 vs. 7.6±2.0 L/min/m2, p=0.19). Peak exercise heart rate remained unchanged following intervention (106±19 vs. 107±16 beats/min, p=0.92), while peak stroke volume index increased by 15% (64±14 vs. 75±17 ml/beat, p=0.04). Workload and O2 consumption at anaerobic threshold increased by 16% (49±16 vs. 59±14 watts, p=0.01) and 10% (11.5±2.9 vs. 12.8±2.2 ml/mg/min, p=0.39) after the intervention.

Conclusion: Personalised home-based physical activity intervention has minimal cost implications for the health service and is safe for CHF patients. It increases daily physical activity levels and improves exercise tolerance and hemodynamic response to exercise.



Increase in Physical Activity Levels

P1943

Cardiac rehabilitation programs in left ventricular systolic dysfunction patients: differences between risk profile and functional capacity according to ejection fraction.

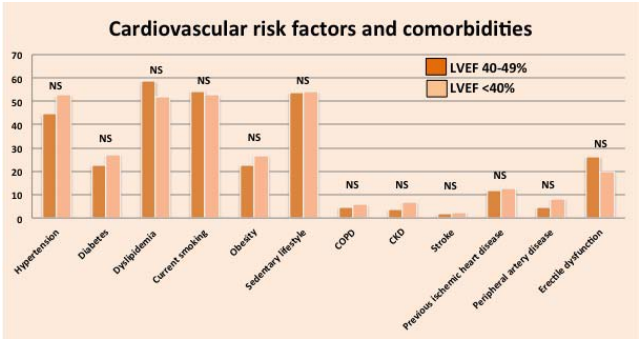
O Oscar Gonzalez Fernandez[1]; FJ Irazusta Cordoba[1]; V Rial Baston[1]; P Meras Colunga[1]; R Dalmau Gonzalez-Gallarza[1]; C Alvarez Ortega[1]; R Mori Junco[1]; S Rosillo Rodriguez[1]; A Castro Conde[1]; JL Lopez-Sendon[1]
[1]*University Hospital La Paz, Cardiology, Madrid, Spain*

Introduction: Cardiac rehabilitation programs (CRPs) in left ventricular systolic dysfunction (LVSD) patients provide optimal medical treatment, as well as supervised exercise, education and counselling. Our purpose was to compare the risk profile and functional capacity according to the ejection fraction (EF) in LVSD patients performing a CRP.

Methods: We made an observational retrospective study including patients with reduced EF (LVEF <40%) and mid-range EF (LVEF 40-49%) admitted to a CRP in our institution between 2006 and 2015. Physical training, optimal pharmacological treatment, medical counselling, nutritional education, and smoking cessation support when needed, were supplied for 8 to 10 weeks. Left ventricular ejection fraction (LVEF) was assessed before and after the program using transthoracic echocardiography, selecting in our study patients with a LVEF <50%. FC was tested before and after the CRP according to the NYHA Functional Classification, in addition to a treadmill stress test (TST). Exercise capacity (EC) was reported in terms of estimated metabolic equivalents of task (METs).

Results: A total of 442 patients were included, mean age 57.93±11.78 years, male 89.6%. Cardiac rehabilitation was performed after a recent acute coronary syndrome in 91.2% of patients. No statistically significant differences depending on the previous cardiovascular risk profile and comorbidities between mid-range EF (mrEF) and reduced EF (rEF) patients were found (table 1). Medical therapy when starting the program showed a significantly higher use of ACEIs/ARBs, MRAs, diuretics and anticoagulants in rEF than mrEF patients (p=0.023, p<0.001, p<0.001 and p=0.003; respectively). Patients with rEF had a worse FC assessed by NYHA class than mrEF patients, class I (43.4% vs 72.4%), II (49.8% vs 25.4%), III (6.3% vs 2.2%), IV (0.5% vs 0%); p<0.001. EC reported in METs was significantly lower in rEF than mrEF patients before (6.22±2.73 vs 7.76±2.38; p<0.001) and after the program (9.82±2.68 vs 10.65±2.42; p=0.003). After completing the CRP an increase in LVEF was observed in both groups (mrEF patients increased LVEF from 43.81±3.09% to 52.53±6.60%, rEF patients from 30.59±5.83% to 42.62±10.75%). FC after the program was significantly higher in the mrEF than the rEF group (I: 92.1% vs 73.4%, II: 7.9% vs 25.5%, III: 0% vs 1.1%; p<0.001). Regarding the heart rhythm, there was a non-significant trend showing an increased prevalence of atrial fibrillation in rEF patients (7.2% vs 3.1%; p=0.06). The dropout rate of the CRP was similar in both groups (11.9% in rEF patients vs 7.8%).

Conclusions: Reduced ejection fraction patients included in a CRP have a lower functional and exercise capacity than mid-range ejection fraction patients, both before and after completing the program. LVSD patients have a high prevalence of cardiovascular risk factors and comorbidities. However, no differences are found according to the left ventricular ejection fraction.



Risk factors and comorbidities

P1944

Long-term effects of cardiac rehabilitation in obese patients

M Marta Braga[1]; A Rocha[1]; H Nascimento[1]; R Pinto[1]; G Pestana[1]; M Tavares-Silva[1]; A Nunes[1]; P Araujo[1]; V Araujo[1]; F Parada-Pereira[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Introduction: Cardiac rehabilitation programs (CRP) improves exercise capacity (EC) and decreases cardiovascular morbidity and mortality after an acute coronary syndrome (ACS). However, some subpopulations are under-represented in CRP, namely obese patients.

Purpose: To compare the EC of obese patients with non-obese patients over 12 months of follow-up after CRP.

Methods: We retrospectively analysed data prospectively collected from patients who underwent CRP after an ACS. Patients were divided in two groups according to their body mass index (BMI): BMI≥30Kg/m2 (obese) and BMI<30kg/m2 (non-obese). EC was assessed with a standard exercise test, including chronotropic index, rate-pressure product, exercise duration, and intensity in metabolic equivalents (METs). EC was evaluated at baseline (T1), end of CRP (T2) and after 12 months of follow-up (T3). The mixed between-within analysis of variance was used to compare groups.

Results: Of a total 469 patients, 108 patients were obese. Except for diabetes and hypertension, there were no additional significant differences at baseline between obese and non-obese patients. Regarding EC, obese showed lower chronotropic index at all three moments (p<0.001), but improved at T2 and T3, like the non-obese group (T1- obese: 63.3±17.0% vs non-obese: 70.6±18.9%; T2- obese: 70.5±13.7% vs. non-obese: 76.6±17.2%; T3- obese: 74.9±16.7% vs non-obese: 77.6±17.7%, within-groups partial Eta square 0.176, p<0.001). The same results

were seen regarding rate-pressure product (T1- obese: 20090 ± 3660 mmHg*bpm vs non-obese: 20600 ± 3910 mmHg*bpm; T2- obese: 22360 ± 4050 mmHg*bpm vs. non-obese: 22410 ± 3930 mmHg*bpm; T3- obese: 23100 ± 4210 mmHg*bpm vs non-obese: 22780 ± 4320 mmHg*bpm, within-groups partial Eta square 0.213, p < 0.001). Both groups improved exercise duration and intensity between T1 and T2, showing a nonsignificant decline in T3 (duration: T1- obese: 7.5 ± 2.1 min vs 8.7 ± 2.2 min; T2- obese: 9.4 ± 1.8 min vs non-obese: 10.6 ± 2.0 min; T3- obese: 9.3 ± 2.0 min vs non-obese: 10.4 ± 2.3 min; intensity: T1- obese 7.8 ± 1.9 METs vs non-obese: 9.2 ± 2.2 METs; T2- obese: 9.4 ± 1.8 METs vs. non-obese: 11.1 ± 2.0 METs; T3- obese: 9.3 ± 1.8 vs non-obese: 11.0 ± 2.2 METs, within-groups partial Eta square 0.47 and 0.38 respectively, p < 0.001). Between-groups comparison showed that non-obese patients achieved a greater duration and intensity than obese patients at all 3 moments (p < 0.001).

Conclusions: Although EC of obese patients was inferior to non-obese patients, our study revealed that CRP significantly improved EC in this population and this benefit persisted after 12 months of follow-up. This data highlights the importance of a greater referral of obese patient to CRP.

P1945

Cardiac rehabilitation in patients with heart failure reduced ejection fraction compared to patients with coronary artery disease preserved ejection fraction: a long term follow up

J Justien Cornelis[1]; C Vrints[2]; E Roelant[3]; T Van Soom[1]; N Possemiers[2]; K Wuyts[2]; E Van Craenenbroeck[2]; P Beckers[2]
[1]*University of Antwerp, Department of Physiotherapy (REVAKI), Antwerp, Belgium*; [2]*University of Antwerp Hospital (Edegem), Department of Cardiology, Antwerp, Belgium*; [3]*University of Antwerp Hospital (Edegem), Department of Scientific Coordination and Biostatistics, Antwerp, Belgium*

Background: Patients with exercise intolerance induced by heart failure reduced ejection fraction (HFrEF) benefit from cardiac rehabilitation as exercise reverses the established prognostic cardiopulmonary parameters assessed through a cardiopulmonary exercise test (CPET). The clinical relevance and prognostic significance of these markers, together with the effect of exercise training in patients with coronary artery disease and preserved ejection fraction (CAD), is dubious.

Methods: The database was searched and 181 patients (CHF: n=35; CAD: n=146) were included between 2004 and 2010. All patients followed an endurance training program in the cardiac rehabilitation centre (38s, 3m, 3x60'/wk, 90%HR@RCP). During the first 24 sessions, the patients trained 5x8´on different training devices. After, exercise time was increased towards 4x10´. At the beginning and the end of the program, a maximal CPET (RER>1.15)(20 or 40 W/min) was conducted. Mortality rate was registered during a 5-year follow-up and survival analyses were performed. Significance was set P < 0.05.

Results: Baseline characteristics of both populations are given for patients with HFrEF (age: 54.8 ± 11.7; EF: 24.2 ± 7.8) and CAD (age: 59.0 ± 10.1; EF: 58.0 ± 9.5). Both groups significantly improved peak VO2, VE/VCO2 slope, HRR-1, Peak PetCO2, half-time of peak VO2, and OUES after 3 months of cardiac rehabilitation. The EqCO2 improved significant in the group with CAD. The patients with CAD improved peak VO2 significantly more (P=0.032) compared to the patients with HFrEF. Secondary parameters improved all significantly in both groups, only for peak(W/VO2) the patients with HFrEF improved significantly (P < 0.001) more. Moreover, the circulatory power improved significantly (P < 0.001) more in CAD. Exercise oscillatory ventilation (n = 4) was present at baseline. The 5-year mortality rate was 17.1% in patients with HFrEF and 5.5% in patients with CAD. The cox-regression analysis illustrated a significant difference (P=0.03) in the 5-year survival comparing both groups. The hazard ratio was 4.9 (P=0.05). Patients who increased their Peak VO2 by 20% (responders) with cardiac rehabilitation were not significant different of the non-responders (P=0.30) and hazard ratio was 0.417 (P=0.31).

Conclusion: A significant positive effect of cardiac rehabilitation in both populations was found. In patients with CAD, exercise training appeared to have more effect on aerobic capacity, circulatory power and EOV, whereas in patients with HFrEF work efficiency enhanced. Despite these improvements, the probability of dying within 5 years was high, however decreased by 58.3% if the patient responded on training. Improvements of prognostic CPET parameters seem to indicate that cardiac rehabilitation benefits all patients with a cardiac disease and perhaps even more the patients with CAD.

P1946

Dynamics of chronic heart failure in patients with rapidly progressive left ventricular remodelling after STEMI

V Valentin Oleinikov[1]; L Salyamova[1]; A Khromova[1]; N Borisova[1]
[1]*Penza State University, Penza, Russian Federation*

Purpose: to study the dynamics of laboratory and functional manifestations of chronic heart failure at 24 weeks in patients with rapidly progressive remodeling of the left ventricle (LV) remodeling after acute myocardial infarction (AMI) with ST-segment elevation (STEMI).

Methods: The study included 62 patients with STEMI. A prerequisite was the presence of hemodynamically significant stenosis of one coronary artery based on the result of coronary angiography. The present study was carried out without a washout period with the full scope of pharmacotherapy on the AMI. All patients underwent echocardiography by MyLab 90 (Esaote, Italy) with the evaluation of end-diastolic volume index (EDV index). Then, the patients were divided into two groups. The first group included 31 people without echocardiographic evidence of left ventricular remodeling and dynamics of EDV index < 8% at 6 months after STEMI. Group 2 consisted of 31 patients with rapidly progressive LV remodeling (EDV index increase >8%). Compared groups were matched for age, sex, number of anthropometric indicators. Initially on days 7-9, and after 24 weeks of follow-up the value of brain natriuretic peptide (BNP) was determined using an immunochemical analysis. A 6-minute walk test was performed at 12 and 24 weeks of myocardial infarction.

Results: at baseline compared subjects did not differ in the level of BNP: group 1 – 24,3 (16,6; 48,2) pg/ml, in group 2 – 32,6 (19,2; 53,8) pg/ml. After 24 weeks in patients without an abnormal growth of EDV index dynamics of BNP was not revealed: 26,6 (18,6; 52,7) pg/ml; in patients with rapidly progressive LV remodeling the values increased to 53,7 (27,0; 96,5) pg/ml (p < 0,05). According to the results of the 6-minute walk test in group 1 after 12 weeks of follow-up the average distance traveled was 506,1 ± 81,1 m. In this case, 0 FC was detected in 29% of cases, 1st FC - in 55%, 2nd FC - 16%. After 24 weeks of STEMI average distance was 612,0 ± 92,9 m (p < 0,05). 0 FC was detected in 46% of cases, 1st FC - in 48%, 2nd FC - 6%. In group 2 initially the average distance was 524,1 ± 67,3 m. 0 FC was detected in 32% of cases, 1st FC - 39%, 2nd FC - 29%. At follow-up, respectively, the values were 514,7 ± 91,3 m, FC 0 - 42%, 1st FC - 23%, 2nd FC - 33%, 3rd FC - 2%.

Conclusion: The patients with rapidly progressive LV remodeling after STEMI showed the deterioration in BNP levels with no significant reduction in tolerance to physical exercise after 24 weeks of follow-up. While in the group without pathological remodeling there was a statistically significant improvement in exercise tolerance in the absence of changes in laboratory signs of heart failure.

P1947

Usefulness of exercised-based cardiac rehabilitation in heart failure patients with preserved ejection fraction

I Burazor[1]; P Seferovic[2]; S Dodic[3]; Y Adler[4]; R Sakurai[5]; Z Cosic[6]; M Moraca[6]; A Kovacevic[6]; S Stevovic[6]; M Andjic[6]; A Ristic[2]
[1]*Institute for rehabilitation, Medical Faculty, Cardiology, Belgrade, Serbia*; [2]*Medical Faculty, University of Belgrade, Clinical Center of Serbia, Belgrade, Serbia*; [3]*Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia*; [4]*Sheba Medical Center, Tel Aviv, Israel*; [5]*The University of Tokyo Hospital, Department of Healthcare Information Management, Tokyo, Japan*; [6]*Institute for rehabilitation, Belgrade, Serbia*

Heart failure is highly prevalent in myocardial infarction survivors and is a major cause of morbidity, mortality and 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 heart failure with preserved ejection fraction (HFpEF) after myocardial infarction Patients and methods: Out of 1854 patients who were admitted to our three weeks in- hospital secondary prevention program – exercised based cardiac rehabilitation, we analyze a total of 199 patients who were admitted early after coronary revascularization (percutaneus coronary interventions or coronary bypass surgery) with HFpEF. The majority of patients were males (64%). The oldest patient was 81 years of age. We noted risk factors and co morbidities. Patients were selected for exercise training after six minute walking test (42%) or exercise stress test (CPX). 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 dyslipidemia. Six minutes walking test was performed and the total distance walked ranged from 160 to 440 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 6% 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 in patients HFpEF. Supervised multidisciplinary cardiac rehabilitation program, including an individualized exercise

component is safe and can improve functional status and exercise tolerance in patient.

P1948

Prognostic factors for STEMI patients after cardiac rehabilitation in single academic cardiologic center.

S Borodzicz[1]; P Balsam[1]; M Peller[1]; R Glowczynska[1]; L Koltowski[1]; P Lodzinski[1]; KJ Filipiak[1]; M Grabowski[1]; G Opolski[1]
[1]Medical University of Warsaw, 1st Chair and Department of Cardiology, Warsaw, Poland

Introduction: Cardiac rehabilitation (CR) has well-established efficiency in improving the prognosis of patients after ST-elevated myocardial infarction (STEMI).
Purpose: The main aim of our study was to analyse early and late factors which may be related to the improved prognosis of STEMI patients who participated in CR programme.
Methods: It was a retrospective analysis of STEMI patients who underwent invasive coronary angiography and percutaneous coronary intervention (PCI) after STEMI followed by CR in years 2007-2013. The group consisted of 141 patients; the average time of follow-up was 30 ± 14 months (max. 96 months). Individual physical capacity was assessed at the beginning of CR by electrocardiographic exercise test. Information on patients' current activity was assessed with validated International Physical Activity Questionnaire (IPAQ). The analysed early factors included: gender, age, body mass index (BMI), hypertension, diabetes mellitus type 2, atrial fibrillation, history of previous MI or stroke, ejection fraction, type of infarction related artery, localization of MI, peak levels of troponin I (TnI), creatine kinase-MB (CK-MB) mass. Late factors included: initial metabolic equivalent of task score (METs), METs after CR, improvement of METs, number of training sessions (12 or 24). The combined end point consisted of: patient's death or another cardiovascular event (stroke, myocardial infarction, any revascularisation).
Results: Higher BMI was associated with better prognosis of patients (Hazard Ratio HR=0.83; 95% Confidence Interval CI 0.71-0.93; p = 0.012). There was observed a trend for the relation between the improvement of METs and better prognosis of patients (HR=0.57; 95% CI 0.38-0.86; p = 0.007). No statistically significant relation between any of the early and late factors and any form of physical activity was found.
Conclusions: Increased BMI, itself a risk factor for coronary artery disease, is a positive prognostic factor for the outcome of CR (phenomenon known as the obesity paradox). Our study also shows that although the absolute value of METs achieved after CR had no significant impact, the thing that seems to improve prognosis is relative improvement of METs.

P1949

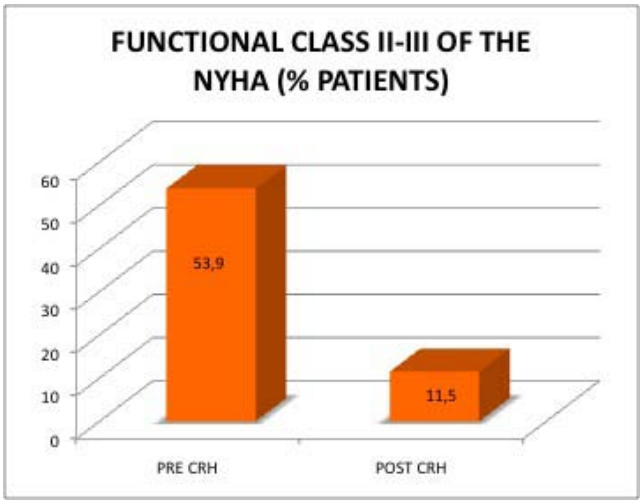
Improvement of functional capacity and other risk factors in the patient with ischemic cardiopathy through the cardiac rehabilitation program

N G Uribe Heredia[1]; J Balaguer Recena[1]; H Alvaro Fernandez[1]; L Gil Fraguas[1]; LG Piccone Saponara[2]; R Arroyo Espliguero[3]; S Moreno Reviriego[3]; E Novo Garcia[3]; M Viana Llamas[3]; C Moreno Vinues[3]; JL Garcia Gonzalez[3]; ME Jimenez Martinez[3]; SM Garcia Ortego[3]; B Tarancon Zubimendi[3]; MA San Martin Gomez[3]
[1]Guadalajara University Hospital, Cardiac Rehabilitation Unit, Guadalajara, Spain; *[2]Hospital General de Ciudad Real, Nefrology, Ciudad Real, Spain*; *[3]Guadalajara University General Hospital, Cardiology Department, Guadalajara, Spain*

Introduction: Coronary heart disease (CHD) is the leading cause of mortality in Europe, causing a significant reduction in physical, psychological and socio-occupational capacity in the short, medium and long term. Cardiac rehabilitation program (CRH) plays an important role in the recovering the patient.
Materials and methods: Observational prospective study. Included all patients with CHD from Sept/2015-Oct/2016 of the CRH. We describe CVRF, demographic, electrocardiographic, echocardiographic; prior and subsequent to the CRH. Statistical analysis SPSS 20. Categorical variables are compared with Chi2. and quantitative (expressed as means ± standard deviation) with Student's T. Statistical significance $p < 0.05$.
Results: 78 patients, mean age 56.9 years, men 92.3%, 60.3% intermediate-high risk, LVEF less than 55%, 34.9% at the start of the CRH, 53.9% NYHA functional class II-III, 52.6% hypertension, 67.9% dyslipidemia, 42.3% obesity, 21.8% diabetes mellitus, 56.4% smokers, 87.9% sedentary, BMI 29.6. At the end of the CRH, NYHA functional class II-III, were reduced to 11,5%. More results in Table 1.
Conclusions: The CRH in patients with CHD is associated with an improvement in functional capacity with better exercise tolerance and fraction left ventricular ejection. In addition to a reduction of resting heart rate, diastolic left ventricular dysfunction, response to exercise, lipid profile, abdominal perimeter, C-reactive protein levels; being these differences statistically significant.

Table 1.

VARIABLES	PRE CRH	POST CRH	P
Functional capacity (METS)	8,3 + 2,5	10,01 + 2,9	< 0,001
Test of 6 minutes (meters)	525,3 + 80,7	572,1 + 95,7	< 0,001
Abdominal circumference (cm)	103,1 + 12,4	101,8 + 12,1	< 0,001
Systolic blood pressure at peak exercise (mmHg)	162,3 + 18,4	158,1 + 14,4	0,04
Diastolic blood pressure at peak exercise (mmHg)	80,9 + 8,1	77,8 + 6,8	< 0,01
Resting heart rate (beats per minute)	71,1 + 10,8	63,6 + 9,8	< 0,001
Recovery time (beats in the first minute)	14,6 + 8,2	18,3 + 8,9	< 0,001
LDL cholesterol (mg/dL)	85,1 + 32,8	72,2 + 26,4	0,003
HDL cholesterol (mg/dL)	39 + 11,2	41,4 + 12	0,005
C-Reactive proteína (mg/L)	3,62 + 4,2	2,04 + 2,6	0,001
B-Type Natriuretic peptide (pg/mL)	77,4 + 124,7	62,4 + 90,4	0,08
Fraction left ventricular ejection (%)	56,2 + 8,3	59,6 + 7	< 0,001
Diastolic left ventricular dysfunction (%)	78,2	32,1	< 0,001



P1950

Different prognostic predictors in cardiopulmonary exercise testing according to the aetiology of systolic heart failure

CMF Christopher Strong[1]; H Dores[1]; M Mendes[1]; N Vale[1]; M Castro[1]; J Carmo[1]; J Mesquita[1]; S Guerreiro[1]
[1]Hospital de Santa Cruz, Cardiology, Lisbon, Portugal

Introduction: The Cardiopulmonary Exercise Testing (CPET) has an important role in the risk stratification and prognostic evaluation of patients with Heart Failure and reduced Ejection Fraction (HFrEF). Several variables in CPET have been validated as independent predictors for a worse prognosis, but, their impact according to the aetiology of the HFrEF has not been established.
Purpose: To evaluate the prognostic value of CPET variables in patients with HFrEF according to the aetiology – Ischemic Vs Nonischemic HF.
Methods: Of all the patients submitted to CPET in our laboratory between 2009 and 2015, those with HFrEF (EF < 40%), NYHA functional class II-III and optimal medical therapy were selected. The following variables of the CPET were studied: Peak VO2, VE/VCO2 slope, exercise oscillatory ventilation, PetCO2 at rest and during exercise, exercise blood pressure response to effort, electrocardiogram changes, heart rate recovery at 1 min and patient reason for test termination. During a mean 44 month follow-up, the independent predictors for the composite endpoint of hospitalization for decompensated heart failure, need for heart transplant and death of any cause, in both groups of patients, were determined using a Cox Regression.
Results: A total of 123 patients were included in the study (average age of 55 ± 11 years; 80% of male gender), 57% with ischemic HFrEF, with the ramped protocol test

being the most commonly used (65% of the cases). Patients with ischemic HFrEF were mostly male, and had a higher mean age. The composite endpoint occurred in 35% of the total sample. In patients with ischemic HFrEF the sole predictor for the composite endpoint was the Peak VO2 (HR 0.79, IC95% [0.69,0.91]; $p < 0.01$), while in those with nonischemic HFrEF the predictors were the Peak VO2 (HR 0.84, IC95% [0.71,0.99]; $p = 0.04$) and the VE/VCO2 slope (HR 1.09, IC95% [1.04,1.14]; $p < 0.01$).
Conclusions: Of the CPET variables studied, the Peak VO2 was an independent predictor for the composite endpoint in both groups, with the VE/VCO2 slope having also been a predictor in the nonischemic HFrEF patients, probably reflecting a lower ventilatory efficiency as a result of the longer chronicity of the cardiac dysfunction.

P1951
Inverse relationship between hemoglobin oxygen saturation measured by pulse oximetry at rest and exercise capacity in the patients with heart failure

N Aizawa[1]; K Nagahama[2]; Y Toma[1]; H Ikemiyagi[1]; T Shinzato[1]; M Iwabuchi[1]; Y Ohya[1]
[1]University of the Ryukyus, Department of Cardiovascular Medicine, Nephrology and Neurology., Nishihara, Japan; *[2]Okinawa Rehabilitation Center Hospital, Okinawa, Japan*

Background: Exercise capacity is a key prognostic factor in the patients with heart failure (HF). Although peak oxygen consumption (peak VO2) measured by maximal symptom-limited cardiopulmonary exercise test (CPET) is the most objective method to determine exercise capacity, a simple tool to predict exercise capacity is required. Hemoglobin oxygen saturation measured by pulse oximetry (SpO2) is a simple and useful tool to evaluate oxygenation. However, the relationship between SpO2 at rest and exercise capacity measured by CPET is unclear.
Purpose: To investigate the relationship between SpO2 at rest and exercise capacity measured by maximal symptom-limited CPET in the patients with HF.
Methods: We examined the association between SpO2 and exercise capacity among 46 patients with HF (age 54 ± 13, male 76%, cardiomyopathy 43%, valvular heart disease 35%, ischemic heart disease 17%) who underwent maximal symptom-limited CPET in our institute.
Results: Peak VO2/weight and peak respiratory exchange ratio were 16.2 ± 5.6 ml/min/kg and 1.2 ± 0.1, respectively. SpO2 at rest inversely correlated with peak VO2/weight ($r = -0.43$, $P = 0.003$). Compared with the patients who had preserved exercise capacity (peak VO2/weight ≥ 11.0 ml/min/kg, $n = 39$), the patients who had low exercise capacity (peak VO2/weight < 11.0 ml/min/kg, $n = 7$) showed significantly higher SpO2 at rest (99.0 ± 0.8 vs 98.0 ± 1.6 %, $P = 0.03$). Multiple regression analysis revealed that higher SpO2 at rest ($\beta = -0.29$, $P = 0.006$), age, BMI and lower hemoglobin, sodium are independent predictors of lower peak VO2/weight.
Conclusion: In patients with HF, higher SpO2 at rest may detect lower exercise capacity.

P1952
Functional testing: comparing the results of 6-minute walk test with handgrip and postural tests

B Leskovar[1]; T Furlan[1]; S Poznic[1]; B Kljucevsek[2]; A Adamlje[1]
[1]Trbovlje General Hospital, Department of Internal Medicine, Trbovlje, Slovenia; *[2]Trbovlje General Hospital, Department of Hemodialyisis, Trbovlje, Slovenia*

Introduction: 6-minute walk test (6MWT) is most widely used for testing functional capacity of heart failure patients. Some patients can't perform it well or at all due to other non-cardiac comorbidities.
Purpose: We wanted to test the correlation of 6MWT with other functional tests (handgrip test, postural tests).
Methods: We performed 6MWT in 30 hemodialysis patients. They performed the test three times in the same setting (before hemodialysis). Handgrip test was performed before hemodialysis three times in three different positions (standing-up, sitting, lying down) using both arms. Postural testing was performed before hemodialysis using the postural test protocol (balance tests, gait speed, chair stand test). Positional influence on handgrip test results was tested with one-way repeated measures ANOVA and functional tests correlation with Pearson's correlation coefficient. We also tested the influence of AVF on handgrip test results (multiple linear regression). In 22 patients with concurrent end-stage kidney disease and heart failure we evaluated possible correlations between echocardiographic parameters, biomarkers and functional tests (multiple linear regression).
Results: Thirty patients (60% male, mean age 64.4 ± 13.3 years, mean ITM 27.1 ± 4.6 kg/m2) performed the 6MWT (mean 65 ± 18% of predicted distance), handgrip test (right arm 23 ± 10kg; left arm 22 ± 10kg), postural tests (10 ± 3 points (of 12 maximum)). Handgrip results were not influenced by body position (right: $F(2.0,56.5)=0.395$, $p = 0.67$; left: $F(1.4,40.7)=1.573$, $p = 0.22$)), neither by the presence of an AVF (right: $F(2,27)=2.268$, $p = 0.123$, $R2=0.144$; left: $F(2,27)=0.991$, $p = 0.384$, $R2=0.068$). All functional tests had a statistically significant positive correlation with each other. In 22 hemodialysis patients with 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), high troponin was the most important prognostic factor of lower LVEF, lower VTI and higher E/A. NT-proBNP was a statistically significant prognostic factor of lower Em and higher E/Em. None of the tested laboratory or echocardiographic parameters were associated with hospitalization rate due to heart failure in the last two years or the results of functional tests. Low VTI was a prognostic factor of longer hospital stay due to heart failure in the last two years.
Conclusion(s): 6MWT can be replaced with other functional tests (handgrip test, postural test) to evaluate functional capacity. This is particularly useful in elderly disabled patients, where 6MWT results are often influenced by their disability to walk for 6 minutes continuously. In addition, handgrip test is not influenced by body position or presence of AVF. In patients with concurrent end-stage kidney disease and heart failure, troponin T was a better prognostic factor of chronic heart failure and none of echocardiographic or laboratory parameters were associated with the results of functional tests.

P1953
Impact of short-term physical training on functional capacity, natriuretic peptids and endothelin in heart failure patients with diabetes mellitus

D Dragan Marinkovic[1]; M Deljanin-Ilic[1]; B Ilic[1]; V Stoickov[1]; S Stojanovic[1]
[1]University of Nis, Medical Faculty, Institute of Cardiology Niska Banja, Nis, Serbia

The positive effects of physical training in patients (pts) with chronic heart failure (CHF) are reflected in improving exercise tolerance, reduce symptoms and less hospitalization, increasing survival and improving quality of life. It has been confirmed that CHF is 2-3 times higher in patients with diabetes mellitus (DM), than for those who do not have DM.
Aim: To evaluate the effects of short-term physical training on physical exercise tolerance and level of markers of neuro-humoral activation and endothelial function, in CHF pts with diabetes mellitus type 2.
Patients and method: The study involved 20 pts (14 males), mean age 62.3 ± 5.7 years, mean EF 36.75 ± 3.34%, NYHA II and III, with DM type 2, and 32 compatible non-diabetic pts with CHF who were assigned to a control group. The mean duration of DM in study group was 10.2 ± 3.6 years. All patients were included in three-week rehabilitation program at 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 parameters, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) an endothelin (ET) were determined.
Results: At the end of rehabilitation, the concentration of neuropeptides, ANP and BNP, were significantly higher compared to the baseline values, in both groups, in a group of diabetics pts and in non-diabetic group, also. (ANP $p = 0.018$; BNP $p = 0.042$). In the group of diabetic pts, there was significantly higher value of BNP compared to the control group after rehabilitation ($p = 0.032$), while there was no significant difference in the values of ANP (ns), between two groups. In contrast, the concentration of ET, after rehabilitation was lower in both groups, but the statistically significance was only in the group of diabetic pts ($p = 0.035$). In both groups, exercise tolerance was improved ($p < 0.005$) as well as quality of life assessed by Minnesota Living With Heart Failure Questionnaire ($p < 0.005$).
Conclusion: Opposite to long, short-term exercise training induced transitory increase of ANP and BNP, and decrease of endothelin in diabetic CHF pts after cardiac rehabilitation. These effects are associated with improvement of exercise tolerance and quality of life.

P1954
Analysis of physical rehabilitation efficiency in patients with chronic heart failure

VL Galenko[1]; TA Lelyavina[1]; MY Sitnikova[1]
[1]The North-Western Federal Medical Research Center named after V.A.Almazov, the research laboratory of chronic heart failure , Saint-Petersburg,, Russian Federation

Introduction: In the world practice, the selection of physical training intensity of CHF patients is based on anaerobic threshold achievement during cardiorespiratory test (CPET). But the majority of patients with severe CHF are not able to achieve it, that requires the use of certain indicators in the appointment of physical training. This alternative indicator can be lactate threshold, which achieved first during the CPET.
Purpose: To evaluate aerobic physical exercise efficiency in CHF patients, selected on the basis of achievement the lactate threshold during CPET.

Methods: 77 patients, CHF NYHA II-III were randomized into two groups - primary (aerobic training) and control (standard treatment of CHF). Main group - 64 patients, mean age 54 ± 12,5 years, body mass index (BMI) 26,46 ± 6,4 kg/m2, among them 46 patients (72%) had III CHF functional class and 18 patients (28%) – II CHF functional class. The control group - 13 patients, age 53 ± 17 years, BMI was 25,4 ± 6.8 kg/m2, 12 patients had III CHF functional class, 1 patient – I. 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 tredmile using hardware "Oxycon Pro", Jaeger, Germany. 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 ± 0.5% and End-diastolic volume decreased by 6 ± 2.0 ml from baseline, QOL was changed by 17.5 ± 8 points (significant regression of symptoms), ET increased by 9 ± 1 points and VO2 peak increased by 4.4 ml/min/kg. In the control group showed an increase EF 4 ± 1,1%, End-diastolic volume decreased by 68 ± 14,8 ml, the change of QOL 14 ± 7,22 points, the increase in ET at 1.5 points, VO2 peak decreased by 1,7 ml/min/kg. Revealed a strong positive correlation between the initial values of VO2 peak and EF (rEF=0,4, p), and between baseline levels of sodium, hemoglobin and the of physical rehabilitation efficiency (rNa= 0,41, p,0,05; rHb = 0,45, $p < 0,05$). There was a positive impact of the initial content of red blood cells (rEr=0,6, p = 0.03), sodium (rNa=0,4, p = 0.05), LV EF (r=0.5, p = 0.05) and level VE at the peak of exercise load (r=0.5,p = 0.01) on training efficiency.Conclusion. Aerobic physical exercise in CHF patients, selected on the basis of lactate threshold achievement during the CPET, is effective in improving values of CPET, EchoCG, QOL and increasing exercise tolerance.

P1955

Randomised pilot study into the effects of low frequency electrical muscle stimulation in advanced heart failure patients

S A Stuart Anthony Ennis[1]; G Mcgregor[1]; T Hamborg[2]; H Jones[3]; R Shave[4]; S Singh[5]; P Banerjee[1]
[1]University Hospitals of Coventry and Warwickshire NHS Trust, cardiac rehabilitation, Coventry, United Kingdom; *[2]university of Warwick, Warwick Medical School, Warwick, United Kingdom*; *[3]Liverpool John Moores University, Sport and Exercise Science, Liverpool, United Kingdom*; *[4]Cardiff Metropolitan University, School of Sport, Cardiff, United Kingdom*; *[5]University Hospitals of Leicester NHS Trust, cardiac and pulmonary rehabilitation, Leicester, United Kingdom*

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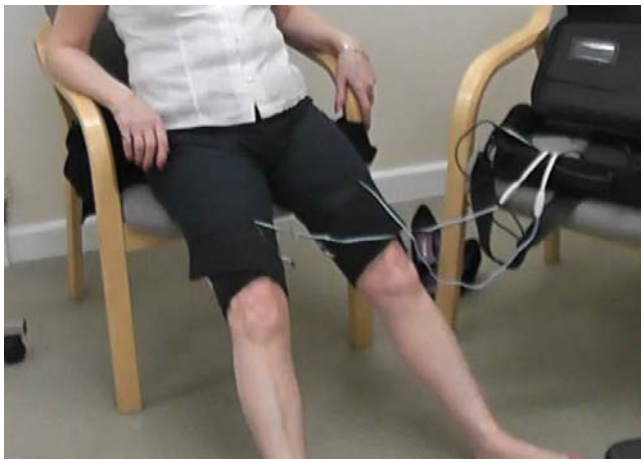
Background: Chronic heart failure patients have limited treatment options and struggle to adhere to exercise training programmes. Low Frequency Electrical Muscle Stimulation (LF-EMS) may have the potential to reduce breathlessness and increase exercise capacity in this cohort. However, the practical feasibility of a randomised controlled trial (RCT) of LF-EMS in this debilitated population has not been established.
Methods: Using a double blind, randomised study design, 60 severe heart failure patients (New York Heart Association class III-IV) were assigned to 8 weeks (5 x 60 mins per week) of either LF-EMS intervention (4Hz, continuous) or SHAM placebo (skin level stimulation only) of the quadriceps and hamstrings muscles. Participants used the LF-EMS straps at home and were supervised weekly. Recruitment, adherence and tolerability to the intervention were measured during the trial as well as physiological outcomes (6 minute walk, quadriceps strength, quality of life and physical activity).
Results: 12 (20%) of the 60 patients (4 LF-EMS, 8 SHAM) withdrew. Reasons for dropout were: deterioration in health (n = 6) family problems (n = 2) device implantation (n = 1) and found the stimulation intolerable (n = 3) Forty One patients (68.3 %), adhered to the protocol for at least 70% of the sessions. The physiological measures indicated improvement in the LF-EMS group in 6 minute walk distance, and quality of life, although not significantly.
Conclusion: Chronic heart failure patients can be recruited to and adhere to LF-EMS studies and find it tolerable. A larger Randomised Controlled Trial (RCT) in the advanced heart failure population is therefore feasible.

Outcome measures all timepoints

Outcome	Time point	LF-EMS	Sham	p-value
6MWD (m)[95% CI]	Baseline	264[222-305]	265[218-312]	0.972
8 weeks		288[242-333]	274[225-323]	0.664
20 weeks		263[214-312]	242[180-305]	0.600
Legstrength(N)[95% CI]	Baseline	218[183-253]	275[235-315]	0.028
8 weeks		209[176-241]	282[235-328]	0.010
20 weeks		182[143-221]	200[149-251]	0.561
QoL(score)[95% CI]	Baseline	53[43-63]	51[42-60]	0.766
8 weeks		45[35-54]	46[36-56]	0.849
20 weeks		54[40-69]	37[18-56]	0.156



Trial participant using LF-EMS

PULMONARY HYPERTENSION

P1956

Residual pulmonary hypertension after endarterectomy: what remains to be clarified?

S Sofia Alegria[1]; MJ Loureiro[1]; AR Almeida[1]; F Ferreira[1]; O Simoes[1]; D Repolho[1]; L Lopes[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal

Introduction: Chronic thromboembolic pulmonary hypertension (CTEPH) is potentially curable by pulmonary endarterectomy (PE). However, residual pulmonary hypertension (PH) after surgery is common, and its impact on long-term outcome is unknown.
Objectives: Evaluate the impact of residual PH and its predictors, as well as the predictors of functional improvement and decrease in NT-proBNP levels.
Methods: Longitudinal analysis of CTEPH patients followed in a reference center for the treatment of PH, submitted to PE abroad. Logistic regression was used to identify predictors of residual PH and of improvement in functional class, NT-proBNP levels and 6-minute walk test (6MWT) distance.
Results: Twenty-one patients (62% females, age 54 ± 12 years) were included. Before surgery 86% were in WHO functional class III or IV, the mean distance walked in the 6MWT was 352 ± 157 meters, NT-proBNP was 1532 ± 1817 pg/mL, mean pulmonary artery pressure (mPAP) was 44 ± 13 mmHg and pulmonary vascular resistance (PVR) was 11.0 ± 5.4 WU. After surgery, 57.9% of the patients had residual PH (mPAP ≥ 25 mmHg and/or PVR> 3 WU), which was associated, among other preoperative parameters, with female gender (p = 0.045), pulmonary artery systolic pressure (PASP) estimated by echocardiogram >79 mmHg ($p < 0.001$) and NT-proBNP >128 pg/mL (p = 0.017). There was no association with cardiopulmonary bypass time. The only predictor of residual PH maintenance was NT-proBNP >128 pg/mL (OR 18.0, 95% CI 1.2-271.5, p = 0.037). During a follow-up of 971 ± 802 days, cardiovascular mortality was 4.8% (n = 1). The presence of residual PH was not associated with overall or cardiovascular mortality, and both functional class improvement and NT-proBNP decrease were similar in patients with and without

residual PH. However, patients with residual PH were more likely to have an increase in 6MWT distance above the mean (90 meters) (p = 0.038). Echocardiographic PASP >81 mmHg (OR 16.5, 95% CI 1.1-250.2, p = 0.043) and invasive PASP >67 mmHg (OR 13.3, 95% CI 1.05-169.6, p = 0.046) were preoperative predictors of improvement of at least 2 functional classes, whereas sildenafil therapy (OR 21.0, 95% CI 1.5-293.3, p = 0.024) was a predictor of increased distance in 6MWT >90 meters. On the other hand, right ventricular systolic dysfunction (OR 20.0, 95% CI 1.4-282.4, p = 0.027), distance in 6MWT < 300 meters (OR 55,0; IC 95% 2,8-1068,4; p = 0,008), and cardiac index < 1.95 L/min/m2 (OR 22.0, 95% CI 1.5-314.3, p = 0.023) were predictors of a decrease in NT-proBNP levels above the mean (1200 pg/mL).

Conclusions: Although the majority of patients submitted to PE mantain residual PH, this is not associated with increased mortality or lack of clinical or laboratory improvement. It remains unclear which hemodynamic cut-offs predict long-term prognosis. This study also suggests that patients with worse clinical, echocardiographic and hemodynamic profile before surgery are those with greater benefit after intervention.

P1957

Circulating biomarkers for the detection of the pre-capillary component in patients with pulmonary hypertension due to left heart diseases

JL Melero Ferrer[1]; S Dolz Gimenez[2]; A Cervero Rubio[1]; IJ Sanchez Lazaro[1]; R Lopez Vilella[1]; V Martinez Sales[2]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Unidad de insuficiencia cardiaca y trasplante. Servicio de Cardiología., Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Instituto de investigación sanitaria La Fe. Unidad de Hemostasia y trombosis., Valencia, Spain*

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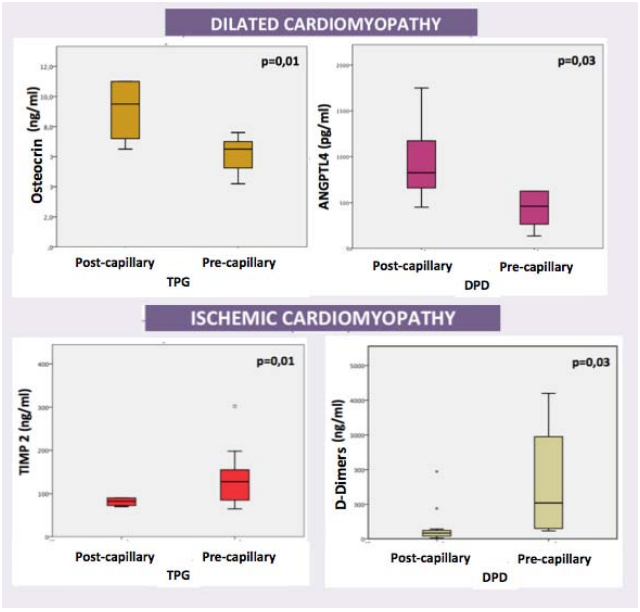
Pulmonary hypertension due to left heart diseases (PH-LHD) is a prevalent disease, which supposes important morbidity and mortality and is associated with right ventricular function impairment. PH-LHD can be classified in post-capillary PH or combined PH, attending to the presence or not of a pre-capillary component (PCP). This component implies the existence of intrinsic pulmonary vascular disease, with serious consequences for the right chambers. It is assumed that in pre-capillary PH-LHD an endothelial dysfunction occurs playing a key role for its development.

The aim of this study is to assess if there is an association among the blood levels of several circulating biomarkers and the presence of PCP.

Fifty five patients with advanced heart failure who underwent a right heart catheterization (RHC) were included. A blood sample from the pulmonary trunk was drawn. Fourteen proteins related with the physiopathological mechanisms of PH-LHD were selected (von Willebrand factor, ADMA, ET-1, VEGF, angiopoietin like 4 –ANGPLT 4 -, cathepsin B, galectin 1, TIMP2, MMP7, osteocrin, NT-proBNP, troponin T, fibrinogen and D-dimers and their levels measured by enzimoimmunoassay (ELISA). Protein levels association with PCP (considered as a transpulmonary gradient –TPG- ≥12 mmHg or a diastolic pressures difference –DPD- ≥ 7 mmHg) was analysed using T-student test.

Among the included patients, 25 had dilated cardiomyopathy (DCM) and 30 had ischemic cardiomyopathy (ICM). In the DCM group, two proteins achieved significant differences; osteocrin (p = . 01) when PCP presence was measured by calculating the TPG, and ANGPTL-4 when PCP presence was measured by using the DPD. In the ICM group three were the proteins that achieved differences; TIMP-2 (p = . 01) using TPG, and VEGF (p = . 02) and D-Dimers (p = . 03) using DPD.

There are several proteins that could be of potential use as biomarkers for detection of thePCP. Based on the aetiology of the heart failure, the selected proteins would be ANGPTL-4 and osteocrin for DCM, and TIMP-2, VEGF and D-Dimers for ICM.



graphics

P1958

The valuable cardiac magnetic resonance imaging parameter for the noninvasive assessment of pulmonary hypertension severity

AV Kazimli[1]; A V Ryzkov[2]; AV Berezina[2]; AV Naymushin[2]; OM Moiseeva[2]
[1]Azerbaijan Medical University, therapy, Baku, Azerbaijan; *[2]Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation*

Pulmonary hypertension characterized by structural and mechanical changes in pulmonary vascular bed. Invasively calculated pulmonary artery (PA) stiffness indeces are associated with mortality in pulmonary hypertension. CMRI-derived pulmonary artery distensibility (PAD) index reflects vascular remodeling in patients with pulmonary hypertension (PH). The aim of the study was to evaluate the relationship between noninvasive PAD index and invasive PA stiffness indeces and basic determinants of PH severity.

Methods: We included 48 pts with PH (mean age 42.8 ± 14.7 yrs, m:f= 13:35): 27 idiopathic pulmonary arterial hypertension (IPAH) pts, 5 scleroderma (Sc) PAH pts, 6 pts corrected congenital heart disease (CCHD) and 10 pts with inoperable CTPEH. All pts underwent 6-min walk test (6MWT), right heart catheterization (RHC), ECHO, CMRI, cardiopulmonary exercise testing (CPX) and serum NT-proBNP level. PA stiffness index and elastic modulus were calculated using data from RHC and CMRİ. PA distensibility index (%) were derived from cross-sectional images of the main pulmonary artery on CMRI and was defined as [(maximum cross sectional area (CSA)-minimum CSA)/ minimum CSA].

Results: We revealed increased PA stiffness index 6.1 (4.6–10.2) and elastic modulus 424 mm Hg (254-678), decreased PAD index in PH pts 10% (9 –16.5). There was a significant negative correlation between PAD index and PA stiffness index (r = –0.90; p < 0.0001), so we derived the formula to calculate the invasive PA stiffness using noninvasive PAD index: PA stiffness index= 102.4/ PAD index. There was also a negative correlation between PAD and elastic modulus (r = –0.91; p < 0,0001). Patients with decreased PAD index < 20 % had higher NT-proBNP level (1558 (738-4341) versus 306 (178-370); p < 0.05) , also ECHO signs of RV systolic dysfunction:lower TAPSE (1.7 ± 0.4 cm versus 2.0 ± 0.4 cm; p = 0,04), tricuspid annular systolic velocity (10 ± 2 versus 12 ± 1 cm/sec; p = 0,007), global RV myocardial deformation (13 ± 4% versus 21 ± 5%; p=0,001) and RV fractional area change (24 ± 7%; p=0,02) and reduced cardiac output which were determined by RHC (4.0 ± 1.1 versus 4.9 ± 1.2 l/min; p < 0,05). Decreased PAD index < 20 % was associated with VO2peak reduction (15 ± 4 vs 20 ± 4 ml/min/kg, respectively; p = 0,04).

Conclusions: Noninvasive CMRI-derived PA distensibility index strongly correlated with PA stiffness indeces, and may be used for noninvasive assessment of PH severity and progression.

P1959

Early ultrasound diagnostic venous pulmonary hypertension

V Kirillova[1]

[1]*Ural State Medical Academy, biochemistry, Ekaterinburg, Russian Federation*

Interstitial and alveolar pulmonary edema is the result of elevated pulmonary veins pressures. The early and correct diagnosis of venous pulmonary hypertension prevents the one of the most common reasons for hospitalization of patients with heart failure and decreases high risk of mortality. The aim of the study was the development early non-invasive diagnostic venous pulmonary hypertension. We investigated pulmonary vein's minimal diameter during atrial systole and pulmonary vein's maximal diameter during heart's diastole by transthoracic echocardiography in 92 chronic heart failure patients (65.4 ± 6.4 years) with preserved left ventricular ejection fraction, complicated by hypertensive disease. All patients hadn't chronic and acute respiratory diseases. The patients were divided into 2 groups: 50 heart failure patients with X-ray signs of pulmonary venous congestion, and 42 heart failure patients with normal pulmonary X-ray pattern. The control group is a 34 people (45.2 ± 5.3 years) without cardiovascular diseases. Values are expressed as means ± SEM. T-test was used when comparing means. $p < 0.05$ was considered statistically significant.

In the present study, we visualized three pulmonary veins: left superior pulmonary vein, left lower pulmonary vein and right upper pulmonary veins by the transthoracic echocardiography. The maximal pulmonary vein's diameter of heart failure patients with X-ray signs of pulmonary venous congestion was increased compared to patients of the control group (24.7 ± 1.1 mm vs 14.7 ± 0.2 mm ($p < 0,001$) and heart failure patients with normal pulmonary X-ray pattern (24.7 ± 1.1 mm vs 15.6 ± 0.6 mm ($p < 0,01$). The minimal diameter of visible pulmonary vein during atrial systole of heart failure patients with X-ray signs of pulmonary venous congestion was increased compared to patients of the control group (14.1 ± 1.0 mm vs 6.4 ± 0.3 mm ($p < 0,001$) and heart failure patients with normal pulmonary x-ray pattern (14.1 ± 1.0 mm vs 7.5 ± 0.7 mm ($p < 0,01$).

The pulmonary vein diameter during heart's diastole is more than 18 mm and the pulmonary vein diameter during atrial systole is greater than 9 mm were observed in the 95% heart failure patients with X-ray signs of pulmonary venous congestion. Thus, if heart failure patients have maximal pulmonary vein's diameter more than 18 mm, and minimal pulmonary vein's diameter greater than 9 mm we can to diagnose venous pulmonary hypertension with probability of 95%. Thus, early diagnosis of venous pulmonary hypertension by the transthoracic echocardiography allow timely will initiate therapy and decreases hospitalizations from decompensated left heart failure.

P1960

Prevalence of pulmonary hypertension and associated comorbidities in mexican patients hospitalized in a tertiary-referral hospital

G K Perez Cortes[1]; L Verdeja-Vendrell[2]; A Orea-Tejeda[2]; DG Gonzalez-Islas[2]; AG Jimenez-Cepeda[2]; AG Navarrete-Penaloza[2]; RN Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; B Robles-Uribe[2]; FA Figueroa-Herrera[2]; SC Torres-Montiel[2]

[1]*Universidad Autonoma Benito Juarez de Oaxaca, Faculty of Medicine and Surgery, Oaxaca de Juarez, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas, Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico*

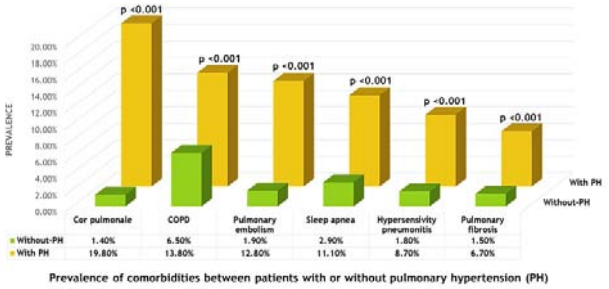
Background: Pulmonary hypertension (PH) is associated with poor quality of life and decreased survival, which vary according its severity and etiology. However, there are only a few large-scale reports on the incidence, prevalence and underlying etiologies of PH.

Purpose: To determine the prevalence of PH and its main comorbidities in Mexican patients hospitalized in a tertiary-referall hospital.

Methods: A cross-sectional study was conducted in hospitalized patient between the years 2014-2016. Comorbidities were assessed according to International Statiscal Classification of Diseases and Related Health Problems 10 th Revision. Subjects older than 18 years were included; subjects with congenital heart defects were excluded.

Results: We included 8,681 patients (age 49.85± 17.90 years). PH prevalence was 3.43% (n = 298). Those patients with PH were older (57.46 ± 15.19 vs. 49.58 ± 17.93, $p < 0.001$) ranging from 18 to 94 years; 60.7% were women. Compared with those without PH, patients with PH had a higher prevalence of cor pulmonale (19.8% vs. 1.4%, $p < 0.001$) and COPD (13.8% vs. 6.5%, $p < 0.001$), of which more than half (56.09% vs. 39.29%, $p < 0.001$) presented with acute exacerbation; pulmonary thromboembolism (12.8% vs. 1.9%, $p < 0.001$); sleep apnea (11.1% vs. 2.9%, $p < 0.001$); hypersensivity pneumonitis (8.7% vs. 1.8%, $p < 0.001$); pulmonary fibrosis (6.7% vs. 1.5%, $p < 0.001$); deep venous thrombosis (3.7% vs. 1.0%, $p < 0.001$); ischemic heart disease (2.3% vs. 1.0%, p 0.042); systemic lupus erythematosus (2.0% vs. 0.4%, $p < 0.001$). The in-hospital stay was 13.62 ± 8.58 days in the PH group and 11.90 ± 12.16 in those without PH.

Conclusions: PH is a condition associated with multiple comorbidities and these are related to higher morbidity and mortality, hence early detection and timely treatment is necessary to reduce economic impact and mortality.



Prevalence of comorbidities between patients with or without pulmonary hypertension (PH)

P1961

Pulmonar hypertension - A strong predictor of mortality among patients admitted with acute coronary syndrome

G Abreu[1]; P Azevedo[1]; C Rodrigues[1]; I Campos[1]; C Braga[1]; C Arantes[1]; J Martins[1]; A Gaspar[1]; J Marques[1]

[1]*Hospital de Braga, Cardiology, Braga, Portugal*

Background: Pulmonary hypertension (PH) is a complex pathophysiological condition, that may result from several scenarios, whose prevalence will likely expand with population aging and heart failure burden.

Aim: To evaluate how pulmonary hypertension can affect the prognosis of patients admitted with acute coronary syndrome.

Methods: We analysed 673 patients admitted consecutively in our coronary care unit with a diagnosis of acute coronary syndrome in a five-year period. Patients were divided in two groups according to pulmonary systolic arterial pressure (PSAP) evaluated by echocardiography. Group 1 – patients with PSAP ≥ 40mmHg (n = 227, 33.7%) and Group 2 – patients with PSAP < 40mmHg (n = 446, 66.3%). For each group we compared clinical and laboratory features, treatment and adverse events. Primary endpoint was the occurrence of 6-month death; follow-up was completed in 97%.

Results: Patients with high PSAP were older (71 ± 13 vs 65 ± 13 years, $p < 0.001$), more frequently obese (23.6% vs 16.7%; $p = 0.037$), had higher prevalence of hypertension (75.3% vs 59.4%; $p < 0.001$), diabetes (36.6% vs 27.1%; $p < 0.001$), and history of previous infarction (22% vs 13.2%; $p < 0.001$). They were under treatment more frequently with diuretics, ACE-inhibitors and calcium channel blockers. On admission, those patients with higher PSAP presented more often with Killip > 1 (38.8% vs 15.0%; $p < 0.001$), anaemia (41.0% vs 25.6%; $p < 0.001$) and renal insufficiency (eGFR < 60 ml/min) (51.8% vs 23.6%; $p < 0.001$). About two thirds had left ventricle dysfunction (62.4% vs 36.9%; $p < 0.001$). Regarding right ventricle function, there were no statiscally differences. During hospitalization, the group with PSAP ≥ 40mmHg presented more frequently atrial fibrillation (22.9% vs 8.7%; $p < 0.001$) and respiratory tract infection (10.6% vs 3.8%; $p = 0.001$), needed more frequently aminergic support (11.5% vs 5.4%; $p = 0.008$) and non-invasive and invasive ventilation support ($p < 0.001$). In-hospital (8.8% vs. 1.6%; $p < 0.001$) and 6-month mortality (18.6% vs. 5.2%; $p < 0.001$) were higher in patients with PSAP ≥ 40mmHg. In multivariate analysis and after adjusting for different baseline characteristics; pulmonary hypertension was related with higher risk of mortality [2.08 HR, 95% CI (1.13 - 3.81), $p = 0.018$].

Conclusion: Pulmonary artery hypertension reveals to be an independent predictor of overall 6-month mortality.

P1962

Pulmonary endarterectomy across borders: results of a program for chronic thromboembolic pulmonary hypertension

S Sofia Alegria[1]; MJ Loureiro[1]; AR Almeida[1]; F Ferreira[1]; O Simoes[1]; D Repolho[1]; L Lopes[1]; H Pereira[1]

[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Introduction: Although it has never been evaluated in randomized trials, pulmonary endarterectomy (PE) is the first-line therapy for chronic thromboembolic pulmonary hypertension (CTEPH). Significant benefits are reported after surgery.

Objectives: To evaluate the clinical, laboratory, echocardiographic and haemodynamic results of PE.

Methods: Longitudinal analysis of CTEPH patients followed in a reference center for the treatment of pulmonary hypertension (PH), submitted to PE abroad.
Results: Twenty-one patients (62% females, age 54 ± 12 years) were included. Before surgery, 85.7% were in WHO functional class III or IV, the distance in the 6-minute walk test (6MWT) was 352 ± 157 meters and the mean NT-proBNP was 1532 ± 1817 pg/mL. On echocardiographic analysis the pulmonary artery systolic pressure (PASP) was 85 ± 20 mmHg, 42.1% had compromised right ventricular (RV) systolic function, 76.5% right atrial (RA) dilatation and 20.0% pericardial effusion. Right heart catheterization revealed a reduced cardiac index in 70.0%, mean pulmonary artery pressure (mPAP) of 44 ± 13 mmHg and pulmonary vascular resistance (PVR) of 11,0 ± 5,4 WU. 43% were medicated with phosphodiesterase-5 inhibitors, 28.6% with endothelin-1 receptor antagonists and 14.3% with prostanoids. The mean cardiopulmonary bypass time was 269 ± 54 minutes and the disease was classified as Jamieson type 2 in the majority of patients (72.7% on the right pulmonary artery and 81.8% on the left). During 971 ± 802 days of follow-up, cardiovascular mortality was 4.8% (n = 1), with death of the only patient undergoing reoperation. After surgery, all patients were in WHO functional class I or II, there was an increase of the distance in 6MWT of 90 ± 107 meters (p = 0.004), NT-proBNP decreased by 1204 ± 1816 pg/mL (p = 0.006) and PASP assessed by echocardiography decreased by 45 ± 22 mmHg (p < 0.001). Recovery of RV systolic function and normalization of AD dimensions were both observed in 44.4% of the patients and none had pericardial effusion. In the haemodynamic evaluation, there was a reduction of the mPAP by 19 ± 12 mmHg (p < 0.001) and of the PVR by 7.3 ± 5.5 WU (p < 0.001). Nevertheless, 57,9% of the patients maintained residual PH (PAPm ≥ 25 mmHg and/or PVR >3 WU). In comparison with the 12 months before PE, there was a reduction in the number and days of hospitalization in the 12 months after surgery (p = 0.014 and 0.018, respectively). Compared to a control population of 10 CTEPH patients not submitted to PE, similar in terms of baseline characteristics, there was a greater improvement in the 6MWT (+90 ± 107 vs. -30 ± 119 meters; p = 0.025), functional class (no patients in class III-IV vs. 62.5%; p < 0.001), mPAP (19 ± 12 vs. 6 ± 3 mmHg; p = 0.032) and PVR (7.30 ± 5.48 vs. 2.09 ± 2.6 WU; p = 0.036), and a reduction in cardiovascular mortality (p = 0.001).
Conclusion: PE was associated with a significant improvement in clinical, laboratory, echocardiographic and haemodynamic parameters, as well as reduction of admissions and mortality.

P1963
Echocardiographic pulmonary artery pressure estimation and risk of recurrent hospitalizations in acute heart failure

E Enrique Santas Olmeda[1]; R De La Espriella[2]; E Valero[1]; A Mollar[1]; J Gonzalez[1]; I Cardells[1]; A Paya[1]; R Heredia[1]; G Minana[1]; A Bayes-Genis[3]; J Lupon[3]; J Sanchis[1]; FJ Chorro[1]; J Nunez[1]
[1]Hospital Clinic Universitari. Universitat de València, Valencia, Spain; *[2]Hospital General Universitario de Valencia, Valencia, Spain*; *[3]Germans Trias i Pujol Hospital, Badalona (Barcelona), Spain*

Background: Pulmonary hypertension (PH) is a strong predictor of mortality in patients with heart failure (HF). However, the relationship between PH assessment, through echocardiographic pulmonary artery pressure (PASP) estimation, and readmission risk burden in acute HF patients remain unclear.
Methods: We prospectively included 2343 consecutive patients discharged for acute HF. PH was estimated by echocardiography through PASP determination in the index admission. Patients were categorized as follows: non-measurable PASP, normal PASP (PASP≤35 mmHg), mild (PASP=36-45 mmHg), moderate (PASP=46-60 mmHg), or severe PH (PASP>60 mmHg). Negative binomial regression method was used to evaluate the association between PASP and recurrent hospitalizations. Estimates were reported as incidence rate ratios (IRRs).
Results: Mean age of the cohort was 72.8 ± 11.2 years, 50.5% were women, and 53.4% exhibited a left ventricular ejection fraction (LVEF) ≥50%. PASP was accurately registered in 1234 (52.7%) patients. Of them, 306 (13.1%) displayed normal PASP, whereas 369 (15.7%), 368 (15.7%), and 191 (8.1%) patients showed mild, moderate or severe PH, respectively. At a median follow up of 2.26 years (interquartile range: 0.77-4.47), 1114 (47.6%) patients died, 4427 all-cause readmissions in 1567 (66.9%) patients, and 1834 HF related-rehospitalizations in 943 (40.2%) patients were recorded. After multivariable adjustment, and compared to patients with normal PASP, only those with severe PH exhibited a higher risk of recurrent admissions (IRR=1.52; 95% confidence interval, 1.14-2.03; p = 0.004). No significant interaction was found with regard to LVEF status (<50% vs. ≥50%; p = 0.803).
Conclusions: Acute HF patients with severe PH, as estimated by echocardiography-derived PASP, are associated with an increased risk of recurrent hospitalizations.

P1964
Prevalence of prognostic factors in pulmonary hypertension

A Adrian Lescano[1]; H Santa Maria[1]; A Lavalle Cobos[1]; D Crippa[1]; N Gonzalez[1]; A Ferro[1]; G Damianich[1]; G Romero[1]; I Constantin[1]; I Fernandez[1]; E Besmalinovich[1]; V Daru[1]; M Gonzalez[1]; H Grancelli[1]
[1]Finochietto Clinic, Buenos Aires, Argentina

Pulmonary hypertension (PH) is a multi-factorial condition associated with high morbidity and mortality. It requires for its diagnosis and treatment a multidisciplinary approach. In the past decades there have been many advances in the epidemiological, pathophysiological and therapeutic knowledge of the disease. However, there is little information available regarding clinical and prognostic factors in patients diagnosed with PH in Latin America.
Pourpose: Determine the prevalence and clinical characteristics of adverse prognostic factors in a population with recent diagnosis of PH.
Methods: Patients with recent diagnosis of PH (< 7 days) confirmed by right heart catheterization, with a mean pulmonary-artery pressure (MPAP) ≥ 25 mm Hg (using a Swan Ganz Catheter) from three heart failure and pulmonary hypertension services were analyzed between March 2012 and December 2016. According to the recommendations of international guides, the following data were recorded: Personal data, PH group (G), clinical features: symptoms, functional class FC. Direct hemodynamic parameters: pulmonary pressures (PP), wedge pressure (WP), right atrium pressure (RA) and cardiac index (CI). Functional: 6 minute walk (6MW) test distance. Echocardiographic variables: right ventricle systolic function (RVSF), tricuspid annular plane systolic excursion (TAPSE), systolic pulmonary pressure and presence of pericardial effusion (PE). Data obtained were analyzed with BioEstat 5.3 program. Adverse prognosis factors identified were: history of heart failure (HF), syncope, advance functional class (III-IV), performance in the 6MW test < 350 m, presence of PE, TAPSE ≤15 RA ≥ 12 e CI ≤ 2,2.
Results: Multicenter, observational, descriptive, consecutive and prospective study. 107 patients where included. 74% women. Mean age was 58,8 (± 19) years, 33% ≥ 70. The mean delay in diagnosis was 24 months after the first sign or symptom recorded. PH group distribution: GI 63%, GII15%, GIII9%, GIV6% and GV6%. FC of presentation: I4%, II 40%, III34% and IV20%. History of HF in 72%, syncope in 23%. 6MW mean distance walked was 320 (± 148) meters, 47 % performed ≤ 350 meters. RHC: MPAP 48.3 (± 16) mmHg, RAP 9.7 mmHG (± 5,2) and ≥ 15 mmHg 27%; CI 2,78 litres/min/mt2 (≤ 2,2 23%). Ecocardiographic data show: 79% impaired FSVD (42% slight, 18% moderate and 19% severe). Mean TAPSE 17.8 (± 4) mm, ≤ 15 mm 37 % and PE in 25%.
Conclusions: In our population with confirmed pulmonary hypertension, with a predominance of group I, we had a high presentation in over 70 years of age. At diagnosis time a high number of patients present adverse prognosis factors. This findings remark the need to use early diagnosis and therapeutic strategies.

P1965
Pulmonary hypertension due to left heart disease and etiology of heart failure

MI Marta Izabela Kaluzna-Oleksy[1]; J Migaj[1]; M Dudek[1]; E Straburzynska-Migaj[1]
[1]Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland

Introduction: Heart failure (HF) is a clinical condition with a miscellaneous background. The most prevalent cause of HF in Europe is coronary artery disease (CAD). Depending on etiology of HF, its natural history may vary. Left heart disease (LHD) is the main cause of pulmonary hypertension (PH), which in turn is considered a risk factor for worse outcomes in patients with heart failure (HF).
Aim: Evaluation of HF patients with reduced ejection fraction (HFrEF) undergoing qualification for heart transplantation with and without pulmonary hypertension due to left heart disease with regard to etiology of HF.
Methods: This was a prospective analysis of 211 patients (both genders) with HFrEF (left ventricular ejection fraction < 40%), with ischemic (ICM) (43%) and non-ischemic cardiomyopathy (NICM) (57%), hospitalized at a tertiary health care center, undergoing qualification process for heart transplantation. The following items were analyzed: medical history, epidemiological data, laboratory test results (including BNP), and chosen parameters obtained in echocardiography, cardiopulmonary exercise testing (CPET) and RHC (thermodilution method). PH was diagnosed according to the ESC guidelines.
Results: Mean age of analyzed population was 51.7 ± 10.3 years. Most patients were men (88%), 73% were in NYHA class 3 and 4. Patients with ICM were significantly older (p = 0.005) and without any gender differences with lower BNP level (p = 0.005) and higher mean aortic pressure measured invasively (p = 0.036). Patients presented PH and ischemic etiology of HF were older (p = 0.005), had lower BNP (p = 0.006) and TSH (p = 0.004) and higher mean pulmonary artery pressure (p = 0.035) and transpulmonary gradient (TPG) measured invasively without any significant differences in echocardiography or CPET.
Conclusions: PH occurred with the same frequency in ICM and NICM group, but

ischemic etiology of HF in PH patients was associated with lower level of BNP and with higher PAPm and TPG with no differences between in echocardiography or CPET.

P1966

Experience with macitentan in patients with pulmonary hypertension in a reference hospital

R Lopez Vilella[1]; I Sanchez Lazaro[1]; MJ Fernandez Megia[2]; C Borras Almenar[2]; E Marques-Sule[3]; R Lopez Reyes[4]; J Roman Ivorra[5]; J Rueda Soriano[6]; S Martinez Penades[7]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Pharmacy department, Valencia, Spain*; *[3]University of Valencia, Physiotherapy Department, Valencia, Spain*; *[4]Hospital Universitario y Politécnico La Fe, Pneumology Department, Valencia, Spain*; *[5]Hospital Universitario y Politécnico La Fe, Rheumatology Department, Valencia, Spain*; *[6]Hospital Universitario y Politécnico La Fe, Valencia, Spain*; *[7]Instituto de Investigación Sanitaria La Fe, Valencia, Spain*

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Background/Introduction: Nowadays, analyzing security and efficacy of macitentan after administering it for any reason is considered to be of special relevance.
Purpose: To describe the clinical profile and the follow-up results (security and efficacy) of patients with PH treated with macitentan.
Methods: From the 1st of July 2015 to the 31st of December 2016 all patients treated with macitentan who were prescribed during hospitalization were retrospectively and consecutively recruited. Demographic, echocardiographic, hemodynamic and clinical data and functional status were assessed.
Results: 13 patients were assessed. 6 patients had group I PH and 6 had group II PH. Table 1 shows the clinical profile, treatment indication and tolerance of 13 patients. It was a well-tolerated treatment for most patients (92%), and 11 of 13 patients (85%) improved their functional class with respect to previous status without having prescribed macitentan. In the follow-up 4 deaths (31%) were registered. Causes of death are shown in table I.
Conclusions: Macitentan is an approved drug for PAH. Nevertheless, our patients have also shown positive results for group II PH. It is a well-tolerated drug in most of our patients, and it has been related with an improvement of the functional class in most cases. Studies with longer follow-up and a larger sample are needed.

RIGHT VENTRICULAR FUNCTION

P1967

Exercise echocardiography to evaluate right ventricular afterload in post pulmonary endarterectomy patients

A R Ana Rita Almeida[1]; L Lopes[1]; MJ Loureiro[1]; D Repolho[1]; AR Pereira[1]; S Alegria[1]; F Ferreira[1]; P Fazendas[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Almada, Portugal

Introduction: Despite near normal resting mean pulmonary artery pressures (mPAP) and pulmonary vascular resistance (PVR) after pulmonary endarterectomy (PEA), abnormal increase in right ventricular (RV) afterload may be apparent during exercise and may explain the reduced exercise capacity that persists in many patients. Right ventricular afterload is better described using measures of both resistive (PVR) and pulsatile load (pulmonary arterial compliance (PAC).
Purpose: Evaluate RV afterload at rest and during exercise in patients after PEA and demonstrate that we can do this evaluation non-invasively with exercise echocardiography (EE).
Methods: Study using information recovered from EE. EE was done using treadmill ergometer and modified Bruce protocol until exhaustion. During exercise they went symptoms, arterial pressure and ECG monitoring
To evaluate RV afterload we used measures of: • total pulmonary vascular resistance (TPVR) = mean pulmonary artery pressure (mPAP)/cardiac output (CO); for this we had to evaluate mPAP = PSAP (pulmonary systolic artery pressure) x0.6 + 2, where PSAP=RV/RA (right atrium) gradient + RA pressure estimate and CO=LVSV(left ventricular stroke volume) (LVOT VTI x LVOT area) x heart rate. RA pressure estimate is as: IVC (inferior vena cava) $<$21 mm and collapsibility index (CI) $>$50% - RAP = 3 mmHg; IVC $>$21mm and CI $<$50% - RAP = 15 mmHg; intermediate values = 8 mmHg.
• compliance pulmonar (PAC) = RVSV (right ventricular stroke volume)/pulmonary pulse pressure (PPP); where RVSV=LVSV in shunt absence and PPP=PSAP-PDAP (pulmonary diastolic artery pressure), where PDAP=PA/RV gradient (in late diastole using pulmonary regurgitation jet) + RA pressure estimate.
We analyze results using SPSS version 21.
Results: The group of post PEA patients consisted of 13 patients at least 6 months after PEA, with mean age of 57.0 ± 11.7 years, 7 females. We verified a significant increase in mPAP (16.2 ± 5.7 at rest (R) vs 36.8 ± 10.3mmHg at peak exercise (PE) ($p < 0.001$)) and in CO (3.8 ± 1.0 at R vs 9.7 ± 2.7 L/min at PE ($p < 0.001$)). The TPVR didn't decrease (4.5 ± 2.0 (R) vs 4.1 ± 1.8 UWood (PE) ($p = 0.512$) and PAC decreased significantly (2.5 ± 3.5 (R) vs 1.3 ± 1.0 (PE) ml/mmHg ($p = 0.01$)).
Conclusions: In patients after PEA, TPVR does not decrease significantly with exercise, unlike what succeeds in healthy people; and CPA decrease significantly, both factors contributing to increase in RV afterload with exercise. It is possible to study TPVR and CPA using exercise echocardiography.

P1969

TAPSE as a simple echocardiographic parameter predicting exercise capacity in patients with advanced heart failure

A Anna Drohomirecka[1]; M Lipczynska[1]; T Rywik[1]; K Kozuch[1]; K Zukowska[2]; K Kodziszewska[1]; K Komuda[1]; T Zielinski[1]
[1]Institute of Cardiology, Warsaw, Poland; *[2]Medical University of Warsaw, Warsaw, Poland*

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Background: Reduced physical activity is an obvious consequence of disease progression in patients with heart failure, as impaired left ventricle function leads to deterioration of mechanisms that regulate response to increased physical exertion. The aim of this study was to determine the echocardiographic factors that affect exercise capacity in patients with advanced heart failure.
Material and methods: Fifty patients referred for evaluation for heart transplantation – 42 men and 8 women (aged 55.5 ± 7.6 years) with advanced heart failure (NYHA II-III/IV, EF≤35%, mean 21.7 ± 5.4%) underwent complex cardiologic assessment, including laboratory tests, echocardiography, cardiopulmonary exercise test (CPX) and right heart catheterization. CPX was performed on a bicycle ergometer according to RAMP protocol 10 Watt/min, measuring i.e. maximum workload, pVO2, pVO2 adjusted for age and sex, anerobic threshold, VE/VCO2 slope, RER, VO2/HR, VO2(WR) slope. Left and right ventricle function and size were assessed using 2D-mode, tissue Doppler and speckle-tracking echocardiography. Statistical correlation between echocardiographic and capacity indexes was tested.
Results: Among all echocardiographic parameters, the tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler-derived right ventricular systolic excursion velocity S' were the most strongly correlated with exercise capacity indexes – statistically significant correlations were noted with, respectively, six and five out of 8 estimated parameters (for example, TAPSE positively correlated with pVO2; r=0.41, $p = 0.003$). Moreover, in patients whose pVO2 value was above the median value in the whole study population, TAPSE was on average 2.2mm higher than in the group with pVO2 below the median (18.04 ± 3.14 vs. 15.83 ± 3.28, $p = 0.02$). Other echocardiographic parameters were correlated with none (i.e., LVEF, LVEDV), only with one (i.e., left and right ventricle GLS) to a maximum of three (i.e., RVOT dimension or RVOT ACT) capacity indexes.
Conclusion: Exercise capacity of patients with advanced heart failure strongly depends on right ventricle function, which can be simply assessed by measuring TAPSE.

P1970

Exercise echocardiography to evaluate right ventricular function in post-pulmonary endarterectomy patients

A R Ana Rita Almeida[1]; L Lopes[1]; MJ Loreiro[1]; D Repolho[1]; AR Pereira[1]; S Alegria[1]; F Ferreira[1]; P Fazendas[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Almada, Portugal

Introduction: Right ventricle (RV) contractile reserve has not been quantified in post-pulmonary endarterectomy (PEA) patients, despite RV function being the main predictor of outcome and exercise capacity, irrespective of any change in PVR.
Purpose: Evaluate RV function at rest and during exercise in patients after PEA, trying to understand the mechanisms that can limit functional capacity and demonstrate that we can do this evaluation non-invasively with exercise echocardiography (EE).
Methods: Study using information recovered from EE. EE was done using treadmill ergometer and modified Bruce protocol until exhaustion. During exercise they went symptoms, arterial pressure and ECG monitoring.
To evaluate RV function we used measures of: RVSVI (right ventricle stroke volume indexed to body surface area) = LVSVI (left ventricle stroke volume indexed to body

surface area)= (left outflow tract (LVOT) area x LVOT VTI)/body surface area; tricuspid annular plane systolic excursion (TAPSE); free RV wall S wave (S wave) and RV fractional area change (RVFAC).
Results: The group of post-PEA patients consisted of 13 patients at least 6 months after PEA, with mean age of 57.0 ± 11.7 years, 7 females.
We verified a significant increase in RVSVI (25.2 ± 7.1 at rest (R) vs 34.7 ± 6.9 mL/m2 at peak exercise (PE) ($p < 0.001$)), in TAPSE (15.6 ± 2.0 (R) vs 20.6 ± 3.3mm (PE) ($p < 0.001$)) and in S wave (9.1 ± 2.6 (R) vs 14.3 ± 3.4 cm/seg (PE) ($p = 0.001$)). RVFAC didn't change significantly with exercise (43.6 ± 9.2 (R) vs 48.5 ± 10.7% (PE) ($p = 0.217$)).
Conclusions: It is possible to study RV function using exercise echocardiography. In patients after PEA the longitudinal function of RV seems to be more preserved than radial function.

P1971

Higher arterial stiffness predicts non-recovery of left ventricular longitudinal function in patients after myocardial infarction treated with percutaneous coronary intervention

E Zharikova[1]; S Villevalde[1]; ZH Kobalava[1]
[1]RUDN Univercity, Moscow, Russian Federation

Objective: Functional recovery or irreversible negative remodeling of injured myocardial segments has different prognostic implication in patients with myocardial infarction (MI) undergoing coronary percutaneous intervention (PCI). Increased pulse wave velocity (PWV), a non-invasive index of arterial stiffness, is one of the important risk factors of cardiovascular events in different clinical conditions. The aim of the study was to assess the relationship between PWV and changes of left ventricular (LV) systolic function in patients with acute MI.
Methods: In 112 patients with acute MI and PCI (68% male, age 61.1 ± 9.5 years (M ± SD), 57.2% with ST-elevation MI (STEMI), smokers 35%, arterial hypertension 83%, diabetes 7%, blood pressure (BP) 128 ± 8/82 ± 87mmHg, LV ejection fraction (LVEF) 48.2 ± 4.6%) arterial stiffness was assessed using applanation tonometry. Global longitudinal peak strain (GLPS) by speckle tracking echocardiography (STE) was calculated in a 16-segment LV model as the average segmental value on the basis of three apical imaging planes. Cardiac adverse remodeling was defined by ratio [follow up - initial LV end diastolic volume (LVEDV)] / initial LVEDV) more than 20%. Mann-Whitney and Spearman tests were considered significant if $p < 0.05$.
Results: Baseline GLPS >20% was not detected in any patient. GLPS increased from 14.4 ± 2.4 to 17.4 ± 3.5% in 4 weeks ($p < 0.05$) and to 18.1 ± 2.7 in 6 months after PCI ($p < 0.05$). GLPS normalized (>20%) in 31 (28%) patients after 4 weeks and 6 months. After 6 months adverse cardiac remodeling was found in 81 (72%) patients (53% STEMI). Achieved GLPS differed significantly in patients with vs without adverse cardiac remodeling (16.7 ± 1.9 vs 21.4 ± 1.2%, $p < 0.001$). Mean carotid-femoral PWV decreased from 11.1 ± 2.1 to 8.7 ± 1.8 m/s, $p < 0.05$. Patients without vs with GLPS normalization in 6 months after PCI were older (62.5 ± 8.5 vs 60.6 ± 9.9 years, $p < 0.05$), more frequent male (71 vs 66.2%, $\chi 2$=11.1; $p < 0.05$), smokers (36.2 vs 31.2%, $\chi 2$=3.4; $p < 0.04$), STEMI (58.7 vs 53%, $\chi 2$=7.7; $p < 0.05$), had higher systolic BP (134 ± 10 vs 130 ± 6 mmHg, $p < 0.03$), baseline PWV (11.4 ± 1.9 vs 10.4 ± 2.6 m/s, $p < 0.03$), lower baseline EF (47.6 ± 4.9 vs 49.6 ± 3.5%, $p < 0.05$). A significant correlation was found between decreased Δ speckle tracking and higher PWV (r=-0.31, $p < 0.05$) and speckle tracking and LVEDV after 6 months (r=-0.75, $p < 0.05$).
Conclusions: 65 % of patients with MI treated with PCI failed to normalize GLPS after 6 months. Adverse cardiac remodeling was revealed in 72% of patients and they more often had non-recovery of left ventricular longitudinal function. Higher baseline PWV is associated with less effective recovery of LV function.

P1972

Left ventricular function in patients with coronary slow flow

A Ali El Sharkawi[1]; MANSOR M Moustafa[2]; M I Mokarrab[2]; N F Ismail[2]; A S Abuarida[1]
[1]National Heart Institute, Cairo, Egypt; *[2]Al-Azhar University, Cairo, Egypt*

Background: The coronary slow flow phenomenon(CSFP) has been linked to myocardial ischemia, life-threatening arrhythmias, sudden cardiac death and recurrent ACS. Hypothesis of its mechanism including early atherosclerosis, microvessel dysfunction, imbalance between vasoconstrictor and vasodilatory factors and platelet function disorder were proposed. How and to what extent do these etiological factors affect left ventricular (LV) function.
Aim: To evaluate LV function in SCF patients.
Material and methods: 100 patients with CSFP and 50 subjects with angiographically normal coronary arteries constituted the control group were included in the study. All are subjected to echocardiography study to determine left ventricular functions.
Results: As regard systolic function measured by modified Simpson's method, ejection fraction was similar in both groups(62.2 ± 5.1 vs 64.4 ± 4.6, $p = < 0.22$. As regard diastolic function, echocardiography showed significantly lower maximal velocity of early diastolic filling (E) and ratio of maximal early to late diastolic filling (E/A)(in the patient group(54.6 ± 6.9 cm/s vs 74.5 ± 12.5 cm/s, $p < 0.001$ and 1.1 ± 0.25 vs 1.44 ± 0.17, $p < 0.001$ respectively). Maximal velocity of atrial diastolic filling (A) and deceleration time of early diastolic filling (DT) were similar. Among tissue Doppler parameters, E' was significantly lower in the patient group(8.6 ± 1.6 cm/s vs 14.9 ± 2.8 cm/s ,$p < 0.001$), E/e' was significantly higher in the patient group (6.4 ± 0.78 vs 5.03 ± 0.83, $p < 0.001$).
Conclusion: Coronary slow flow phenomenon is associated with left ventricular diastolic dysfunction.

Echocardiograpghic parameters

	CSFPn=100	Control valuen=50	p
LVESD (cm	3.26±0.59	3.14±0.53	0.64
LVEDD (cm)	5.15±0.5	5.02±0.52	0.3
EF (modified Simpson) (%)	62.2±5.1	64.4±4.6	0.22
LVEDV (mL/m2)	101.7±30.2	100.2±26.2	0.84
LVESV (mL/m2)	45.7±16.2	42.2±13.2	0.39
E wave (cm)	54.5 ± 6.9	74.5 ±12.5	<0.001
A wave (cm)	50.5 ±10.3	51.6± 9.	0.318
E/A	1.1± 0.25	1.44±0.17	<0.001
DT(msec)	216.3 ± 42.9	220±21.	0.72
IVRT	100.2 ±14.2	92.6±16.4	0.19
e' (cm/s)	8.6 ± 1.67	14.9 ± 2.78	<0.001
E/e'	6.4 ± 0.78	5.03 ± 0.83	<0.001

P1973

Systolic left ventricular dysfunction in isolated mitral stenosis

N Nada Tabebi[1]; R Hammami[1]; B Rekik[1]; L Abid[1]; S Kammoun[1]
[1]Hedi Chaker University Hospital, cardiology, Sfax, Tunisia

Mitral stenosis is a long term complication and the most important sequel of acute rheumatic fever.The dogma is that there is no left ventricular deficiency during mitral stenosis (MS). The aim of the study is to determine left ventricular (LV) dysfunction by tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE) in MS patients who had no clinical signs of heart failure.
Methods: Our study was an observational study. The population included 44 patients with isolated mitral stenosis and mitral valve area < 2 cm2 (Group 1) and 44 healthy control subjects (Group 2). Standard echocardiographic methods, TDI and STE were performed to assess LV functions in all participants.
Results: Mean age was 39 years old ± 12 with female predominance. Left ventricular (LV) ejection fraction (EF) was in the normal ranges in both groups (60.04 + - 4.8% vs61,75 ± 6,9% , $p = 0,21$).
Systolic myocardial velocity was significantly lower in Group 1 than in Group 2 (10.1 ± 1.7 cm/sec vs 11.29 ± 1.6 cm/sec, $p = 0.04$).The peak of global longitudinal strain GLS was significantly lower in Group 1 than in Group 2 ($p = 0.009$). Indeed, the apical systolic strain was significantly lower in Group 1 than in Group 2 (-22.49 + - 8.22 % vs-26.75 + -5.35, $p < 0.001$ f). The same results were found with basal and median systolic strain ($p < 0.001$ both). There is no correlation between severity of MS and the degree of systolic dysfunction particularly between mean GLS and mitral area (r=0.157, $p = 0.31$).
Conclusion: Through our study, we demonstrated that LV dysfunction in patients with isolated MS and normal EF. The speckle tracking imaging may be useful to detect LV function in early stage of mitral stenosis.

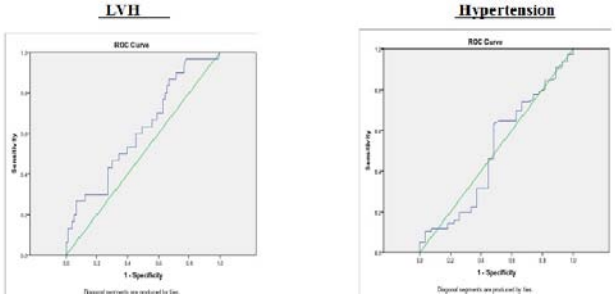
P1974

The impact of chronic cytomegalovirus infection on left ventricular hypertrophy

R Siliste[1]; C Carmen Cristescu[2]; C Dita[2]; AM Vintila[1]; C Grancea[2]; S Ruta[2]
[1]Coltea Clinical Hospital, Cardiology, Bucharest, Romania; *[2]Stefan S Nicolau Virology Institute, Virology, Bucharest, Romania*

Background: Recent studies revealed a possible relationship between cytomegalovirus (CMV) infection and cardiac disease, more specific atherosclerosis, hypertension and left ventricular hypertrophy (LVH). Characterized by a lifetime latency in mieloid cell lineage cells, but with high propensity for fibroblasts and

epithelial cells, and ability to periodically reactivate in subclinical events, CMV maintains a permanent, variable inflammatory response that contributes to arterial wall damage.
The aim of our cross-sectional prospective study was to demonstrate the impact of chronic cytomegalovirus infection on hypertension and left ventricular hypertrophy.
Methods: One hundred and three patients aged between 22 and 65 years old, 55 women and 48 men, mean age 55.5 years old, with or without known cardiac disease were enrolled in the study from february to december 2016. An informed consent approved by the local Ethics Commitee was signed by every patient before the participation to our study. At enrollement each patient filled a questionary concerning risk factors for cardiac disease (cigarrette smoking, alcohol, diabetes, obesity, serum cholesterol levels, family risk factors). All patients underwent blood tests to determine their cholesterol levels and a quantitative immunoenzymatic test for specific CMV IgG antibodies (Dia.Pro Diagnostic Bioprobes SRL, Italy) and all of them carried out a complete physical examination with arterial blood pressure measurement and a cardiac ultrasound. Left ventricular mass and left ventricular mass indexed to total body surface area were determined using the Devereaux modified formula. IBM SPSS version 19 softwear was used for the results' database and for their processing.
Results: IgG CMV antibodies were positive in all patients enrolled in our study demonstrating a very high seroprevalence for CMV in Romanian population in the fifth decade of life. From the total of 103 patients, 76 were diagnosed with hypertension (45 women and 31 men) and only 30 with LVH (20 women and 10 men). The ROC curve for LVH and hypertension did not demonstrate a very good accuracy for CMV as a prediction factor alone for any of these two conditions, but had a higher sensitivity for LVH.
Conclusions: Our study showed that chronic CMV infection can not be considered a prediction factor alone neither for hypertension nor for left ventricular hypertrophy in a 100% positive population for IgG CMV antibodies. However, in addition to other cardiac risk factors, chronic CMV infection might bring its contribution to the severity of cardiac disease by reactivation (high titers of IgG specific antibodies with positive titers of IgM antibodies) and this is why further studies need to be conducted.



ROC curve

P1975

Can the severity of acute dyspnea predict the type of heart failure?

R Zeimaite[1]; J Celutkiene[2]; A Vinikovas[1]; I Jonauskiene[3]; A Mebazaa[4]; A Kavoliuniene[3]; D Kablucko[2]; K Stasaitis[3]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; *[2]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; *[3]Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; *[4]University Paris Diderot , U942 Inserm, Hospital Lariboisière, Paris, France*

On behalf of: GREAT network
Funding Acknowledgements: The work was supported by Research Council of Lithuania, grant Nr. MIP-049/2015 The work was approved by Lithuanian Bioethics Committee, Nr. L-15- 01.

Background/Introduction: Dyspnea is one of the most common symptoms of acute heart failure patients presenting to emergency rooms. If the severity of acute dyspnea is associated with the type of heart failure according to the new classification of the 2016 ECS Heart failure guidelines, remains unclear.
Purpose: We aimed to determine if the severity of acute dyspnea could be a predictor of the specific type of heart failure as distinguished in the new ESC classification.
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the emergency department with acute dyspnea due to decompensated heart failure (HF) and other reasons. Study parameters: left ventricular ejection fraction (LVEF), dyspnea points and presence of atrial fibrillation (AF) were collected at the time of admission. Data of 387 study patients (mean age 70.3 years) with final HF diagnosis were included in the study and divided into three groups according to LVEF, measured at the time of admission or using latest available echocardiography data: HF with reduced ejection fraction (HFrEF) group with LVEF less than 40% (n = 173), HF with mid range ejection fraction (HFmrEF) with LVEF 40-49% (n = 47) and HF with preserved ejection fracture (HFpEF) with LVEF >50% (n = 167). Patients were asked to rate dyspnea by visual-analog dyspnea scale (VADS) from 1 to 10 points; point range of 0-3, 3-6 and 6-10 was defined as low, moderate and high intensity dyspnea, respectively. Using random number generator, 47 patients were randomly selected to each of three groups. Subsequently, data of 141 patients were analyzed using SPSS v23 statistical package with One-way ANOVA.
Results: Of 141 examined patients 65 (46.1%) were female, 76 (53.9%) were male. Heart failure with mid range ejection fraction was found in 12.1%, HFrEF in 44.7% and HFpEF in 43.2% of study population. Mean of dyspnea points in HFrEF group was 6.3 ± 2.9, in HFmrEF group 7.3 ± 2.3 and in HFpEF group 7.5 ± 7.5 with no statistically significant difference (p = 0,053).
Conclusion: In the prospective observational cohort the majority of acute HF patients complained of high intensity dyspnea with no differences of intensity between the three types of heart failure.

	Dyspnea severity		Gender		AF		
Low	Moderate	High	F	M	-	+	
HFrEF	6	12	29	18	29	15	32
HFmrEF	5	5	37	21	26	23	24
HFpEF	3	9	35	26	21	25	22

HFPEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

P1976

Effect of drug treatment on quality of life in heart failure with preserved ejection fraction: a systematic review and meta-analysis of randomised controlled trials

S Zheng[1]; FTS Chan[2]; S Ayis[3]
[1]King's College London, London, United Kingdom; *[2]Imperial College Healthcare NHS Trust, London, United Kingdom*; *[3]King's College London, Department of Primary Care and Public Health Sciences, London, United Kingdom*

BACKGROUND: Clinical drug trials in heart failure with preserved ejection fraction (HFpEF) have failed to consistently demonstrate mortality-reducing effects. Improvements in quality of life are of equally significant clinical importance and an outcome that has not been the focus of clinical trials.
Purpose: To examine whether clinical trials in HFpEF demonstrate improvements in quality of life compared with placebo or standard medical therapy.
Methods: We systematically searched MEDLINE, Embase and CENTRAL for randomised controlled trials (Jan 1996 to May 2016) assessing pharmacological treatments in HFpEF on quality of life. Inclusions/exclusions were adjudicated and data extracted by two independent investigators. The primary efficacy outcome examined was mean difference in quality of life (measured using the Minnesota living with heart failure questionnaire) between treatment and control groups. Trials were classified by drug type: beta-blockers (BB), angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA) and other drug classes.
Results: Of 3561 articles identified in the search, nine trials reported the treatment effects on quality of life as measured by the MLHFQ, including a total of 3510 patients (BB: 116, ACEi: 166, ARB: 2460, MRA: 444, Other: 324). Overall estimate showed that treatment was associated with statistically improved mean difference favouring treatment group (MD: -1.63, 95% CI: -2.94 to -0.31, P=0.001) (Figure 1). By individual class, only ARBs showed statistically significant difference favouring treatment (-1.84, 95% CI -3.55 to -0.14), with ACEi and MRA showing a non-significant trend favouring treatment.
Conclusion: While quality of life scores were improved in HFpEF patients in clinical trials, the clinical significance of this small difference is uncertain. Trends in improvements were found with other drug classes that block renin-angiotensin-aldosterone axis (ACEi and MRA), though this was limited by small numbers of patients. Our study found that few trials measured quality of life as an outcome. It will be of increasing importance to determine if there are other benefits of treatments beyond mortality-reducing effects, including their effects on hospitalisation rates and exercise capacity.

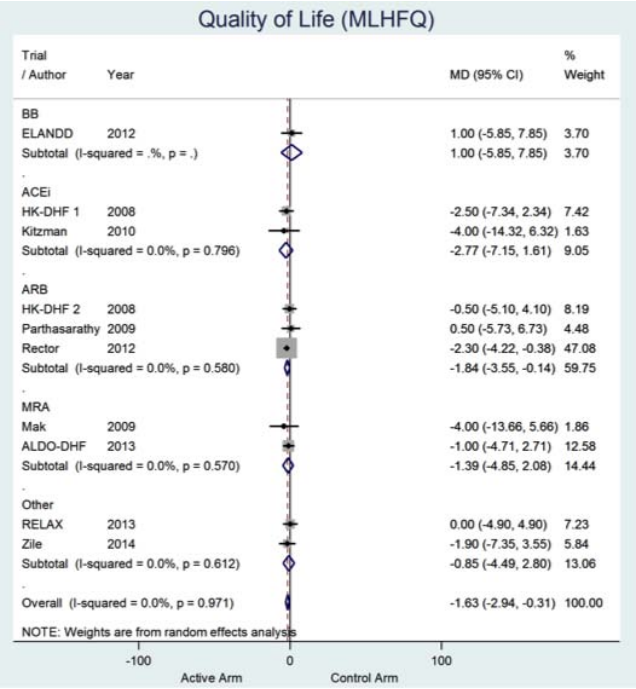


Figure 1. Quality of Life (MLHFQ)

P1977

Prognostic impact of blood pressure values in patients with heart failure with preserved ejection fraction

H Hugo Antunes[1]; ML Goncalves[1]; L Abreu[1]; B Marmelo[1]; J Gil[1]; I Pires[1]; D Moreira[1]; I Almeida[1]; M Correia[1]; C Cabral[1]
[1]*Hospital Sao Teotonio, Cardiology, Viseu, Portugal*

Introduction: Arterial hypertension (HT) is an important cardiovascular risk factor, with an increased risk of morbidity and mortality, especially with the increased risk of ischemic heart disease and stroke.
Objectives: To assess the impact of blood pressure (BP) values in patients (P) with heart failure with preserved ejection fraction (HFpEF).
Methods: We identified all P admitted for HF in a single center between 01/01/2009 and 31/12/2014. Only P with HFpEF were included. We considered 2 groups, according to BP values at admission: Systolic blood pressure (sBP)> 140 mmHg (gHyper) and sBP < 120 mmHg (gHypo). We excluded all P with sBP < 90 mmHg at admission and those who had intermediate sBP (between 120-139 mmHg).
Clinical, imaging and analytical parameters were evaluated. We compared in-hospital mortality (IHM), the combined endpoint (death / hospitalization for HF) at 12 and 24 months (M) and the survival curves of each group.
Results: Of a total of 1006 P, 350 met the inclusion criteria, 59.7% female, 79.4 ± 8.5 years.
In-hospital mortality was 3.7%. The combined endpoint at 12M was 46.0% and 58.6% at 24M.
The gHyper represents 68.6% of the P. Female predominance was found in both groups (gHyper 60% vs 59.1%, p> 0.05), mean age 79.3 ± 8.6 years (vs 79.6 ± 8.2 years, p> 0.05) and mean sBP of 167.2 ± 24.1 mmHg (vs. 109.5 ± 8.7 mmHg).
Evaluating comorbidities, 39.6% of gHyper had diabetes and 83.8% had previous diagnosis of hypertension, compared with 24.5% (p = 0.006) and 52.7%, respectively (p < 0.001). There was a trend for gHyper to have a history of ischemic heart disease more frequently (11.7% vs 5.5%, p = 0.055). Prevalence of atrial fibrillation in gHypo (65.7% vs 54.2%, p = 0.044). The two groups were similar in the remaining comorbidities.
The value of BNP in gHyper on discharge was 282 ± 354 (vs 433 ± 609, p = 0.043) and the urea value on admission was 61.9 ± 30.9 (vs77.5 ± 39.4, p < 0.001). The gHyper evolved more frequently with acute renal injury (21.8% vs 10.9%, p = 0.014). There was no statistically significant difference in hospital mortality between the two groups (gHyper 2.9% vs 5.5%, p = 0.244). There were a greater number of events in combined endpoint at 12 and 24M in gHypo (54.2% vs 46%, p = 0.05 and 67.0% vs 55.0%, p = 0.048). Survival curves showed that P with sBP < 120 mmHg had worse outcome at 12 and 24 M (p = 0.028 and p = 0.021, respectively).
Conclusion: This study showed that although gHyper have a higher number of cardiovascular risk factors, they appear to have a more favorable short and medium-term prognosis. Survival curves showed that gHypo have a greater number of adverse events at both 12 and 24M.
These results raise the hypothesis that aggressive BP control could be unfavorable in P with HFpEF.

P1978

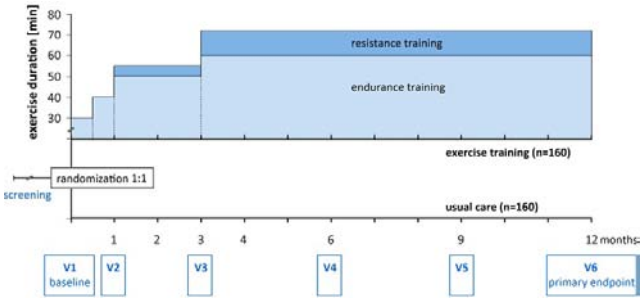
Exercise training in diastolic heart failure (Ex-DHF): rationale and design of a multicentre, prospective, randomized, controlled, parallel group trial

F Edelmann[1]; A Anna Bobenko[1]; G Gelbrich[2]; G Hasenfuss[3]; C Herrmann-Lingen[4]; A Duvinage[5]; S Schwarz[5]; T Trippel[1]; R Lindhorst[1]; D Morris[1]; E Pieske-Kraigher[1]; HD Duengen[1]; R Wachter[3]; M Halle[5]; B Pieske[1]
[1]*Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany*; [2]*University Julius Maximilian of Wurzburg, Institute for Clinical Epidemiology and Biometry, Wurzburg, Germany*; [3]*University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*; [4]*University Medical Center Gottingen (UMG), Depatment of Psychosomatic Medicine and Psychotehrapy, Gottingen, Germany*; [5]*Technical University of Munich, Depatment of Prevention, Rehabilitation and Sports Medicine, Munich, Germany*

Aims: Heart failure with preserved ejection fraction (HFpEF) is a common disease with high incidence and increasing prevalence. Patients suffer from functional limitation, poor health-related quality of life (HRQoL), and reduced prognosis. A pilot study in a smaller group of HFpEF patients showed that structured, supervised exercise training (ET) improves maximal exercise capacity, diastolic function and physical quality of life. However, the long-term effects of ET on patient related outcomes remain unclear in HFpEF.
Methods: The primary objective of Ex-DHF is to investigate whether a 12-months supervised ET can improve a clinically meaningful composite outcome score in HFpEF patients. Components of the outcome score are maximal exercise capacity, NYHA functional class, global self-rated health, diastolic function, hospitalizations and all-cause mortality.
After undergoing baseline assessments to determine whether ET can be performed safely, 322 patients in 11 trial sites with stable HFpEF were randomized 1:1 to supervised ET in addition to usual care or to usual care alone. Patients randomized to ET perform supervised endurance/resistance ET (3 times/week at a certified training centre) for 12 months. At baseline and during follow-up, anthropometry, echocardiography, cardiopulmonary exercise testing and HRQoL evaluation are performed. Blood samples are collected to examine various biomarkers. Overall physical activity, training sessions, and adherence are monitored and documented throughout the study using patient diaries, heart rate monitors and accelerometers.
Conclusions: The Ex-DHF trial is the first multicentre trial to assess the long-term effects of a supervised ET program on different outcome measures in patients with HFpEF.

Inclusion/exclusion criteria of Ex-DHF
Inclusion criteria-Stable symptomatic heart failure with preserved ejection fraction (diagnosis according to the recommendations of the European Society of Cardiology):· a.NYHA II-III, peakVO_2 <25ml/kg/min· b.LVEF ≥ 50%·c. E/e' > 15 or 15 ≥ E/e' > 8 and any of the following: NT-proBNP > 220 ng/L or atrial fibrillation-Age ≥ 18 years-Symptom severity and heart failure medication were stable during the last 4 weeks-General ability of the patient to declare willingness to participate in this trial-Written informed consentExclusion criteria-Non-cardiac causes for heart failure like symptoms:· a.chronic obstructive pulmonary disease (COPD) GOLD stages ≥ II· b.Anaemia (Hb < 11mg/dl)· c.Significant renal dysfunction (eGFR < 30 ml/min/1.73m^2 BSA)· d.Significant peripheral artery disease (Fontaine ≥ IIb)· e.Musculoskeletal disease that contribute to reduced exercise performance· f.Specific cardiomyopathy (e.g. amyloidosis etc.)· g.Haemodynamically significant valvular disorders-Significant coronary artery disease (current angina pectoris CCS ≥ II or positive stress test, myocardial infarction or coronary artery bypass graft within the last 3 months)-Any inability or contraindication to participate in CPET or in an exercise program (e.g. physiological, mental) or to supply essential information (e.g. questionnaire, diary)-Ineffective control of resting blood pressure (BP ≥ 140/90mmHg or BP ≥ 160/100mmHg with ≥ 3 antihypertensive drugs) or of resting heart rate (HR ≥ 100bpm)-Expected low compliance (e.g. by travel distance to trial site; planned absences longer than 4 weeks during follow up) or ongoing drug abuse-Pregnant or nursing women-Concomitant participation in other interventional clinical trials

peakVO2: maximum oxygen intake; LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; BSA: body surface area; CCS: Canadian Cardiovascular Society; CPET: cardiopulmonary exercise testing; BP: blood pressure; HR: heart rate



Flow Chart

P1979

Left atrial volume index predicts major adverse cardiovascular events in patients with ischemic chronic heart failure with preserved ejection fraction and renal dysfunction

D Dmytro Lashkul[1]; VD Syvolap[1]
[1]*Zaporizhzhya State Medical University, Zaporizhzhya, Ukraine*

The incidence of heart failure and chronic kidney disease has been steadily increasing and will further increase due to ageing of the general population and better treatment of acute cardiac and renal diseases. Identification of new reliable markers for diagnosis, analysis, prognosis of mortality and prevention of hospitalization is still necessary, it is not well known whether left atrial volume index (LAVi) has predictive value for prognosis in patients with ischemic chronic heart failure with preserved ejection fraction (HFpEF) and renal dysfunction.
Purpose: This study was aimed to assess the association between LAVi and outcomes in ischemic HFpEF with renal dysfunction patients.
Methods: We enrolled a total of 243 (80.3% men, mean age 58.7 ± 9.3 years) in-hospital patients diagnosed as HFpEF is due to ischemic heart disease. Clinical and echocardiographic data at baseline were collected. Glomerular filtration rate (eGFR) calculated by the formula MDRD (Modification of Diet in Renal Disease). Mean GFR was 78.1 ± 18.1 ml/min/1.73m^2, mean ejection fraction 59.2 ± 8.4 %.The patients were followed for the development of major adverse cardiovascular (CV) events, including hospital readmission for decompensate heart failure, acute myocardial infarction, sudden cardiac death, stroke.
Results: During 3-year follow-up period, 54 adverse CV events occurred (32 hospital readmission for heart failure, seven sudden cardiac death, five fatal and five non-fatal AMI, five stroke). In a multivariate Cox model, LAVi ≥12.96 cm^3/m^2 [OR: 9.69, 95% CI: 2.5-37.5, p = 0.001], eGFR ≤71.25 ml/min/1,73m^2 (OR: 6.91, 95% CI: 1.73-27.5, p = 0.006) were independent predictors for major adverse CV events in ischemic HFpEF patients with renal dysfunction.
Conclusions: LAVi is a predictor of major adverse CV events independent of clinical and other echocardiographic parameters in ischemic HFpEF patients with renal dysfunction.

P1980

The comorbidity in patients with heart failure and preserved ejection fraction depending on age

Y Yulia Kushnir[1]; A Anduyschenko[1]; A Homeniuk[1]
[1]*Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine*

The aim of our study was to analyze the frequency of comorbid diseases and the characteristics of treatment of patients with chronic heart failure (HF) and preserved ejection fraction (EF) depending on age.
Background: Despite the advances in medicine, heart failure is still the most common complication of many cardiovascular diseases and a major factor of mortality of old people. Number of patients with chronic heart failure and preserved ejection fraction is increasing, but there are no approved treatment recommendations yet.
Methods: retrospective analysis of 198 patients with heart failure and preserved ejection fraction (m - 106 pts, f - 92 pts). Patients were divided into 3 groups according to age: 1st - 40-59 years old (n = 74), 2nd - 60-75 (n = 73), 3rd - >75 years old (n = 51). The average EF (M ± m) - (63,8 ± 6,3)%. The presence of arterial hypertension, anemia, chronic obstructive pulmonary disease (COPD), diabetes, thyroid dysfunction, body mass index, renal dysfunction, intracardiac hemodynamics diseases were analyzed.
Results: Comorbidity was observed in all examined patients. 169 pts had arterial hypertension. Revealed age changes in the comorbidity: prevalence increases with age changes in renal function (29,7% in the 1st group, 26% in 2nd and 29,4% in the 3rd), hypothyroidism (25,7% in the 1st group, 38,4% in the 2nd group and 23,5% in the 3rd), COPD (2,7% in the 1st group, 10,2% in the 2nd group and 7,8% in the 3rd), anemia (16,3% in the 1st group, 32,9% in the 2nd group and 39,2% in the 3rd group), hyperuricemia (16,2% in the 1st group and 21,6% in the 3rd). Thus in all age groups more than half of patients had obesity, hypertension, stable angina and a quarter of patients - diabetes. Heart attack and atrial fibrillation are more common for patients aged 60-75 years (31,5%). End-systolic size and end-systolic volume were the highest in the second group, than may indicate bad prognosis (41,8% and 21,3% accordingly). Increased size of the left atrium, the average pressure in the pulmonary artery and aortic root changes were higher among patients over 75 years (4,4 ± 1,1 sm, 34,2 ± 4,3 mmHg and 13% accordingly). Appointment of medical therapy met the requirements in virtually all cases. Determined increase in prescription of loop diuretics in the 3rd group (70,5%) and low frequency of use of beta-blockers in the 1st group (63,5%). Metabolic therapy which does not meet the requirements of evidence is still used very often (from 50% in the 1st group and 25,5% in the 3rd).
Conclusions: A high level of comorbidity in patients with chronic heart failure and preserved ejection fraction that increases with age was revealed.

P1981

Machine-learning based exploration of variability of longitudinal myocardial velocities in heart failure with preserved ejection fraction

S Sanchez-Martinez[1]; N Duchateau[2]; T Erdei[3]; G Kunszt[4]; A Degiovanni[5]; E Carluccio[6]; A G Fraser[3]; G Piella[1]; B Bijnens[1]
[1]*University Pompeu Fabra, Barcelona, Spain*; [2]*Inria, Asclepios research project, Sophia-Antipolis, France*; [3]*Cardiff University, Wales Heart Research Institute, Cardiff, United Kingdom*; [4]*Oslo University Hospital, Department of cardiology, Oslo, Norway*; [5]*University of Eastern Piedmont, Department of cardiology, Novara, Italy*; [6]*University of Perugia, Perugia, Italy*

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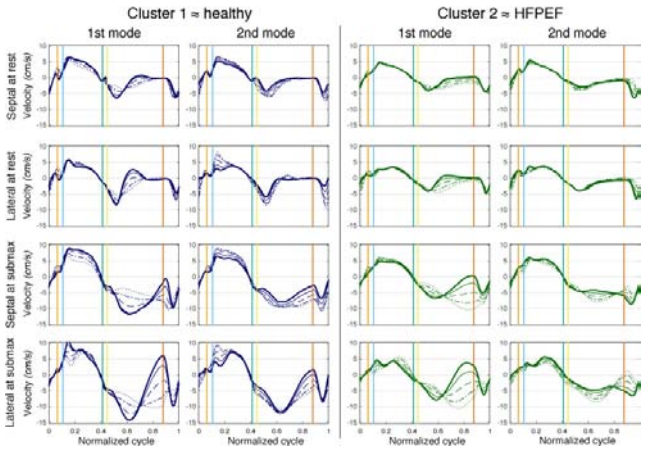
Purpose: Current diagnosis of heart failure with preserved ejection fraction (HFPEF) is suboptimal since the consensus recommendations oversimplify abnormalities by only considering simplified key markers of disease, often derived from myocardial velocity patterns (e.g., E/e' and E/A ratio, deceleration time). These diagnostic criteria are based on the expertise of highly trained cardiologists. However, complex mechanical interactions or subtle discriminative markers of disease could pass unnoticed even to the most expert eye. We investigate whether a comprehensive machine-learning based analysis of multiple myocardial velocity profiles, acquired during stress echocardiography, can identify characteristic patterns of cardiac (dys-)function.
Methods: Longitudinal velocity traces from 33 healthy subjects (67 ± 4 years) and 72 HFPEF (72 ± 6 years, diagnosed according to the Consensus Statement on HFPEF, 2007) were examined. Data came from tissue Doppler acquisitions at rest and submaximal exercise at the basal septum and lateral wall of the left ventricle. Each cardiac phase was identified and used to temporally align the velocity profiles. Unsupervised machine learning (multiple kernel learning algorithm) was used to fuse the heterogeneous velocity patterns and to reduce their complexity. Agglomerative hierarchical clustering was performed on this set to identify naturally-occurring groupings within the population. The variability explained by the identified groups was reconstructed by means of advanced regression techniques.
Results: The agreement between the found groups and the clinical diagnosis was high (Kappa = 72.6%). In the figure, the curves range from -2 (solid line) to +2 (dotted line) standard deviations along the indicated modes of each group. The HFPEF group with respect to the healthy group showed: lower overall velocity amplitude; more pronounced diastolic fusion, especially prominent in the septal velocity at exercise; higher diastolic delay, especially in the exercise patterns; and more frequent inter-atrial contraction delay. A detailed analysis of cases classified differently by the algorithm, compared with the clinical labels, confirmed that they had subtle abnormalities that had been overlooked when applying current diagnostic criteria.
Conclusion: The method proposed is automatic, objective, and independent of the diagnosis suggested by the consensus recommendations. The variability analysis of the velocities within each of the identified groups was consistent with the clinical knowledge about the HFPEF mechanical abnormalities, and revealed possible diagnostic features non-considered to date, as is the case of the delay in the atrial contraction dynamics – recently suggested as an indicator of HFPEF. Furthermore, our study confirms that machine-learning based assessment of the cardiac function at exercise is helpful when characterizing the HFPEF syndrome.



P1982

Left atrial pacing for the treatment of heart failure with preserved ejection fraction associated with interatrial dyssynchrony. Results from a randomized cross-over study

J-C Jean-Christophe Eicher[1]; B Mouhat[1]; G Bertaux[1]; M Montoy[1]; S Hassam[1]; G Laurent[1]

[1]*University Hospital Center (CHU) Dijon, Dijon, France*

Background: Heart failure with preserved ejection fraction (HFpEF) is still an orphan disease. We recently reported that interatrial conduction delay (IACD) could be a causal factor in some patients.
Purpose: To confirm the effects of left atrial (LA) pacing in patients with HFpEF associated with IACD.
Methods: Patients presenting with HFpEF (LVEF > 50%, NYHA III, or NYHA II and ≥ 1 hospitalization for CHF during the past year) were enrolled if echocardiography showed 1) an interatrial mechanical delay > 70 ms (difference between P-A' intervals at the mitral and tricuspid annulus); 2) a shortening of the mitral A wave duration > 30 ms (difference between the tricuspid and mitral A wave durations). After informed consent, a double chamber pacemaker (PCM) was implanted with the atrial lead screwed into the coronary sinus. After 1 month, baseline parameters were collected, then a randomized, double-blind crossover study was conducted with 3-month duration periods (PCM on then off vs off then on). At the end of the crossover, patients were asked which mode they preferred. Echocardiographic parameters, 6-minute walking distance and Nt-proBNP levels were studied at the end of each period.
Results: 15 patients were studied. 1 patient was excluded because of definitive atrial fibrillation (AF). 3 patients had acute CHF during the off period requiring the activation of the PCM. Compared to the baseline and "off" periods, the active period resulted in significant improvements of most parameters (table). At the end of the study all the patients chose the "on" mode.
Conclusion: LA pacing in patients with HFpEF and IACD improves LA emptying, LV filling, 6-min walking distance and Nt-proBNP levels. This technique could represent a promising treatment in some selected patients.

Table

	"off" mode	"on" mode	p
aortic VTI (cm)	23.6 ± 6.1	23.2 ± 6.5	NS
mitral E wave velocity (cm/s)	123.8 ± 23.5	107.2 ± 19.4	0.03
mitral A wave velocity (cm/s)	42 ± 12.1	60.2 ± 14.6	0.0001
E/A	3.1 ± 0.8	1.8 ± 0.4	0.002
E/e'	21.5 ± 7.1	16.1 ± 4.1	0.04
mitral A wave duration (ms)	119 ± 25.2	180 ± 19.7	0.08
interatrial mechanical delay (ms)	99 ± 21	-46 ± 77.3	0.003
systolic pulmonary artery pressure (mmHg)	47.2 ± 10.9	36.6 ± 8.04	0.0009
Nt-proBNP (pg/mL)	1854 ± 1824	1504 ±1574	0.04
6-min walking distance (m)	288 ± 130	310 ± 105	0.04

P1983

Latent class echocardiographic phenotypes predict adverse outcomes in heart failure with preserved ejection fraction: A secondary analysis of TOPCAT

DP David Peter Kao[1]; KM Flint[1]; M Merrill[1]

[1]*University of Colorado Denver, Denver, United States of America*

Funding Acknowledgements: University of Colorado Center for Women's Health Research Seed Grant

Background: Heart failure with preserved ejection fraction (HFpEF) is associated with structural and functional myocardial remodeling. Primary combinations of remodeling components in HFpEF have not been described.
Purpose: To identify complex echocardiographic phenotypes in HFpEF.
Methods: 647 patients with symptomatic HF and an LVEF ≥45% enrolled in the Americas underwent echocardiography. Phenotypes were identified using latent class analysis based on LV structure, global longitudinal strain, left atrial volume index (LAVIx), diastolic dysfunction (DD), average E/E', and RV fractional area change. The primary outcome was a composite of CV death, aborted cardiac arrest, or HF hospitalization.
Results: 4 phenotypes were identified (Table), which corresponded to subjects with little LVH, no DD and RV dysfunction (206, 31.8%); intermediate LVH with (76, 11.7%) and without DD (246, 38.0%), and significant LVH with DD (119, 18.4%). Other defining factors included LAVIx and E/E' average, suggesting variation in LV filling pressure. Phenotypes were associated with significantly different rates of the primary outcome (27-42%, chi-square p = 0.025).
Conclusions: Cluster-based echocardiographic phenotyping identified subpopulations of HFpEF patients with varying combinations of LVH, DD, LV filling pressure and RV function that were predictive of poor clinical outcomes.

Phenotype characteristics

	Type 1	Type 2	Type 3	Type 4
Trait, N (%)	206 (32)	246 (38)	76 (12)	119 (18)
Cardiac structure††				
Normal	50 (24)	31 (13)	12 (16)	0 (0)
Concentric remodeling	107 (52)	94 (39)	20 (26)	8 (7)
Eccentric hypertrophy	9 (4)	22 (9)	3 (4)	11 (9)
Concentric hypertrophy	39 (19)	97 (40)	41 (54)	100 (84)
Global long. strain >-15.6%††	72 (68)	25 (18)	25 (65)	52 (89)
LA volume index, ml/m^2 >41††	39 (23)	6 (3)	0 (0)	54 (52)
Diastolic dysfunction††				
Grade 1-2	120 (100)	60 (39)	0 (0)	17 (33)
Grade 3	0 (0)	97 (62)	17 (36)	18 (35)
Grade 4	0 (0)	0 (0)	30 (64)	16 (31)
E/E' average > 15††	4 (5)	45 (38)	28 (85)	31 (72)
RV factional area change ≤ 0.45††	55 (82)	0 (0)	46 (73)	30 (34)
Primary outcome*	55 (27)	74 (30)	28 (37)	50 (42)

*p < 0.05 ††p < 0.001

P1984

Essentials for understanding clinical trials outcomes after interventions in heart failure patients with preserved ejection fraction. insights from the aldo-DHF cohort.

R Ruhdja Lindhorst[1]; AB Bobenko[1]; TDT Trippel[1]; KN Nolte[2]; GH Hasenfuss[2]; HDD Duengen[1]; GG Gelbrich[3]; RW Wachter[2]; BP Pieske[1]; FE Edelmann[1]

[1]*Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany*; [2]*University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*; [3]*University Julius Maximilian of Wurzburg, Institute for Clinical Epidemiology and Biometry, Wurzburg, Germany*

Aims: Understanding the probability for not just randomly changes in key parameters from echocardiography (E/e', E/a), cardiopulmonary exercise testing (CPET) (peak VO2, VE/VCO2,VO2 AT) and six minute walk test (6-MWT) (walking distance, borg scale) is very important for the interpretation of clinical trials' results after interventions in heart failure patients with preserved ejection fraction (LVEF < 50%).

Table 1

	Mean Difference	Standard Deviation	Upper limit	Bottom limit	T-test significance
E/e'	0,14	1,48	3,07	-2,72	0,016
E/a	0,001	0,19	0,38	- 0,38	0,9
Peak VO2(ml/kg/min)	0,18	1,50	3,09	-2,81	0,062
VE/VCO2 slope(ml/kg/min)	0,05	3,73	7,36	-7,25	0,77
VO2 AT	0,09	2,12	4,23	-4,06	0,41
6-MWD	8,63	41,31	72,34	- 89,60	< 0.001
Borg	0,18	1,29	2,36	2,71	0,006

Altman plots could not be uploaded

Methods: We analysed the results from the repeatingly after a week performed echocardiography, CPET and 6-MWT on 422 patients of the Aldo DHF trial with a mean age 67 years and NYHA II-III. The examiantions at baseline and after a week (+/- 1 day) were implemented under stable clinical conditions without any changes in medication. To visualize the values of E/e', E/a, peak VO2, VE/VCO2,VO2 AT, walking distance, borg scale and their limits Bland Altman analysis were used.
Results: As the Altman plot indicates one could not find any systematic bias for the different measurements. There is a low-retest probability for 6-MWT's distance and Borg scale as well as for the common used echocardiographic value E/e' (t-test significance: 0,016). Only CPET shows a good reliability for peak VO2, VE/VCO 2 slope and VO2 AT (t-test significance: 0,062/0,77/0,41) and e/a (t-test significance: 0,9).
Conclusion: We have to rethink our concept regarding the usefulness E/e' for any finding in clinical trials for HfpEF populations since it is not reliable, suprisingly. CPET parameters in contrast to the commonly used E/e' seem to be reliable with a high retest probability and therefore are strongly recommended for evaluation of clinical trial's interventions in cohorts with HfpEF. Changes in value within the the mean difference and the standard deviation are likely to be random findings and have no significance for any intervention's influence. Since 95 % of variations in measurements with no intervention are within the values of the upper and bottom limits of the table 1, you will expect the opportunity of 'real' findings beyond these limits.

P1985

Heart failure with preserved ejection fraction as risk factor of mortality after cardiothoracic surgery

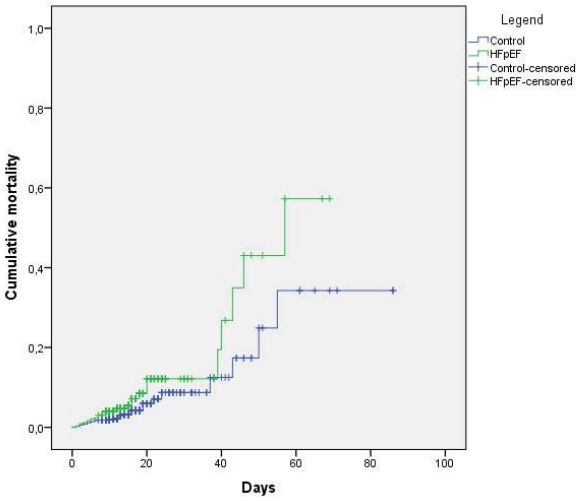
F Nicot[1]; P Baudinaud[1]; A Brusset[1]; P Estagnasie[1]; P Squara[1]; L S Nguyen[1]
[1]Clinique Medico-Chirurgicale Ambroise Pare, Critical Care Department, Neuilly sur Seine, France

Background: Heart failure (HF) with preserved ejection fraction (HFpEF) is a syndrome that occurs in one-half of all patients with HF. While considered an important risk factor of adverse medical outcomes, its prognostic role in cardiac and thoracic surgery is still unclear. We aimed to investigate its prognostic value after cardio-thoracic surgery.

Baseline characteristics

	Control (n = 1316)		HFpEF (n = 427)	
Age (years)	67,3	+/-11,3	71,5	+/-10,8
Male gender	975	(74,1%)	263	(61,6%)
Weight (kg)	77,6	+/-15,0	74,3	+/-15,6
Height (cm)	169,7	+/-8,9	167,7	+/-9,4
EuroSCORE II	2,4	+/-3,4	4,5	+/-5,7
Brain natriuretic peptide (pg/ml)	168,7	+/-376,4	481,8	+/-604,1
Aortic surgery	58	(4,4%)	11	(2,6%)
Isolated CABG	719	(54,6%)	66	(15,5%)

continuous data presented as mean +/- standard deviation, categorical data as number (%). HFpEF: heart failure with preserved ejection fraction; CABG: coronarby artery bypass surgery



Cumulative mortality

Methods: In a four-year prospective cohort, among patients having LVEF ≥ 50%, we compared postoperative intrahospital mortality after cardiothoracic surgery between HFpEF and control patients. HFpEF was defined as symptomatic HF with LVEF ≥ 50%, New York Heart Association functional class ≥ 2 and elevated BNP (above 100 pg/ml). Cox model regression was used for statistical analysis with adjustment on EuroSCORE II.
Results: 1743 patients were included, among whom 427 (24.5%) presented HFpEF. Global postoperative intrahospital mortality was 4.1%. Mortality was higher among HFpEF patients (7.0% vs 3.2%, p-value < 0.001). In multivariate analysis, HFpEF was independently associated with postoperative intrahospital mortality (adjusted hazard-ratio=1.6 (95CI 1.0-2.6), p = 0.049).
Conclusion: In our cohort, HFpEF was a risk factor of mortality after cardio-thoracic surgery.

P1986

Prognostic stratification in heart failure with preserved ejection fraction: an attainable score in daily clinical practise

P Paula Martinez Santos[1]; I Vilacosta[2]; E Batlle Lopez[3]; A De La Rosa Riestra[1]; B Sanchez Sauce[3]; B Herreros Ruiz Valdepenas[3]; E Espana Barrio[3]; J Jimenez Valtierra[3]; MD Martin Rios[4]
[1]Hospital de Fuenlabrada, Cardiology, Madrid, Spain; *[2]Hospital Clinic San Carlos, Cardiology, Madrid, Spain*; *[3]University Hospital Alcorcon Foundation, Cardiology, Madrid, Spain*; *[4]Foundation Jimenez Diaz, Madrid, Spain*

Background an aim: Several variables have been related to a poor prognosis among heart failure with preserved ejection fraction (HFpEF) patients. We aimed to develop a score to select those with the highest clinical risk among hospitalized HFpEF patients.

Table 1. Prognostic index

Risk factor	Yes	No
Age >80	16 points	0
NT proBNP ≥ 2087 ng/l	16 points	0
Long term supplemental oxygen therapy	13 points	0
TAPSE < 15 mm	17 points	0
TOTAL	62 points	0
Risk stratification		
	n	Mortality
Low risk	2	7,4%
Moderate risk	5	18,5%
High Risk	20	74,1%

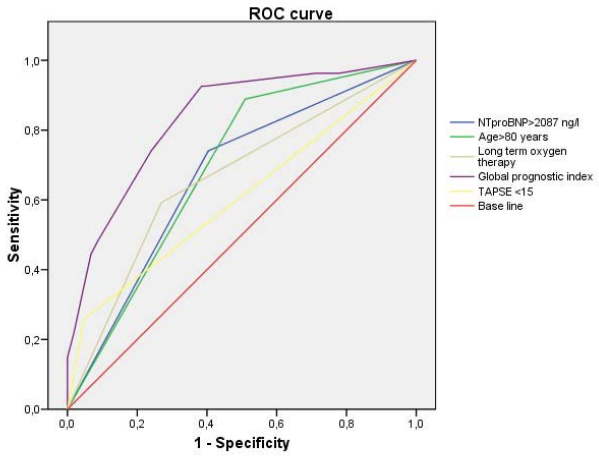


Figure 1

Methods: We prospectively included 154 consecutive patients who were admitted for HF and had a left ventricular ejection fraction (LVEF) >50%. All patients were followed during one year after hospital discharge. We analysed the information on cardiac and comorbid candidate prognostic predictors in a multivariable model to predict 1-year outcome. Then, we multiplied the model regression coefficients by 10 according to the formula: Prognostic index score = 10xβ1 (variable1) + 10xβ2 (variable2) + … 10xβn (variablen). ROC plot analysis compared the prognostic utility of the factors related to a poor prognosis.
Results: Mean age was 81 years (SD 9) and 63% were female. The mortality rate was 25.2%. In the multivariable analysis, four variables were associated to a higher risk of mortality: age over 80 years (OR 5.27; 1.38-20.06 CI 95%, p = 0.015), plasma NT proBNP higher than 2087 ng/l (OR 5.42; 1.79-16.38 CI 95%, p = 0.003), indication of chronic oxygen therapy (OR 3.98; 1.39-11.38 CI 95%, p = 0.010) and right ventricular systolic dysfunction (OR 5.48; 1.21-24.78 CI 95%, p = 0.027). We established three risk categories based on 50th and 75th percentiles. Table 1 summarizes the results from the risk stratification according to the amplified formula of the logistic regression coefficients model for 1-year mortality. The ROC curve (Figure 1) was 0.83 (95% CI, 0.74 to 0.92, p < 0.0001).
Conclusions: Our score, based on accessible clinical characteristics, allows the prediction of 1-year mortality among HFpEF hospitalized patients.

P1987

Possibility of the CAVI as the risk factor of development of heart failure with preserved left ventricular ejection fraction

K Takagi[1]; N Sato[1]; S Ishihara[1]; W Shimizu[2]
[1]Nippon Medical School Musashi-Kosugi Hospital, Department of Cardiology and Intensive Care Unit, Kanagawa, Japan; [2]Nippon Medical School, Department of Internal Medicine and Cardiology, Tokyo, Japan

Backgrounds: Heart failure (HF) is pandemic with high morbidity and mortality, and is becoming a worldwide economic burden. Although many studies have been conducted to identify characteristics of patients with HF with reduced ejection fraction (HFrEF), characteristics and pathophysiologic features of patients with HF with preserved ejection fraction (HFpEF) remain unclear. Hypertension(HT) and diabetes mellitus(DM) 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 defined the HF patients whose left ventricular EF(LVEF) was less than 50 as HFrEF, and the patients whose LVEF was more than 50 as HFpEF. We enrolled the patients who were hospitalized for acute heart failure and examined CAVI from April 2013 to March 2015. And during the same study period, HT or DM or dyslipidemia patients with preserved LVEF who did not present with HF symptoms and had never been diagnosed or treated for HF were also enrolled as patients without HF. 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. And the exclusion criteria included HFrEF. A total of 46 patients with HFpEF and 230 patients without HF were enrolled in this study.
Results: There were no differences in age (74 ± 11, 69 ± 12), sex (male: 58.7%, 58.7%) between HFpEF and without HF. The CAVI was significantly higher in patients with HFpEF compared with patients without HF (10.07[9.00-10.60] vs. 9.15[7.91-10.10]; P=0.001) (Fig. 1).
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.

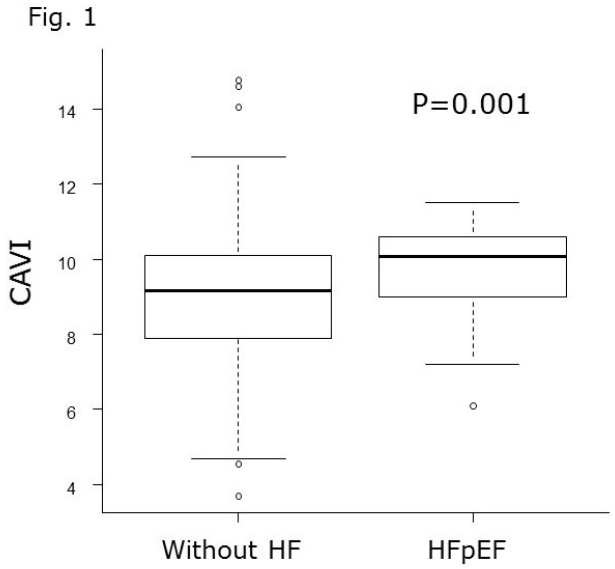


Fig. 1

P1988

Association of levels of BNP plasmatic with prediction of mortality in study cohort in south Brazil

E Eduardo Pitthan[1]; HV Hirakata[1]; BJ Barbisan[1]
[1]Institute of Cardiology of Rio Grande do Sul, Porto Alegre, Brazil

Background: The diagnosis of HF in elderly patients in clinical basis is difficult due to comorbidities. The BNP is used as a diagnostic and prognostic tool in HF, but is not sufficiently studied in the elderly.
Objective: To evaluate the association of plasma BNP levels with diagnostic accuracy of HF and long-term prognostic validation.
Methods: Six hundred and thirty-four consecutive patients presenting with suspected HF in the Emergency Room of a tertiary hospital in southern Brazil participated in this cohort study. All patients underwent BNP measurement (Biosite - POCT) as the institution protocol were included between March 2006 and September 2012. Following the Gold Standard (Fig.1) for diagnosis of HF, consisting of history and physical examination, ECG, chest X-ray, echocardiogram Uni and Two Dimensional Color Doppler. The sample was divided into 3 groups: SHF (Systolic Heart Failure), HFPEF (Preserved Ejection Fraction Heart Failure) and NHF (In Heart Failure), and patients were followed for 78 months. The study endpoint was mortality identified by the certificate of death of the Mortality Information Service (SIM).
Results: Most patients (59.6%) were female, the mean age was 77 ± 8 years, 40.5% over 80 years. The majority (46.8%) had a diagnosis of HFPEF and BNP median 335 pg/ml, 25% presented SHF and BNP median of 573 pg/ml and 28% did not meet the criteria for NHF and median BNP 45 pg/ml (Kruskal-Wallis's test; p < 0.005) fig. 1. Ejection fraction less than 44% was observed in 18.6%. BMI was greater than30kg/m^{2}in 38.6% and less than 22kg/m^2 at 13%. Cardiomegaly was prevalent in 72.7%, congestion in 70.7%, 52.5% had pleural effusion, and 18% EEC less than 30ml/h. Half of the deaths were caused by HF. In the group with SHF was 79 deaths (49%) with a BNP median of 800 pg/ml (Fig.2) and the 80 survivors median 383 pg/ml (p < 0.005). In HFPEF group occurred most deaths that computed 157 deaths (52% of the group) with a median of BNP 380 pg /ml and 140 survived with a median 245 pg/ml (p < 0,005). The NHF group had 40 deaths (22% of the group) with BNP median of 59pg/ml and 138 survivors, median of 36 pg/ml (p < 0,005).Survival analysis in 78 months (6.5 years) was performed by Kaplan-Meier curve. Two hundred seventh six deaths were recorded in the total group (42%) (Fig3).The group SHF with a 27-month mean survival time (MST), the group HFPEF with a 52-month MST, the NHF group more than 50% survived.
Conclusion: The BNP level showed association with the mortality index. BNP is an

independent prognostic biomarker for long-term mortality in patients with HF in all ages. The BNP shows good accuracy for diagnostic to HF.

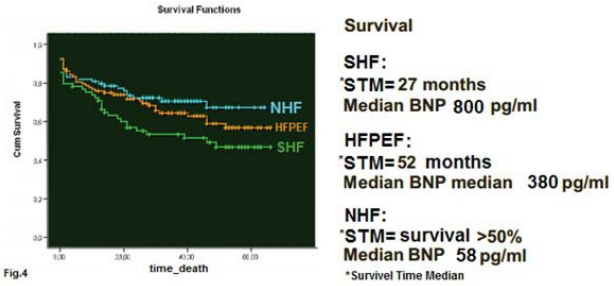


Fig.4

P1989

Results of 3-week rehabilitation in patients with heart failure with reduced and preserved ejection fraction

Y Yuriy Dovgalyuk[1]; IE Mishina[1]; SL Archipova[1]; MV Kudryashova[1]; AA Guduhin[1]; LY Kornilov[1]; LL Yarchenkova[1]; VV Belova[1]; NN Panueva[1]
[1]*Ivanovo State Medical Academy, Ivanovo, Russian Federation*

Objective: to evaluate the impact of 3-week cardiac rehabilitation (CR) program on the exercise tolerance, lipid blood profile, blood pressure in patients with heart failure and reduced ejection fraction (HFrEF) and in patients with heart failure and preserved ejection fraction (HFpEF).
Methods: 26 patients with HFrEF (mean age – 57.3 ± 11.2 years; men – 80.8%, women – 19.2%) and 94 patients with HFpEF (mean age – 59.2 ± 6.1 years; men – 70.2%, women – 29.8%) were underwent an inpatient 3-week CR program. The CR program consisted of physical exercise, lifestyle modification, and pharmacotherapy. Exercise tolerance, serum lipoproteins, blood pressure were assessed at baseline and follow-up.
Results: Patients with HFrEF compared to those with HFpEF more often had risk factors such as diabetes mellitus (23.1% vs. 11.7%, p < 0.0001) and smoking (57.7% vs. 22.3%, p < 0.0001). The rate of patients that achieved lower LDL cholesterol (<100 mg/dl), total cholesterol (<200 mg/dl) and triglyceride (<150 mg/dl) values at discharge was high in patients with HFrEF compared to those with HFpEF (88.5% vs. 75.5%, p < 0.05). There was no difference in blood pressure between two groups at baseline. At discharge systolic blood pressure was substantially lower in the HFrEF group compared to the HFpEF group (115.6 ± 27.2 vs. 127.1 ± 14.2 mmHg, p = 0.01). Maximal power during exercise test improved substantially both in HFrEF group (from 89.8 ± 21.2 to 127.4 ± 34.0 Watts, p < 0.01) and in HFpEF group (from 99.7 ± 12.1 to 130.2 ± 16.8 Watts, p < 0.001). The distance covered in the 6-min walk test was significantly greater after the 3-week cardiovascular training both in patients with HFrEF (393.4 ± 78.7 vs. 452.9 ± 92.5, p < 0.05) and in patients with HFpEF (420.7 ± 48.6 vs. 474.6 ± 57.1, p < 0.05).
Conclusion: patients with HFrEF and HFpEF both benefited from participation in 3 week CR program, as their lipid profile, blood pressure and exercise tolerance improved.

P1990

Clinical pattern of HF-pEF and role of comorbidity in development of HF-pEF

Y Dubolazova[1]
[1]*the National Research Center for Preventive Medicine, Moscow, Russian Federation*

Purpose: To study clinical pattern and role of comorbidity in development of HF-pEF, to evaluate association between comorbidity and NT-proBNP and galectin-3 in HF-pEF.
Methods: 30 patients with HF-pEF (>50%) (17 women, 13 men, age 65 ± 8) were included in the study. All patients were undertaken physical examination, evaluation of comorbidity, clinical state rate scale, 6 minute walk test, echocardiography, tissue doppler imaging, evaluation of plasma NTproBNP and galectin3 levels.
Results: The mean age was 65 years. Main complaints were dyspnea and fatigue (100% and 83%). Dyspnea at rest, edema, orthopnea were found in 6%, 46% and 6% of patients. Decompensation in HF-pEF patients was accompanied by weight gain in 30%. Small bubbling rales was found in 53%, tachycardia in 30%, third heart sound in 7 %, jugular venous distention in 40%, hepatomegaly in 20% of HF-pEF patients. Mean exercise tolerance was 334 m. by 6 minutes walk test. Dyslipidemia was found in 70%, obesity in 53% and fatty liver in 60% of patients. T2DM in 13%. Arterial hypertension was found in 93%, CAD in 60%, COPD in 16% of HF-pEF patients. History of ACS and stroke had 16% and 10% of patients. Atrial fibrillation was found in 23%, HF NYHA I-II in 53%, HF NYHA III-IV in 46%. The mean NT-proBNP level was 153,2 fmol/mL. Mean galectin3 plasma level was 0,98 ng/mL. The higher mean NT-proBNP level was associated with more expressed signs and symptoms of HF (r = 0,46, p < 0,05, 95% CI). The higher mean NT-proBNP level is associated with lower exercise tolerance in HF-pEF patients (r = –0,41, p = 0,02, 95% CI) and worse clinical state (r = 0,48, p = 0,006, 95% CI). Direct correlation between plasma level of NT-proBNP and dyslipidemia (r=0,47, p = 0,007, 95%CI), fatty liver (r=0,42,p = 0,02, 95%CI) and obesity (r=0,34,p = 0,05, 95% CI) was found. Direct correlation between mean plasma level of galectin3 and LV EF in HF-pEF patients was found (r = 0,45, p = 0,012, 95% CI). There was no correlation between galectin3 mean plasma level and signs and symptoms of HF, exercise tolerance and clinical state in HF-pEF patients.
Conclusions: Clinical pattern of HF-pEF is indistinct. Main comorbidities are obesity, AH and CAD. Obesity, dyslipidemia and fatty liver probably could lead to development and progression of HF-pEF. NT-proBNP could be used to identify decompensated HF-pEF. Galectin3 cannot be used as biomarker of decompensation of HF, but can help to indentify HF-pEF patients. Combined use of NTproBNP and galectin3 allows identifying patients with decompensated HF-pEF.

P1991

Heart failure in patients with hypothyroidism

NINO Latsabidze[1]
[1]*Elizabeth Blackwell Hospital, Cardiology, Tbilisi, Georgia Republic of*

The cardiovascular system is the main target organ of thyroid hormone. Overt hypothyroidism decreases myocardial contractility, and diminished myocardial contractility reduces thyroid hormone metabolism. Subclinical hypothyroidism also exhibits impairment of left ventricular diastolic function that returns to normal after thyroid hormone replacement. We investigate 12 with overt hypothyroidism, 15 with subclinical hypothyroidism subjects. The patients were evaluated for cardiac disease by physical examination, electrocardiography, and echocardiography. Serum samples were taken for free thyroxine (fT4), TSH, NT-pro BNP before and after achievement of euthyroidism in patients.
Results: Basal mean NT-pro BNP level of overt hypothyroid group was significantly higher than the subclinical hypothyroid group (98.8 ± 63.0 vs 43.40 ± 23.66 pg/ml, P < 0.001). Mean NT-pro BNP significantly decreased after achievement of euthyroidism in both group (P=0.002). Basal NT-pro BNP level was negatively correlated with heart rate in hypothyroid group (r: –0.6, P=0.03).
Conclusion: Studies to date suggest that thyroid hormone is one of the important factors that regulate serum NT-pro BNP level. Thus, in patients without severe cardiac dysfunction, elevated NT-pro BNP level may be suggestive for both group - as overt hypothyroid, as subclinical hypothyroidism too.

P1992

Heart failure with preserved ejection fraction in black african people. what is the profile?

K A Kassi Anicet Adoubi[1]; E Soya[1]; C Konin[1]; A Adoh[1]
[1]*Institut de cardiologie d'Abidjan, Abidjan, Cote d'Ivoire*

Background: regional variations exist in heart failure with preserved ejection fraction (HFpEF).
Objectives: To determine clinical characteristics of HFpEF among black African patients.
Methods: We analyzed data from 302 consecutive black African patients hospitalized for heart failure in our institute (Ivory Coast) and followed up during one year. We considered HFpEF (group1), heart failure with mid-range (HFmrEF), group 2 and reduced ejection fraction (HFrEF), (group3) as defined in 2016 ESC guidelines for HF.
Results: Forty seven patients (18.7%) had HFpEF, 44 (17.5%) HFmrEF and 160 patients (63.7%) HFrEF; Fifty-one patients had excluding structural heart diseases. There was no gender difference (36.2% of female (group 1), 45.5% (group 2), and 32.5%, p = 0.28) but HFpEF patients were older (62.1 ± 17 years (group 1), 60 ± 15.2 (group 2), 52.2 ± 1.2 (group 3); p < 0.0001). These patients were more often admitted with pulmonary edema (27.7% (group 1), 9.1% (group 2), 11.3% (group 3), p = 0.01) and had more often comorbidities (4.1 ± 1.7 (group 1), 3.9 ± 2.1 (group 2), 3.3 ± 1.7 (group 3) p = 0.004). Hypertension was its most frequent aetiology (63.8%).

Survival was better (569.9 ± 38.4 days (group 1) vs 456.1 ± 24.7 days (group 3); (log-rank = 4.61; p = 0.032).

CELLULAR BIOLOGY

P1993

The effect of pharmacological KATP channels activation on contractile function and gene expression of isolated neonatal rat cardiomyocytes under doxorubicin induced oxidative stress

T Drevytska[1]; K Tarasova[2]; O Linnyk[1]; V Dosenko[1]
[1]*Bogomoletz Institute of Physiology, Department of general and molecular pathophysiology, Kiev, Ukraine*; [2]*National O.O. Bohomolets Medical University, Kiev, Ukraine*

Doxorubicin (DOX) is one of the most effective chemotherapeutic agents. This drug is anthracycline antibiotic and at the same time cardiotoxic agent due to activation of the free-radical oxidation that leads to the progressive heart failure. This requires the search of the grounded approaches for its' use in pharmacological correction of the heart activity. The activator of ATP-depended potassium (KATP) channels contradicts to the doxorubicin action normalizing the biochemical indexes of oxidative stress and histological changes in the heart. The aim of the work is to study the mechanisms of the potential cardioprotector - fluorine-containing analogue of diazoxide - action on the contractile function of cardiomyocytes and gene expression in these cells under DOX induced oxidative stress. Ventricular myocytes were isolated from 2-days-old Wistar rats by enzymatic digestion. After 48-hours of cultivation cardiomyocytes were treated for 1 h with doxorubicin hydrochloride (2.5μM) and with or without fluorine-containing analogue of diazoxide – 7-difluoromethoxy-3-methyl-1,2,4-benzothiadiazine-1,1-dioxide (40 μM). Mechanical properties of rat ventricular cells were assessed using the Myocyte Contractility Recording System IonOptix. RNA isolation was performed using phenol-chloroform extraction with guanidine isothiocyanate. cDNA was synthesized by reverse transcription. Real-time PCR was for quantitative evaluation of HIFs subunits, GLUT-1, GLUT-4, and TERT mRNA. Data are present as means ± SE of four independent experiments. The analysis of variance was performed using one-way ANOVA. The equality of variances between groups was analyzed using the Level test. Cardiomyocytes under the administration of DOX contracted more frequently and arrythmically comparing to the control, but their shortening was significantly weaker. Cells perfused with the solution containing diazoxide analogue, demonstrated increase of the shortening amplitude comparing to the control and decrease of the contraction and relaxation time. Combined action of DOX and diazoxide analogue improved cardiomyocytes contractile activity (lowered the beating rate, stabilized the rhythmicity of contractions) and increased the velocity parameters comparing to the DOX and control groups. Combined action of DOX and diazoxide analogue increased expression of mRNA of HIF-1α, GLUT-1, GLUT-4 and TERT genes and reduced the expression of HIF-3α comparing to the use of DOX only. The data obtained allow us to suppose that the significant antiarrythmic and cardioprotective effects of the KATP channels activator can be explained in particularly by its' property to suppress mRNA of HIF-3α gene expression. These results might represent a potential therapeutic approach for the protection of the heart from the doxorubicin-induced free-radical oxidation and progressive heart failure.

P1994

Role of platelet surface receptor expression and blood group in predicting risk of bleeding with aspirin

R Khalil[1]; E Dunne[2]; D Kenny[3]
[1]*Royal College of Surgeons in Ireland, School of Medicine, Dublin, Ireland*; [2]*Royal College of Surgeons in Ireland, Department of Molecular and Cellular Therapeutics, Dublin, Ireland*; [3]*Royal College of Surgeons in Ireland, Clinical Research Center, Dublin, Ireland*

Aspirin (ASA) is the first-line therapy for the secondary prevention of cardiovascular events(1). Platelet response to ASA is highly variable between individuals, and is associated with varying risks of bleeding. This study examined the role of platelet surface receptors and blood group in determining this risk of bleeding attributable to ASA.

Platelet GPIb-IX-V receptor binds Von Willebrand Factor (VWF) and initiates platelet aggregation by capturing platelets to damaged subendothelium. GPIIb/IIIa receptor binds fibrinogen and is essential in the formation of a primary platelet plug by mediating cross-linkage of platelets. We recruited 20 healthy volunteers and administered 300mg ASA. We evaluated the standard response of ASA to Arachidonic Acid-induced platelet aggregation using Light Transmission Aggregometry. Plasma TxB2 (product of activated platelets) and Glycocalicin (soluble GPIb normally found in plasma) were measured using ELISA. The surface expression of GPIIB/IIIa and GPIb were measured using flow cytometry.

LTA and post-ASA TxB2 demonstrated standard effects of ASA on platelet aggregation ($p < 0.0001$, student t-test, n=19 and $p < 0.0001$, student t-test, n=20 respectively). Donors with blood group O had significantly less surface expression of GPIb counts compared to non-O donors ($p = 0.0288$, student t-test, n=10). Interestingly, both groups had almost identical Glycocalicin post-ASA, suggesting that the reduced GPIb expression in blood group O can't be explained by shed plasma GPIb.

Our results suggest for the first time that blood group plays a crucial role in platelet CD42b receptor expression, independent of plasma Glycocalicin levels. This can be used to possibly determine the individual risk of ASA bleeding.

GENE AND CELL THERAPY

P1995

Assessment of grafts patency and diastolic dysfunction in patients after coronary artery bypass grafting and cell-based therapy.

A Nemkov[1]; V Komok[1]; S Beliy[1]; V Lukashenko[1]; YI Zhang[1]; A Kobak[1]; E Babenko[1]; B Afanasiev[1]
[1]*St-Petersburg State Pavlov Medical University, St-Petersburg, Russian Federation*

Background: It is very little known about influence of cell-based therapy on diastolic dysfunction in patients after coronary artery bypass grafting (CABG) and intramyocardial injection of bone marrow stem cells (BMSC).

Purpose: Assessment of grafts patency and diastolic dysfunction in patients after CABG and cell-based therapy.

Methods: Patients with coronary artery disease were randomly divided on 3 groups: group 0 - control n=36, patients received only CABG; group 1- patients received CABG and intramyocardial injections of BMSC n=25; group 2- patients received CABG and intramyocardial and intracoronary injections of BMSC n=17.

1 year after operation clinical assessment, echocardiography and angiography was performed.

Preliminary results. All patients are alive. Decreasing of functional class of angina pectoris, graft patency, improvement of diastolic dysfunction was more dramatically achieved in patients of group 2.

Conclusion: intramyocardial and intracoronary injections of BMSC is a safe and useful procedure during CABG for patients with coronary artery disease and diastolic dysfunction.

ISCHEMIA - REPERFUSION - PRECONDITIONING - POSTCONDITIONING

P1996

High-intensity lipid-lowering therapy prevents pathological left ventricle remodeling after STEMI

AN Parkhomenko[1]; OI Irkin[1]; IA Iaroslav Lutay[1]; AA Stepura[1]; SP Kushnir[1]; DA Bilyy[1]
[1]*National Scientific Center "M.D. Strazhesko Institute of cardiology, MAS of Ukraine", Kiev, Ukraine*

According to current guidelines, statin therapy is indicated for all ACS patients regardless of the initial cholesterol level. However, the effects of different lipid-lowering regimes on left ventricular remodeling in patients after STEMI have been insufficiently studied.

The study involved 135 STEMI patients admitted an average of 4.5 hours after symptoms onset and treated with primary PTCA. Lipid-lowering treatment was prescribed immediately after hospital admittance. Patients were randomly assigned to one of four groups treated by average (group I and group II) or high (group III and group IV) intensity lipid-lowering therapy. Group I (26 patients) was assigned to atorvastatin 10 mg /ezetimibe 10 mg combination, group II (24 patients) - to atorvastatin 40 mg, group III (42 patients) - to atorvastatin 40 mg/ ezetimibe 10 mg combination, and group IV (43 patients) – to atorvastatin 80 mg. Echocardiography was performed to all the patients during the first 24 hours after symptoms onset and 90 days after MI development. LV dilatation was defined as at least 25% increase of end-diastolic volume.

Patients from groups III and IV showed a tendency to the reduction of post-MI LV dilatation after 3 month of treatment (figure 1). High intensity lipid-lowering therapy (figure 2) reduced the risk of LV remodeling by 30% ($p < 0.05$), that was also associated with significantly higher LDL reduction. Without initial differences,

on the 90th day the average LDL level was 1.63 ± 0.1 in pts with high intensity treatment vs. 2.21 ± 0.2 mmol /l in patient with therapy of average intensity ($p < 0.01$).

Conclusion: The use of high-intensity lipid-lowering therapy with achievement of target LDL levels after STEMI can reduce the incidence of post-MI LV dilatation and may prevent heart failure development.

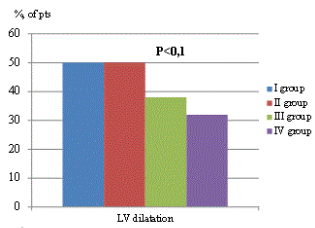


Figure1.

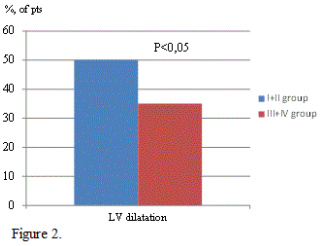


Figure 2.

P1997

Can we predict heart failure after anterior ST-elevated myocardial infarction?

S Snezana Tadic[1]; A Stojsic-Milosavljevic[1]; A Ilic[1]; M Stefanovic[1]; S Stojsic[1]; M Sladojevic[1]; R Jung[1]; J Dejanovic[1]
[1]*Institute of CVD Vojvodina, Sremska Kamenica, Serbia*

Objective: Patients with ST-elevated myocardial infarction (STEMI) treated by primary angioplasty (pPCI) will develop left ventricular remodeling in one third of the cases, which is main cause of heart failure (HF) and mortality. The purpose of this study is to determine early angiographic predictors.

Methods: 210 patients with a first acute anterior STEMI were included. All participants underwent echocardiography after 6 months, after which they were divided into two groups: remodeling (n = 55; 26%) and non-remodeling (n = 155; 74%). The criteria for remodeling was increasing of left ventricular end-diastolic volume >20% after 6 months.

Results: The group with remodeling had more frequent MACE during one year follow-up: repeated hospitalizations (61.8% vs 22.6%; $p < 0,0001$), myocardial infractions (20% vs 7.1%; $p = 0.007$), repeated coronary angiography (45.5% vs 18.1%; $p < 0,0001$), repeated PCI ((30.9% vs 11%; $p = 0.001$) and mostly re-hospitalizations due to HF (40% vs 2.6%; $p < 0.0001$). Mortality rate was 5.5%. We identified a lot of statistically significant differences between remodeling and non-remodeling groups, among them angiographic parterres: proximal localisation of RIA (63.6% vs 43.9, $p = 0,041$), occlusion of RIA (90.9% vs 69%, $p = 0,001$), lower TIMI flow before pPCI (average 0.09 vs 0.31, $p = 0,001$) and after pPCI (average 2.75 vs 2.91, $p = 0,003$), lower blush grade after pPCI (3.55 vs 3.75, $p = 0,015$), no-reflow phenomenon (40% vs 1.9%, $p < 0,0001$) and use of GP IIb/IIIa (40% vs 24.5%, $p = 0,029$). The most powerful independent early predictors were: no reflow phenomenon (OR=30.031 95% CI, $p < 0.0001$), diastolic dysfunction in the first 24hrs (OR=27.7 95% CI, $p < 0.0001$) and at admission Killip class 2-4 (OR=3.4 95% CI, $p = 0.003$), by multi-variant regression analysis. Also, strong predictors were incomplete ST-resolution- STR (OR 2.0 95% CI, $p = 0,024$) and Wall motion score index (WMSI)>2 (OR 21.6 95% CI, $p < 0.0001$), by uni variant regression analysis.

Conclusions: Some angiographic parameters as: no-reflow phenomenon, proximal localisation and occlusion of RIA, lower TIMI flow and blush grade after pPCI, use of GP IIb/IIIa, can identified high-risk group for post-infarction remodeling in the patients with a first acute anterior STEMI, treated by pPCI. Development of diastolic dysfunction, heart failure on admission, incomplete STR and WMSI>2 are strong predictors too. Remodeling patients will have a more frequent incidence of MACE, heart failure and mortality.

P1998

Myocardial infarction in the elderly (about 120 cases)

A Alaeddine Jalled[1]; NEJEH Ben Halima[2]
[1]*University of Tunis El Manar, cardiology departement, La Marsa, Tunisia*; [2]*IBN EL Jazzar hospital , cardiology departement, kairouan, Tunisia*

Background: Due to high mortality and the increasing aging population, acute myocardial infarction in the elderly is a public health issue; the event is often marked by severe major complications that influence the prognosis in the short and medium term.

Methods: We report a descriptive retrospective study involving 120 patients (55 men and 65 women) aged 75 or more admitted to the cardiology department Kairouan (Tunisia) for a myocardial infarction. They are collected between 2002 and 2013.

Results: The incidence of myocardial infarction in patients over 75 years between 2002 and 2013 is 14.6%. the age means of the population is 78.8 ± 3.05 years, ranging from 75 to 94 years. Hypertension is the most common risk factor found: 65% while 32.5% were diabetics and 16.7% were smokers. Only 40.8% of the population were supported in the first 06 hours while 13.4% after 12 hours. Among 120 patients, reasons for admission to the ED included chest pain(62.5%) , digestive symptoms 16.7%, dyspnea 8.3%, malaise 8.3 % and vigilance disorders in 4.2% of cases. Compared with those who presented with chest pain , patients admitted for other reasons are more women ($p < 0.01$) , diabetics ($p < 0.01$) having kidney failure($p = 0.03$), they waited longer before going to the hospital (prehospital delay >12 hour: 31.5 % vs 6.8 % $p < 0.01$ •A myocardial revascularization treatment was performed in 72 patients (60%). It was a thrombolysis in 35% of cases and angioplasty in 25% of cases, the remaining(40%)were treated medically. During the study period we notice an improvement in the use of reperfusion and a decrease of using medical strategy. At the hospital phase the overall mortality rate was 15.8%,The statistical logistic regression analysis has identified as significant predictors factors of mortality :female sex($p = 0.04$); diabetes($p = 0.01$); kidney failure ($p = 0.05$); the anterior territory of the infarction ($p = 0.02$); the myocadiel infarction complicated by acute heart failure ($p = 0.01$) or cardiac shock ($p < 0.01$) and finally the abscence of a revascularization ($p = 0.01$).

Conclusion: Take charge of elderly patients with STEMI is not easy especially that atypical clinical symptom are common and severe but chronological age should not be an exclusive criteria of decision and even a factor of “loss of chance”. we should use the specific reperfusion treatments which improve the prognosis of these patients.

P1999

Prognostic impact of anemia on long-term mortality in patients with reduced ejection fraction following acute myocardial infarction

L Savic[1]; I Mrdovic[1]; M Asanin[1]; G Krljanac[1]; R Lasica[1]; B Kastel[1]
[1]*Clinical Center of Serbia, Institute for Cardiovascular Disease, Emergency Hospital, Belgrade, Serbia*

Purpose: Anemia is a relatively common disorder in patients with acute myocardial infarction. The aim of this study is to analyse prognostic impact of anemia at admission on five year mortality in patients with reduced ejection fraction (EF) following ST-elevation myocardial infarction (STEMI).

Method: We included 589 consecutive STEMI patients who were treated with primary percutaneous coronary intervention (pPCI). Reduced EF was defined as being ≤40%. Anemia was defined as baseline hemoglobin level <13g/dl in men and <12g/dl in women. Patients presenting with cardiogenic shock were excluded.

Results: Anemia at admission was present in 69 (11.7%) patients. Median hemoglobin on admission was 11g/dl(10-12g/dl) in anemic patients and 14g/dl(13-15g/dl) in patients without anemia, $p < 0.001$. Compared with patients without anemia, patients with anemia were older, and presented more often with heart failure (Killip class II and III); they were more likely to be women to have lower baseline creatinine clearance and lower systolic blood pressure at admission; they had more often 3-vessel coronary disease on initial angiogram. Therapy at discharge and the duration of dual antiplatelet therapy during follow up did not differ among analysed patients. Five year all-cause mortality rate was significantly higher in patients with anemia as compared with those without anemia: 43.9% vs 17.8%, $p < 0.001$ (Figure 1). After multivariable adjustements in Cox regression model anemia at admission was an independent predictor of all-cause mortality-HR 1,95 (95%CI 1,30-3,29), $p = 0.021$, besides (older) age, Killip class II-III at admission, baseline renal dysfunction and postprocedural flow TIMI < 3.

Conclusion: In analysed patients with reduced ejection fraction following STEMI the presence of anemia at admission is associated with 2-fold increase in long-term mortality

Figure 1. Kaplan-Meier curves estimating estimatimg the probabillity of 5-year mortality according to teh presence of anemia

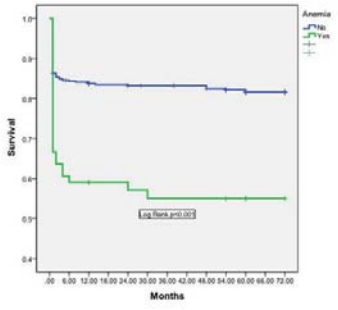


Figure 1.

P2000

The evaluation of treatment retention to dual therapy with antiplatelet drugs in real clinical practice

SV Malchicova[1]; NS Maksimchuk-Kolobova[1]
[1]*Kirov State Medical Academy, Kirov, Russian Federation*

Objective: to evaluate the retention of patients, who had an acute coronary syndrome (ACS), to dual therapy with antiplatelet drugs (DTAD) in real clinical practice.
Materials and methods: The study involved 41 patients with earlier ACS and whom DTAD was recommended were during 12 months. The average age was 62,3 ± 8,7 years old, from them 23 women and 18 men. Patients were divided into 4 groups depending on the prescription of ACS. 10 patients were involved in the group 1 (1 month after ACS), 13 patients in the group 2 - (3 months after ACS), 10 people in the group 3 and 4 (6 months and no more than 12 months, respectively). Treatment retention was evaluated by use of telephone survey on the number of patients who is taking the drug.
Results: Treatment retention to DTAD was 90% already after 1 month after earlier ACS, and only 60% of patients followed the recommendations for anti-thrombotic therapy by the end of the year after ACS. At the same time, retention to therapy by acetylsalicylic acid was 90% throughout the year. The retention to clopidogrel was 100% at 1 and 3 months after ACS, it decreased to 80% over 6 months , and to 60% over 12 months. The reasons for refused treatment were: 50% of patients stopped taking drugs because of adverse drug reactions fear, 25% because of well-being, for 25% of patients clopidogrel was canceled by doctor.
Conclusions: Nevertheless on the proven effectiveness of DTAD in prevention of complications after ACS and reducing the risk of death, the treatment retention to DTAD is still insufficient in real clinical practice, decreasing to 12 months after ACS until 60%. The main way to increase the treatment retention to DTAD is to hold the explaining actions to physicians by patients about the need to keep to recommendations.

VASCULAR BIOLOGY, OTHER

P2001

The senescent CD8+ T cell population is expanded in chronic kidney disease patients and correlated with arterial stiffness

JY Kim[1]; JC Youn[2]; SW Choi[2]; SW Han[2]; KH Ryu[2]; S Park[3]; EC Shin[4]
[1]*Yonsei University College of Medicine, Division of Cardiology, Seoul, Korea Republic of*; [2]*Dongtan Sacred Heart Hospital, Division of Cardiology, Hwaseong, Korea Republic of*; [3]*Yonsei University College of Medicine, Division of Cardiology, Severance Cardiovascular Hospital, Seoul, Korea Republic of*; [4]*Korea Advanced Institute of Science and Technology, Laboratory of Immunology and Infectious Diseases, GSMSE, Daejeon, Korea Republic of*

Funding Acknowledgements: Basic Science Research Program through the NRF of Korea funded by the Ministry of Science, ICT & Future Planning (NRF-2015R1C1A1A02036645)

Background: Chronic kidney disease (CKD) is associated with increased arterial stiffness, which is a well-known predictor of future cardiovascular events. However, the underlying mechanisms of arterial stiffening in CKD are not well known. Accelerated immune aging, characterized by expansion of immunosenescent T cell fraction might be involved in the pathogenesis of arterial stiffening in CKD.
Purpose: We aimed to evaluate the relationship between arterial stiffness and immunosenescent T cell (CD8+CD57+ or CD8+CD28- T cell) fraction in patients with CKD.
Methods: Four hundred and twenty-nine consecutive hypertensive patients with CKD (266 male, mean age 61 ± 10 years) who registered in Cardiovascular and Metabolic Disease Etiology Research Center - High Risk Cohort (CMERC-HI, NCT02003781) were enrolled. Arterial stiffness was evaluated by pulse wave velocity (PWV) and the frequency of CD57+ or CD28- senescent T cells in peripheral blood lymphocytes were examined by multicolor flow cytometry.
Results: Senescent CD8+ T cell fraction showed significant tendency to increase according to CKD stages (CD8+CD57+ T cell fraction, $p < 0.001$; CD8+CD28- T cell fraction, $p < 0.001$). Multivariate analysis revealed that CD8+CD57+ T cell fraction is independently associated with PWV even after adjustment with age, gender, body mass index, renal function and systolic blood pressure (β=0.102, $p = 0.038$). Next, we asked if CMV-specific CD8+ T cells correlate with the expansion of senescent T cells and increased arterial stiffness. To this end, we are currently under investigation for CMV-specific CD8+ T cell responses using 9 different CMV antigens (pp65, IE-1, IE-2, UL94, pp150, pp71, glycoprotein B, US3, UL48) by IFN-γ ELISpot assay.
Conclusion: In CKD patients, CD8+CD57+ T cell fraction are expanded and independently associated with increased arterial stiffness. These findings may explain the role of immunosenescence in the pathogenesis of accelerated arterial stiffening in patients with CKD.

P2002

Relationship between body composition and endothelial dysfunction in heart failure patients and chronic obstructive pulmonary disease

AG Abril Guadalupe Jimenez Cepeda[1]; D Gonzalez-Islas[2]; A Orea-Tejeda[2]; G Perez- Cortes[2]; A Navarrete-Penaloza[2]; L Verdeja- Vendrell[2]; R Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; A Figueroa-Herrera[2]; B Robles Uribe[2]; SC Torres-Montiel[2]
[1]*Universidad Autonoma del Noreste, Nutricion Clinica , Saltillo, Mexico*; [2]*Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clínic , Mexico, Mexico*

Background: Chronic obstructive pulmonary disease (COPD) is associated with a high risk of cardiovascular mortality and endothelial dysfunction, there is known that when endothelial dysfunction increases the GOLD increase too, in the same way the prevalence of cachexia in patients with Heart failure (HF). However, there is not information about linking body composition and endothelial function, or this mechanisms in patients with HF and COPD.
Objectives: To evaluate if there is a relationship between endothelial dysfunction (ED) and type of body composition in patients with HF and COPD.
Methods: A cross-sectional study included patients older than 18 years with a confirmed diagnosis of COPD and HF who decided to participate. Body composition was classified according to the electrical bioimpedance by vector analysis (BIVA) in 3 groups: normal body composition, obesity and cachexia. Endothelial function was assessed by photoplestimography. ED was considered in those with a time index of maximum amplitude / over total time of the pulse curve (TAM / TT index) > 0.30 at 120 seconds post ischemia.
Results: 88 patients (56.8% female and 43.2% male) were recruited; age mean was 70.89 ± 11.77 years. The most frequent co-morbidities were COPD, 81.8% of which 45.2% were by biomass, 47.9% by smoking, and the rest were mixed; systemic hypertension 55.7%, diabetes 18.2%, obstructive sleep apnea syndrome 15.9%, pulmonary thromboembolism 13.6% and dyslipidemia 12.5%. The prevalence of endothelial dysfunction (ED) was 63.5%. There was a higher prevalence of ED in obese subjects (78.6%) compared to normal and cachectic body composition (78.3% and 52.1%, $p = 0.044$, respectively). The TAM / TT index was 0.38 ± 0.08 in obese subjects, 0.34 ± 0.05 in normal and 0.32 ± 0.06 in cachectic $p = 0.02$.
Conclusions: In this subjects prevalence of ED is high and predominates in obese subjects. Probably caused by adipokines domination upon the endothelium and that may the reason of a high risk in this patients.

BASIC SCIENCE - TRANSLATIONAL BIOMARKERS AND CARDIO-RENAL SYNDROME

P2004

Ranolazine partially blunts ado trastuzumab emtansine related cardiotoxicity

N Nicola Maurea[1]; C Coppola[2]; G Piscopo[2]; G Riccio[3]; D Rea[4]; R De Vecchis[5]; C Maurea[2]; G Sorrentino[2]; C De Lorenzo[6]; M De Laurentiis[7]
[1]National Cancer Institute G. Pascale, Naples, Italy; *[2]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCCS, Division of Cardiology, Naples, Italy*; *[3]Federico II University of Naples, Department of Pharmacy, Naples, Italy*; *[4]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCCS, Animal Facility, Naples, Italy*; *[5]Elena d'Aosta Hospital, Department of Cardiology, Naples, Italy*; *[6]University 'Federico II', Department of Molecular Medicine and Medical Biotechnology , Naples, Italy*; *[7]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCSS, Department of Breast Surgery and Cancer Prevention, Naples, Italy*

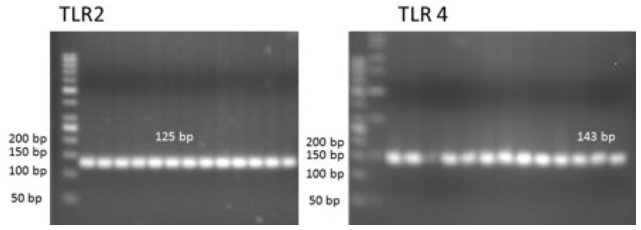
Background: Ado trastuzumab emtansine (TDM1) is a novel antibody–drug conjugate consisting of trastuzumab (TRAS) covalently linked to the highly potent microtubule inhibitory agent DM1 via a stable thioether linker. TDM1 is used in metastatic ErbB2 positive breast cancer patients, previously treated with TRAS and taxane. Although, the potential cardiotoxic effects of TDM1 have not yet been fully elucidated, they can include all the mechanisms of TRAS-related cardiotoxicity, such as changes in Ca2+ regulation related to blockade of ErbB2, PI3K-Akt and MAPK pathways. Here, we aim to elucidate whether Ranolazine (RAN), administered after TDM1 treatment, blunts or not cardiotoxicity in vivo and in vitro.
Methods: In vitro, human fetal cardiomyocytes (HFC) were treated with TDM1 for 3 days and then treated in the absence or presence of RAN for 3 days. Cell viability was assessed by cell counting and MTT assay. To evaluate cardiac function in vivo, C57/BL6 mice, 2-4 months old, were daily treated with TDM1 (44.4 mg/kg/day). At day 0 and after 7 days, fractional shortening (FS) and ejection fraction (EF) were measured, by M/B mode echocardiography, and radial and longitudinal strain (RS and LS) were evaluated using 2D speckle-stracking. These measurements were repeated after 5 days of RAN treatment (305 mg/Kg/day), started at the end of TDM1 treatment.
Results: RAN reduces TDM1 toxicity in HFC, as evidenced by the higher percentage of viable cells treated with TDM1 + RAN with respect to the cells treated with TDM1 alone ($p < 0.01$). In in vivo studies: after 7 days with TDM1 administration, FS decreased to 53.6 ± 0.9%, versus 61.0 ± 0.8 % (sham), ($p < 0.01$), and EF decreased to 85.5 ± 3.5 % versus 91.0 ± 0.8% (sham), ($p < 0.01$). Moreover, RS decreased to 20.92 ± 3.2 % versus 42.2 ± 10.1% (sham) ($p < 0.01$), and LS decreased to -15.5 ± 2.8 % versus -23.6 ± 6.7% (sham), ($p < 0.01$).
In mice treated with TDM1 and, successively treated with RAN for 5 days, the indices of cardiac function partially recovered: FS 58 ± 2.4 % ($p < 0.05$), EF 88.8 ± 1.7 %, ($p < 0.05$), RS (35.7 ± 8.2 %, $p > 0.05$), whereas the alteration of LS persists even after treatment with RAN (-17.3 ± 3.7 %, $p > 0.05$)
Conclusions: Here we show that in vivo RAN post-treatment reduces cardiotoxic effects due to TDM1, as demonstrated by the recovery of FS, EF and RS values. As expected, RAN increases cell viability of HFC treated with TDM1.

P2005

Customized laboratory TLR4 and TLR2 detection method from peripheral human blood for early detection of doxorubicin induced cardiotoxicity

M Trofenciuc[1]; A Pop-Moldovan[1]; D Darabantiu[1]; M Tomescu[2]; R Christodorescu[2]; H Branea[2]; T Pirvanescu[2]; M Puschita[1]
[1]"Vasile Goldis" Western University of Arad, Faculty of Medicine,County Emergency Clinical Hospital, Arad, Romania; *[2]University of Medicine Victor Babes, Timisoara, Romania*

Background: 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%. Exclusion criteria consisted of: previous anthracycline therapy, previous radiotherapy,history of heart failure or chronic renal failure, atrial fibrillation, 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: blood collection, RNA isolation, cDNA reverse transcription, qRT PCR and quantification of the relative expression. At enrolment all patients were evaluated clinically, an ECG and an echocardiography were performed.
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 ηg/μl. 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 ± 0.19 and for TLR4 0.15 ± 0.04. The corresponding values for the patients who did not develop diastolic dysfunction were 0.16 ± 0.07 for TLR2 ($p = 0.01$) and 0.11 ± 0.10 for TLR4 ($p = 0.2$).
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.



Genetic amplification

P2006

Cardiotoxic effects of the novel anti-ErbB2 agent Ado trastuzumab emtansine

N Nicola Maurea[1]; C Coppola[2]; G Piscopo[2]; G Riccio[3]; R De Vecchis[4]; C Maurea[2]; G Sorrentino[2]; C De Lorenzo[5]; M De Laurentiis[6]
[1]National Cancer Institute G. Pascale, Naples, Italy; *[2]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCCS, Division of Cardiology, Naples, Italy*; *[3]Federico II University Hospital, Department of Pharmacy, Naples, Italy*; *[4]Elena d'Aosta Hospital, Department of Cardiology, Naples, Italy*; *[5]University 'Federico II', Department of Molecular Medicine and Medical Biotechnology , Naples, Italy*; *[6]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCSS, Department of Breast Surgery and Cancer Prevention, Naples, Italy*

Background: Ado trastuzumab emtansine (TDM1) is a novel antibody–drug conjugate consisting of trastuzumab (TRAS) covalently linked to the highly potent microtubule inhibitory agent DM1 via a stable thioether linker. TDM1 is used in metastatic ErbB2 positive breast cancer patients, previously treated with TRAS and taxane. Although the potential cardiotoxic effects of T-DM1 have not yet been fully elucidated, they can include all the mechanisms of TRAS-related cardiotoxicity, such as blockade of ErbB2,PI3K-Akt and MAPK pathways. Furthermore, since TDM1 is also used in combination with other anti-ErbB2 agents, the risk of cardiotoxic side effects could be further increased. Here, we aim to assess the cardiotoxic side effects of TDM1 in vitro and in vivo.
Methods: To evaluate the cardiotoxic effects of TDM1 in vitro, human fetal cardiomyocytes (HFC) and cardiomyoblasts (H9C2) were treated, for 3 days, in the absence or in the presence of increasing concentrations of TDM1 and TRAS. Moreover, to assess the cardiac function in vivo, C57/BL6 mice, 2-4 months old, were daily treated with TDM1 (44.4 mg/kg/day). At day 0 and after 7 days, fractional shortening (FS) and ejection fraction (EF) were measured, by M/B mode echocardiography, and radial and longitudinal strain (RS and LS) were evaluated using 2D speckle-stracking.
Results: TDM1 shows a higher toxicity on HFC and H9C2 cells with respect to TRAS. TDM1 clearly causes more marked changes in HFC cell morphology, cells, that indeed lost their typical features to assume distorted forms (rounded-shape). In in vivo studies: after 7 days with TDM1, FS decreased to 53.6 ± 0.9 %, versus 61.0 ± 0.8 % (sham), ($p < 0.01$), and EF decreased to 85.5 ± 3.5 % versus 91.0 ± 0.8% (sham), ($p < 0.01$), RS decreased to 20.9 ± 3.2 % versus 42.2 ± 10.1 % (sham), ($p < 0.01$), LS decreased to -15.5 ± 2.8 % versus -23.6 ± 6.7 % (sham), ($p < 0.01$).
Conclusions: Here we show for the first time the cardiotoxic effects of TDM1, both in in vitro, and in vivo models.

P2007

Cardiorotective effect of non-peptidic pkr1 agonist against anthracycline-cardiotoxicity.

A Adeline Gasser[1]; M Charavin[1]; B Escoubet[2]; N Messaddeq[1]; L Desaubry[1]; CG Nebigil[1]
[1]*University of Strasbourg, Strasbourg, France*; [2]*University Paris Diderot , Paris, France*

ABSTRACT Doxorubicin induced cardiotoxicity is a well-recognized complication of chemotherapy, and its prevention remains an important challenge in cancer survivorship. An angiogenic hormone prokineticin via its receptor PKR1 promotes angiogenesis, differentiation of cardiac stem cells, and survival of the cardiomyocytes. PKR1 has been recently shown to protect heart against myocardial infarction in mice model. Thus, we hypothesized that PKR1 agonist can be a promising target to prevent doxorubicin-mediated cardiotoxicity.
Methods and Results: In vitro, we showed that IS20 attenuates apoptosis induced by DOX treatment in H9c2 cardiomyocytes and human epicardial derived progenitor cells. However, IS20 does not interfere DOX-mediated cytotoxicity in cancer cell line. In vivo, IS20 administration in juvenile mice model promotes survival, proliferation and differentiation of WT1 + EPDCs into vasculogenic cells. Similarly, IS20 on chronic mice model preserves vascular structure, reduces apoptosis and inflammation. IS20 also improves systolic and diastolic parameters that impaired by DOX.
Conclusions: Multi effects of IS20 on the activation of cardiac progenitor cells, cardiac cells survival, vascular stability and cardiac parameters show a strong cardioprotective potential of PKR1 agonist that can be used in cancer patients during anthracyclines chemotherapy.

P2008

Growth differentiation factor 15 as a predictor of acute kidney injury formation

IR Vishnevskaya[1]; HF Barahmeh[2]
[1]*Government institution "L.T. Malaya Therapy National institute of the National academy of medical sci", Kharkiv, Ukraine*; [2]*V.N. Karazin Kharkiv National University, Kharkiv, Ukraine*

The development of acute kidney injury (AKI) in patient with acute coronary syndrome (ACS), especially in those who underwent angiography, is an actual problem, because it worsens the prognosis. In order to diagnose this condition in time the search for biomarkers is going. Stress-induced marker growth differentiation factor 15 (GDF 15), a member of the transforming growth factor-β cytokine superfamily is being actively studied.
Purpose: to determine the prognostic significance of GDF 15 and other markers in development of AKI in patients with ACS.
Methods: 73 patients were enrolled with different forms of ACS (55 male and 18 female), mean age was 61, 8 ± 1, 3 years. All patients underwent a baseline investigation which includes: standard electrocardiography, echocardiography, angiography and determination of marker of myocardial necrosis – cardiac troponin T. Based on the results of the examination glomerular filtration rate (GFR) was calculated by Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI). 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 level of GDF 15 was determined during the first day of hospitalization (normal range of GDF 15 < 1200 pg / ml).
Results: By comparing selected groups significant difference was found in creatinine level and GFR in both groups ($p < 0.001$; $p < 0.01$, respectively). The effects of various variables were assessed on formation of AKI in patients with different level of GFR. To identify the main risk factors for AKI, we have used logistic regression (LR): ejection fraction of left ventricle (area under curve (AUC) 0.7; $p < 0.01$; 95% confidence interval (CI): 0.560 – 0,842), GDF 15 (AUC 0.77; $p < 0.03$; 95% CI: 0.53 – 0.92) and age (AUC 0.77; $p < 0.01$) were main risk factors for predicting development of AKI. During the statistical analysis the predictive value for estimated parameters was calculated: GDF 15 > 2200 pg/ml (specificity (Spe) 87%, sensitivity (Se) 65%), ejection fraction of left ventricle >46% (Spe 80 %, Se 71 %), age >55 year (Spe 39 %, Se 96 %) We have developed a prognostic model to predict reduced kidney function formation (AUC 0.8; $p < 0.001$). This model with 96% of Se and 68% of Spe can predict development of AKI in patients with different levels of GFR after ACS.
Conclusion: the prognostic multifactor model can be used in clinical practice to improve risk stratification in patients with ACS to prevent formation of AKI.

P2009

Neladenoson, a partial adenosine A1-receptor agonist, improves mitochondrial function in skeletal muscle of dogs with chronic heart failure

HN Hani Sabbah[1]; RC Gupta[1]; V Singh-Gupta[1]; K Zhang[1]; J Xu[1]; B Albrecht-Kuepper[2]
[1]*Henry Ford Hospital, Detroit, United States of America*; [2]*Bayer AG, Wuppertal, Germany*

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Background: Exercise intolerance (Ex-Int) is a feature of chronic heart failure (HF) and in particular, HF with preserved ejection fraction (HFpEF) and attributable, in part, to skeletal muscle (SM) abnormalities of fiber type composition and mitochondrial (MITO) dysfunction. In patients and dogs with HF, SM aerobic, MITO-dependent, type-I fibers decrease in number while anaerobic type-II fibers increase; a maladaptation that contributes to Ex-Int. We previously showed that chronic therapy with capadenoson, a partial adenosine A1-receptor agonist (pA1RA), improves LV function in HF dogs and therapy with neladenoson (NELA), a novel pA1RA, normalizes MITO function in failing cardiomyocytes. This study examined the effects of NELA on MITO function in SM biopsies from normal (NL) dogs and dogs with microembolization-induced HF.
Methods: Fresh SM open biopsies (˜6 grams) were obtained from the hind leg Vastus Lateralis muscle of 6 NL and 6 HF anesthetized dogs. Samples were cut into thin sections, divided into 4 equal portions, and one portion each incubated in 0 (vehicle), 3, 10, and 30 nM concentration of NELA respectively for one hour at 37°C. At end of incubation, MITO were isolated from SM and their function assessed. MITO ADP-stimulated state-3 respiration (ADPresp) was measured using a Strathklein respirometer, MITO complex-IV (COX-IV) activity was measured polarographically and MITO maximum rate of ATP synthesis (ATPsyn) was measured using the bioluminescent ApoSENSOR assay kit.
Results: Increasing concentration of NELA had no effect on measures of MITO function in SM from NL dogs (Table). In SM from HF dogs, depressed levels of MITO ADPresp, ATPsyn, and COX-IV activity increased significantly in a dose-dependent manner after exposure to NELA (Table).
Conclusions: The results indicate that NELA improves MITO function of SM of dogs with HF. These improvements can potentially reduce/reverse Ex-Int in HF.

MITO Function Measures

	Vehicle	3 nM NELA	10 nM NELA	30 nM NELA
NL Dogs (n = 6)				
ADPresp (nAtom Oxygen/min/mg protein)	164±15	161±16	165±13	166±15
ATPSyn (RFU/µg protein)	8835±423	8788±475	8821±524	9051±468
COX-IV Activity (nAtom Oxygen/min/mg protein)	2459±210	2488±316	2545±311	2412±267
HF Dogs (n = 6)				
ADPresp nAtom Oxygen/min/mg protein)	98±5	113±9	171±19*	162±14*
ATPSyn (RFU/µg protein)	3829±440	4210±460	5923±627*	5407±440*
COX-IV Activity (nAtom Oxygen/min/mg protein	1583±197	1745±239	2734±313*	2524±268*

*=$p < 0.05$ vs. vehicle

P2010

Regulation of the balance between cardiac and skeletal muscle triadin by a heart-enriched antisense long non-coding RNA

L Zhang[1]; A Salgado-Somoza[1]; M Vausort[1]; P Leszek[2]; Y Devaux[1]
[1]*Luxembourg Institute of Health, CVRU, Strassen, Luxembourg*; [2]*Institute of Cardiology, the Heart Failure and Transplantology Department, Warsaw, Poland*

Background: Ribonucleic acids (RNAs) are molecules with key roles in cell biology. In the recent years, the so called long non-coding RNAs (lncRNAs), which do not encode for proteins, showed multiple functions in cardiac pathophysiology and they were found to be dysregulated in the failing heart. However, their role in heart failure development is still poorly undrestood.
Purpose To investigate the regulation and function of heart-enriched lncRNAs in the failing heart.
Methods: Public datasets in combination with in-house data were used to identify heart-enriched lncRNAs regulated in heart failure. Biopsies from 43 failing and 23 control human hearts, as well as different mouse organs were used for wet-lab experiments. Gene expression was assessed using quantitative PCR. GapmeRs or

a CRISPR/dCas9-VPR activation approach were used to modulate the expression of lncRNAs in murine cardiomyocytes HL-1.
Results: Analysis of a RNA-seq dataset of 15 Caucasian tissues allowed the identification of 415 heart-enriched lncRNAs. After data mining, we selected a genome region harboring the Triadin (TRDN) gene, that encodes for a protein involved in calcium release from the endoplasmic reticulum and which is associated with cardiac hypertrophy. Five lncRNAs from nonCode4.0 database were localised on the antisense strand of TRDN gene. One of them (arbitrarily named TRDN-AS) was positively correlated with the cardiac isoform of TRDN and negatively correlated with the skeletal muscle isoform of TRDN. Expression levels of TRDN-AS and cardiac TRDN – but not skeletal muscle TRDN – were elevated in biopsies from human failing hearts compared to control hearts (Figure 1a). A mouse homolog of TRDN-AS (Trdn-AS) was identified and found mostly in the nuclear compartment of murine cardiomyocytes HL-1. Activation of the transcription of Trdn-AS using specific guide RNAs in combination with a CRISPR/dCas9-VPR system resulted in an increase of the ratio between cardiac and skeletal muscle isoforms of Trdn (Figure 1b). Down-regulation of Trdn-AS expression using gapmeRs had no effect on the cardiac/skeletal muscle ratio.
Conclusion: We identified a lncRNA named TRDN-AS which regulates the balance between cardiac and skeletal muscle isoforms of TRDN at the epigenetic level. Since TRDN is associated with heart failure, these results suggest a role for TRDN-AS in the development of heart failure. Figure legend. a) Expression levels of TRDN-AS, cardiac and skeletal muscle isoforms of TRDN in left ventricular biopsies from 23 control and 43 failing human hearts. b) Regulation of Trdn isoforms by Trdn-AS. HL-1 cardiomyocytes were co-transfected with SP-dCas9-VPR and gRNA_Cloning Vector with (specific guide RNA, sgRNA) or without (Control) target sequence. Cells were harvested after 48h. 5 independent experiments were performed.

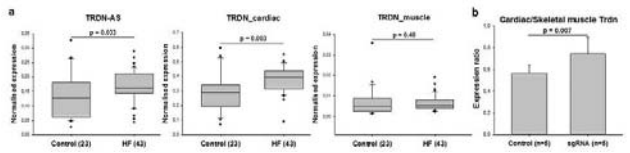

Figure 1

P2011

Iron availability and the expression of genes of oxidative and non-oxidative metabolic pathways in primary human cardiac myocytes cultured upon mechanical stretch

MM Dziegala[1]; M Kasztura[1]; K A Kobak[1]; J Bania[2]; L Kiczak[3]; K Josiak[4]; W Banasiak[5]; P Ponikowski[4]; E A Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland; *[2]Wroclaw University of Environmental and Life Sciences, Department of Food Hygiene and Consumer Health, Wroclaw, Poland*; *[3]Wroclaw University of Environmental and Life Sciences, Department of Biochemistry, Pharmacology and Toxicology, Wroclaw, Poland*; *[4]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; *[5]Military Hospital of Wroclaw, Centre for Heart Diseases, Wroclaw, Poland*

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Background: Iron is presumed to play an essential role in the oxidative energy metabolism of cardiomyocytes. Different iron availability introduced to primary human cardiac myocytes is anticipated to affect the expression of genes involved in oxidative and non-oxidative metabolic pathways in these cells.
Purpose: The aim of the study was to investigate the response of genes involved in non-oxidative glycolysis and oxidative mitochondrial metabolism to increased or reduced iron availability in the environment of human primary cardiac myocytes when cultured upon mechanical stretch.
Methods: Primary human cardiac myocytes (HCM) were cultured for 48 hours: 1) in static conditions; 2) upon mechanical stretch; at the optimal versus reduced versus increased iron concentration (iron chelation with100μM deferoxamine, DFO; iron supplementation with 200μM ammonium ferric citrate, AFC). We analysed the mRNA expression of the genes involved in non-oxidative metabolism: pyruvate kinase (PKM2) and lactate dehydrogenase A (LDHA), as well as genes of mitochondrial enzymatic complexes involved in oxidative metabolism: NDUFS1 (subunit of complex I), UQCRFS1 (subunit of complex III), COX4I1 (subunit of complex IV) and ATP5B (subunit of complex V) using qPCR.
Results: HCM cells when exposed to mechanical stretch demonstrated, as compared to the cells cultured in static conditions, an increased mRNA expression of PKM2 ($p < 0.001$) and LDHA ($p < 0.0001$), suggesting an enhanced glycolysis. Additional exposition of the cells to the reduced iron availability caused further increase in mRNA expression of PKM2 ($p < 0.05$) and LDHA ($p < 0.05$). The AFC treatment during mechanical effort resulted, as compared to the cells cultured upon mechanical stretch and optimal iron concentration, in an increased mRNA expression of PKM2 ($p < 0.05$) and a decreased expression of LDHA ($p < 0.05$). Notably, in case of AFC treatment expression of PKM2 increased to a lesser extent compared with that in case of DFO treatment ($p < 0.05$). Upon mechanical stretch HCM demonstrated, as compared to the cells cultured in static conditions, an increase in mRNA expression of NDUFS1, UQCRFS1, COX4I1 and ATP5B (all $p < 0.05$), suggesting an enhanced mitochondrial oxidative pathway. Additional DFO treatment resulted in a decrease in expression of NDUFS, UQCRFS1, COX4I1 and ATP5B (all $p < 0.05$).The analogous alterations were observed upon AFC treatment during mechanical stretching; however, mRNA expression of NDUFS1, UQCRFS1, COX4I1 and ATP5B decreased to a lesser extent compared with that in case of DFO treatment (all $p < 0.01$).
Conclusions: Reduced iron availability during mechanical effort enhances non-oxidative metabolic pathway and resulting lactate formation, whilst decreasing mitochondrial oxidative pathway in human cardiac myocytes. On the other hand, iron supplementation during mechanical effort may act in a protective manner, reducing lactate formation pathway.

P2012

PPARalpha in cardiac energy metabolism regulation in chronic heart failure due to ischemic heart disease

AD Voronova[1]; MP Valikhov[1]; TG Kulikova[1]; OV Stepanova[1]; VP Masenko[1]; RS Akchurin[1]
[1]Cardiology Research and Production Center, Moscow, Russian Federation

One of the main causes of chronic heart failure (CHF) is ischemic heart disease (IHD). Cardiac ischemia is usually the result of hypoxia. The CHF progression is accompanied with alterations in cardiac energy metabolism, failing hearts become energy deprived. Recent scientific studies have shown that the cardiac energy metabolism is under the transcriptional control of nuclear receptors, such as peroxisome proliferator activated receptors (PPARs). These transcription factors act as molecular sensors in response to extracellular and intracellular changes, regulating the expression of the target genes. The downregulation of PPAR-alpha has been shown in the studies in mice model of ischemic cardiomyopathy. Our purpose was to study the role of PPAR-alpha and target genes in the regulation of cardiac energy metabolism in ischemic heart disease.
In order to characterize the metabolic phenotype in IHD, RT-qPCR was used to measure mRNA expression of the nuclear receptor PPAR-alpha - a key regulator of fatty acid beta-oxidation, and target genes: Long-Chain Acyl-CoA Dehydrogenase (LCAD, a key enzyme of beta-oxidation); Cardiac Carnitine Palmitoyl-Transferase-1 (CPT-1, the other principal outer mitochondrial membrane fatty acid transporter); Cluster-of-Differentiation 36 (CD36, also known as Fatty-Acid Translocase (FAT); Heart Fatty-Acid-Binding Protein (HFABP) in surgical specimens of auricle from patients with ischemic heart disease (IHD, $n = 10$) and human non-diseased myocardium autopsy specimens ($n = 5$).
Transcript expression levels of PPAR-alpha, CD36, CPT-1 and LCAD decreased in IHD in comparison to human non-diseased myocardium autopsy specimens. The significant up-regulation of HFABP in IHD was observed in the study.
These data indicate the occurrence of metabolic disorders in ischemic heart disease - an energy metabolism shifting from cardiac fatty acid oxidation as a primary energy source to glucose oxidation. It can be assumed that the regulation of the cardiac energy metabolism is possible by acting on PPAR-alpha, CD36, CPT-1, LCAD and HFABP. Whether downregulation of PPAR-alpha is an adaptive response in IHD remains unclear. It is likely that inhibitors or activators of mitochondrial fatty acid oxidation can be used for metabolic therapy of CHF due to IHD.

P2013

A single systemic injection of AAV9-hIGFBP2 prevents left ventricular hypertrophy and dysfunction in metabolic syndrome

MF Evaristi[1]; M Barutaut[1]; WF Peacock[2]; P Fournier[1]; C Caubere[1]; G Murat[1]; C Dambrin[1]; P Trochet[3]; P Davault[3]; F Koukoui[1]; M Galinier[1]; F Smih[1]; P Rouet[1]
[1]UMR UT3 CNRS 5288, Evol. Medicine, Obesity and heart failure: molecular and clinical investigations, Toulouse, France; *[2]Baylor College of Medicine, Emargency Medicine, Houston, United States of America*; *[3]FUJIFILM VisualSonic, Amsterdam, Netherlands*

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Aims Metabolic syndrome (MetS) is a known risk factor for cardiovascular events. It is characterized by central obesity plus any two of dyslipidemia, insulin resistance, and hypertension. Obese and diabetic patients with MetS have low plasma insulin-like growth factor binding protein 2 (IGFBP2). Our first aim was to investigate IGFBP2 cardiac expression in MetS patients and in a mice model of MetS. The second aim was to assess if gene therapy with adeno-associated virus 9 carrying human

IGFBP2 (AAV9-hIGFBP2) could reduce MetS associated left ventricular hypertrophy in mice.
Methods and Results: We measured plasma IGFBP2 by ELISA and cardiac mRNA IGFBP2 expression in MetS patients by RT-qPCR. Both plasma levels and heart expression of IGFBP2 were decreased in patients with MetS vs. control patients. Further, in a C57BL/6J mouse model of diet-induced MetS, found similar left ventricular mRNA IGFBP2 expression. Finally, we demonstrated for the first time that in MetS mice with decreased cardiac IGFBP2 mRNA levels, human IGFBP2 can be induced by a single AAV9-hIGFBP2 injection, and that the increased IGFBP2 prevents left ventricle wall thickening, hypertrophy and dysfunction.
Conclusions: Human plasma and cardiac IGFBP2 are decreased in MetS patients. In mice, restoration of cardiac IGFBP2 expression level prevents MetS associated left ventricular dysfunction and hypertrophy. These clinical and animal data suggest that IGFBP2 is a new cardiac marker and therapeutic target in MetS to prevent heart remodeling consistent with heart failure.

P2014
Association between the gut microbiota composition, low-grade inflammation and blood pressure in patients without heart failure from moscow and moscow region

DA Daria Kashtanova[1]; ON Tkacheva[2]; YUV Kotovskaya[3]; AS Popenko[4]; AV Tyaht[4]; DG Alekseev[5]; SA Boytsov[6]
[1]National Research Center for Preventive Medicine, "Research of Age and Age-associated Conditions" Department, Moscow, Russian Federation; *[2]Russian National Research Medical University, Russian Clinical Research Center for Gerontology, Moscow, Russian Federation*; *[3]Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*; *[4]Federal State Institution "Federal Scientific Clinical Center of Physical-Chemical Medicine (FMBA), Moscow, Russian Federation*; *[5]Moscow Institute of Physics and Technology, Moscow, Russian Federation*; *[6]National Research Center for Preventive Medicine, Moscow, Russian Federation*

Introduction: Mechanisms of interaction between the gut microbiota composition and cardiovascular diseases are actively investigated. The aim of the study was to assess the relationship between the gut microbiota composition, inflammatory markers and level of blood pressure (BP) in apparently healthy individuals living in Moscow and Moscow region.
Materials and Methods: The study included untreated subjects aged from 25 years to 76 years carefully selected through exclusion of cardiovascular diseases by means of clinical and laboratory evaluation, ECG, treadmill test, echocardiography, carotid ultrasound examination. Eight hundred and fifty eight subjects were screened and only 92 met the selection criteria. Highly sensitive C-reactive protein (CRP) concentration was measured (immunoturbidimetry method) and interleukin-6 (IL-6) was measured by immunoenzyme method. DNA was isolated from 2 ml of stool samples. Preparations for further sequencing and sequencing of the V3-V4 variable regions of the 16S rRNA gene were done according to recommended protocol 16S metagenomic sequencing Library Preparation. Statistical analysis was performed on the R programming language, version 3.1.0. Statistical analysis for comparing the groups of samples was performed using the generalized linear models and Mann-Whitney test (corrected for multiple comparisons false discovery rate).
Results: 92 participants were included (26 men), arterial hypertension of 1 degree was detected in 34 participants (37%). Average SBP was 120 ± 18,6 mmHg. Gram-negative opportunistic bacteria of the genus Prevotella were more presented in patients with systolic blood pressure (SBP) >140 mmHg than in normotensive subjects ($p < 0.001$). It was found that SBP was higher in patients whose microbiota contained more bacteria of the genus Blautia ($p = 0.002$). The average CRP level among the participants was 3.50 ± 4.39mg/l. CRP level was ≥5mg/in 12 participants. High CRP levels were positively associated with gram-negative opportunistic pathogens of the Serratia ($p < 0.001$) and Prevotella ($p = 0.002$) genera. Prevotella was also positively associated with IL-6 ($p = 0.008$), which average value was 5.57 ± 5.45 pg/ml, in 24 patients it was ≥10pg/ml.
Conclusions: The results show the relationship between the increased SBP, low-grade inflammation and higher representation of gram-negative opportunistic pathogens which are capable of producing endotoxins and genus Blautia which is able to activate the secretion of tumor necrosis factor-alpha and pro-inflammatory cytokines.

P2015
The absence of leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1) does not influence cardiac repair after acute myocardial infarction in mice

GHJM Ellenbroek[1]; JJ De Haan[1]; IE Hoefer[1]; L Timmers[2]; MAD Brans[1]; SM Van De Weg[1]; PAFM Doevendans[2]; G Pasterkamp[3]; L Meyaard[4]; SCA De Jager[1]
[1]University Medical Center Utrecht, Experimental cardiology, Utrecht, Netherlands; *[2]University Medical Center Utrecht, Cardiology, Utrecht, Netherlands*; *[3]University Medical Center Utrecht, Clinical Chemistry and Hematology, Utrecht, Netherlands*; *[4]University Medical Center Utrecht, Immunology, Utrecht, Netherlands*

Background: Heart failure after acute myocardial infarction (MI) depends on infarct size and adverse left ventricular (LV) remodelling, both depending on extent and quality of the inflammatory response. Leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1) is an inhibitory leukocyte receptor. The aim of this study was to investigate the role of LAIR-1 in the extent of inflammation, infarct size and adverse LV remodelling after MI.
Methods & Results: Wildtype (WT) and LAIR-1-/- mice were either subjected to ischemia-reperfusion or permanent left coronary artery (LCA) ligation. In mice subjected to ischemia-reperfusion, infarct size (IS) was comparable between WT and LAIR-1-/- mice as a percentage of the area at risk (37.0 ± 14.5 vs. 39.4 ± 12.2%, $p = 0.63$) and as a percentage of the LV (14.2 ± 7.4 vs. 14.9 ± 7.0%, $p = 0.80$). In mice subjected to permanent LCA ligation, end-diastolic (133.3 ± 19.3 vs. 132.1 ± 27.9 μL, $p = 0.91$) and end-systolic volumes (112.1 ± 22.2 vs. 106.9 ± 33.5 μL, $p = 0.68$) did not differ between both groups, as assessed by echocardiography four weeks after MI. Similarly, no differences were observed in inflammatory cell quantification or collagen deposition in the infarcted area.
Conclusion: The absence of LAIR-1 does not influence infarct size, nor does it affect inflammation, fibrosis formation and adverse LV remodelling four weeks after MI.

P2016
Association of M235T polymorphism of angiotensinogen gene and lipid parameters in heart failure patients with type 2 diabetes mellitus.

OO Medentseva[1]; MM Udovychenko[1]; IS Rudyk[1]
[1]L.T.Malaya Institute of Therapy, Department of Clinical Pharmacology and Pharmagenetics of non-communicable diseases, Kharkiv, Ukraine

Background: Polymorphism of angiotensinogen (ATG) gene M235T could be associated with coronary artery disease (CAD). Dyslipidemia have been reported as one of the main pathophysiological mechanism contributing to CAD. It's well known that arterial hypertension and CAD play an important role in unfavorable course of heart failure with preserved ejection fraction (HFpEF) development. On the other hand, the association of M235T polymorphism of ATG gene and lipid parameters in heart failure patients with type 2 diabetes mellitus (T2DM) is not well researched.
Purpose: To investigate the parameters of lipid metabolism in diabetic and non-diabetic subjects carrying different types of M235T polymorphism of ATG with HFpEF.
Methods: One hundred and thirty-three patients (58 males and 75 females; mean age 61,78 ± 9,7 years) with HFpEF were examined. One hundred patients were carriers of 235T allele (MT + TT genotypes), 33 patients were homozygous carriers of 235M allele of M235T polymorphism of ATG. T2DM had 83 patients and 49 were non-diabetic patients. By using of polymerase chain reaction, different genotypes of M235T polymorphism of ATG were determined. The lipid metabolism parameters were performed by using kits of reagents "NUMAN" (Germany). Continuous variables as median (25th, 75th percentile) are expressed. Mann-Whitney U test was used for nonparametric comparisons. All statistical tests were 2-tailed and $p < 0,05$ was considered statistically significant.
Results: In the group of T2DM subjects levels of serum total cholesterol ((6,00 (5,00 : 6,80) vs to 5,10 (4,30 : 5,90) mmol/l), very low-density lipoprotein-cholesterol ((0,92 (0,62 : 1,33) vs 0,69 (0,47 : 0,83) mmol/l) and triglycerides ((2,10 (1,50 : 2,95) vs 1,6 (1,15 : 1,85) mmol/l, respectively) were increased comparing with the group of non-diabetic patients, carrying the 235T allele of M235T polymorphism, ($p < 0,005$). No significant differences in lipids parameters such as levels of serum total cholesterol ((5,85 (4,57 : 7,05) vs to 5,65 (4,7 : 6,77) mmol/l), very low-density lipoprotein-cholesterol ((0,88 (0,67 : 1,15) vs 0,85 (0,55 : 0,98) mmol/l) and triglycerides ((2,05 (1,80 : 2,57) vs 1,9 (1,22 : 2.20) mmol/l) were found in M235M carriers with T2DM and without it, respectively, ($p > 0,05$).
Conclusions: The most unfavorable lipid parameters profile had diabetic patients with HFpEF and MT + TT genotypes of M2335T polymorphism of ATG.

P2017
Usefulness of CHA2DS2-VASc score in predicting stroke and death in patients with heart failure: the korean acute heart failure registry

H-Y Hyun-Young Park[1]; MK Son[1]; M-C Cho[2]; B-H Oh[3]
[1]Korea National Institute of Health, Department of Cardiovascular and Rare Diseases, Cheongju, Korea Republic of; *[2]Chungbuk National University College of Medicine, Cheongju, Korea Republic of*; *[3]Seoul National University Hospital, Internal Medicine, Seoul, Korea Republic of*

Background: The CHA2DS2-VASc score is commonly used for stroke risk stratification in patients with atrial fibrillation (AF). Its predictive accuracy in patients with heart failure (HF) is unclear.

Purpose: To determine whether CHA2DS2-VASc predicts stroke and death in patients with HF with and without AF.
Methods: The Korean Acute Heart Failure registry (KorAHF), an ongoing, a prospective observational multicenter cohort study from 2011-2014, was used in the study. We excluded patients with a diagnosis of cancer or chronic obstructive pulmonary disease before HF. The study sample comprised 1,840 patients with AF, and 2,756 patients without AF.
Results: During 1-year follow-up period, among HF patients with and without AF, the stroke occurred 3.7% (n = 68) and 2.6% (n = 73), respectively; incidence rate per 100 person-years without AF were 3.7, 1.1, 3.5, 3.1, 3.9, 5.7, and 6.4 for CHA2DS2-VASc scores of 1 through ≥7, respectively. The all-cause death occurred 21.6% (n = 398) and 20.7% (n = 570) in patients with and without AF, respectively; incidence rate per 100 person-years were as follows, for CHA2DS2-VASc scores of 1 through ≥7, respectively: (1) with AF: 12.0, 13.4, 28.2, 27.7, 33.5, 41.0, and 47.7 and (2) without AF: 16.6, 13.9, 17.4, 26.5, 37.5, 41.7, and 51.9. Each 1-point increase in the CHA2DS2-VASc score was significantly associated with increased risk of stroke in HF patients without AF (HR=1.15, 95% CI=1.00–1.32) and all-cause death in HF patients with and without AF (HR=1.18, 95% CI=1.12–1.25 in patients with AF, and HR=1.19, 95% CI=1.13–1.25 in patients without AF, respectively). The CHA2DS2-VASc score performed modestly in this HF population (for stroke without AF, and all-cause death with and without AF, 1-year C statistics, 0.59 [95% CI, 0.52–0.65], 0.62 [95% CI, 0.59–0.65], and 0.64 [95% CI, 0.61–0.66], respectively).
Conclusions: Among patients with HF, the CHA2DS2-VASc was significantly associated with and was able to modestly predict the risk of stroke and death, except stroke in patients with AF.

P2018
Clinical application of human iPS cells for the treatment of patients with severe congestive heart failure

K Keiichi Fukuda[1]; J Fujita[1]; S Tohyama[1]; T Seki[1]; S Yuasa[1]
[1]*Keio University School of Medicine, Tokyo, Japan*

Funding Acknowledgements: Grant from Japanese Government

Although heart transplantation can drastically improve the survival, shortage of the donor heart is a serious problem. The regenerative medicine of the failing heart had been long awaited. To address this question, we had developed novel methods to induce human iPS cells from circulating human T lymphocytes using Sendai virus containing Yamanaka 4 factors. We had screened the factor that were expressed in future heart forming area of the early mouse embryo, found several growth factors and cytokines that can induce cardiomyocytes differentiation and proliferation, and applied them to human iPS cells. We performed transcriptome of the metabolic enzymes and fluxome analysis using 13glucose and 13lactic acid on ES/iPS cells and cardiomyocytes, and found that their metabolic pathways were completely different. Based on these findings, we purified cardiomyocytes using glucose-free lactate-supplemented medium. Purity of the cardiomyocytes was >99%, and they did not make teratoma formation. The transplanted cardiomyocytes using our technique can survive in the heart with more than 90%, and can show physiological growth after transplantation. Transplantation of ES/iPS-derived cardiomyocytes into the infarcted myocardium could improve cardiac function in rat and porcine model. We expect the combination of these techniques can achieve future heart regeneration.

BASIC SCIENCE - MOLECULAR BASIS

P2019
The cell death-associated protein kinase, RIPK1, is phosphorylated in cardiomyocytes in response to pro-inflammatory cytokines or oxidative stress.

KA Rostron[1]; SJ Leonard[1]; SJ Fuller[1]; PH Sugden[1]; A Clerk[1]
[1]*University of Reading, School of Biological Sciences, Reading, United Kingdom*

Funding Acknowledgements: British Heart Foundation

Introduction: Myocardial infarction is associated with oxidative stress, inflammation and production of pro-inflammatory cytokines [e.g. tumour necrosis factor alpha (TNFα), interleukin-1 beta (IL1β)]. In T cells, TNFα signals via RIPK1. Ubiquitinylated RIPK1 is protective, activating NFκB, p38-MAPKs and JNKs. Deubiquitinylation of RIPK1 induces apoptosis, whilst phosphorylation and kinase activation switches the mode of cell death from apoptosis to an alternative, more damaging form, necroptosis.
Purpose: Our aims are to determine how RIPK1 is regulated in cardiomyocytes and its role in the cardiomyocyte response to pro-inflammatory cytokines or oxidative stress. Our hypothesis is that RIPK1 is phosphorylated and activated by these stresses, and its activation status influences cardiomyocyte survival vs. death.
Methods and results: Phosphorylation of protein kinases is associated with the appearance of reduced mobility bands on immunoblots. The effects of TNFα, IL1β or H2O2 (a physiologically relevant oxidative stress) on RIPK1 were studied initially in neonatal rat ventricular myocytes (NRVMs). TNFα (20 ng/ml) induced appearance of reduced mobility bands (indicating multiple phosphorylations) in 5-15 min, with return to the basal state by 2 h. IL1β (>1 ng/ml) induced appearance of similar bands in 5-15 min, but the response was greater and more prolonged. H2O2 (>0.2 mM) induced the same degree of response as IL1β, but this was maximal at 1-2 h. These reduced mobility bands are consistent with phosphorylation rather than ubiquitinylation in terms of relative molecular mass. Anion-exchange chromatography also indicated RIPK1 was phosphorylated. Gel filtration chromatography showed RIPK1 (74.8 kDa predicted molecular weight) elutes in a complex of 150-170 kDa in control cells and forms higher molecular weight complexes with IL1β. The degree of RIPK1 phosphorylation in response to IL1β was concentration-dependent. Activation of p38-MAPK was assessed by immunoblotting using phosphospecific antibodies. The concentration-dependency of p38-MAPK phosphorylation in response to IL1β mirrored that of RIPK1 phosphorylation. Moreover, p38-MAPK inhibitors (SB203580, BIRB-796) attenuated the appearance of reduced mobility bands induced by IL1β. The concentration-dependency for this inhibition was similar to that for inhibition of phosphorylation of MAPKAPK2 (an established p38-MAPK substrate). Adult male rat hearts were perfused in the Langendorff mode with IL1β (15 min) in the absence/presence of SB203580. Consistent with the results from NRVMs, IL1β induced the appearance of reduced mobility bands and this was inhibited by SB203580, confirming that the results are relevant for the adult heart.
Conclusions: RIPK1 is phosphorylated in response to IL1β in cardiomyocytes and perfused adult rat hearts, and this is mediated via p38-MAPK signalling. Since p38-MAPK is activated downstream of RIPK1, this is likely to be a feedback system.

P2020
HFWM: Regulation of cardiac pacemaker activity by PDE4 isoforms

D Mika[1]; AM Gomez[1]; G Vandecasteele[1]; R Fischmeister[1]
[1]*INSERM UMR-S 1180, Univ. Paris-Sud, Université Paris-Saclay, Châtenay-Malabry, France*

Funding Acknowledgements: CORDDIM, Fondation Lefoulon-Delalande, ANR Jeune Chercheuse-Jeune Chercheur

Background: Numerous epidemiological and clinical studies have revealed a positive correlation between heart rate (HR) and cardiovascular morbimortality. The autonomic nervous system is the major extracardiac determinant of HR. During sympathetic stimulation, the activation of β-adrenergic receptors (βAR) induces an increase in cAMP levels, leading to a positive chronotropic effect. Among the 5 cAMP-PDE families expressed in the heart, PDE4 is critical for controlling excitation-contraction coupling (ECC) during βAR stimulation in atrial and ventricular cells. PDE4 may also be important for automaticity. 3 genes encode for cardiac PDE4s: pde4a, pde4b and pde4d. Their respective contribution to the regulation of pacemaker activity remains ill-defined.
Methods: The total enzymatic PDE activity was determined in mouse sinoatrial node (SAN) tissue as the cAMP hydrolytic activity measured in the absence of PDE inhibitor and the fraction corresponding to PDE4 activity was assessed by including the PDE4 inhibitor Ro-20-1724 (10 μM). The in vitro pacemaker activity was assessed by measuring the spontaneous Ca2+ transients in Fluo4-loaded-SAN intact tissue. Images were obtained using confocal microscopy.
Results: Ro-20-1724 increased the beating rate of intact mouse SAN and increased PKA-phosphorylation levels of key ECC actors (ryanodine receptor, phospholamban). PDE4 enzymatic activity was found to account for 60% of the total cAMP-PDE activity in SAN. The 3 isoforms PDE4A, 4B and 4D were found to be expressed in mouse SAN. In PDE4D-, but not in PDE4B-deficient mice, Ca2+ homeostasis was altered in control conditions and after βAR stimulation. Indeed, ablation of PDE4D induced a decreased beating rate and an increased Ca2+ spark frequency in control and βAR-stimulated conditions.
Conclusion: Our preliminary results reveal that PDE4 controls pacemaker function in mice and that PDE4D ablation strongly perturbs normal SAN activity.

P2021
HFWM: - Title: The natural autophagy-inducer spermidine protects the aging heart and promotes longevity in mice

M Abdellatif[1]; T Eisenberg[2]; A Schmidt[1]; W A Linke[3]; C Muehlfeld[4]; J Sadoshima[5]; S Kiechl[6]; G Kroemer[7]; F Madeo[2]; S Sedej[1]
[1]*Medical University of Graz, Division of Cardiology, Graz, Austria*; [2]*Institute of Molecular Biosciences, NAWI Graz, University of Graz, Graz, Austria*; [3]*Ruhr*

University Bochum (RUB), Department of Cardiovascular Physiology, Bochum, Germany; [4]*Hannover Medical School, Institute of Functional and Applied Anatomy, Hannover, Germany*; [5]*New Jersey Medical School, Department of Cell Biology and Molecular Medicine, Newark, United States of America*; [6]*Innsbruck Medical University, Department of Neurology, Innsbruck, Austria*; [7]*Centre de Recherche de Cordeliers, Equipe 11 labellisée Ligue contre le Cancer, Paris, France*

Purpose: Aging is associated with increased risk of cardiovascular disease and death. One of the theories of aging postulates an age-dependent decline in autophagy, a major cellular repair process associated with rejuvenation. Here, we tested if dietary supplementation of the natural autophagy-inducer spermidine protects against cardiac aging.
Methods: Spermidine (3mM) was supplemented in the drinking water of pre-aged (18-month-old) C57Bl/6 wild-type male mice for 5 months. Cardiomyocyte-specific autophagy-deficient male mice (Atg5fl/fl/MLC2aCre+, 4-month-old) that were fed spermidine for 3 months were employed to test whether the effects of spermidine are autophagy-dependent. A comprehensive in vivo and in vitro cardiac characterization was performed using echocardiography, invasive hemodynamics, confocal and electron microscopy, immunoblotting, high-resolution respirometry and ultrastructural analysis of cardiomyocytes by design-based stereology. Another subset of C57Bl/6 mice was followed up for lifespan estimation and survival analysis. In humans, a correlational study between dietary spermidine intake (as assessed by food questionnaires) and cardiovascular disease was carried out (Bruneck Study).
Results: Dietary spermidine supplementation extended median lifespan (by ~10%) and exerted cardioprotective effects through reduction of cardiac hypertrophy and preservation of diastolic function in old mice. Spermidine-fed mice showed enhanced cardiac autophagy, mitophagy, mitochondrial respiration and mechano-elastical properties of cardiomyocytes in vivo, coinciding with increased titin phosphorylation and suppressed subclinical inflammation. Age-related effects on subcellular cardiomyocyte composition were reversed by spermidine, as reflected by increased relative mitochondrial and myofibrillar volumes and a reduced (mitochondria- and myofibril-free) sarcoplasmic volume. Spermidine failed to promote cardioprotection in the mice that lack autophagy in cardiomyocytes. In humans, higher spermidine intake was correlated with lower blood pressure and lower risk of cardiovascular disease (e.g. fatal heart failure).
Conclusion: Our results suggest dietary intake of spermidine as a novel and feasible strategy against aging-associated cardiovascular disease.

P2024

HFWM: Endogenous proteasome regulation in the myocardium supports increased systolic function upon chronic, but not acute beta-adrenoreceptor signaling

FA Trogisch[1]; F Koser[1]; A Jungmann[2]; OJ Mueller[2]; M Hecker[1]; O Oliver Drews[1]
[1]*Heidelberg University, Institute of Physiology and Pathophysiology, Heidelberg, Germany*; [2]*University Hospital of Heidelberg, Department of Internal Medicine III: Cardiology, Angiology and Pneumology, Heidelberg, Germany*

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Introduction: The ubiquitin-proteasome pathway participates in the regulation of protein function and signaling via targeted proteolysis. Increasing evidence suggests that its function is dynamically adjusted in cardiac remodeling and failure. A shared mechanism in hypertrophic remodeling of the myocardium appears to be endogenous proteasome regulation via Lmp2. However, the role of cardiac Lmp2 in hypertrophic remodeling and heart failure is not known.
Purpose: Towards this end, we investigated whether cardiac Lmp2 is required for hypertrophic remodeling in response to continuous β-adrenoreceptor signaling as observed in several cardiovascular disease conditions associated with reduced cardiac output.
Methods & Results: Lmp2 had no apparent impact on cardiac development and function as observed in adult Lmp2 knock out (KO) mice, which were indistinguishable from wildtype littermates (wt). Continuous treatment of those mice with the β-adrenergic agonist isoproterenol for 4 days (30mg/kg/d) increased systolic function as well as posterior wall thickness in both groups. In contrast, chronic isoproterenol treatment for 7 days caused a loss of systolic function in Lmp2 KO animals while cardiac function was maintained in wildtypes (fractional shortening/FS: -32% vs. wt, $p < 0.01$, $n \geq 9$). To attribute a support of cardiac function to proteasome regulation via Lmp2 in cardiomyocytes, Lmp2 expression was reconstituted via cardiotropic gene transfer using adeno-associated virus serotype 9. Furthermore, Lmp2 expression was driven by a recombinant cardiac myosin light chain promoter. Lmp2 gene transfer had the effect that two forms of Lmp2 were expressed in the myocardium: full-length and processed Lmp2. Without isoproterenol, processed Lmp2 levels were similar to those in wt hearts. Upon isoproterenol treatment, full-length Lmp2 decreased reciprocally proportional to an increase in processed Lmp2. Endogenous Lmp2 processing is part of proteasome assembly, indicating that Lmp2 gene transfer restored the endogenous mechanism for proteasome regulation. Lmp2 gene transfer did not impact cardiac function under baseline conditions and upon isoproterenol administration for 4 days. In contrast, Lmp2 gene transfer fully restored systolic function in Lmp2 KO mice treated for 7 days with isoproterenol albeit the mice were born and matured without the gene. In contrast, control gene transfer did not restore systolic function in Lmp2 KO mice treated with isoproterenol for 7 days (FS: +33% Lmp2 vs. luciferase gene transfer, $p < 0.01$, $n \geq 8$). Notably, reduced systolic function was associated with exacerbated hypertrophic remodeling.
Conclusions: Cardiac proteasome regulation via Lmp2 sustains systolic function during hypertrophic remodeling upon chronic β-adrenoreceptor stimulation, but does not interfere with cardiac muscle mass or function under unchallenged conditions and short-term β-adrenoreceptor signaling.

P2025

Evaluation of the cardiovascular profile of a novel nitroxyl donor BMS-986231 in chronically instrumented dogs with normal cardiac function and pacing-induced cardiomyopathy

CL Del Rio[1]; JC Hartman[2]; J Reardon[3]
[1]*QTest Labs, LLC, Columbus, Ohio, United States of America*; [2]*Pharmaceutical R&D Consulting, LLC, Loveland, Colorado, United States of America*; [3]*HemoShear Therapeutics, LLC, Charlottesville, Virginia, United States of America*

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Background: BMS-986231 is a novel nitroxyl (HNO) donor that releases HNO, a molecule linked to positive inotropy, lusitropy and vasodilation.
Purpose: Assess BMS-986231 effects on haemodynamics and load-independent left ventricular (LV) mechano-energetic parameters in conscious, chronically instrumented normal dogs and dogs with pacing-induced heart failure (HF).
Methods: BMS-986231 was given as a 180-min intravenous (IV) infusion (50 μg/kg/min) in 8 dogs with normal cardiac function (CTRL), and at 3 doses (25, 50, 75 μg/kg/min) per animal in 6 dogs with pacing-induced cardiomyopathy (HF). ECG and pressure waveforms were recorded continuously; heart rate, arterial pressure and LV mechanical/geometric indices were measured at baseline and at 30, 60, 90 and 180 mins after infusion start (and at 60 mins post-infusion in HF dogs). After the 180-min infusion in normal dogs, an IV bolus of plasma volume expander was administered to restore cardiac preload and further assess BMS-986231 effects.
Results: (Mean [±SEM] % vs. baseline) BMS-986231 (at 180 mins) led to significant ($p < 0.05$) dose-dependent reductions in mean arterial (CTRL: -14 [1]%, HF: -7 [2] to -15 [1]%) and LV end-systolic pressures (CTRL: -18 [2]%, HF: -8 [2] to -17 [1]%), arterial elastance (CTRL: -23 [3]%, HF: -22 [1] to -35 [2]%) and systemic vascular resistance (CTRL: -16 [2]%, HF: -16 [3] to -29 [2]%), indicating decreased afterload. BMS-986231 also significantly decreased filling pressures (CTRL: ~-4 mmHg, HF: ~-3 to -7 mmHg) and preload. Tau (CTRL: -6 [1]%, HF: -14 [3] to -18 [4]%) and the slope of the end-diastolic pressure volume relationship (CTRL: -28 [7]%, HF: -17 [2] to -39 [6]%) were significantly decreased, suggesting positive lusitropy. Ejection fraction (CTRL: 12 [1]%, HF: 23 [2] to 41 [6]%) and the slopes of the end-systolic pressure volume (CTRL: 19 [2]%, HF: 11 [1] to 29 [1]%) and the preload-recruitable stroke work (CTRL: 12 [1]%, HF: 10 [1] to 22 [1]%) relationships increased dose-dependently with BMS-986231, suggesting positive inotropy. In normal dogs, acute restoration of LV preload by volume expansion significantly increased stroke volume (SV) (16 [4]%) and cardiac output (CO) (17 [3]%), while induced positive lusitropy/inotropy was preserved. In HF dogs, BMS-986231 resulted in significant dose-dependent increases in CO (14 [1] to 20 [2]%) and SV (18 [1] to 28 [5]%). BMS-986231-mediated improvements in load-independent cardiac function, SV and CO in HF were sustained at 60 minutes post-infusion. In all cases, BMS-986231 significantly reduced the pressure volume area (CTRL: -25 [4]%, HF: -28 [10] to -43 [6]%), suggesting decreased myocardial oxygen demand.
Conclusions: BMS-986231 produced significant and dose-dependent vasodilation, as well as inotropic and lusitropic effects, and had no meaningful impact on heart rate or markers of myocardial oxygen demand. BMS-986231 may therefore be useful in treating patients with acute decompensated HF.

P2027

ASB1 differential methylation closely relates to left ventricular function and stroke volume in ischaemic cardiomyopathy patients

E Esther Rosello-Lleti[1]; A Ortega[1]; E Tarazon[1]; C Gil-Cayuela[1]; F Lago[2]; JR Gonzalez-Juanatey[2]; L Martinez-Dolz[1]; M Portoles[1]; M Rivera[1]
[1]*Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain*; [2]*Instituto de Investigación Sanitaria de Santiago, Cellular and Molecular Cardiology Research Unit, Santiago de Compostela, Spain*

Funding Acknowledgements: National Institute of Health [PI13/00100; PI14/01506], CIBERCV [CB16/11/00261], the European Regional Development Fund (FEDER), RETICS [12/0042/0003].

Background: Ischemic cardiomyopathy (ICM) leads to impaired contraction and ventricular dysfunction causing high rates of morbidity and mortality. Epigenomics has allowed the identification of epigenetic signatures in human diseases.
Purpose: In this human pre-transplant study, we aimed to analyse the differential epigenetic patterns of ASB gene family in a group of ICM patients and relate these alterations to the hemodynamic and functional status of patients.
Methods: Epigenomic analysis was carried out using 16 left ventricular (LV) tissue samples, 8 from ICM patients undergoing heart transplantation and 8 from control (CNT) subjects without cardiac disease. We increased sample size up to 13 ICM and 10 CNT for RNA-sequencing analysis.
Results: We found two hypermethylated profiles (cg09969882 and cg11189868) in the ASB1 gene that showed a differential methylation of $0.17\Delta\beta$ and $0.26\Delta\beta$, respectively, $P < 0.05$ for both. Notably, the second methylation pattern was strongly related to end-systolic and diastolic left ventricular diameters (r=-0.743, P=0.035 for both), stroke volume (r=-0.929, P=0.001) and LV ejection fraction (r=-0.849, P=0.008). ASB1 showed a down regulation in mRNA levels (-1.2 fold, $P < 0.05$).
Conclusions: Our findings link a specific ASB1 methylation pattern to LV structure and performance in end stage ICM, and provide new insights and raising questions regarding which is the functionally relevant genome for the ischemic failing myocardium.

P2028
HFWM: Upregulation of cathepsin A induces left ventricular remodeling

L Lisa Lang[1]; M Hohl[1]; M Mayr[2]; AG Nickel[1]; A Mueller[3]; C Maack[1]; M Boehm[1]; T Sadowski[4]; D Linz[1]
[1]Saarland University Hospital, Internal Medicine III, Homburg, Germany; *[2]King's College London, London, United Kingdom*; *[3]Saarland University Hospital, Radiology, Homburg, Germany*; *[4]Sanofi Aventis, Frankfurt am Main, Germany*

Introduction: The serine carboxypeptidase cathepsin A (CatA) is located in lysosomes and in the extracellular matrix. CatA is involved in multiple pathophysiological processes including degradation of extracellular peptides and oxidative stress response. Additionally, CatA enzymatic activity has been proposed to mediate bradykinin breakdown and alternative angiotensin II production. Therefore, CatA may be an interesting target to prevent arrhythmias, cardiac hypertrophy and heart failure.
Methods: We used a proteomics approach to identify new substrates for CatA. Conditioned medium of cardiac fibroblasts was digested with CatA and analyzed by mass spectrometry. A transgenic mouse model (CatA-TG) was used to investigate the role of a heart-specific CatA-overexpression on left ventricular (LV) remodeling. Transaortic constriction (TAC) was performed in C57/Bl6N mice for 24 hours, 3 days, 5 days, 7 day, 14 days and 42 days to determine the time course of CatA-expression. Afterwards, we conducted TAC for 3 days (acute) and 6 weeks (chronic) and treated these mice with the CatA-inhibitor SAR1 (30mg/kg/day). Placebo-treated mice served as controls. At the age of 6 weeks LV function was determined by magnetic resonance imaging (MRI).
Results: Using proteomics the extracellular superoxide dismutase (SOD3) was identified as a novel candidate substrate due to a substantial downregulation upon CatA-digestion (Ctr: 24084 ± 13731 Vs. CatA: 611 ± 456 $p < 0.0001$). In CatA-TG mice an increased CatA protein expression and activity resulted in a significant decrease in SOD3 protein concentration (WT: 1.03 ± 0.04 Vs. CatA-TG: 0.58 ± 0.04 IOD/GAPDH; $p < 0.01$) and higher levels of oxidative stress (WT: 4.01 ± 0.61 Vs. CatA-TG: 7.51 ± 1.15 μmol/mg tissue/min; $p = 0.05$), which was associated with increased apoptosis and enhanced fibrosis content (WT: 5.41 ± 0.2 Vs. CatA-TG: 6.46 ± 0.31 %; $p < 0.05$). Using a TAC-timeline we observed that CatA expression increased at day 3 (≈1.8-fold; $p = 0.0003$) and went down to baseline after 2 weeks. CatA upregulation went hand in hand with increased expression of the hypertrophy-marker brain natriuretic peptide, profibrotic connective tissue growth factor, and collagens 1a, 3a and 5a. Due to the differential regulation of CatA during TAC, we treated animals for 3 days and 6 weeks (when CatA was down-regulated to control level) with the selective orally available CatA-inhibitor SAR. At 3 days after TAC, SAR-treated animals were protected against up-regulation of collagen 1a (Placebo: 8.74 ± 2.09 Vs. SAR: 1.15 ± 0.19; $p = 0.003$). TAC still induced hypertrophy of cardiomyocytes, increased LV mass and decreased ejection fraction (determined by MRI) in SAR-treated mice.
Conclusions: These findings identified up-regulation of CatA as a novel mechanism causing LV remodeling and SOD3 depletion, which in turn contributes to the cardiac phenotype begetting oxidative stress–dependent LV remodeling. CatA may therefore represent a potential therapeutic target in heart failure.

P2029
Relationship among LRP1 expression, Pyk2 phosphorylation and MMP-9 activation in post-myocardial infarction left ventricular remodeling

E Revuelta[1]; CSB Soler-Botija[1]; L Nasarre[2]; A Benitez-Amaro[2]; D De Gonzalo-Calvo[2]; A Bayes-Genis[1]; V Llorente-Cortes[2]
[1]Germans Trias i Pujol Hospital, Badalona (Barcelona), Spain; *[2]Cardiovascular Research Center (CSIC-ICCC), Barcelona, Spain*

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Introduction: Left ventricular (LV) remodeling after myocardial infarction (MI) is a crucial determinant of the clinical course of heart failure. Matrix metalloproteinase (MMP) activation is strongly associated with LV remodeling post-MI. Elucidation of plasma membrane receptors related to the activation of specific MMPs is fundamental for treating adverse cardiac remodeling post-MI.
Purpose: The aim of current investigation was to explore the potential association between the receptor low-density lipoprotein receptor-related protein 1 (LRP1) and MMP-9 and MMP-2 spatiotemporal expression post-MI.
Methods: A total of 46 male C57/Bl6 mice were used in this study; MI was induced occluding permanently left anterior descending coronary artery. Animals were sacrificed at 1, 10 and 21 days post-operation. In vitro studies were carried out with MEF and PEA13 fibroblasts; cells were exposed to hypoxia in an H35 Hypoxic/Anoxic Workstation with 94% N2 and 5% CO2.
Results: Real-time PCR and Western blot analyses showed that LRP1 mRNA and protein expression levels, respectively, were significantly increased in peri-infarct and infarct zones at 10 and 21 days post-MI. Confocal microscopy demonstrated high colocalization between LRP1 and the fibroblast marker vimentin, indicating that LRP1 is mostly expressed by cardiac fibroblasts in peri-infarct and infarct areas. LRP1 also colocalized with proline-rich tyrosine kinase 2 (pPyk2) and MMP-9 in cardiac fibroblasts in ischemic areas at 10 and 21 days post-MI. Cell culture experiments revealed that pPyk2 protein levels and MMP-9 activity were reduced to minimal levels in LRP1-deficient fibroblasts compared to control fibroblasts. These results indicate that both Pyk2 phosphorylation and MMP-9 activation require LRP1 in hypoxic fibroblasts.
Conclusion: Our results suggest that LRP1 plays a major role in MMP-9 upregulation in cardiac fibroblast post-myocardial infarction and highlight the potential role of LRP1 modulation for treatment of cardiac remodeling.

P2030
Zeb2 protects the heart from ischemic damage.

MM Gladka[1]; A Kohela[1]; D Versteeg[1]; B Molenaar[1]; H De Ruiter[1]; V Groenewold[1]; G Lacraz[1]; D Huylebroeck[2]; M Giacca[3]; E Van Rooij[1]
[1]Hubrecht Institute, Molecular Cardiology, Utrecht, Netherlands; *[2]Erasmus Medical Center, Rotterdam, Netherlands*; *[3]International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy*

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Following ischemic damage the heart undergoes extensive remodeling in response to the massive loss of cardiomyocytes in the area of injury. This will result in multiple processes including production and activation of the fibroblasts needed for proper infarct healing, however prolonged activation can be detrimental for cardiac contractility and can lead to heart failure. To maintain a proper cardiac function after an ischemic event it is crucial to preserve a proper healing of the infarct but at the same time increase the number of surviving cardiomyocytes.
Here we identify a novel function of the transcription factor Zeb2 in cardiomyocytes that it is necessary for proper infarct healing and for cardiomyocytes survival and function. Our data show that Zeb2, downstream of activated Hif1 alpha, is upregulated in cardiomyocytes in response to ischemic stress and declines 2 weeks after the injury. While cardiomyocyte specific deletion of Zeb2 did not induce an overt phenotype at baseline, after myocardial infarction (MI) deletion of Zeb2 worsened cardiac contractility, infarct healing, and survival. Transcriptome profiling of cardiac tissue of mice subjected to MI indicated that deletion of Zeb2 from cardiomyocytes leads to a significant inhibition of genes involved in fibroblast activation and proliferation, survival of cardiomyocytes and angiogenesis. Conversely AAV9-mediated cardiac delivery of Zeb2 promotes ECM related gene expression that prevents cardiac rupture and dysfunction.
To unveil the molecular mechanisms behind the cardioprotective effect of Zeb2 we performed mass spectrometry on conditioned medium from cardiomyocytes overexpressing Zeb2 and we identified Thymosin beta4 (Tmsb4) as one of the main secreted proteins. In line with this discovery, siRNA mediated Zeb2 inhibition in hypoxic neonatal cardiomyocytes abolished not only Zeb2 but also Tmsb4 expression, further verifying the regulation of Tmsb4 by Zeb2 in hypoxic cardiomyocytes. This is likely due to multiple conserved Zeb2 binding motifs in the 5kB proximal promoter region of the Tmsb4 gene.

Our data indicate that the Hif1 alpha-mediated increase in Zeb2 in cardiomyocytes in response to ischemic stress activates cardiac fibroblasts for proper infarct healing and promotes Tmsb4 secretion from heart muscle cells, which activates a downstream pro-survival response in injured cardiomyocytes. These findings reveal Zeb2 as a cardioprotective factor during ischemic injury, which may hold great promise for future heart failure therapies.

P2031

HFWM: Selective HDL-raising gene transfer counteracts cardiac hypertrophy, reduces fibrosis, and improves cardiac function in mice with chronic pressure overload

R Amin[1]; I Muthuramu[1]; F Jacobs[1]; B De Geest[1]
[1]*KU Leuven, Cardiovascular Sciences, Leuven, Belgium*

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Purpose: Epidemiological studies support an independent inverse association between high-density lipoprotein (HDL) cholesterol levels and heart failure incidence. The effect of selective HDL-raising human apo A-I gene transfer on cardiac remodelling induced by transverse aortic constriction (TAC) was evaluated.
Methods: Gene transfer with 5 x 1010 genome copies of an adeno-associated viral serotype 8-human apo A-I (AAV8-A-I) vector containing a hepatocyte-specific expression cassette was performed in C57BL/6 low-density lipoprotein receptor deficient (LDLr-/-) mice at the age of 12 weeks and was followed by TAC or sham operation two weeks later. Invasive hemodynamic measurements and morphometric and immunohistological analysis was performed 8 weeks after TAC or sham operation.
Results: Septal wall thickness was reduced by 16.5% ($p < 0.001$) 8 weeks after TAC in AAV8-A-I mice ($n = 24$) compared to control TAC mice ($n = 39$). The anti-hypertrophic effect of HDL-raising human apo A-I gene transfer was confirmed by a 16.5% ($p < 0.01$) reduction of cardiomyocyte cross-sectional area after TAC. Capillary density was 15.7% ($p < 0.05$) higher and interstitial fibrosis was 45.3% ($p < 0.001$) lower in AAV8-A-I TAC mice compared to control TAC mice. The lung weight in AAV8-A-I TAC mice was not increased compared to sham mice and was 13.3% ($p < 0.05$) lower than in control TAC mice. Atrial weight was 2.05 ($p < 0.001$) higher in control TAC mice than in control sham mice whereas no increase of atrial weight was observed in AAV8-A-I TAC mice. The peak rate of isovolumetric contraction was 18.4% ($p < 0.01$) higher in AAV8-A-I TAC mice ($n = 17$) than in control TAC mice ($n = 29$). Improved diastolic function following selective HDL-raising gene transfer was evidenced by a 17.5% ($p < 0.05$) increase of the peak rate of isovolumetric relaxation, a 15.4% ($p < 0.05$) shortening of the time constant of isovolumetric relaxation, and a significantly ($p < 0.01$) reduced end-diastolic pressure. Moreover, parameters of diastolic function were significantly ($p < 0.05$) better in AAV8-A-I sham mice ($n = 12$) than in control sham mice ($n = 10$). The 3-nitrotyrosine-positive area (%) in the myocardium quantified by immunohistochemistry was increased 7.73-fold ($p < 0.001$) and 3.57-fold ($p < 0.001$) in control TAC mice and in AAV8-A-I TAC mice, respectively. The 3-nitrotyrosine-positive area was 57.6% ($p < 0.001$) lower in AAV8-A-I TAC mice than in control TAC mice, indicating decreased nitro-oxidative stress. Compared to control TAC mice, the number of cleaved caspase-3 positive cells was reduced by 46.7% ($p < 0.05$) in AAV8-A-I TAC mice.
Conclusions: Selective HDL-raising human apo A-I gene transfer exerts anti-hypertrophic effects, reduces interstitial fibrosis, and improves systolic and diastolic function in a model of pressure overload-induced cardiomyopathy.

P2032

HFWM : post-transcriptional regulators of superoxide dismutase 2 as new biomarkers of left ventricular remodeling post-myocardial infarction.

E Emilie Dubois-Deruy[1]; O Beseme[1]; J Fielder[2]; A Pfanne[2]; P Mulder[3]; P Amouyel[1]; V Richard[3]; C Bauters[1]; T Thum[2]; F Pinet[1]
[1]*Institute Pasteur of Lille, U1167, Lille, France*; [2]*Institute for Molecular and Translational Therapeutic Strategies (IMTTS), Hannover, Germany*; [3]*INSERM U1096, ROUEN, France*

Purpose: After myocardial infarction (MI), 30% of patients develop a left ventricular remodeling (LVR) which remains a major complication and a strong predictor of both heart failure (HF) and death after MI. Our main objective is to identify new biomarkers of this pathology.
Methods: We used an experimental HF-rat model in which MI is induced by left coronary ligation to perform a proteomic analysis of left ventricle (LV). By bioinformatical analysis with Ingenuity Pathway Analysis (IPA), we identified 13 microRNAs potentially modulated during HF. We then quantified these microRNAs in left ventricle (LV) and plasma in our rat model of HF post-MI and in a cohort of patients with different degrees of LVR (REVE-2 study).
Results: By proteomic and phosphoproteomic analysis in a HF-rat model, we identified 45 proteins differentially modulated in LV. We then performed a bioinformatical analysis with IPA to identify molecular targets involved in their regulation. We identified 13 miRNA regulating 8 proteins, mostly involved in oxidative stress and metabolism, two main pathways involved in HF progression. We quantified in LV of HF-rats an increased levels of miR-23a-3p (x1.5, $p = 0.029$) at 7 days post-MI, of miR-377-5p (x3.5, $p = 0.014$), miR-21-3p (x2.6, $p = 0.013$) and miR-21-5p (x2.3, $p = 0.004$) at 2 months post-MI and of miR-222-3p at both time (7 days : x3, $p = 0.025$; 2 months: x2.1, $p = 0.005$). To analyze their potential as biomarkers, we quantified these miRNA in plasma and observed a decreased expression at 7 days post-MI and an increased expression at 2 months post-MI for miR-21-5p (7 days : /1.6, $p = 0.002$; 2 months: x6.2, $p = 0.007$), miR-23a-3p (7 days :/3.2, $p = 0.006$; 2 months: x6.6, $p = 0.004$) and miR-222-3p (7 days : /6, $p = 0.0002$; 2 months: x1000, $p = 0.0001$).
Interestingly, these 3 miRNA regulate superoxide dismutase 2 (SOD2), the major mitochondrial anti-oxidant enzyme. We then quantified an increased SOD2 expression in LV of HF-rats at 2 months post-MI (x1.6, $p = 0.029$), without modulation at 7 days post-MI. Plasmatic levels of SOD2 were not modulated in HF-rats.
We then quantified SOD2 and its post-transcriptional regulators in human plasma of patients with or without LVR in REVE-2 cohort. SOD2 increased in plasma of LVR patients 1 year after MI (x6.5, $p = 0.044$). Expression of miR-21-5p, miR-23a-3p, miR-222-3p decreased 7 days after MI (/10, respectively $p = 0.010$; $p = 0.049$; $p = 0.020$) and increased 3 months after MI in plasma of LVR patients (x10, respectively $p = 0.018$; $p = 0.002$; $p = 0.007$). Lastly, we demonstrated direct regulation of SOD2 by miR-222-3p by using mimic and miR-222 inhibitors in human cardiomyocytes.
Conclusion: We demonstrated for the first time the potential interest of miR-21-5p, miR23a-3p and miR-222-3p, 3 microRNAs involved in SOD2 regulation, as new biomarkers of LVR post-MI.

P2033

HFWM: Molecular and functional characterization of MICRA, a circular RNA predicting the development of heart failure after acute myocardial infarction

Y Devaux[1]; M Vausort[1]; A Salgado-Somoza[1]; L Zhang[1]; P Leszek[2]; DR Wagner[3]
[1]*Luxembourg Institute of Health, CVRU, Strassen, Luxembourg*; [2]*Institute of Cardiology, the Heart Failure and Transplantology Department, Warsaw, Poland*; [3]*Hospital Centre, Luxembourg, Luxembourg*

On behalf of: Cardiolinc network

Background: Predicting outcome after acute myocardial infarction (AMI) is challenging. Identification of patients at risk of developing left ventricular (LV) remodelling leading to heart failure would be a major achievement towards personalized medicine. Existing biomarkers such as brain natriuretic peptides have limited applications due to lack of specificity and stability in the few hours following AMI. Novel biomarkers are needed to improve risk stratification. Both microRNAs and long noncoding RNAs circulating in the blood have shown some potential to predict outcome after AMI. Whether circular RNAs (circRNAs), a novel class of noncoding RNAs formed by back splicing, could be used as biomarkers of heart failure was, until recently, unknown. Using in silico bioinformatics analyses, we identified one circular RNA named MICRA for Myocardial Infarction-associated Circular RnA. MICRA was a robust predictor of LV remodelling in two independent cohorts of AMI patients (JACC 2016).
Purpose: To provide a molecular and functional characterization of MICRA.
Methods and Results: MICRA is a 874 nucleotides-long circRNA formed mainly from exon 1 of the zinc finger protein 609 (ZNF609) gene located on chromosome 15q22. The functions of ZNF609 and MICRA are unknown.
First of all, the circularity of MICRA was demonstrated using quantitative PCR with divergent primers, a TaqMan probe spanning the junction site, sequencing, northern blotting, cloning and over-expression in HEK293 cells, and digestion with RNase R (RNase R is able to digest linear RNAs but not circRNAs).
Then, MICRA expression was measured in whole blood samples obtained at admission in 409 AMI patients. MICRA was positively correlated with the ejection fraction (r=0.18, $p = 0.001$) and negatively correlated with the NYHA score at 4 months (OR 0.33 [0.14-0.74], $p = 0.007$), consistent with a protective role of MICRA.
MICRA was predominantly expressed by lymphocytes and was positively correlated with CD8 and FoxP3, markers of suppressive T regulatory cells which are known to play a protective role in the infarcted heart. In CD8 + CD25 + T cells isolated from healthy donors and activated in vitro by anti-CD3/CD28 beads and interleukin-2, MICRA was decreased and IL10 and FoxP3 were increased (Figure).
MICRA was readily expressed in the human heart and was up-regulated in failing ($n = 22$) compared to non-failing ($n = 5$) hearts ($P < 0.01$). MICRA was positively

associated with CD3 and CD8, suggesting that its over-expression in failing hearts was attributable to infiltrated blood lymphocytes.
Finally, MICRA was very weakly expressed or absent in plasma, serum, and exosome-enriched plasma fractions.
Conclusion: We have characterized MICRA, a novel circRNA predicting the development of heart failure after AMI. MICRA is expressed by lymphocytes and may participate in the function of T regulatory cells after AMI. Further investigation of the therapeutic potential of these findings is warranted.

P2034
Saliva: linking oral health with heart failure

X Xi Zhang[1]; B Schulz[2]; T Walsh[1]; J Atherton[3]; K Kostner[4]; C Punyadeera[1]
[1]Queensland University of Technology, Institute of Health and Biomedical Innovation, Brisbane, Australia; *[2]University Of Queensland, School of Chemistry and Molecular Biosciences, Brisbane, Australia*; *[3]Royal Brisbane and Women's Hospital, Cardiology, Brisbane, Australia*; *[4]Mater Adult Hospital, Cardiology, Brisbane, Australia*

Background: Heart failure (HF) is a severe complication that affects 26 million people world-wide and the incidence is growing due to an aging population. The lack of early screening program for HF hinders early detection and targeted treatment and contributes greatly to the mortality of HF. Human saliva contains a large number of circulating proteins that can serve as indicators of the body's health and well-being. Previous research from us and others have demonstrated the possibility of detecting cardiac specific biomarkers in saliva. These biomolecules enter saliva through diffusion, active transport or filtration.
Purpose: We aimed to investigate the diagnostic potential of saliva for HF.
Methods: Saliva samples were collected from age-matched healthy controls (n = 20) and HF patients (n = 40). We employed an unbiased approach to investigate the salivary proteomics profiles of HF patients and healthy controls using SWATH-Mass Spectrometry. Potential candidate proteins were identified based on their abundance levels in saliva and their biological functions. These findings have further been validated using biological and technical replications.
Results: This unbiased approach identified six candidate proteins in saliva and this panel of six proteins correlated with disease severity. These six candidates were then combined into a prediction model using logistic regression. At the optimal cut-off point, the panel demonstrated excellent diagnostic performance (sensitivity = 77.1% and specificity = 71.4% and AUC = 0.84).
Conclusion: We were able to identify proteins in human saliva that can distinguish HF patients from healthy controls. Prior to clinical implementations, these findings should be verified in larger asymptomatic patient cohorts. There is evidence that salivary proteins can be used in developing early screening/diagnosing tools for HF.

P2035
HFWM: Erythrocyte nitrosyl-hemoglobin reflects endothelial function and vascular nitric oxide bioavailability in vivo

F Dei Zotti[1]; I Lobysheva[1]; C Beauloye[1]; JL Balligand[1]
[1]Institute of Experimental and Clinical Research (IREC), Brussels, Belgium

On behalf of: FATH
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Reduced bioavailability of nitric oxide is a hallmark of endothelial dysfunction in metabolic and cardiovascular diseases,but its quantification in circulating blood remains a challenge.NO can form iron-nitrosyl complexes with hemoglobin(5-coordinate-α-HbNO) in erythrocytes(RBCs).We hypothesized that this complex,predominantly formed in venous blood,reflects bioavailability of vascular NO and endothelial function in vivo.We developed a modified subtraction method using EPR to quantify it in RBCs from mouse,rat and human venous blood.We HbNO observed in RBC from the three species ex vivo.The circulating concentration was 425nM in rodents and 92nM in human venous blood.NO could be supplied from vascular or intraerythrocytic NOS.We detected eNOS proteins in RBC from rodent and human.To test eNOS functionality,we measured nitrite/nitrate production and HbNO formation in human RBCs and from eNOS(+/+) and eNOS(-/-)mice in vitro and its sensitivity to NOS or arginase inhibitors.Nitrite and HbNO signals increased after arginase inhibition and were abrogated upon NOS inhibition in human and eNOS(+/+) but insensitive to these modulators in eNOS(-/-)RBCs.HbNO signal from venous RBCs was minimally sensitive to NOS inhibitor ex vivo,suggesting that intraerythrocytic NOS contributes little compared with vascular eNOS or other NO sources reaching RBCs in vivo.We found that upon exposure to exogenous NO donor,the formation of HbNO was higher in hypoxic conditions (1%of O2:0.018+/-0.002 μmolHbNO/μmol)compared to room air(0.0036+/-0.0004 μmolHbNO/μmol) and inversely correlated with ratio of oxy- to deoxy- forms of Hb.The stability of pre-formed HbNO was higher under hypoxia(17%degradation after 30 min1%of O2 vs 49%room air),and preserved at 21% of O2 by incubation with catalase (CAT:2μM HbNO/L vs 0.5μM HbNO/L untreated controls),whereas superoxide dismutase had minimal effect.CAT inhibition increased ROS formation in RBCs,measured by FACS analysis of DCFDA fluorescence.This suggested that HbNO formation is sensitive to oxidative degradation,possibly by H2O2.We compared circulating HbNO levels in venous RBCs from normal volunteers or patients with cardiovascular diseases and found decreased HbNO in patients(0.141+/-11μmol/L vs0.22+/-12μmol/L in volunteers;N=38 and48).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 biovailability and/or oxidative stress ex vivo.

P2036
Evidence-based nursing interventions which improve heart failure patients under mechanical circulatory support outcomes: an integrative review

T Teresa Pessoa[1]; T Leal[2]
[1]Hospital Lisbon North, Hospital Santa Maria, Lisbon, Portugal; *[2]ESEL, Lisboa, Portugal*

Background: Heart Failure (HF) is a major and growing issue in Public Health worldwide. Mechanical Circulatory Support (MCS) is a non pharmacologic therapeutic recommended to highly selected patients. Advanced Nursing Practice requires nurses to have actualized scientific knowledge in their specialty area, integrating it with the empirical knowledge derived from daily practice of patient centered care.
Purpose: To identify and describe evidence-based nursing interventions which improve the outcomes of patients with HF under MCS.
Methods: Integrative literature review based on a systematic research in MEDLINE, CINAHL and Cochrane databases and manual search on Google and Researchgate of original articles and literature reviews published between January 1st, 2010 and August 31st, 2016. There have been included studies related to adult HF patients with formal indication or under MCS in which the first author was a nurse. The studies related to patients under MCS devices such as intra-aortic baloon counterpulsion or venovenous extracorporeal membrane oxygenation have been excluded.
Results: From the 41 articles included, the nursing interventions evidence-based found in this integrative review were grouped in four nursing care areas such as perioperative care, patient and caregiver education, post-discharge care and palliative care, particularly focused on clinic and hemodynamic evaluation, MCS device management, anticoagulation management, immobility prevention and control, nutritional support, rehabilitation and functional readaptation, self-care facilitation, infection prevention and control, decision making, advanced directives, end of life support and support of systems.
Conclusion: HF patients centered care under MCS is complex, requires teamwork and relational skills, and it depends on the best available evidence-based scientific knowledge, on stakeholders' life experience and on context and environment specificity in which we find ourselves. Patient outcomes can be improved by prevention and early identification of MCS related complications. There is a need to standardize practices and to develop protocols and guidelines to improve nursing care in this particular group of patients. The creation and implementation of training programs on MCS could be an advisable way to improve advanced nursing practice.

P2037
The protective effect of aerobic exercise preconditioning in female rats with hypoxic pulmonary hypertension depends on the female sex hormone

N Natalia Medvedeva[1]; N Pankova[1]
[1]M.V. Lomonosov Moscow State University, Biology Department, Moscow, Russian Federation

Introduction: The influence of exercise preconditioning on the development of pulmonary hypertension (hPAN) is studied a long time. However, the answer has not been received. It was 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. It was shown that exercise to improve endothelial function (Mereles 2006). The same mechanism underlies the protective effect of female sex hormones on the development of pulmonary hypertension. Can these influences interact? The aim of current research was to study the effect of aerobic exercise preconditioning on the degree of hPAN in the gonadectomized female rats and rats with preserved ovaries.
Methods and design: Female Wistar rats were used. They were divided into 8 groups, four were with hPAH (H) and four without (C). Two groups from (H) and (C) rats were gonadectomized (HG and CG) and two were with ovaries (HN and CN). One group from HG,CG,HN,CN were with exercise preconditioning (groups HGEx, CGEx,HNEx,CNEx) and one group were without exercise (groups

Table P2038: Parameters of the experimental

	Control	MCT	MCT + G1	MCT effect	Estrogen effect	Interaction effect
Pulmonary Accelerationtime (ms)						
SHAM	45.0 ± 0.8	33.2 ±1.2*	43.2 ± 0.7†	P < 0.05	P < 0.05	P < 0.05
OVX	44.3± 1.3	20.7 ± 0.6*	38.1± 1.0†			
RV free wall thickness(mm)						
SHAM	0.5 ± 0.03	1.0 ±0.03*	0.6 ± 0.03†	P < 0.05	P < 0.05	P < 0.05
OVX	0.5± 0.02	1.8± 0.09	0.7± 0.03			
RVSP (mmHg)						
SHAM	30.7 ± 2.3	46.9 ± 3.9*	29.8 ± 1.3†	P < 0.05	P < 0.05	No
OVX	33.1 ± 0.8	60.2 ± 4.9*	29.1 ± 1.9†			
RV PLB/SERCA2a expression ratio						
SHAM	0.28±0.09	0.94 ± 0.1*	0.7±0.05†	P < 0.05	P < 0.05	P < 0.05
OVX	0.26±0.04	1,02±0.08*	0.30±0.08†			

Mean ± S.E.M of 5-7 rats per group. *P <0.05 compared with corresponding control rats; †P <0.05 compared with corresponding monocrotaline rats. SHAM, intact; OVX, ovariectomized; RV, right ventricle; RVSP, right ventricular systolic pressure; MCT, monocrotaline; PLB, phospholamban; SERCA2a, sarco-endoplasmic reticulum Ca2 + -ATPase 2a.

Table P2039: Cardiac remodeling and hemodynamics

Group	LVEF	LVESP	LVESPVR	LVEDP	LVEDPV	RVESP	RVEDP	Coronary Relaxation
Lean	80±1	135±6	22.5±1.4	2.40±0.40	1.17±0.08	18.5±1.8	2.36±0.41	88±2
Zucker	82±1	157±6*	20.9±1.5	4.12±0.43*	3.84±0.26*	36.6±4.3*	4.99±1.10*	30±2*
Zucker + macitentan	83±1	132±4†	19.8±1	1.90±0.23†	1.66±0.12†	3.3±0.41†	3.30±0.41†	87±3†

Left Ventricular Ejection Fraction (LV EF; %), LV end-systolic pressure (LVESP; mmHg), LVESP-Volume Relation (LVESPVR; mmHg/relative volume unit), LV end-diastolic pressure (LVEDP; mmHg), LVEDP-volume relation (LVEDPVR; mmHg/relative volume unit) RV end-systolic pressure (RVESP; mmHg) RV end-diastolic pressure (RVEDP; mmHg); Coronary relaxation (% at Ach 3.10-5 M). *: p <.05 vs. Lean; †: p<.05 vs. Zucker.

HGC,CGC,HNC,CNC) The procedures followed the FELASA/ICLAS for use of the laboratory animals, 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%).For exercise preconditioning rats were subjected to exercise training (aerobic swimming during 30 min/day.) for a period of 2 weeks to hypoxia. Right ventricular (RV) hypertrophy was calculated as RV weight /w.h. Systolic right ventricle pressure (SRVP) was measured.

Results: Two weeks after chronic hypoxia exposure all (H) groups of rats developed hPAH. In rats of (H) groups average SRPV was on78% more than SRPV in rats of C groups ($p < 0,05$). Between rats of all C groups were not difference in the magnitude of SPRV. However the degree of disease was different in groups (H): the magnitude of SRPV was significantly smaller in HGEx rats than in HNEx and HGC (50,58 + 1,54 vs.66,86 + 4,30 vs.61,1 + 5,7 mm Hg $p < 0.05$). There were not differences in SRPV between HNC, HNEx and HGC groups. In hypoxia gonadectomized rats were not difference in RV hypertrophy. But in hypoxia rats with ovaries the magnitude of RV hypertrophy was significantly smaller in group with exercise preconditioning (26,29 + 2.80 vs. 23,49 + 2,51 $p < 0,05$).

Conclusions: Aerobic exercise preconditioning has a protective effect on the development of hypoxic pulmonary hypertension in the female rats. The effect depends on the female sex hormone. A reduction of systolic right ventricle pressure in the gonadectomized rats and a decrease in right ventricle hypertrophy in rats with preserved ovaries observed.

P2038

Activation of a new estrogen receptor (GPER) ameliorates cardiopulmonary dysfunction in female rats with pulmonary hypertension.

G Gisele Zapata-Sudo[1]; AKNA Allan Kardec Nogueira De Alencar[1]; AMS Ananssa Maira Da Silva[1]; GCM Guilherme Carneiro Montes[1]; TLM Tadeu Lima Montagnoli[1]; SM Sabrina Martinez[1]; LV Luiza Villarinho[1]; VNC Valeria Nascimento Cunha[1]; AF Aline Fraga[1]; HW Hao Wang[2]; LG Leanne Groban[2]; CAMF Carlos Alberto Manssour Fraga[1]; RTS Roberto Takashi Sudo[1]
[1]Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; *[2]Wake Forest University, Winston-Salem, United States of America*

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Introduction: Pulmonary hypertension (PH) is a disease of women, and induces right ventricle (RV) failure. Hypothesis: The activation of an estrogen receptor (GPER) by the agonist G1 was evaluated in monocrotaline (MCT)-induced PH female rats.

Methods: Depletion of estrogen was performed by oophorectomy (OVX; n = 18) in female Wistar rats. Experimental groups included SHAM or OVX rats that received a single injection of MCT (60 mg/kg, i.p.) for PH induction followed by administration of vehicle or G1 (400 μg/kg/day s.c.) for 14 days after PH onset (n = 7 per group).

Results: MCT injection and estrogen loss led to a decrease in pulmonary acceleration time and an increase in RV hypertrophy in PH rats and MCT-related changes were attenuated by treatment with G1 ($P < 0.05$; Table 1). RV pressure (RVP) was higher in MCT-injected rats and this increase in OVX group was higher than that in SHAM. G1 reduced RVP in both SHAM and OVX rats (Table 1). G1 normalized the expression of calcium handling proteins in the RVs (Table 1). G1 reduced pulmonary arteries wall fibrosis and hypertrophy in both MCT-treated SHAM and OVX rats ($P < 0.05$).

Conclusion: G1 reversed cardiopulmonary dysfunction in female rats, a finding that may have important implications for the treatment of PH in women.

P2039

Improved metabolic syndrome-related right and left ventricular dysfunction by the dual ETA-ETB receptor antagonist macitentan.

M Marianne Lachaux[1]; N Harouki[1]; N Peschanski[1]; L Nicol[1]; A Dumesnil[1]; J-P Henry[1]; S Renet[1]; I Remy-Jouet[1]; M Iglarz[2]; V Richard[1]; P Mulder[1]
[1]INSERM U1096, ROUEN, France; *[2]Actelion Pharmaceuticals, Basel, Switzerland*

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Background: WHO group II pulmonary hypertension (PH due to left heart disease), represents a major health problem with significant morbidity and poor prognosis. Endothelin (ET) receptor blockade is a promising therapeutic approach, since ET-1 is a key player in PH and is probably involved in the development of left heart disease and cardiac hypertrophy and fibrosis via both ETA and ETB receptors. However, whether ET receptor blockade exerts protective effects on PH due to left heart disease is unknown.

Purpose: To evaluate the effects of dual ET receptor antagonism in a rat model of metabolic syndrome-related right and left ventricular dysfunction.

Methods: We assessed in Zucker fa/fa rats the effects of long-term (90 days) macitentan treatment (ETA/ETB receptor antagonist; 10 mg/kg/day as food additive) on LV and RV remodeling/function (MRI), LV and RV hemodynamics (catheterization) and coronary function (myograph).

Results: After 3 months, untreated Zucker rats presented both LV diastolic dysfunction (elevation of LV End-Diastolic Pressure (EDP) and LV End-Diastolic Pressure Volume Relation (EDPVR) without change in LVESPVR) associated with increased collagen deposition. Simultaneously, left coronary artery relaxation to acetylcholine was impaired. Zucker rats developed PH and RV dysfunction characterized by increases in RVESP and RVEDP. Macitentan significantly prevented LV and RV dysfunctions as well as coronary dysfunction, associated with a reduced LV collagen density (Lean: 0.93 ± 0.10 %; Zucker: 1.32 ± 0.13 %, $p < 0.05$ vs lean; Zucker + macitentan: 0.76 ± 0.06 %, $p < 0.05$ vs Zucker).
Conclusions: The dual ET receptor antagonist macitentan prevents LV diastolic dysfunction and reduces RV pressure in a model of PH due to left heart disease.

P2040

Benefit of combined therapy with Sildenafil and LASSBio-1359 in preventing monocrotaline-induced rat pulmonary hypertension.

RT Roberto Takashi Sudo[1]; FIC Fabio Indias Carvalho[1]; AKNA Allan Kardec Nogueira De Alencar[1]; AMS Ananssa Maira Da Silva[1]; SM Sabrina Martinez[1]; CAMF Carlos Alberto Manssour Fraga[1]; EJB Eliezer Jesus Barreiro[1]; GZS Gisele Zapata-Sudo[1]
[1]*Federal University of Rio de Janeiro, Rio de Janeiro, Brazil*

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Background and Purpose: Pulmonary hypertension (PH) is characterized by enhanced pulmonary vascular resistance, subsequent right ventricle (RV) pressure overload, which ultimately results in right-sided heart failure and death. This study was designed to assess if the effectiveness of a combined therapy with sildenafil, a phosphodiesterase type 5 inhibitor (PDE5i), and LASSBio-1359, a new adenosine A2A receptor (A2AR) agonist, is superior to either compound alone in mitigating monocrotaline (MCT)-induced rat PH.
Experimental Approach: For in vitro study, an isobolographic analysis was performed to identify a possible synergistic relaxation effect between sildenafil and LASSBio-1359 in rat pulmonary artery (PA). For in vivo protocol, PH was induced in male Wistar rats by a single intraperitoneal injection of MCT at a dose of 60 mg/kg. Rats were divided into the following groups: control (saline injection only), MCT + vehicle, MCT + sildenafil (34 μg/kg/day), MCT + sildenafil (170 μg/kg/day), MCT + LASSBio-1359 (34 μg/kg/day), MCT + LASSBio-1359 (170 μg/kg/day) and MCT + combination of sildenafil and LASSBio-1359 (34 μg/kg/day each one). Fourteen days after MCT injection, rats were treated daily with oral administration of the regimen therapies or vehicle for 14 days. Cardiopulmonary system function and structure were evaluated by echocardiography. RV systolic pressure (RVSP) and pulmonary artery endothelial function were further measured.
Key Results: Isobolographic analysis showed synergistic interaction between sildenafil and LASSBio-1359 in rat PA arteries. In vivo monotreatment with low-dosages (34 μg/kg/day) of both compounds did not reverse the deleterious effect of PH on PA flow, pulmonary vasculature reactivity, RV structure and function, but combined modality of a PDE5i with an A2AR agonist ameliorated all these PH-related abnormalities of the cardiopulmonary function and structure in MCT-challenged rats.
Conclusion and Implications: In vitro and in vivo synergism interaction between sildenafil and LASSBio-1359 suggest a combined use of both compounds to improve life-quality and outcomes of a higher population of patients with PH in the future.

P2041

Ivabradine improves left ventricular twist and untwist in the hypertrophied heart and preserves contraction-relaxation coupling.

M Jozwiak[1]; J Melka[1];
M Rienzo[1]; A Bize[1]; L Sambin[1]; L Hittinger[1]; A Berdeaux[1]; JB Su[1]; B Bouhemad[2]; B Bijan Ghaleh[1]
[1]*INSERM U 955 Equipe 03, Creteil, France*; [2]*University Hospital of Dijon, Service d'Anesthesie Reanimation, Dijon, France*

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Background: Tightly coupled and abnormal left ventricular (LV) isovolumic contraction and relaxation are observed during chronic hypertension and LV hypertrophy. These altered systolic and diastolic functions are associated with maladaptive LV responses to tachycardia. However, isovolumic periods do not reflect the whole cycle and more global assessment is needed. Interestingly, LV twist and untwist are LV myocardial deformation that occurs during the overall systole and diastole, respectively.
Purpose: To investigate contraction-relaxation coupling using LV twist and untwist analysis and to determine the effect of acute heart rate (HR) reduction with ivabradine (1 mg/kg iv) on global systolic and diastolic function in a pig model of chronic hypertension.
Methods: Eight chronically instrumented pigs received angiotensin II infusion during 28 days to induce chronic hypertension. LV function was investigated by combining hemodynamic and echocardiographic measurements. All measurements were performed at Day 0 and at Day 28 while angiotensin II infusion was stopped.
Results: Chronic infusion of angiotensin II significantly increased LV posterior and septal wall thicknesses as well as the estimated LV mass, indicating LV hypertrophy. HR increased by 15%. LV untwist was significantly reduced (-104 ± 8 vs. -154 ± 9 °.s-1, at Day 0 vs 28, respectively, $p < 0.05$), showing global LV diastolic dysfunction. Concomitantly, LV twist was also significantly altered (11 ± 1 vs. 16 ± 1 °, at Day 0 vs 28, respectively $p < 0.05$), showing global LV systolic dysfunction. Interestingly, there was a strong relationship between LV twist and untwist so that the ratio between LV twist and untwist remained unchanged between Day 0 and Day 28 (0.107 ± 0.013 vs. 0.108 ± 0.012, p = NS). It suggests that contraction-relaxation coupling was preserved with the development of LV hypertrophy. In this context, ivabradine decreased HR by 25% (from 86 ± 5 to 63 ± 3 beats/min, $p < 0.05$) and significantly improved both LV twist (from 11 ± 1 to 14 ± 1°, $p < 0.05$) and LV untwist (from -104 ± 8 to -146 ± 5°.s-1, $p < 0.05$), showing that HR reduction with ivabradine improved both global systolic and diastolic LV functions. In addition, ivabradine did not alter contraction-relaxation coupling, as shown by the unchanged absolute ratio between LV twist and untwist at baseline and after ivabradine administration (0.108 ± 0.012 vs. 0.100 ± 0.004).
Conclusions: LV twist and untwist were altered in this model of chronic hypertension and LV hypertrophy but they remained tightly coupled. Acute HR reduction with ivabradine improved both LV systolic and diastolic functions without altering contraction-relaxation coupling.

RAPID FIRE 7 - ACUTE HEART FAILURE

2064

The degree of pulmonary congestion measured by non-invasive lung impedance is the key determinant of heart failure hospitalizations: Lessons from the extended IMPEDANCE-HF trial.

M Michael Kleiner Shochat[1]; A Shotan[1]; M Kazatsker[1]; A Asif[1]; I Kleiner[2]; JM Weinstein[2]; I Dahan[1]; D Blondheim[1]; S Meisel[1]
[1]Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel; [2]Saroka Medical Center, Cardiology, Beer Sheva, Israel

Results of the IMPEDANCE-HF trial have shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The main trial was extended for an additional year to accrue more data on predictors of hospitalizations due to HF. The main aim of the study was to prove that HF patients with higher degree of long-standing pulmonary congestion are hospitalized more often.

Methods: Study population included 266 patients, with HF and LVEF≤35% in New York Heart Association class II-IV. Patients were randomized (1:1) to a control group treated by clinical assessment and a monitored group whose therapy was also assisted by LI. Patients were examined and LI measured monthly in our outpatient clinics. Noninvasive LI measurements were performed with the high-sensitive device. Assessment of the degree of pulmonary congestion was by the new index LIR, measured at each visit and calculated as LIR = {1- [currently measured LI/ normal baseline (calculated for each patient)] × 100} expressed as percentage. The annual average LIR for each patient was calculated as the mean of all LIR measurements at each consecutive year of follow-up.

Results: The total follow-up period was 634 years in the monitored group and 483 years in the control group ($p = 0.001$). Groups were similar with respect to baseline characteristics. There were 228 and 431 HF hospitalizations (mean 0.54 and 1.29 per × year of follow up) in the monitored and control groups, respectively ($p < 0.001$). There were 54, 35, 22 and 74, 62, 49 all-cause, cardiac and HF-associated death cases in the monitored and the control groups, respectively ($p < 0.001$). Figure 1 shows the dynamics of pulmonary congestion in study groups during the follow-up period as represented by LIR, demonstrating a significantly lower level of pulmonary congestion in the monitored group compare with the control group during the study ($p < 0.001$).

Conclusion: The Extended IMPEDANCE-HF demonstrated that pre-emptive LI-guided therapy of HF patients reduced pulmonary congestion significantly more effectively than by treatment according to clinical assessment only. This effect appeared to be consistent during the whole study period. Since groups were similar with respect to baseline characteristics, we proposed that the main reason for reducing the number of HF hospitalizations and improving survival was better decongestion achieved in the monitored group.

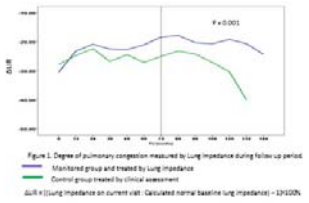


Figure 1

2065

Impact of nitrate use on morbility and mortality in acute heart failure

L Reis[1]; A Fernandes[1]; C Lourenco[1]; R Teixeira[1]; P Dinis[1]; M Madeira[1]; J Ribeiro[1]; L Puga[1]; I Almeida[1]; J Nascimento[1]; L Goncalves[1]
[1]University Hospitals of Coimbra, Coimbra, Portugal

Introduction: The current pharmacological treatment in acute heart failure (AHF) consists mainly of the use of diuretics in addition to vasodilators or inotropes. The drugs recently studied in AHF have shown no impact on the prognosis. For years, nitrates have been used to treat patients (P) with AHF (recommendation IIa according to the guidelines of the European Society of Cardiology of 2016) however, there is limited evidence of the impact of nitrates on morbidity and mortality of these P.

Purpose: To evaluate the prognostic impact of the early administration (first 24 hours) of intravenous nitrates in P admitted by AHF.

Methods: Retrospective study with 264 P admitted in a cardiac intensive care unit, between February 2010 and November 2016. P with adequate arterial pressure were selected for nitrates therapy (systolic arterial pressure> 90mmHg, N=227) and divided into 2 groups - G1: nitrates, N=103 and G2: no-nitrates, N=124. Demographic, laboratory, echocardiographic variables and in-hospital mortality were compared. Clinical follow-up (5 years) was performed targeting for readmission with AHF and mortality.

Results: The population mean age was 69 ± 14 years old with a majority of male (78%). The etiology was ischemic in 28% of the P and 46% had left ventricular ejection fraction (LVEF)≤35%. Readmission with AHF occurred in 42% and in-hospital mortality and during follow-up was 11% and 36%, respectively.

The groups presented similar clinical and analytical characteristics: congestive HF (G1 100% vs 91% G2, $p = 0.52$), presence of cardiovascular risk factors, NT-proBNP values (G1 16972 ± 21511 pg/nL vs G2 19028 ± 41691 pg/nL , $p = 0.357$), creatinine on admission (G1 159 ± 113 μmol/L vs G2 149 ± 192 μmol/L, $p = 0.23$), chronic kidney disease (G1 46% vs G2 44%, $p = 0.25$) and cardio-renal syndrome (G1 56% vs G2 57%, $p = 0.23$). They were similar regarding LVEF (G1 38 ± 12% vs G2 34 ± 14%, $p = 0.10$) and presence of coronary artery disease (G1 47% vs G2 47%, $p = 0.24$). There were no differences in the diuretic dosage (G1 174 ± 119mg vs G2 152 ± 97mg, $p = 0.15$) and in the use of noninvasive ventilation (G1 62% vs 38%, $p = 0.60$).

In-hospital mortality (G1 56% vs. G2 44%, $p = 0.83$) and during follow-up (G1 61% vs G2 39%, $p = 0.58$) were similar, however we found that patients of G1 had a shorter hospital stay (G1 11 ± 7.9 days vs G2 15 ± 15 days, $p = 0.001$) and a lower percentage of readmission with AHF (G1 31% vs. G2 39%, $p = 0.018$).

Conclusions: In our population the early use of intravenous nitrates in P with AHF had no impact on mortality. However, it's associated with a shorter hospital stay and a lower readmission rate due to AHF.

2066

Utilization of proton pump inhibitors in patients with atrial fibrillation is associated with hospitalization for de novo acute heart failure

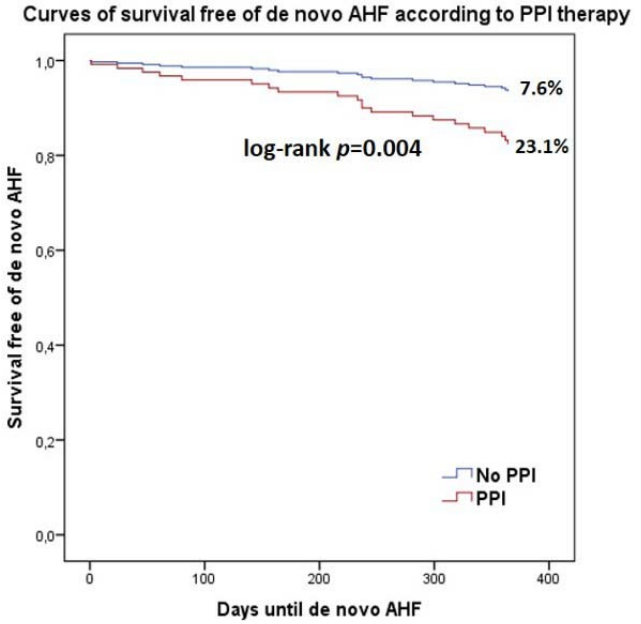
J B Augusto[1]; M Borges Dos Santos[1]; D Roque[1]; D Faria[1]; H Ferreira[1]; J Urzal[1]; C Santos[2]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal; [2]Hospital Santo Andre, Leiria, Portugal

Background: Proton pump inhibitors (PPIs) are frequently used among patients with atrial fibrillation (AF). In patients under PPI therapy, anaemia due to both iron and vitamin B12 deficiencies may ensue.

Purpose: We aimed to evaluate the incidence of hospitalization for de novo acute heart failure (AHF) at 12-month follow-up in patients with atrial fibrillation who were under PPI therapy.

Methods: We included retrospectively 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period. Among them, 423 patients were admitted for in-hospital management. Patients who had previous known heart failure (n = 101), who were under antiplatelet therapy (aspirin, clopidogrel and/or ticagrelor) (n = 109) and those with history of dyspepsia, gastroesophageal reflux, peptic ulcer disease or gastrointestinal bleeding (n = 30) were

excluded. We recorded the haematocrit (Htc) nadir during in-hospital stay. We further determined the proportion of PPI prescription at discharge. Primary outcome was the incidence of hospitalization for de novo AHF 12 months after discharge.
Results: We included 172 AF patients who were successfully discharged and followed for 12 months (mean age of 69.3 ± 12.8 years, 37.2% males). A total of 30.8% (n = 53) had a PPI prescription at discharge. In all of these cases, PPIs were also prescribed during in-hospital stay. Nadir Htc during hospitalization was significantly lower in patients under PPI therapy (median of 37.4 vs. 40.4%; p = 0.003). Kaplan-Meier analysis (Figure) showed that patients with AF who were taking PPIs had a higher incidence of de novo AHF 12 months after discharge (23.1 vs. 7.6%; log-rank p = 0.004). Cox regression analysis controlled for age and chronic kidney disease showed that PPI therapy was an independent predictor of de novo AHF (HR 2.90; CI 95% 1.22 – 6.90; p = 0.016).
Conclusions: Approximately one third of the AF patients were treated with PPI, the vast majority without formal indication. PPI overuse was associated with anaemia and hospitalization for de novo acute heart failure and therefore its use must be carefully weighted in clinical practice.



Survival free of de novo AHF

2067

Missed opportunity to minimise risk of admission with acute decompensated heart failure (ADHF) during pre-hospital phase of care

J Mc Cambridge[1]; C Keane[1]; M Walshe[1]; P Campbell[1]; F Rathore[1]; PR Kalra[2]; MR Cowie[3]; J Riley[3]; R O' Hanlon[1]; M Ledwidge[1]; J Gallagher[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland; *[2]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*; *[3]Royal Brompton Hospital, London, United Kingdom*

Funding Acknowledgements: Enterprise Ireland, ResMed, Boston Scientific, Cardiomark

Introduction: Heart failure (HF) admission rates present a major challenge. There is a paucity of data relating to the pre-hospital phase of care prior to admission with ADHF.
Purpose: To achieve a more complete understanding of this pre-hospital period, which may highlight ways we can improve pre-hospital care and thereby prevent admission.
Method: As part of an ongoing multicentre study analysing care pathways in patients admitted to hospital with ADHF (de novo patients, DN, and recurrent admitters, RA), focus was placed on the pre-hospital period to assess duration of symptoms, numbers seeking pre-hospital medical assessment, the nature of any intervention prescribed and (for RA) reporting of weight gain. This analysis is taken from one of the study centres. Data were gathered from clinical patient surveys, conducted by a HF nurse specialist.
Result: Of a total of 113 patients, 57 (50.4%) were DN and 56 (49.6%) were RA. A symptom duration of >3 days was reported in 76.4% (42) of DN and 64.2% (34) of RA. Of RA, 75% (42) reported monitoring their weight and 57.1% (24) of those noted a weight gain of >2kg over two days with their symptoms. Of those who noted a weight gain, 79.2% (19) reported it to a doctor prior to admission. There was a high number seeking pre-hospital medical assessment (via a GP/HF/general cardiology clinic): 66.7% (38) of DN and 67.9% (38) of RA. Cardiology review (general/HF) was more common in RA than DN (39.3% vs. 3.5% respectively, p = 0.000); while more DN were reviewed by a GP only than RA (63.2% vs. 28.6%, p = 0.000). Of DN who were seen by a GP only, 11.1% (4) were prescribed a HF-directed intervention (HFI, commencement of a diuretic or alteration of an established diuretic regimen) and of RA who were seen by a GP only, 12.5% (2) were prescribed an HFI.
Conclusion: Due to the prolonged duration of symptoms and high rate of patients seeking medical advice in the community, there is both time and opportunity in which to implement a more effective HFI. Improved patient education and recognition of HF features by GP's with streamlined access to outpatient specialist assistance may allow for earlier appropriately directed HFI, potentially reducing the risk of admission.

	De Novo (DN)	Recurrent Admitters (RA)
Pre-hospital Assessments(no. of patients, all reviews)	38 (66.7%)	38 (67.9%)
Pre-hospital Assessments(no. of patients, GP only reviews)	36 (63.2%)	16 (28.6%)
Treatment given by GP's*(no. of patients)	HFI: 4 (11.1%) Other**: 15 (41.7%) Nothing: 18 (50%)	HFI: 2 (12.5%) Other**: 4 (25%) Nothing: 10 (62.5%)
*to those 36 DN and 16 RA patients reviewed only by a GP prior to admission**primarily antibiotics with or without steroids		

2068

The weekend effect - a distraction to actual associations with in hospital mortality - a large single centre experience

C Broughton[1]; S Davies[1]; CS Kwok[1]; S Anderson[1]; J Brough[1]; N Cotton[1]; F Umar[1]; A Appaji[1]; I Crossley[1]; S Duckett[1]; D Barker[1]; A Patwala[1]; U Kadam[2]; M Mamas[2]; DK Satchithananda[1]
[1]University Hospital North Midlands, stoke-on-trent, United Kingdom; *[2]Keele University, stoke-on-trent, United Kingdom*

Introduction: The data as to whether weekend admissions increase in patient mortality in acute heart failure (AHF) admissions are conflicting. Multi-centre outcomes for weekend admissions may be confounded by multiple institutional factors. We present the largest, single centre data examining whether in hospital mortality is associated with weekend admissions in comparison to other routinely collected patient data.
Methods: Routinely collected hospital episode data were analysed from January 2012 - December 2016 for emergency admissions with AHF to our university teaching hospital serving a population of 600000. Patients were identified by standardised national codes identifying AHF hospitalisation. All patients admitted on Saturday or Sunday were weekend admissions. Comparisons between survivors and all deaths, and weekday vs weekend admissions were made using unpaired Students t test and Chi 2 test as appropriate. P values of <0.05 were statistically significant.
Results: 4417 patients were admitted during the study: 3873 survived to discharge (in hospital mortality 12.3%). 21.3% (941/4417) were admitted at the weekend. The table below demonstrates comparative data for: for the total group, survivors vs. in hospital deaths, all patients weekday vs. weekend admissions. ** = $p<0.05$. There were no significant demographic, length of stay early or late in hospital mortality differences in AHF patients admitted during the weekend. AHF patients surviving to discharge are younger, less co-morbid and have shorter lengths of stay than patients with AHF who die in hospital.
Conclusions: There is no evidence of a 'weekend effect' on in hospital mortality in nearly 4500 admissions with AHF. We have demonstrated that in hospital mortality depends more on: pre-existing patient characteristics (e.g. extreme age, number of co-morbidities) and by in-patient factors reflected in the length of stay than by weekend admission date.

Table 2068

	Total AHF admissions n=4417	AHF survivorsn=3873	AHF in hospital deaths n=544	AHF admitted on a week day n=3476	AHF admitted at weekend n=941
Mean age (sd) in years	76.8(13.2)	76(13.4)**	83 (9.4)	76.6 (13.1)	77.6 (13.3)
% female	52	52	53	52	54
Mean number of co-morbidities (sd)	7.8 (10.1)	7.2 (9.8)**	11.5 (11.7)	7.8 (10.2)	7.6 (9.9)
Mean length of stay (sd) in days	7.5 (3.8)	7 (3.7)**	11.4 (2.4)	7.5 (3.8)	7.6 (3.8)
Died within 48 hrs of admission as % of total admissions	2.9	na	2.9	2.7	3.5
Died within 48 hrs as a % of total deaths	23.1	na	23.1	21.9	27.5
Total in hospital mortality as a % of admissions	12.3	na	na	12.2	12.8

Comparison between demographics and early and late in hospital mortality of patients with AHF based on survival or day of admission

2069

Biventricular unloading: an efficacious concept to rescue patients in refractory cardiogenic shock

JT Tongers[1]; J-T Sieweke[1]; LC Napp[1]; F Zauner[1]; D Berliner[1]; C Kuehn[2]; A Haverich[2]; J Bauersachs[1]; A Schaefer[1]
[1]*Hannover Medical School, Cardiology and Angiology, Hannover, Germany*; [2]*Hannover Medical School, Department of Cardiothoracic, Transplantation and Vascular Surgery, Hannover, Germany*

Funding Acknowledgements: Abiomed research funding

The prognosis of cardiogenic shock (CS) remains substantial although advances have been accomplished over the past decades. Amongst patients with CS mortality remains more than 40%, which is even worth in cases of refractory CS. In recent years, devices for transient mechanical support such as microaxial pump (Impella) or veno-arterial extracorporeal membrane oxygenation (vaECMO) have changed the field. Timing, efficacy, monitoring, weaning and many other aspects of the management of mechanical support are fairly unknown. This is particularly true for the case of combined mechanical support, where experiences are scarce.

We evaluated 55 consecutive patients (age 53 ± 2 yrs, 45 male/10 female) who were biventricularly supported by vaECMO and Impella microaxial pump due to refractory CS despite goldstandard intensive care. Cardiogenic shock resulted from cardiomyopathy (40%), STEMI (17%), NSTEMI (7%), and arrhythmia (15%). During the ICU-course patients were critically ill: e.g. 93% mechanical ventilation, 53% dialysis, 38% resuscitation. Impella and vaECMO were inserted and removed percutaneously via femoral access (duration of dual mechanical support: 107 ± 72 hrs). The length of ICU-/in-hospital stay was 12 ± 2 and 27 ± 5 days. Following the installation of mechanical support, hemodynamics stabilized while number and dosing of catecholamines could be reduced (dobutamine: BL 5.6 ± 4.2, 24-hrs 2.9 ± 3.1, 72-hrs 2.2 ± 2.7 mg/kg/min, $p < 0.0001$ vs. BL; norepinephrine BL 0.5 ± 0.6, 24-hrs 0.2 ± 0.3, 72-hrs 0.2 ± 0.3 mg/kg/min, $p < 0.0001$ vs. BL). As a measure of an improved periphery, lactate levels normalized rapidly (BL 8.5 ± 6.4, 24-hrs 2.4 ± 1., 72-hrs 2.1 ± 2.4 mmol/L, all $p < 0.05$ vs. BL). Although our patient cohort clearly constitutes a negative selection of CS patients with a devastating prognosis, in-hospital survival in our fragile population was only 42%. By contrast a substantial number of patients at-risk were rescued: 19 patients were bridged to recovery, and another 13 patients were bridged to VAD-implantation. Notably, in not a single patient weaning mechanical support had to be reinstalled after successful weaning, which positively reflects on our weaning concept of mechanical support devices. Furthermore, the safety profile of biventricular support was reasonable (11% DIC, 7% leg ischemia, 7% stroke, 6% compartment). In only 3 patients minor vascular access site problems occurred.

In conclusion, biventricular unloading by combined mechanical support using Impella microaxial pump vaECMO is efficacious in stabilizing and rescuing high-risk patients with refractory cardiogenic shock.

2070

Should we start ECLS and maintain the support after 24h for refractory cardiogenic emergencies?

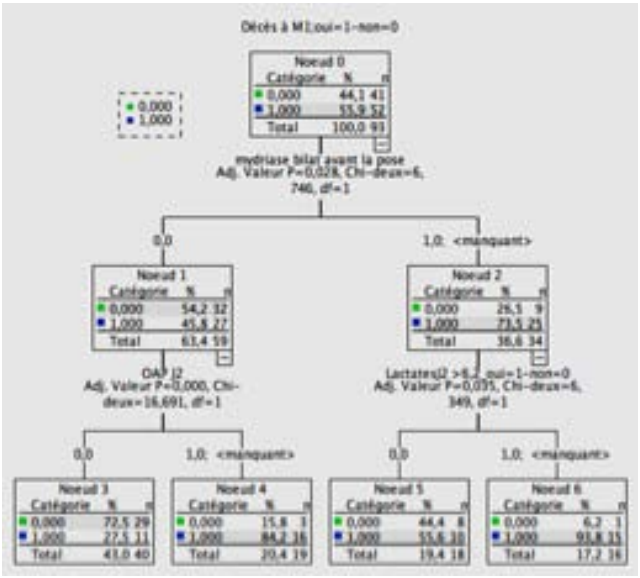
N Hernandez[1]; JM Conil[2]; B Georges[2]; T Seguin[2]; F Bounes[2]; L Crognier[2]; S Silva[3]; C Biendel[4]; V Minville[3]; B Marcheix[5]; C Delmas[2]
[1]*Civils Hospices of Lyon, Centre Hospitalier Lyon Sud-pôle anesthésie réanimation, Lyon, France*; [2]*Toulouse Rangueil University Hospital (CHU), Service de reanimation polyvalente, Toulouse, France*; [3]*University Hospital of Toulouse, Pôle anesthésie-réanimation, Toulouse, France*; [4]*Toulouse Rangueil University Hospital (CHU), USIC, federation des services de cardiologie, Toulouse, France*; [5]*Toulouse Rangueil University Hospital (CHU), service de chirurgie cardiaque, Toulouse, France*

Introduction: Extracorporeal life support (ECLS) has taken an important place in the treatment of cardiogenic shock (CS) or refractory cardiac arrest (CA). Because the decision is taken in extreme emergency, the real challenges are the good patient selection and the early reassessment. The aim of this study was to research prognostic factors of 30-days mortality before and 24h after ECLS implantation for CS or CA.

Material and methods: All patients undergoing ECLS in our tertiary center during a 2-year period were prospectively included. The ECLS were managed with a multidisciplinary protocol based on consensus. Clinico-biological data were collected just before and 24h after ECLS implantation. These data were compared between survivors and deceased at one month.

Results: 94 patients were included with predominance of males (66%) and a median age of 53 years. ECLS was implanted for CA under resuscitation (29.8%), acute CS (37.2%), CS after CA (22.3%) and CS due to end-stage heart failure (10.6%). The 30-days mortality was 56.4%. Regarding the data before the implantation, a multivariate analysis (survival Cox model at 30 days) showed the influence of AMI (RR=3.06, IC95% [1.43-6.56]), bilateral mydriasis (RR=2.87, IC95% [1.30-6.31]), and a high lactate rate (RR=1.10, IC95% [1.02-1.18]). Regarding data 24h after ECLS, bilateral mydriasis before ECLS (RR=2.87, IC95% [1.34-6.07]), H24 arterial lactate rate>6.2mmol/l (RR=4.04, IC95% [1.96-8.32]) as well as acute pulmonary edema occurrence in the first 24h (RR=2.37, IC95% [1.20-4.70]) are significative prognostic markers of mortality. CHAID's segmentation method represented the patients' survival using the H24 covariables with a prevision of 75.3% and may help to stop or maintain ECLS after 24h of support (figure).

Conclusion: Simple biological and clinical parameters as initial mydriasis and a high lactate rate could help the ECLS decision. Moreover, the segmentation based on initial mydriasis, H24 lactate>6.2mmol/l and acute pulmonary edema 24h after ECLS support could serve to the early reassessment of the support for CA or CS.



Death prediction after 24h of ECLS

2071

Specialist input is the main determining factor for outcome in patients admitted with acute heart failure

N Al-Refaie[1]; M Phillips[2]; M Ashton[3]; S Lucas-Jones[3]; A Wong[3]
[1]John Radcliffe Hospital, Oxford, United Kingdom; [2]Princess of Wales Hospital, Bridgend, United Kingdom; [3]Princess of Wales Hospital, Cardiology Department, Bridgend, United Kingdom

Introduction: Acute heart failure (AHF) is associated with high mortality rates. UK national heart failure audit has highlighted higher in-patient mortality in patients who were managed by non-specialists, and the importance of specialist follow up.
Purpose: Compare in-patient mortality rates with 30 days, 6 months and 1 year mortality rates based on place of care, and determine the effect of specialist follow up on mortality rates.
Method: Retrospective analysis of data on 250 patients who were discharged with the primary diagnosis of heart failure from year 2014-2015.
Results: Inpatient mortality rate is significantly lower in patients treated in a cardiology ward compared to other medical wards (13% Vs. 23%, p value=0.03), however, 30 days, 6 months and 1 year mortality rates are not significantly different, although the trend still shows preference to the patients who were managed in the cardiac ward (30 days: 21.5% Vs. 25%, p value=0.3) (6 months: 32% Vs. 43%, p value=0.07) (1 year: 39% Vs. 46%, p value=0.16). Patients who were managed in cardiology ward were more likely to be followed up by specialists in the community (table 1). And patients who were followed up by HF specialists, regardless of the place of care were associated with significantly lower 6 months and 1 year mortality rates, compared to patients who were not followed up (6 months: 20% Vs. 35%, p value=0.04. 1 year: 26% Vs. 42%, p value=0.037).
Conclusions: In-patients mortality rate is significantly lower in AHF patients managed in cardiology ward. Similarly, specialist follow up was associated with lower mortality post discharge. These findings are likely to be attributed to better optimization of evidence based medicines, more comprehensive assessment, and patients' monitoring. This study highlighted that importance of specialist input in the management of such complex condition

	Cardiology ward N=158	Other medical wards N=92	P value
ECG	97%	88%	0.0002
Echo	92%	68%	0.0001
ACE inhibitors/ACE blockers	70%	67%	0.3
Beta blockers	77%	67%	0.04
Spironolactone/Eplerenone	46%	37%	0.09
Heart failure MDT	22%	13%	0.09
HF discharge planning	72%	60%	0.05
HF nurse follow up	22%	11%	0.03
Cardiology outpatient referral	34%	13%	0.0002

2072

In acute heart failure with reduced ejection fraction beta blocker has no beneficial effect on 1-year mortality in patients with slow discharge heart rate

J J Jin Joo Park[1]; CH Yoon[1]; DJ Park[2]; IH Chae[1]; DJ Choi[1]
[1]Seoul National University Bundang Hospital, Division of Cardiology,, Seongnam, Korea Republic of; [2]Hangang Sacred Hospital, Division of Cardiology, Seoul, Korea Republic of

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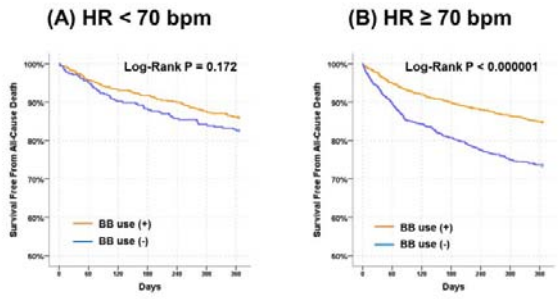
Background: Many hospitalized heart failure patients with reduced ejection fraction (HFrEF) have low heart rate at discharge. Low heart rate may be a sign for reduced sympathetic activity, and the effect of beta blockers may be reduced in those patients as well.
Methods: The Korea Acute Heart Failure (KorAHF) registry consecutively enrolled 5,625 patients hospitalized for acute HF. In this analysis we included patients with HFrEF (LVEF $<40\%$). Low heart rate was defined as <70 beats per minute (bpm). The primary outcome was 1-year all-cause death according to the heart rate.
Results: Of 3,088 patients with HFrEF, 852 (29%) had low heart rate and 57.3% received beta blocker at discharge. There was a significant interaction between discharge heart rate and beta blocker use (P for interaction <0.001). In Kaplan-Meier survival analysis patients with beta blocker had lower 1-year all-cause mortality only in patients with high heart rate, but not in those with low heart rate (Figure). Similar findings were observed both in patients with sinus rhythm and atrial fibrillation.
In a Cox-proportional hazard regression analysis, beta blocker prescription at discharge was associated with 29% reduced risk for 1-year mortality in patients with high heart rate (hazard ratio [HR], 0.71; 95% confidence interval [CI], 0.57-0.89, $P=0.003$), but not in patients with low heart rate (HR, 0.91; 95% CI, 0.61-1.37; $P=0.656$).
Conclusions: In hospitalized patients with HFrEF every third patient has a low heart rate at discharge and the beneficial effect of beta blocker on 1-year outcomes may be limited only to patients with high heart rate at hospital discharge.



Mortality According to Heart Rate

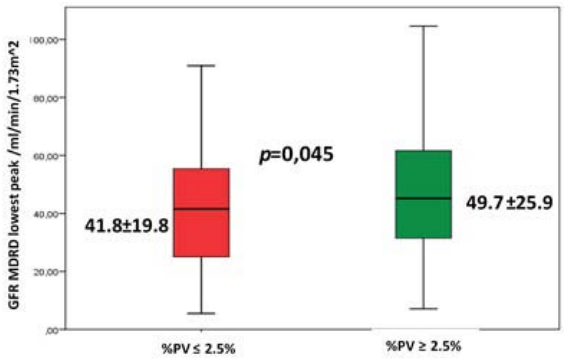
2073

Plasma volume and its relation with glomerular filtration rate in patients admitted with acute decompensated heart failure

D David Cabrita Roque[1]; J Augusto[1]; A Sachetti[1]; D Faria[1]; A Gaspar[1]; L Melo[1]; T Bernardo[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal

Background: Excessive depletion of vascular volume after diuretic therapy for acute decompensated heart failure (ADHF) is common and may lead not only to activation of the angiotensyn-renin-aldosterone system but also to acute kidney injury. Our aim is to evaluate the relation between the degree of contraction of vascular volume, using the percentage of alteration in the plasma volume and the glomerular filtration rate (GFR), after the use of diuretics, in patients admitted with ADHF.
Methods: Retrospective study of 258 patients (74.2 ± 17.3 years, 45.7% male) admitted in the emergency department between January and June 2016, for ADHF, defined by the presence of ≥ 2 signs or symptons of heart failure. All the patients were treated with diuretic therapy. We evaluate the diference between admission and discharge values of hemoglobin (ΔHb), hematocrit (ΔHtc), sodium (ΔNa), and the GFR evaluted by the Modification of Diet in Renal Disease (MDRD). The relative change in plasma volume (%PV) from admission until discharge was estimated by: {([Hb admission/Hb discharge]x[(100-Htc discharge)/(100-Htc admission)])-1}x100.
Results: Of the 258 patients admitted with ADHF, we excluded 11.6% ($n=30$) for missing laboratory values or description of blood loss/need of blood transfusion during hospital stay. After diuretic therapy (average of maximum dose of furosemide administered 69.3 ± 17.3mg), the incidence of increase in the %PV was 61% ($n=139$) and in the decrease was 39% ($n=89$). We further divide the patients in two groups according to the average %PV (2.5%): group 1 with preserved volume [%VP $>2.5\%$ (from $>2.5\%$ to 44%, n=101], and the group 2 with diminished volume [%VP $<2.5\%$ (from -13.8% to $<1.5\%$, n=127]. There were no statistically significant difference regarding ΔNa (average of 0.73 ± 3.52mEq for group 1 vs. 1.52 ± 4.56mEq for group 2, $p=0.396$). Patients in the group 2 showed greater positive variations of ΔHb (group 1 average of -1.34 ± 0.78 g/dl vs. group 2 0.57 ± 1.01g/dl $p=<0.001$) and in ΔHtc (group 1 average of $-4.66\pm2.69\%$ vs. group 2 $2.21\pm3.23\%$, $p=<0.001$). We also conclude that patients in the group 2, with volume contraction, where those who, during hospital stay, had the lowest GFR (average of 49.7 ± 25.9 ml/min/1.73m2 for group 1 vs 41.8 ± 19.8ml/min/1.73m2 for group 2, $p=0.045$, statistically significant).
Conclusions: The present study establish a relation between the percentage of alteration in the plasma volume and the lowest peak value of GFR (acute kidney injury), in patients with ADFH, treated with diuretic therapy. Besides that, the values

of hemoglobin and hematocrit seems to be the most useful laboratory values to evalute congestion vs contraction of volume. The sequential evaluation of the percentage of variation in the PV could be a useful tool to avoid the overuse of diuretic therapy in these patients and prevent the ocorrence of acute kidney injury during hospital admission.

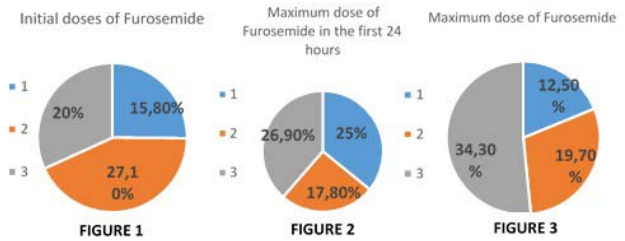


2074

Relation between the dose of loop diuretics and worsening renal function during hospitalization for acute decompensated heart failure

D David Cabrita Roque[1]; J Augusto[1]; A Sachetti[1]; D Faria[1]; A Gaspar[1]; L Melo[1]; T Bernardo[1]; J Simoes[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal*

Background: Worsening renal function (WRF) during heart failure (HF) hospitalization is common. Loop diuretics are increasingly being considered as a potential cause of worsened HF outcomes, perhaps via WRF. However, the magnitude of worsening in renal function attributable to loop diuretics is not well defined.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for acute decompensated heart failure. Admission, maximum and discharge values of creatinine (Cr) were collected, along with first dose, dose in the first 24 hours of admission and maximum dose of furosemide (Fur), the only loop diuretic in the hospital prescription set. We further divided each of the preceding parameters according to dose of Fur: Group 1 - Low (<40mg); Group 2 - Medium (40-80mg); and Group 3 - High (>80mg). The first Cr value or estimated glomerular filtration rate (eGFR) in the emergency department was considered baseline. A 20% relative decrease in eGFR defined WRF.
Results: We included 228 patients (45.6% male, 74.6±16.4 years). Baseline Cr was 1.47±0.87mg/dl, maximum Cr was 1.79±1.07mg/dl and discharge Cr was 1.38±0.73mg/dl. The average initial dose of Fur was 39.6±32.2mg; the average maximum dose in the first 24 hours was 88.4±73.9mg and the average maximum dose was 69.7±39.2mg. There were no significant association between the various doses of Fur and the incidence of WRF: initial doses of Fur (incidence of WRF: Group 1 15.8% vs. Group 2 27.1% vs. Group 3 20.0%, p=0.137; figure 1), maximum dose in the first 24 hours (incidence of WRF: Group 1 25.0% vs. Group 2 17.9% vs. Group 3 26.9%, p=0.289; figure 2) and the maximum dose of Fur (incidence of WRF: Group 1 12.5% vs. Group 2 19.7% vs. Group 3 34.3%, p=0.128; figure 3).
Conclusions: While loop diuretic exposure and its dose is empirically associated with WRF among hospitalized HF patients, this study demonstrate that the association between WRF and the dose of furosemide, in three separate times during acute decompensated heart failure hospitalization, can not be made, and so, loop diuretics explain little of the variability in renal function during hospitalization.



Incidence of WRF according to group

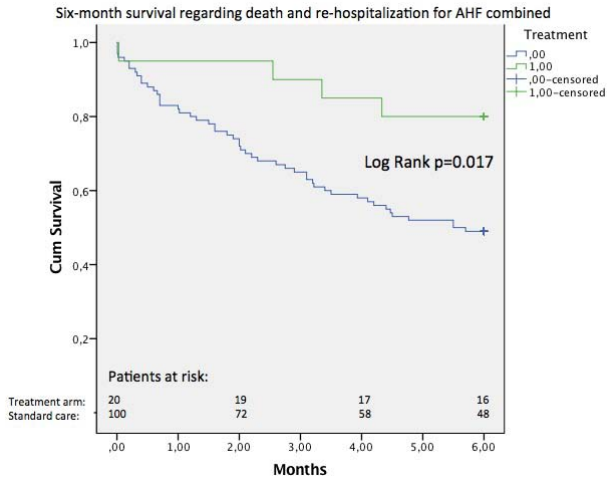
2075

Ultrasound-guided treatment in Acute Heart Failure based on lung ultrasound and cardiac filling pressures- greater decongestion despite shorter hospitalization and improved survival

JG Oehman[1]
[1]*Turku University Hospital, Cardiology , Turku, Finland*

On behalf of: DYSPNEA study group

Introduction: -Treatment for acute heart failure (AHF) is ineffective and hospitalizations long and expensive, as there is virtually no prognostically beneficial treatment available -Lung ultrasound (LUS) and focused echoardiography allow monitoring of pulmonary congestion and cardiac filling pressures during AHF treatment, and may be done sequentially using the same probe -Echo- and LUS-guided therapy could allow aggressive decongestive therapy in AHF while monitoring hemodynamics, but has not been studied to date
Purpose: To investigate the efficacy and safety of ultrasound-guided therapy in AHF using a focused cardiothoracic ultrasound protocol (CaTUS), combining medial E/e', IVC index (based on diameter and respiratory variation) with LUS
Methods: After enrolling 100 AHF patients for follow-up purposes, we enrolled an additional 20 patients who received aggressive decongestive therapy guided by CaTUS, based on a pre-specified treatment protocol-All patients had the CaTUS done on a daily basis, alongside clinical parameters and laboratory samples -The treatment protocol aimed for resolution of pulmonary congestion, normalization of E/e' and a plethoric IVC, while monitoring renal function, electrolytes and clinical parameters
Results: Patients in the treatment arm had a significantly larger mean(±SD) reduction in all congestion parameters, i.e. E/e' (6.48±2.9 vs. 2.62±4.6, p=0.001) , % reduction in BNP (35.9±26 vs. 16.6±61, p=0.029), IVC index (1.91±1,1 vs. 0.38±0.8, p<0.001), cumulative fluid loss (5.47±5.3 vs. 3.07±3.0, p<0.001)(p<0.05 for all) despite a significantly shorter hospitalization (3.7±2.0 vs. 6.9±4.2 days, p<0.001) as compare to patients in the standard care arm -A larger proportion in the treatment arm were also asymptomatic (95 % vs. 72 %, p=0.036) and free of any signs of pulmonary congestion on LUS (80 % vs. 53 %, 0.039), and had a lower mean E/e' (14.4±3.1 vs. 18.0±4.1, p<0.001), mean IVC index (1.02±1.0 vs. 1.82±0.76, p=0.005) and median(25%-75% IQr) BNP (249 (172-408) vs. 426 (242-1015), p=0.011 at discharge, without any significant difference in any of these parameters on admission-There was a trend towards less adverse events in terms of acute kidney injury and symptomatic hypotension in the treatment arm (p=0.617 and 0.378)-Patients in the treatment arm seemed to have an improved six-month survival regarding the combined endpoint of death and re-hospitalization for AHF compared to the conventional treatment group (Figure), although the treatment group was small for prognostic purposes
Conclusion: CaTUS-guided aggressive AHF treatment resulted in greater decongestion during shorter, and thus propaply cheaper, hospitalization, and may be associated with an improved prognosis



6-month survival, combined endpoint

			Peripheral oedema None (A)	Mild (B)	Moderate (C)	Severe (D)	Total
NYHA Class of symptoms	IV	Age %Female	6% (7,218) 80 44%	7% (8,403) 81 48%	11% (13,625) 81 45%	10% (11,824) 79 40%	34 (41,070)
III	Age %Female	9% (10,219) 78 41%	11% (12,298) 79 45%	17% (20,020) 80 43%	7% (7,708) 78 37%	44 (50,245)	
I/II	Age %Female	9% (10,571) 75 36%	7% (8,308) 79 44%	4% (4,808) 80 46%	1% (1,750) 80 38%	21 (25,437)	
Total			24 (28,008)	25 (29,009)	32 (38,453)	18 (21,282)	

2076

Characteristics and outcome of patients according to the severity of peripheral oedema and breathlessness, a report from national (england & wales) heart failure audit

A Shoaib[1]; M Mamas[2]; S Thackray[3]; M Rashid[1]; R Perveen[3]; A Raza[3]; A Shote[4]; S Hardman[5]; T Mcdonagh[4]; H Dargie[6]; A Mohamed[7]; ALC Clark[3]; JGFC Cleland[6]
[1]Keele University, Academic Cardiology, Stoke on Trent, United Kingdom; *[2]University of Keele, Academic Cardiology, Stoke on Trent, United Kingdom*; *[3]University of Hull, Department of Academic Cardiology, Hull, United Kingdom*; *[4]King's College Hospital, London, United Kingdom*; *[5]Whittington Hospital, Cardiology Department, London, United Kingdom*; *[6]University of Glasgow, Glasgow, United Kingdom*; *[7]Whiston Hospital, Liverpool, United Kingdom*

Introduction: Heart failure is a common reason for hospital admission. Patients presenting with pulmonary and peripheral oedema may be seen as two ends of a spectrum with many patients presenting with a mixed picture. The purpose of the present analysis is to describe patient characteristics according to the severity of oedema and NYHA class, their length of hospital stay and mortality during the index admission and after discharge.
Methods: National Audit Data were collected from April 2007 to March 2013 in more than 90% of hospitals in England & Wales. Patients with a confirmed discharge diagnosis of heart failure were divided by severity of peripheral oedema (severe, moderate, mild and none) and NYHA class (IV, III, II/I) – creating 12 groups. Patients' characteristics and mortality during the index hospital admission for up to three years after discharge were reported.
Results: Amongst 136,790 patients, the median age was 79 years, 58% were women, 81% were treated with ACEi/ARB, 67% with beta-blockers and 40% with MRA at discharge. Only 34% of patients had breathlessness at rest or minimal exertion at the time of admission and 18% had severe peripheral oedema.
Prevalence of LVSD was highest in group I-II/A (71%) and lowest in group I-II/D (49%). Median length of index admission stay was determined by the severity of peripheral oedema rather than NYHA class: 12 days for severe, 9 days for moderate, 7 days for mild and 6 days for no peripheral oedema. The highest index admission mortality during was observed in group IV/D (18%) followed by III/D (13%) and lowest in groups I-III/A (6%). After median follow-up 344 (IQR 94-766) days), mortality was 60% for IV/D and 56% for III/D compared to 46% for IV/A and 40% for III/A (. Hazard ratios for death in the above groups were 2.26, 2.09, 1.49 and 1.28 respectively (for all P- < 0.001) compared to group I-II/A.
Conclusion: The severity of peripheral oedema rather than of breathlessness or LVSD is the more important determinant of length of stay and prognosis in patients with heart failure. However, the prognosis of patients recently hospitalised with heart failure remains poor despite a high uptake of disease modifying medication.

2077

Intravenous ivabradine in low cardiac output syndrome treated by dobutamine following cardiac surgery: a phase II trial

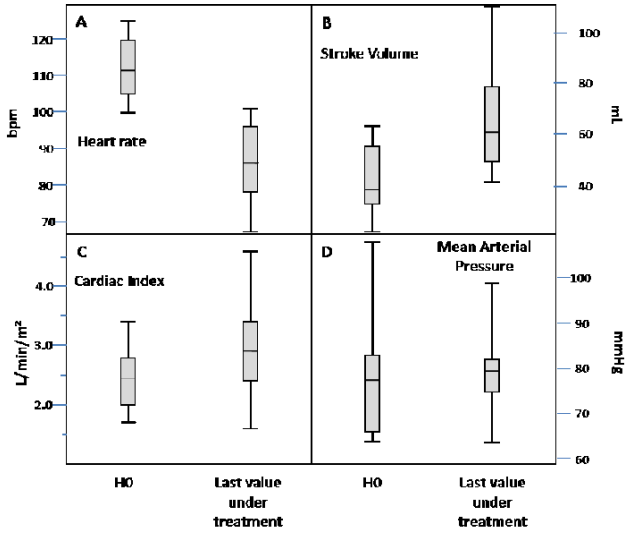
L S Nguyen[1]; P Squara[1]; J Amour[2]; B Cholley[3]
[1]Clinique Medico-Chirurgicale Ambroise Pare, Critical Care Department, Neuilly sur Seine, France; *[2]Hospital Pitie-Salpetriere, Anesthesiology and Critical Care Medicine Department, Paris, France*; *[3]Hôpital Européen Georges Pompidou, Université Paris Descartes, Anesthesiology and Critical Care Medicine Department, Paris, France*

Funding Acknowledgements: Servier

Background: Dobutamine is the first-line treatment for low cardiac output syndrome (LCOS) after cardiac surgery, but induces sinus tachycardia. We aimed to assess the intravenous (i.v.) ivabradine in patients presenting LCOS with dobutamine-induced tachycardia following elective coronary artery bypass graft surgery.
Methods: In a phase 2 multi-center randomized placebo-controlled trial, i.v. ivabradine was infused in patients presenting sinus tachycardia (heart rate (HR) > 100 bpm) after dobutamine initiation. Primary endpoint was the number (%) of patients having their HR reduced between 80 and 90 bpm for > 30 minutes. Secondary endpoints were hemodynamic parameters measured by Swan-Ganz catheter.
Results: Thirteen (93%) patients treated by ivabradine reached the primary endpoint, compared to 2 (40%) in the placebo group ($p < 0.05$). Ivabradine significantly decreased HR (112 to 86 bpm ($p < 0.001$)) while increasing cardiac index (2.5 to 2.9 l/min/m^2 ($p < 0.05$)), stroke volume (38.0 to 60.0 ml ($p < 0.001$)) and systolic blood pressure (110 to 125 mmHg ($p < 0.05$)). These parameters remained similar in the placebo group. Five (35.7%) patients developed atrial fibrillation in the ivabradine group.
Conclusion: Intravenous ivabradine reduced HR in patients presenting with LCOS treated with dobutamine after CABG surgery, without impairing cardiac output. This beneficial effect should be confirmed with larger trials.

Baseline characteristics		
	Ivabradine group (n = 14)	Placebo group (n = 5)
Age (years)	61 [59 ; 67]	54 [53 ; 59]
Male gender (%)	11 (79)	5 (100)
BMI (kg/m^2)	27.5 [25.8 ; 28.9]	26.2 [25.9 ; 29.7]
HR (bpm)	73.5 [65.0 ; 89.0]	75.0 [67.0 ; 77.0]
SBP (mmHg)	120 [112 ; 130]	115 [114 ; 125]
LVEF (%)	32 [25 ; 38]	35 [27 ; 39]
EuroSCORE	5.5 [4.5 ; 6.5]	4.0 [3.5 ; 6.5]
Hypertension(%)	9 (64.3)	3 (60.0)
Diabetes(%)	7 (50.0)	2 (40.0)
Heart Failure(%)	7 (50.0)	3 (60.0)

BMI: body-mass index; HR: heart rate; SBP: systolic blood pressure; LVEF: left ventricule ejection fraction.



Hemodynamics: ivabradine group

2078

Effect of tolvaptan administration on renal function in the acute phase of congestive heart failure

Y Kawase[1]; R Hata[1]; T Tada[1]; K Kadota[1]

[1]Kurashiki Central Hopistal, cardiovascular medicine, Kurashiki, Okayama, Japan

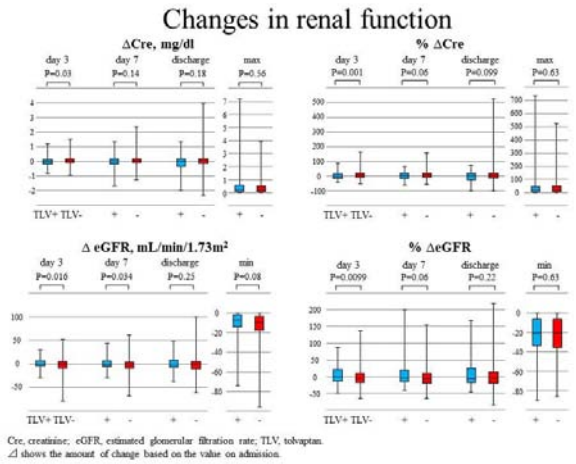
Background: Tolvaptan has been widely used as a diuretic drug in the acute phase of congestive heart failure. However, how it affects renal function has not been clarified sufficiently.

Purpose: To clarify the effect of tolvaptan administration on renal function in the acute phase of congestive heart failure.

Methods: We retrospectively investigated 1038 consecutive patients hospitalized for congestive heart failure between February 2015 and December 2016 and enrolled 556 patients in the study sample, excluding those with end stage renal dysfunction (estimated glomerular filtration rate [eGFR] <15 mL/min/1.73m2), acute coronary syndrome, tolvaptan use prior to admission, and insufficient data. We divided the 556 patients into two groups based on the use and non-use of tolvaptan within 2 days after admission: 111 patients (tolvaptan group) and 445 patients (non-tolvaptan group). The primary outcome measure was defined as $\geq$20% decline in eGFR from the value on admission, and its rate on day 3, day 7, and at the time of discharge was compared between the two groups.

Results: The mean age of the tolvaptan group was 79.3 ± 12.1 years and that of the non-tolvaptan group was 77.2 ± 13.6 years. Renal function on admission was significantly worse in the tolvaptan group than in the non-tolvaptan group (creatinine, 1.22 [0.87 to 1.72] versus 1.01 [0.80 to 1.32], $p < 0.001$; eGFR, 38.7 [24.8 to 54.7] versus 48.7 [35.7 to 63.1], $p < 0.001$). The figure shows creatinine, % creatinine, eGFR, and % eGFR on day 3, day 7, and at the time of discharge, respectively. shows the amount of change based on the value on admission. On day 3, $\geq$20% decline in eGFR was observed in 20% of the study sample (113/556 patients), and its rate was significantly lower in the tolvaptan group than in the non-tolvaptan group (10/111 patients [9.0%] versus 103/445 patients (23.2%), $p < 0.001$). On the other hand, on day 7 and at the time of discharge, there were no significant differences between the two groups. Multivariate analysis showed that tolvaptan administration in the acute phase significantly reduced the rate of $\geq$20% decline in eGFR on day 3 (adjusted odds ratio, 0.35; 95% confidence interval, 0.16 to 0.71, $p = 0.003$).

Conclusion: In the acute phase, tolvaptan administration to patients with congestive heart failure may prevent renal function from worsening.



MODERATED POSTER SESSION 6 - THERAPY

2079

Granulocyte colony-stimulating factor in patients with a large anterior wall acute myocardial infarction to prevent left ventricular remodeling (the RIGENERA trial): 10 years follow-up- FINAL RESULTS

D Domenico D'amario[1]; AM Leone[1]; F Cannata[1]; F Graziani[1]; F Cobianchi Bellisari[1]; M Massetti[1]; L Galiuto[1]; AG Rebuzzi[1]; F Crea[1]
[1]*Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy*

Background: Granulocyte-colony stimulating factor (G-CSF) has been clinically tested in ST-elevation myocardial infarction (STEMI) patients with controversial results.
Purpose: Aim of the study was to determine the long-term safety, feasibility and efficacy of stem cell mobilization following G-CSF as a treatment for acute myocardial infarction.
Methods: 41 patients were randomized 1:2 to G-CSF therapy (n = 14) or conventional therapy (n = 27) from June 2003 to May 2006, in order to assess the potential efficacy of G-CSF administration on cardiac function evaluated by conventional echocardiography, in patients with a first large anterior AMI and a LV ejection fraction < 50% despite successful percutaneous revascularization of the infarct-related artery. Exclusion criteria were cardiogenic shock, uncontrolled myocardial ischemia or arrhythmias, malignancies, severe infections, hematologic diseases, splenomegaly on abdominal echocardiography and age >80 years. Patients randomized to G-CSF therapy were treated with lenograstim at a dose of 10 μg/kg/day for 5 days starting ≥ 5 days after AMI and/or a complete revascularization. The 10 year follow-up was completed, 3 patients were lost to follow-up: the final population consisted of 38 patients (12 in G-CSF group and 26 in control group). LV function and NYHA functional class evaluation was performed at follow up, together with quality of life and life expectancy assessed by Minnesota Living with Heart Failure Questionnaire (MLHF) and The Seattle Heart Failure Model (SHFM) respectively.
Results: No differences were found in the two groups in term of LVEF and LVESV. Remarkably, a significant increase was detected in control group when considering the difference (Delta) in LVEDV between baseline and follow up ($p < 0.05$). This result was coupled with a reduction in the incidence of adverse LV remodeling in the G-CSF group (48% Control vs 8% G-CSF; $p = 0.01$). Moreover, patients treated with G-CSF referred a better quality of life and a lower burden of symptoms, compared to control patients, as shown by MLHF score ($p = 0.05$) and NYHA functional class ($p = 0.04$). The mean life expectancy, evaluated with the SHFM, was significantly higher in the G-CSF group then control (15 ± 4 years vs 12 ± 4 years $p = 0.05$). At 10 years, deaths were two fold higher in the control compared to G-CSF group, although this difference was not statistically significant (19% vs 8%; $p = 0.39$), most likely due to the paucity of the population.
Importantly, the incidence of recurrent MI, in-stent restenosis and occurrence of malignancies was similar in G-CSF-treated patients and controls.
Conclusions: The final analysis ot the 10-year data from the RIGENERA trial represent the longest available follow-up on the safety and efficacy of G-CSF treatment in STEMI patients. The administration of G-CSF is not only safe but also associated with a documented reduction of adverse ventricular remodeling after large anterior STEMI and better quality of life.

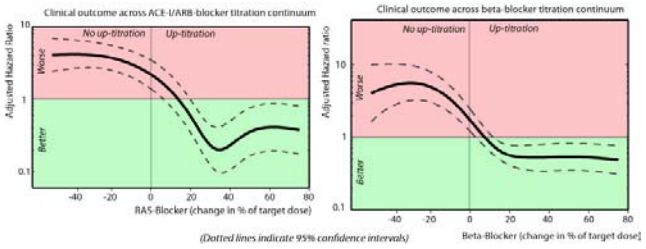
2080

Feasibility and benefit of neurohumoral blocker uptitration following cardiac resynchronization therapy

P Pieter Martens[1]; FH Verbrugge[1]; P Nijst[1]; PB Bertrand[1]; M Dupont[1]; WH Tang[2]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*; [2]*Cleveland Clinic Foundation, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland, United States of America*

Funding Acknowledgements: Pieter Martens is supported by a doctoral fellowship by the Research Foundation – Flanders (FWO, grant-number: 1127917N

Background: Cardiac resynchronization therapy (CRT) improves mortality and morbidity on top of optimal medical therapy in heart failure with reduced ejection fraction (HFrEF). Although CRT is considered as a step-on option after optimal medical treatment, its beneficial effects with regards to reverse remodelling, could allow for further uptitration of neurohumoral blockers despite optimal baseline of medical therapy.
Methods: Doses of angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB) and beta-blockers were retrospectively evaluated in 650 consecutive CRT patients, implanted between October, 2008, and August, 2015. All 650 patients were on individually optimal dose at the time of implant. Uptitration was calculated as the difference in percent of target dose between CRT-implantation and six month follow-up. Outcome was measured as the combined end-point of heart failure admission or all-cause mortality.
Results: Uptitration was performed in 45.4% (n = 191) of patients for ACE-I/ARB and 56.8% (n = 283) for beta-blockers, in patients who were not at maximal target dose at implantation. ACE-I/ARB were uptitrated on average 39 ± 20% of target dose and beta-blockers 44 ± 20% of target dose. During a mean follow-up of 37 ± 22 months, a total of 148 events occurred for the combined endpoint of heart failure admission and all-cause mortality. Uptitration versus no-uptitration following CRT was associated with an adjusted hazard ratio of 0.54 (0.32-0.91; $p = 0.022$) for ACE-I/ARB and 0.63 (0.41-0.99; $p = 0.044$) for beta-blocker therapy on the combined end-point of heart failure and all-cause mortality. Figure 1 illustrates the relationship between post-implant dose adaptation for ACE-I/ARBs and Beta-blockers, versus the adjusted hazard ratio for the combined endpoint depicted on a continuous scale. Patients in the uptitration group exhibited a similar low risk for death or heart failure admission as patients treated with the maximal dose at the time of CRT-implant (ACE-I/ARB $p = 0.133$, beta-blockers $p = 0.709$).
Conclusions: Following CRT, a majority of patients are capable of tolerating higher dosages of neurohumoral blockers. Uptitration of neurohumoral blockers after CRT implantation associates with improved clinical outcome, even matching patients treated with the guideline-recommended target dose at the time of implant.



2081

Relation of biological and functional LV remodeling to obstruction in hypertrophic cardiomyopathy. A rest and exercise echocardiographic study with longitudinal strain measurement

F Flore Morio[1]; TLT Le Tourneau[1]; NP Piriou[1]; CC Cueff[1]; JMS Serfaty[1]; KW Warin[1]; JNT Trochu[1]
[1]*University Hospital of Nantes Nord Laennec, Nantes, France*

Introduction: Outflow tract obstruction is thought to be involved in left ventricular (LV) remodeling in sarcomeric hypertrophic cardiomyopathy (HCM).
Objective: To determine the influence of obstruction to biological parameters of remodeling and global longitudinal strain (GLS) in HCM.
Material and Methods: Patients with HCM who accepted to participate to this study were included. Transthoracic echocardiography at rest and exercise with GLS measurement was carried out. Blood was sampled before and early after exercise.

Patients were divided into 3 groups according to the presence of an obstruction at rest (OHCM), effort (Latent obstruction: LOHCM), or none (HCM).
Results: We included 40 HCM patients, 7 OHCM, 19 LOHCM and 14 NOHCM. Troponin T and NTproBNP levels at rest were significantly higher in OHCM compared to NOHCM (19.5 ± 10 vs 10 ± 5.8 ng/L, p = 0.017 and 1184 ± 389 vs 520 ± 388ng/l, P=0.005). Troponin T and NTproBNP levels at rest were correlated with the outflow tract peak gradient (r=0.49, p = 0.001 and r=0.41, p = 0.005, respectively) and with the alteration of GLS (r=0.51, p = 0.001 and r=0.46, p = 0.003, respectively). After exercise ST2, IL6, GDF15, Troponin T and NTproBNP increased significantly in OHCM + LOHCM while only NTproBNP increased in NOHCM. In multivariate analysis post-exercise Troponin T (β=0.57, P < 0.0001) was a determinant of GLS at rest. MMP9 (β=-0.44, P=0.004) and TGFβ (β=0.54, P=0.001) at rest, and post-exercise Troponin T (β=0.57, P < 0.0001) were independent determinants of exercise GLS.
Conclusion: In HCM, biological parameters of remodeling are correlated to obstruction and GLS. Exercise in obstructive forms of HCM induces a significant increase in multiple biological parameters of remodeling. Troponin T level is a strong predictor of GLS alteration both at rest and exercise.

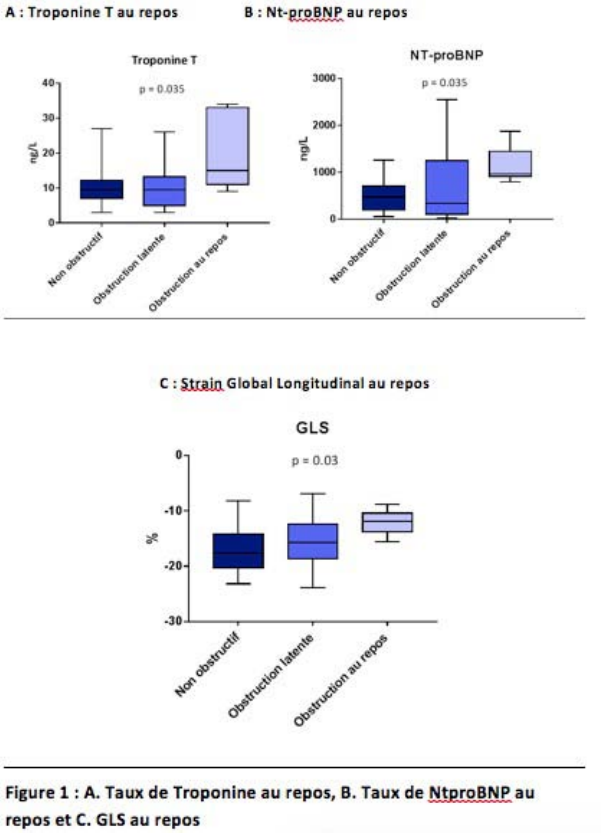


Figure 1 : A. Taux de Troponine au repos, B. Taux de NtproBNP au repos et C. GLS au repos

Figure 1

2082

Early phase 99Tc-HMDP scintigraphy: a rapid and reliable technique for the diagnosis and typing of cardiac amyloidosis

A Arnault Galat[1]; AVG Van Der Gucht[2]; AG Guellich[1]; DB Bodez[1]; ASC Cottereau[2]; SG Guendouz[1]; LH Hittinger[1]; JLDR Dubois-Rande[1]; VPB Plante-Bordeneuve[3]; EI Itti[3]; MM Meignan[2]; TD Damy[1]; JR Rosso[2]
[1]*University Hospital Henri Mondor, Cardiology, Creteil, France*; [2]*University Hospital Henri Mondor, Nuclear medicine, Creteil, France*; [3]*University Hospital Henri Mondor, Neurology, Creteil, France*

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.
Aims: To compare accuracy of early (10 min) versus late (3h) cardiac fixation of 99mTc-HMDP at scintigraphy in diagnosing and typing CA.
Methods: 135 patients refereed for suspicion of CA were prospectively evaluated using 99mTc-HMDP scintigraphy. Myocardial tracer accumulation was semi-quantitatively measured and visually scored at early and late phases of bisphosphonate scintigraphy.
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 ventricular hypertrophy) and without amyloidosis served as controls. Early 99mTc-HMDP cardiac uptake was found in 68 patients whose late visual score was ≥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-HMDP heart/mediastinum ratio ≥1.115 predicts a late visual score ≥1 which differentiated CA from other causes of LVH (100% sensitivity, 97% specificity). Early heart / mediastinum ratio ≥1.210 discriminated TTR-CA from AL with perfect accuracy (100% sensitivity and specificity).
Conclusions: Early phase 99mTc-HMDP-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 avaibility of scintigraphy.

2083

Less invasive ventricular reshaping provides sustained reduction of heart failure symptoms

CS Schmitz[1]; PN Neuzil[2]; IS Skalsky[2]; LL Labrousse[3]; HS Sievert[4]; CF Frerker[5]; TS Schmidt[5]; KK Kuck[5]; MB Biffi[6]; AC Calafiore[7]; DP Pacini[6]; RDB Dibartolomeo[6]; GD Davidavicius[8]; G Kalinauskas[8]; K Rucinskas[8]
[1]*University Hospital of Munich, Munich, Germany*; [2]*Na Homolce Hospital, Prague, Czech Republic*; [3]*Hospital Haut Leveque, Bordeaux-Pessac, France*; [4]*CardioVascular Center Frankfurt, Frankfurt am Main, Germany*; [5]*Asklepios Clinic St. Georg, Hamburg, Germany*; [6]*University of Bologna, Cardiology, Bologna, Italy*; [7]*Prince Sultan Cardiac Center, Riyadh, Saudi Arabia*; [8]*University Hospital Santariskiu Klinikos, Vilnius, Lithuania*

Funding Acknowledgements: BioVentrix, Inc.

Background: A new technique described as Less Invasive Ventricular Enhancement (LIVE) was performed to reduce and reshape the left ventricle after anteroseptal infarction without cardiopulmonary bypass. Access in the early series was via median sternotomy and later using a hybrid transcatheter approach. We report survival, functional and echocardiographic results at 2 years.
Methods: All patients had MRI or CT demonstrating scars in the anteroseptal wall and symptoms of heart failure NYHA class II/III. Coronary lesions were always treated before the procedure. Significant MR was an exclusion criteria. LIVE was achieved using the Bioventrix Revivent Myocardial Anchoring System. Titanium anchors were delivered to the right side of the interventricular septum. An external anchor was fitted onto a tether to allow apposition of the LV free wall to the scarred septum.
Results: Eighty-six patients were treated from August 2010 till March 2016. Baseline EF was 30 ± 8% and ESVi 72 ± 28 ml/m^2. Four patients (4.7%) died in-hospital and 1 (1.2%) had a stroke. Two-year survival was 89.2%. In 57 patients who completed 2-year follow up, EF improved (+13%) and LVESVI reduced (-27%). NYHA class reduced (2.6 ± 0.5 to 1.8 ± 0.7, P < 0,001), 6-minutes walking test increased (353 ± 108 to 432 ± 102 minutes, P < 0.001) and Minnesota Living with Heart Failure score reduced (41 ± 21 to 24 ± 19, P < 0.001). Serial echocardiograms and functional evaluations (@6,12,24 months) demonstrated sustained improvements.
Conclusions: Excellent survival and sustained improvement of echocardiographic and functional parameters are obtained using the Less Invasive Ventricular Enhancement technique. In patients with no significant MR and/or myocardial ischemia, ventricular reduction and reshaping, when performed off-pump using the Revivent myocardial anchors, demonstrates long term decrease in heart failure symptoms.

2084

A natriuretic peptides clearance receptor agonist reduces pulmonary artery pressures and enhances cardiac performances: new hope for PH due to HF

E Eroum A Egom[1]; T Feridooni[2]; RB Pharithi[1]; V Maher[1]; Y El-Hiani[2]; KS Pasumarthi[2]; H Ribama[3]
[1]*Adelaide & Meath Hospital, Dublin, Ireland*; [2]*Dalhousie University, Halifax, Canada*; [3]*ECTRS Ltd, Dartmouth, Canada*

Funding Acknowledgements: ECTRS Ltd

In patients with left ventricular heart failure (HF), the development of pulmonary hypertension (PH) is common and represents a strong predictor of death. PH due to HF is a disabling and life-threatening disease for which there is currently no single marketed pharmacological agent approved. Furthermore, despite recent advances in the pathophysiological understanding, there is as yet no prospect of cure of this deadly clinical entity, and the majority of patients continue to progress to right ventricular failure and die. There is, therefore an urgent unmet need to identify novel

pharmacological agents that will prevent the progressively increasing or reverse the already elevated pulmonary artery pressures while enhancing cardiac performance in HF. We here reported, for the first time, that a specific natriuretic peptides clearance receptors (NPR-C)' agonist, the ring-deleted atrial natriuretic peptide analogue, cANF4-23 (cANF) reduces pulmonary artery pressures and enhances cardiac performance including left ventricular inotropy in mice, using a pressure-loop (P-V) conductance catheter system (Table 1). Natriuretic peptides clearance receptors' agonists may therefore represent a novel and attractive therapeutic option for PH due to HF, and have the potential to ultimately improve morbidity and mortality for millions of people affected with PH due to HF.

Table 1

Haemodynamic Parameters	Baseline	After administration of cANF	95% Confidence interval
SW (mmHg*µL)	688.72±10.73	1274.80±7.34†	-610.04 to -562.12
CO (µL/min)	5099.40±23.25	4519.60±24.70†	466.64 to 692.96
SV (µL)	14.71±0.08	14.84±0.08*	-0.49 to 0.23
Ves (µL)	4.79±0.08	1.45±0.09†	2.99 to 3.71
Ved (µL)	18.48±0.27	13.45±0.08†	4.36 to 5.72
Heart Rate (bpm)	346.64±0.51	304.60±0.00*	Z-Statistic = -2.06
EF (%)	77.53±1.36	92.59±0.52†	-19.52 to -10.61
Ea (mmHg/µL)	3.40±0.03	5.69±0.06†	-2.48 to -2.09
PowMax (mmHg*µL/s)	4681.40±285.98	10727.60±492.07†	-7415.53 to -4676.87
dP/dt max (mmHg/s)	4186.60±5.12	7005.00±24.49†	-2885.73 to -2751.07
dP/dt min (mmHg/s)	-3412.20±17.43	-4945.20±60.07†	1352.48 to 1713.52
Tau (ms)	8.46±0.04	10.71±0.04†	-2.38 to -2.12

Haemodynamic Parameters

2085

Effect of aortic valve opening pattern on endothelial functions after continuous flow left ventricular assist device implantation

E Kaya[1]; E Simsek[1]; S Nalbantgil[1]; A Akilli[1]; P Ozturk[2]; C Engin[2]; T Yagdi[2]; M Ozbaran[2]

[1]Ege University, Faculty of Medicine, Department of Cardiology, Izmir, Turkey; [2]Ege University, Faculty of Medicine, Department of Cardiovascular Surgery, Izmir, Turkey

Background And Objective: Recent studies have shown that endothelial functions are negatively affected by decreased pulsatile flow in the arterial system following implantation of continuous flow left ventricular assist device (CF-LVAD). During systole aortic valve opening patterns differs among CF-LVAD patients and effects on endothelial functions of these patterns have not been studied in detail. In this study after CF-LVAD implantation associations with aortic valve opening patterns and endothelial functions are evaluated.

Methods: Forty three CF-LVAD patients (pre-implantation NYHA class III-IV) and as a control group 35 NYHA class II heart failure (HF) patients were included in the study. Control group had just baseline testing however CF-LVAD group had pre implantation and 3 months after post implantation endothelial function testing with flow mediated vasodilatation (FMD) method. CF-LVAD patients were divided into three subgroups according to the opening patterns of aortic valve with echocardiography; as complete opening, intermittent opening, constantly closed; and the effects of these patterns on endothelial functions were investigated.

Results: Mean FMD was significantly lower in pre- CF-LVAD patients than control group. (% 5.4 ± 0,94 vs. % 7.6 ± 1.11, P < 0.001). Three months after CF-LVAD implantation, mean FMD was % 3.7 ± 0,81 and significantly lower than pre implantation. (p < 0.001). Between subgroups of aortic valve opening patterns, patients with closed and intermittent opening patterns had significantly decreased endothelial functions. (% 5.02 ± 1.16 vs. % 3.37 ± 0.91, p = 0.001; % 5.8 ± 1.61 vs. % 4.30 ± 2.46, p = 0.024 respectively) However patients with complete opening aortic valve pattern did not have any statistically difference. (% 4.72 ± 1.06 vs. % 4.67 ± 1.16, p = 0,135) (Table 1)

Conclusions: Diminished pulsatile flow after CF-LVAD implantation impairs endothelial functions. Complete opening of the aortic valve in each systole may provide enough pulsatile flow to the peripheral arterial system to prevent the development of endothelial dysfunction. CF-LVAD implantation should be performed before complete loss of the left ventricular contractility reserve to save complete opening aortic valve pattern and endothelial functions.

Table 1

	BeforeCF-LVAD impl.FMD(%)	AfterCF-LVAD impl.FMD(%)	p
Opening Aortic Valve (n = 18)	4,72±1,06	4,67±1,16	0,135
Closed Aortic Valve(n = 21)	5,02±1,16	3,37±0,91	0,001
Intermittent OpenningAortic Valve(n = 4)	5,80±1,61	4,30±2,46	0,024

Mean FMD values of patients with different aortic valve opening patterns before and after CF-LVAD implantation

2086

Spironolactone reduces all-cause mortality in women but not men with heart failure with preserved ejection fraction enrolled in TOPCAT from the Americas

DP David Peter Kao[1]; KM Flint[1]; M Merrill[1]

[1]University of Colorado Denver, Denver, United States of America

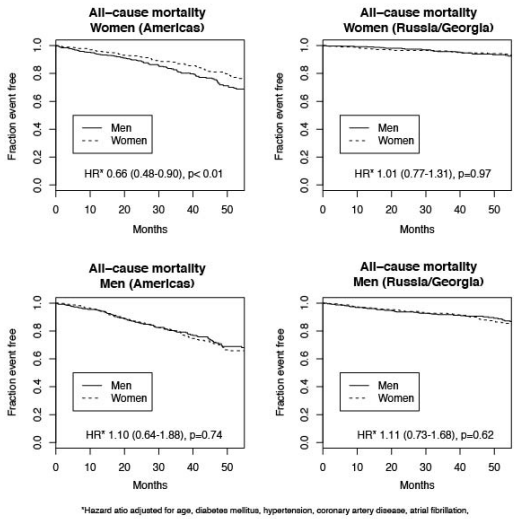
Background: Large clinical trials of treatments for heart failure with preserved ejection fraction (HFpEF) have suggested differences between women and men in several clinical outcomes but not treatment response. Sex differences in outcomes and treatment response in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) trial have not yet been reported.

Purpose: To characterize sex differences in outcomes and treatment response in subjects enrolled in TOPCAT.

Methods: 3445 patients with symptomatic heart failure and an LVEF ≥45% were randomized to spironolactone or placebo with mean follow-up 3.3 years. The primary outcome was a composite of cardiovascular (CV) death, aborted cardiac arrest, or HF hospitalization. Secondary outcomes were all-cause mortality and hospitalization. Outcomes were stratified by sex, treatment arm and enrollment region (Americas vs. Russia/Georgia). Treatment effect of spironolactone was determined using time-to-event analysis.

Results: 1775 women (882 from the Americas) were enrolled vs. 1670 men (785 from the Americas (p = 0.053). Overall, rates of all the primary outcome, all-cause mortality, and hospitalization were significantly lower in women vs. men (17 vs. 22%, 12 vs. 19%, 42 vs 49%, p < 0.001). In subjects from the Americas, rates for women vs. men of the primary outcome (27 vs. 32%, p = 0.04) and all-cause mortality (19 vs. 25%, p = 0.004) were significantly different, but hospitalization was not (59 vs. 61%, p = 0.33). In subjects from Russia/Georgia, rates of the primary outcome (6 vs. 12%), all-cause mortality (6 vs. 11%) and hospitalization (26 vs. 34%) were lower in women than men (p < 0.001 for all). Outcome rates by region, sex, and treatment arm are shown in the Table. Spironolactone was associated with reduced all-cause mortality in women in region 1 only, even when adjusted for age, diabetes mellitus, hypertension, atrial fibrillation, coronary artery disease, and COPD (HR 0.66, p = 0.008). (Figure)

Conclusions: Women with HFpEF had lower rates of most adverse outcomes than men. The benefit of spironolactone previously observed in the Americas appears driven by reductions in mortality in women only.



All cause mortality by sex and region

Table 2086: Outcomes by sex and treatment arm, N(%)

	Americas				Russia/Georgia			
	Female		Male		Female		Male	
	Spiro	Placebo	Spiro	Placebo	Spiro	Placebo	Spiro	Placebo
Primary outcome	111(25)	130 (30)	131 (30).	150 (34)	26 (6)	30 (7)	48 (12)	45 (11)
All-cause mortality	70 (16)	98 (22)*	112 (25)	107 (24)	25 (6)	28 (6)	47 (12)	43 (11)
Hospitalization	252 (57)	268 (61)	274 (62)	268 (81)	121 (27)	107 (24)	133 (34)	136 (34)

*p = 0.014. Spiro=spironolactone

2087

Intrarenal venous flow alterations during transition from euvolemia to intravascular volume expansion in heart failure patients with reduced ejection fraction

P Petra Nijst[1]; P Martens[1]; M Dupont[1]; W Tang[2]; W Mullens[1]
[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium; [2]Cleveland Clinic Foundation, Cleveland, United States of America

Background: Diuretic capacity relates to intrinsic renal function but also to renal blood flow. Intrarenal blood flow alterations may help better understand impaired volume handling in heart failure (HF).
Objectives: To study 1) intrarenal flow patterns in chronic HF patients with reduced ejection fraction (HFrEF) during the transition from euvolemia to intravascular volume overload, and 2) the relationship between intrarenal flow patterns and diuretic efficiency.

	HFrEF (n = 40)
Baseline characteristics- Age- Ischemic etiology	65±1283%
Laboratory values- eGFR (ml/min + 1.73m2)- NT-proBNP (ng/L)	64±26670[225;1383]
Baseline echocardiographic values- Left ventricular ejection fraction- E/E'- IVC max (mm)- estimated CVP	36±1012±615±5 6±2
Intrarenal doppler ultrasonograpy- Resistive index- venous impedance index- continuous flow pattern	0.6±0.10.2±0.3 68%

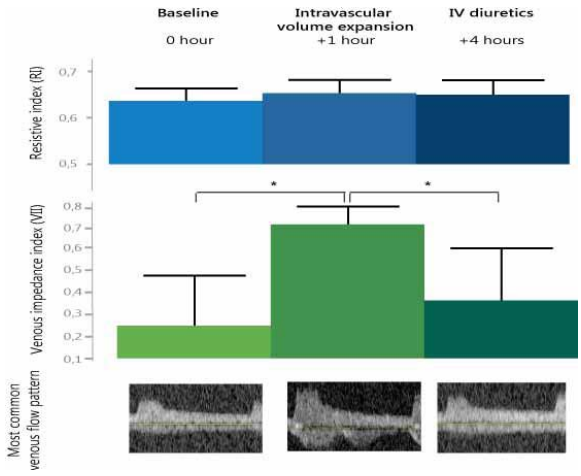


Figure 1

Methods: Arterial resistive index (RI), venous impedance index (VII) and venous flow pattern (continuous vs discontinuous) were assessed in 40 euvolemic HFrEF patients by intrarenal Doppler ultrasonography at baseline, during 3 hours of intravascular volume expansion with 1-liter hydroxyl ethyl starch 6%, and 1 hour after the administration of a loop diuretic. Clinical parameters, echocardiography, and laboratory values were assessed. Cumulative urine output was collected after 3 and 24 hours.
Results: In response to intravascular volume expansion VII increased significantly (0.2 ± 0.3 to 0.7 ± 0.2; p < 0.001) (Figure 1). This was reversed after IV diuretic administration. In contrast, RI changed non-significantly after expansion (0.6 ± 0.1 to 0.7 ± 0.1; p = 0.131). There was a non-significant change in echocardiographic estimates of central venous pressure (from 6 ± 2 mmHg at baseline to 7 ± 2 mmHg during expansion). The median VII during intravascular volume expansion was 0.74. Compared to patients with VII above the median during intravascular volume expansion, patients with lower VII generated a greater spontaneous and loop diuretic-induced amount of diuresis (0.6 ± 0.2 vs 0.4 ± 0.3 L/3 hours; p = 0.025 and 2.5 ± 0.4 vs 1.8 ± 0.5 L/24 hours; p = 0.001) and natriuresis (1.2 ± 0.4 vs 0.7 ± 0.5 g/3u ;p = 0.002 and 5.9 ± 1.2 vs4.1 ± 1.4; p = 0.005).
Conclusion: In HFrEF patients, intravascular volume expansion results in greater rise in VII than RI, before a significant change in cardiac filling pressures could be demonstrated. Impaired renal venous flow is correlated with less diuretic efficiency. Intrarenal venous flow patterns may be of additional interest to evaluate renal congestion.

2088

Therapeutic potential of phosphodiesterase 5 inhibitors in patients with heart failure with preserved ejection fraction (HFpEF) and combined post- and pre-capillary pulmonary hypertension (Cpc-PH).

T Kramer[1]; K Orlova[1]; F Gerhardt[1]; D Dumitrescu[1]; H Ten Freyhaus[1]; S Baldus[1]; S Rosenkranz[1]
[1]Cologne University Hospital - Heart Center, Clinic III for Internal Medicine, Cologne, Germany

Background: The prevalence of heart failure with preserved ejection fraction (HFpEF) is increasing and frequently associated with pulmonary hypertension (PH), which is associated with a poorer prognosis. The current ESC/ERS guidelines subdivide post-capillary PH into isolated post-capillary PH (Ipc-PH) and combined post- and pre-capillary PH (Cpc-PH). The latter is hemodynamically defined by a mean pulmonary artery pressure (PAPm) ≥25 mmHg, a pulmonary artery Wedge pressure (PAWP) >15 mmHg and a diastolic pressure gradient (DPG) ≥7 mmHg and/or a pulmonary vascular resistance (PVR) >3 WU. However, the therapeutic consequences of this subclassification are entirely unclear. Preliminary studies on phosphodiesterase 5 inhibitors (PDE5i) in PH-HFpEF yielded contradictory results. We specifically investigated the efficacy and safety of PDE5i in patients with HFpEF and Cpc-PH.
Methods: In 40 hemodynamically precisely characterized patients with HFpEF and Cpc-PH who were treated with a PDE5i (sildenafil 60 mg/d, n=24 or tadalafil 40 mg/d, n=16) for at least 12 months, the therapeutic effect on 6 minute walk distance (6MWD), WHO functional class (WHO-FC), echocardiographic parameters, right ventricular (RV) function and laboratory parameters (NTproBNP) was evaluated 3, 6, 9, and 12 months after the initiation of treatment.
Results: The average patient age was 73 ± 9 years, 53% were female, and comorbidities were frequent (75% atrial fibrillation, 78% arterial hypertension, 35% diabetes). Initially, 38 patients (95%) were in WHO-FC III and 2 patients (5%) in WHO-FC II. Prior to treatment initiation, PAPm was 45.6 ± 1.6 mmHg, PAWP 20.9 ± 0.8 mmHg, DPG 6.1 ± 1.0 mmHg, PVR 6.1 ± 0.5 WU, and RAP was 12.5 ± 1.0 mmHg. After 12 months of PDE5i therapy, the 6MWD substantially increased from initially 277 ± 17.0 to 340 ± 17.7 m, resulting in a net increase of 63 m (p < 0.001). The proportion of patients in WHO-FC I/II increased from 5% at baseline to 37.5% after 12 months of therapy. In addition, there was moderate improvement in RV function at 12 months (TAPSE 18.8 ± 0.8 vs. 16.9 ± 0.7 mm at baseline, p = 0.01), and NTproBNP levels decreased from 3.191 ± 559 ng/L at baseline to 2.130 ± 472 ng/L at 12 months (-33%, p = 0.004). Importantly, body weight of the patients remained constant throughout the observation period (71.7 ± 3 kg initially vs. 71.5 ± 2 kg at 12 months), so that the changes in measured parameters may not be attributable to optimized volume status and reduced left ventricular filling pressure. No deaths occurred in the investigated group, and the typical side effects of PDE5i (headache, flushing, nasal congestion) were observed.
Conclusion: These data indicate that precisely characterized patients with HFpEF and Cpc-PH who tolerate PDE5i may benefit from targeted therapy. A randomized study in this particular sub-population is warranted.

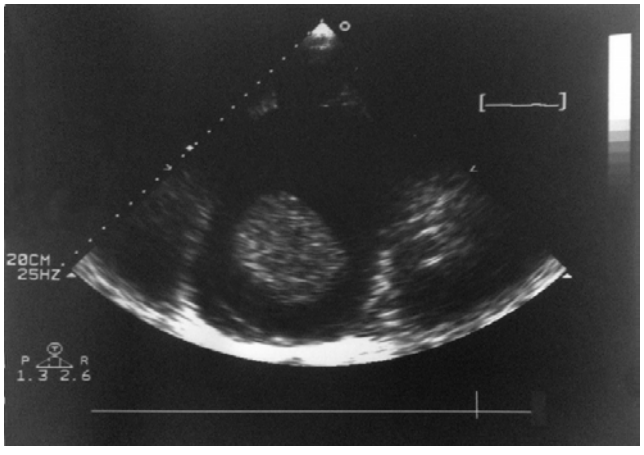
CLINICAL CASE CORNER 6 - HEART (AND PERIPHERAL!) MUSCLE DISEASE

2089

Endomyocardial fibrosis with a giant atrial thrombus

J Jose Costa[1]; A Damasceno[2]
[1]*Sao Joao Hospital, Internal Medicine, Porto, Portugal*; [2]*Maputo Central Hospital, Cardiology, Maputo, Mozambique*

Background: Endomyocardial fibrosis (EMF) is a rare type of restrictive cardiomyopathy that is seen in young people who live in tropical countries. The etiology is still unknown, being nutritional deficit and infections the most discussed hypothesis. It can affect the right, left or both ventricles, and the clinical presentation will depend on which chamber is most affected.The basic histologic lesion is endomyocardial fibrosis that involves the ventricular muscle. This will lead to high ventricular filling pressures and atrioventricular regurgitation with subsequent atrium dilatation. This dilatation is associated with arrhythmic problems and the formation of thrombus that can lead to pulmonary embolism and sudden death.The diagnosis is made with echocardiography that shows a thickened endocardium in the ventricle wall. In right EMF there is an obliteration of the trabecular layer of the right ventricle with a reduction of the diameter and a tricuspid annulus dilatation with severe regurgitation. Clinical case: The authors present the case of a 19 years-old female patient with a 2-year history of dyspnea for large efforts. She denied chest pain, fever, cough or palpitations. She did not have any specific sign on physical examination or any abnormality on laboratorial evaluation. On the X-Ray she presented with cardiomegaly. The EKG presented a right axis deviation, and atrial fibrillation. Echocardiography showed endomyocardial fibrosis of the right ventricle with dilatation of the right atrium with a giant thrombus. She was put on diuretics and heart failure medication, and was proposed for cardiac surgery. Due to the high risk of embolization, the patient didn't take anticoagulant therapy.
Conclusion: EMF is a rare cause of cardiomyopathy of unknown etiology in tropical and underdeveloped countries. It affects mostly young people in some geographical area and carries a very high burden in these communities. This is a rare condition with a low medical awareness. Since the world is going through a globalization process with a high mobility of populations, which can increase the diagnosis of EMF in developed countries, the authors are trying to raise awareness of the medical community to the existence and treatment of EMF, especially in countries that can receive patients from tropical areas.



Atrial Thrombus

2090

A rare etiology of left ventricular hypertrophy: mitochondrial cardiomyopathy

JSS Seo[1]
[1]*Inje University Pusan Paik Hospital, Busan, Korea Republic of*

Mitochondrial disease is a heterogeneous systemic disorder and a rare cause of left ventricular hypertrophy (LVH). A 48-year-old woman with diabetes mellitus underwent evaluation for cardiomegaly. Echocardiography showed concentric LVH and a restrictive diastolic pattern. While left ventricular ejection fraction was preserved, global longitudinal and radial strains were decreased. Cardiac magnetic resonance imaging demonstrated LVH and subepicardial delayed enhancement of the anterolateral and inferolateral walls of the left ventricle. Endomyocardial biopsy with transmission electron microscopy showed accumulation of varying-sized abnormal-shaped mitochondria in the myocytes including electron-dense inclusion and disoriented cristae. DNA sequence analysis revealed heteroplasmy of m.3243A>G and wild type. Therefore, mitochondrial cardiomyopathy, leading to diagnosis of mitochondrial encephalomyopathy, lactic acidosis, and stoke-like episodes (MELAS syndrome). Diagnosis of mitochondrial disease based on cardiac symptoms is unusual because cardiac symptoms or signs present later than other neurologic or systemic symptoms. Referrals for cardiac evaluation typically come from neurologists or geneticists who have diagnosed a mitochondrial disease. Interestingly, in this case, there were no prominent neurologic symptoms. It is unique for prominent LVH without significant neurologic symptoms to suggest MELAS syndrome. In conclusion, we should consider the mitochondrial cardiomyopathy as a rare cause of LVH when there are no definite neurologic symptoms.

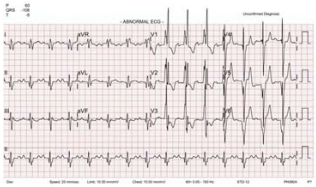
2091

A rare case of Fabry cardiomyopathy requiring permanent pacemaker and implantable cardioverter-defibrillator despite enzyme replacement therapy

SH Sang Hyun Park[1]; JY Chin[1]; KT Jung[1]; YJ Choi[1]; WH Kim[1]; KW Kang[1]
[1]*Eulji University Hospital, Daejeon, Korea Republic of*

A 55-year-old male farmer referred to our hospital due to ECG abnormality, dyspnea on exertion and cardiac enzyme elevation after diagnosis of scrub typhus at local clinic. Cardiac troponin-T was mildly elevated (0.169 ng/mL, normal range: 0-0.1 ng/mL). A 12-leads electrocardiogram (ECG) revealed normal sinus rhythm with 1st degree atrioventricular block (AVB), complete right bundle branch block (RBBB) and pathologic Q wave in I, II, aVL, V5 and V6. (Figure 1) Transthoracic echocardiogram showed diffuse severe concentric hypertrophy of the left ventricle (LV) of an average ventricular wall thickness of 30 mm. (Figure 2) A dynamic left ventricular outflow track obstruction LVOT) was observed during the Valsalva maneuver. Right ventricle (RV) was also hypertrophied (RV free wall thickeness, 9mm). Cardiac magnetic resonance imaging revealed diffuse delayed hyper-enhancement with various degrees of transmurality.
More detailed familial history taking informed that his younger brother and older sister suffered from cardiac problem. His oldest sister died of sudden cardiac death at the age of 60. Genetic disorder was suspected and confirmed as Fabry diasese (FD) via GLA gene sequencing. A missense mutation was identified at exon 6 within a GLA gene. The mutation is known to cause FD of a cardiac variant type by literature review. Additionally 4 family members were confirmed to have FD with same mutation.
Index patient initiated enzyme replacement therapy (ERT) with intravenous agalsidase-beta via outpatient department (OPD). Follow-up ECG showed first degree AVB and left bundle branch block (LBBB). (Figure 3) He experienced two episodes of syncope and frequently complained of dizziness during OPD follow-up. ECG revealed complete AVB. (Figure 4) Beta blocker was discontinued more than two weeks after that. However, complete AVB didn't improve. Permanent pacemaker (PPM) which has a function of implantable cardioverter-defibrillator (ICD)

was implanted considering that he has high risk features of sudden cardiac death such as syncope, severe hypertrophy of LV septal wall and family history of sudden cardiac death. Peak pressure gradient of LVOT markedly decreased to 36mmHg after PPM implantation from 63mmHg before that. Symptoms of dyspnea and dizziness also markedly improved.
Progression of Fabry cardiomyopathy can lead to severe conduction dysfunction such as complete AVB requiring PPM despite ERT. It needs to check ECG serially to identify the progression of conduction disturbance in patients with conduction dysfunction at baseline to prevent cardiac events.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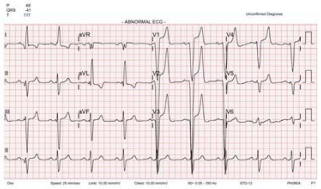
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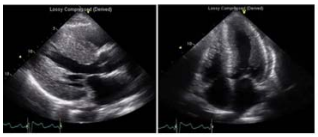
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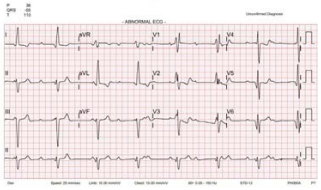
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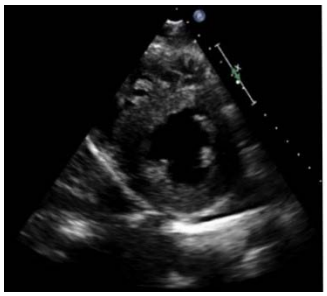
ECG and Echocardiography

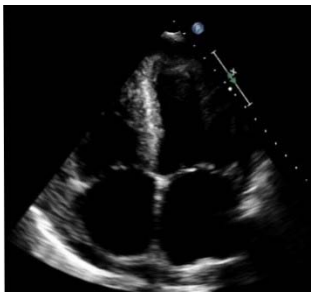
2092

Cardiac amyloidosis: a difficult journey to diagnosis

PM Paulo Maia Araujo[1]; A Nunes[1]; S Amorim[1]; MB Campelo[1]; H Baldaia[2]; P Rodrigues-Pereira[2]; R Bergantim[3]; A Andrade[4]; MJ Maciel[1]
[1]Sao Joao Hospital, Cardiology, Porto, Portugal; *[2]Sao Joao Hospital, Pathology, Porto, Portugal*; *[3]Sao Joao Hospital, Clinical Hematology, Porto, Portugal*; *[4]Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*

The present case refers to a 63-years-old women, with hypertension, dyslipidemia and history of unilateral nephrectomy (for nephrolithiasis), without any other relevant medical history and no family history of cardiac diseases. She was admitted to hospital for progressive dyspnea, with a 3-month evolution time. At admission, she had evident signs of congestive heart failure (HF). Electrocardiogram showed low limb lead voltage and poor precordial R-wave progression. Echocardiogram (TTE) revealed severe left ventricular (LV) systolic dysfunction due to global hypocontractility, without dilatation of cardiac chambers, but with moderate LV hypertrophy (LVH); right ventricular function was preserved. Coronariography excluded epicardial coronary disease. For better characterization, a cardiac magnetic resonance was performed, showing a marked increase in myocardial mass with concentric LVH, global hypokinesia with severe LV dysfunction and subendocardic late gadolinium enhancement, almost circular, in all ventricular plans. These findings were suggestive of infiltrative cardiomyopathy, with a high suspicion of amyloidosis. Laboratorial tests for amyloidosis were all negative, including serum and urinary immunofixation, free light chains (FLC) assay and nuclear imaging with DPD. Tests for another possible etiologies of infiltrative cardiomyopathy were negative as well. Bone marrow biopsy was negative and endomyocardial biopsy revealed an unspecific inflammatory infiltrate, without amyloid deposits. Rectum and abdominal fat biopsies were also negative for amyloidosis. After initial compensation, the clinical status deteriorated again, with progression to severe biventricular dysfunction. Thus, diagnostic workup was repeated and a high FLC lambda/kappa ratio, previously normal, was found. Given the high suspicion of AL cardiac amyloidosis, bone marrow biopsy was repeated, this time showing infiltration of plasma cells with positive immunohistochemistry to lambda FLC. Therefore, it was performed an immunohistochemistry review of myocardial biopsy, that revealed the deposition of lambda FLC also in myocardial tissue, making the definitive diagnosis of AL cardiac amyloidosis. Chemotherapy (Cth) with bortezomib, dexamethasone and cyclophosphamide was initiated. However, there was progression to terminal HF and evaluation for cardiac transplantation (CTr) was started, with the perspective of being followed by autologous stem cell transplantation (ASCT). During evaluation of extracardiac organ amyloid involvement, colonoscopy with rectum biopsy was repeated and it revealed amyloid deposition in the rectum tissue. Given the involvement of an extracardiac organ and the associated absence of hematologic response to Cth, disease progression was assumed and the patient was withdrawn from CTr evluation. After clinical compensation, she was discharged from hospital with indication for comfort measures and 2 months later, the patient died. This case shows that the diagnosis of cardiac amyloidosis remains a clinical challenge, in a disease in which early diagnosis is fundamental to a better prognosis. Laboratory tests may be negative and even analysis of tissue biopsies may give misleading results. These difficulties may lead to delays in establishing a definitive diagnosis, with significant negative effects on the prognosis. Improvements in diagnostic approach can promote the earlier beginning of Cth, slowing the disease progression and allowing therapies, such as CTr and ASCT.





TTE: Thickened and hyperechogenic walls

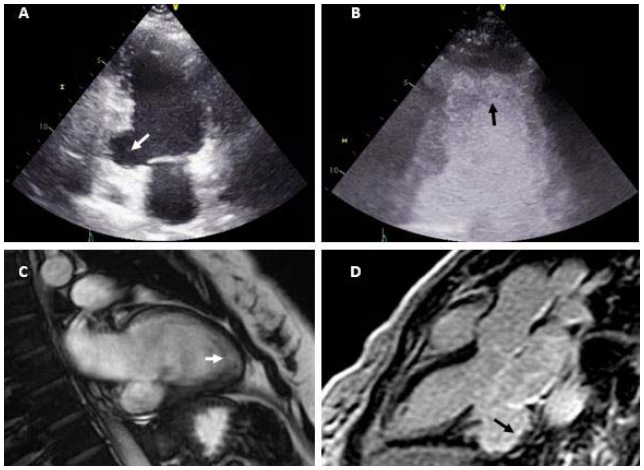
2093

Non-compaction cardiomyopathy with multiple embolic events, a new association to a sarcomeric gene mutation.

R Morales Murillo[1]; E Fortuny Frau[1]; P Pericas[1]; J Pons Llinares[1]; M Noris Mora[1]; M Massot Rubio[1]; R Gonzalez Colino[1]
[1]University Hospital Son Espases, Cardiology, Palma de Mallorca, Spain

Introduction and Case Report Description: Left ventricular non-compaction (LVNC), is a rare form of cardiomyopathy characterized by deep intertrabecular recesses communicated with the ventricular cavity. Since different diagnostic criteria have been proposed, final diagnosis can be challenging. We report the case of a 29-year-old woman, without known cardiovascular risk factors, family history of a brother with degenerative muscle dystrophy and a personal history of pontine stroke of unclear origin, due to the occlusion of the vertebrobasilar artery at the age of 25. No previous history of heart disease was reported. Although she had no cardiovascular symptoms at any time, she was referred to our hospital after the finding of high density monomorphic ventricular ectopic heart beats that were confirmed on an EKG Holter.
Description of the problem, procedures, techniques and/or equipment used: We performed a transthoracic echocardiogram (TTE) that showed a basal inferior aneurism (Fig A). Contrast TTE exposed hyper-trabeculated areas on the lateral and apical walls (Fig B). Cardiac resonance objectivised myocardial thinning involving lateral wall and apex with augmented trabeculation, meeting criteria of non-compaction, and confirmed the presence of an aneurism of 36 x 17mm (Fig C). Left ventricular (LV) function was preserved. Myocardial suppression sequences revealed sub-endocardial late enhancement of the aneurism, which suggested a chronic ischemic origin (Fig D). Coronary angiogram showed normal coronary arteries. The patient had a brother with degenerative myopathy and a father with onset of atrial fibrillation at young age, so we performed genetic testing that found a heterozygous mutation on the sarcomeric gene MYH6. QUESTIONS, PROBLEMS OR POSSIBLE DIFFERENTIAL DIAGNOSIS. It was proposed that the stroke in addition to an asymptomatic myocardial infarction were most likely caused by multiple embolism originated in the left ventricle non-compacted areas and the ectopic heartbeats were originated on the scarred area. Treatment with betablockers was started, substantially diminishing the ectopic heart beats and anticoagulation therapy with warfarin was considered necessary.
Answers and discussions: LVNC is a genetically heterogeneous disorder associated with several gene defects. It is known that MYH6, encoding myosin heavy chain 6, has a vital role in heart development. Mutations in MYH6 have been related to hypertrophic cardiomyopathy, dilated cardiomyopathy and atrial septal defects. Yet, to our knowledge this would be the first case linked to LVNC. Regarding the prognosis, although the classic triad of heart failure, arrhythmias and embolic events has been described, possible clinical presentation are very variable and prevention and treatment of the complications are the main therapeutic goals.
Conclusions and implications for clinical practice. Given that this is the first association of the disease with an MYH6 mutation, it should be considered of uncertain clinical significance. However, it is of big importance its segregation in the progenitors and family susceptible of being carrier of the mutation to determine its implication in the development of the disease. The prevention of embolic events is an issue still discussed, in the past there was a tendency of giving anticoagulants to all patients with LVNC, now days some only recommend it on determined cases like patients with LV dysfunction, atrial fibrillation and previous embolic events. Even

though there is no robust data to support it, anticoagulation therapy in our patient seems to be justified.



2094

A challenging case of rare cardiomyopathy and its clinical implications

A Adriana Covaliov[1]; C Radulescu[1]; L Antohi[1]; R Radu[1]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*

Introduction: Left ventricular non-compaction or 'spongy myocardium' is a rare congenital cardiomyopathy characterized by prominent trabeculations and intertrabecular recesses that communicate with the ventricular cavity rather than the coronary circulation.
Case description: We present a case of 49 years old male with history of an ischemic stroke one month ago, who was admitted to hospital because of clinical signs and symptoms of left heart failure with extreme breathlessness, anxiety and profuse diaphoresis, symptoms developed in the last 12 h during an intercurrent respiratory infection. Physical examination revealed tachypnea, severe hypoxemia, the 3rd heart sound h and crackling rales extended to upper lungs with a systolic blood pressure of 170/90 mmHg. Electrocardiogram showed sinus tachycardia with QRS duration of 130 ms and negative T waves in V5, V6, DI, AVL. First echographic evaluation at the emergency room showed a dilated left ventricle with severe systolic disfunction and the response to initial supportive therapy was good. The levels of brain natriuretic peptide after 24 h from the acute event was 2504 pg/ml. Later transthoracic echocardiogram reevaluation showed a left ventricle enlargement with severe systolic dysfunction (calculated ejection fraction 25%) and proeminent trabeculation, sponge-like appearance, especially in the mid and apical areas of the left ventricle suggestive for non- compaction cardiomyopathy (Fig 1). The mitral and tricuspid regurgitation were mild. Also, transesophageal echocardiogram revealed a mobile, heterogeneous, echodense structure located in intertrabecular recesses, probably thrombi (Fig 2). The patient had no significant arrhythmias during his hospital stay. After evidenced based heart failure theraphy with loop diuretics, ACE inhibitors, spironolactone and b blockers his symptoms improved significantly. Also anticoagulation therapy was added. Follow-up examinations during 6 month showed an improved exercise capacity quantified by cardiopulmonary test and BNP levels dropped with more than 70 percent. Transthoracic and transesophageal echocardiography reevaluation revealed a better systolic function (EF calculated 34 %) with the decrease of end-systolic volume and no more thrombi were seen in the cardiac cavities after 6 month of oral anticoagulation. The aetiological investigations were completed with a normal coronarography exam and a cardiac IRM which confirmed the non-compacted cardiomiopathy in the apical areas. (Fig 3) The patient was advised to continue the evidenced based heart failure therapy treatment with no indication at the moment for cardiac transplantation. All first-degree relatives were advised to undergo screening echocardiogram.
Conclusions: This case illustrates a rare non-compaction cardiomyopathy diagnosed at mid age after clinical presentation with de novo acute heart failure. Evidenced based heart failure theraphy had unexpectably good results which could be explained by the response to neurohormonal therapy for heart failure of the compaction myocardium areas with beneficial effects on metabolic and adrenergic abnormalities. One of the complications of this cardiomyopathy is intraventricular thrombosis complicated in this case with ischemic stroke just one month before diagnostic. Also, the response to anticoagulant theraphy was excellent with no more thrombi seen on follow up and more thromboembolic events.

2095

Rapidly manifested heart failure treated with left ventricle assist device and heart transplantation in patient with Becker muscular dystrophy

V Bajoras[1]; G Zuoziene[1]; V Maneikiene[1]; V Janusauskas[1]; A Zorinas[1]; K Rucinskas[1]
[1]*Faculty of Medicine of Vilnius University, Clinic of Cardiac and Vascular Diseases, Vilnius, Lithuania*

Introduction: We describe a rare case of Becker muscular dystrophy (BMD) which presented by rapidly progressing heart failure (HF), without primary expressed clinical signs of neuromuscular disease and was treated with left ventricle assist device (LVAD) and heart transplantation. Description: 22 y/o previously healthy male presented to our hospital with shortness of breath on exertion (NYHA class III), orthopnoea lasting for a few weeks. Physical examination was unremarkable. Blood tests were in normal range, except for BNP (2132 ng/l), CK (1964 U/l) and CK-MB (31 mcg/l). Transthoracic echocardiography (TTE) and magnetic resonance imaging indicated dilated cardiomyopathy (DCM) with severe restrictive mitral valve (MV) regurgitation, LVEF 25%. VO2 max on spiroergometry was 15.5 ml/kg/min. Endomyocardial biopsy demonstrated non-specific changes of DCM. Successful MV repair was performed. Patient's exercise tolerance improved (NYHA class II), and LVEF increased up to 38% postoperatively with medical HF treatment at one year follow up. At the same visit slightly reduced strength of lower extremities was noted, and BMD was diagnosed clinically as there was no possibility to perform specific genetic examination at the time. HF was progressing gradually and two years after the surgery patient deteriorated to NYHA class IV with LVEF 15%, VO2 9.2 ml/kg/min, PA pressure 80/50, PCWP 44/40mmHg and PVR 8 WU. Patient was listed for heart transplantation and LVAD was implanted as a bridge to heart transplantation. Six months after the procedure patient's condition improved significantly, patient was in NYHA class II with PVR 2.6 WU. Heart transplantation was successfully performed 1 year after LVAD implantation. Patient was treated with a small dose of prednisolone, calcineurin inhibitor (CNI), and mycophenolate mofetil postoperatively. Inherited BMD was confirmed by detecting deletions in dystrophin gene of the patient and his brother. 3 months after heart transplantation, rapid deterioration of kidney function (creatinine 329 mcmol/l), and rapid increase of ALT and AST level (467 and 341 U/l respectively) were observed. Due to possible drug induced kidney and liver injury immunosuppressive therapy was revised and CNI was withdrawn. Subsequently, patient's kidney and liver function improved. Every attempt to initiate CNI or rapamycin resulted in increase of creatinine, liver enzymes and bilirubin. As a consequence of reduced immunosuppression patient developed humoral rejection. Despite treatment with monoclonal antibody therapy and plasmapheresis heart function could not be recovered. After 40 days in the intensive care unit, patient died of multiple organ dysfunction syndrome induced by sepsis.
Conclusions: Becker muscular dystrophy can present with heart failure due to DCM even before symptoms of muscular dysfunction appear. Patients with BMD may be more susceptible to the side effects of immunosuppression and should be considered for LVAD implantation as a destination therapy if they develop severe heart failure resistant to medical treatment.

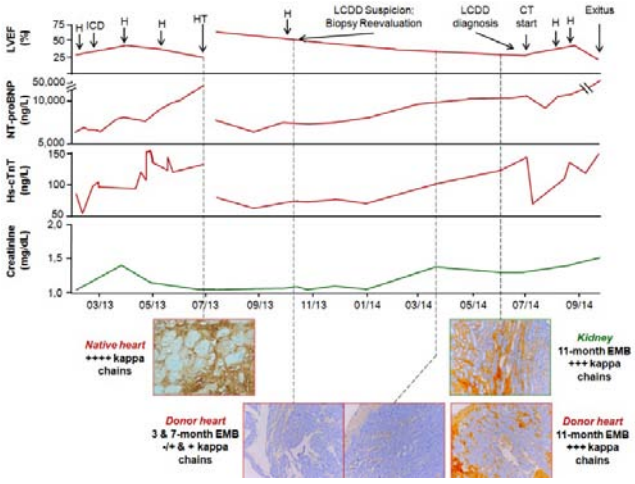
2096

Cardiac light chain deposition disease relapsing in the transplanted heart

A Alberto Aimo[1]; G Vergaro[2]; A Pucci[3]; A Paolicchi[3]; S Bernazzali[4]; G Buda[3]; C Passino[1]; M Emdin[1]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*Gabriele Monasterio Foundation, Pisa, Italy*; [3]*University of Pisa, Pisa, Italy*; [4]*Polyclinic Santa Maria alle Scotte, Siena, Italy*

Light chain deposition disease (LCDD) is characterized by the deposition of monoclonal light chains (LCs) causing tissue inflammation and damage. Renal failure is a hallmark of LCDD, whereas heart failure (HF) is infrequent, and has been almost constantly reported in combination with severe renal impairment. Heart transplantation (HT) has never been described in patients with LCDD. Herein, we report a case of undiagnosed LCDD with selective cardiac phenotype, relapsing after heart transplantation. A 44-year-old man was hospitalized because of dyspnoea, cough and ankle oedema, worsening over 4 months. HF with reduced ejection fraction was diagnosed: echocardiography and magnetic resonance showed a dilated left ventricle with normal mass, global hypokinesis, and patchy septal fibrosis; at coronary angiography, epicardial arteries were normal. Biohumoral evaluation disclosed increased plasma N-terminal fraction of brain natriuretic peptide and troponin T, and normal serum creatinine; no clear monoclonal peak was present, but serum protein immunofixation revealed a monoclonal component (IgG kappa).

Endomyocardial biopsy (EMB) demonstrated non-specific interstitial inflammation; negative Congo red stain excluded amyloidosis. Despite guideline-recommended therapy including implanted cardiac defibrillator, declining cardiac function and refractory symptoms required urgent HT, 4 months later. The patient recovered his health for three months, then symptoms and cardiac dysfunction recurred. At that point, cardiac histology was re-evaluated, and immunohistochemistry revealed massive kappa chain accumulation in the native heart. In addition, a borderline positivity for kappa chains was found in an EMB performed 3 months after the HT. The suspicion of LCDD was raised, but was contested because of normal kidney function. Another EMB, 4 months later, resulted slightly positive for kappa chains. A consensus on the LCDD diagnosis was eventually reached 11 months after the HT, when an evident kappa chain accumulation was detected in both a third EMB and a renal biopsy. A therapy with melphalan and desamethasone was then started, causing a transient clinical improvement. Nonetheless, the patient died two months later because of systemic Cytomegalovirus infection. LCDD should be considered whenever unexplained HF is associated with evidence of a plasma cell dyscrasia, even if renal function is preserved. As in this case, rapid deterioration of cardiac function can occur, with just 8 months from the onset of symptoms to urgent HT. We report for the first time that graft dysfunction can develop 3 months after HT and before LC deposits become evident. Early diagnosis and prompt initiation of a treatment for the haematological disorder are probably crucial in order to improve the natural history of LCDD-related HF.



2097

Cardio pulmonary exercise testing detects ventricular tachycardia at peak exercise in 28 year old soccer player

CH Dall[1]; H Rasmusen[2]
[1]*University of Copenhagen, Dept. of Cardiology, Dept. of Physical Therapy & Institute of Sports Medicine, Bispebjerg Hospital, Copenhagen, Denmark*;
[2]*Department of Cardiology, Bispebjerg Hospital, Copenhagen, Denmark*

Background and purpose: Physical exercise plays an important role in preventing chronic disease and in maintaining health throughout life. Nevertheless, in some subjects intensive exercise can trigger a cardiopulmonary event (nausea, syncope or a fatal cardiovascular episode). This occurs primarily in the context of an underlying inherited or genetic cardiac disorder. The purpose of this study is to describe a case challenged by the ability to reproduce symptoms using the conventional assessment techniques.
Case description: A 28 year old male having presented several episodes of syncope and near syncope, while playing soccer, was referred to cardiopulmonary screening. He has no family history of sudden cardiac death.
Outcome: The golden standard assessments (i.e. resting ECG, Holter monitoring, echocardiography, coronary angiography) could not detect arrhythmia or reproduce pathology/symptoms in this case. Conversely a supplementary screening using a Cardio Pulmonary Exercise Test (CPET) reproduced symptoms, so that the subject experienced an episode of ventricular tachycardia (VT) lasting for 11 seconds at peak workload/peak VO2 and the ECG returned subsequently to normal level without intervention.
Discussion: In this case report the CPET reproduced symptoms. None of the conventional assessment techniques detected any arrhythmia or pathology/symptoms when testing at rest. Using the VO2peak and the respiratory exchange ratio as guidance is pivotal in the CPET testing. Especially for athletes, this can be important because the peak workload and VO2peak is much higher than in average subjects. There is a risk that the conventional assessment techniques are not sensitive enough when assessing athletes only presenting symptoms at peak workload.
Conclusion: and implication Measurements that are able to reproduce symptoms should be included as a supplement to conventional assessment techniques particularly in the evaluation of cardiac symptoms in relations to intense physical exercise in athletes. In patients with arrhythmia but without structural changes the CPET becomes important in reproducing symptoms. Based on the reproduced symptoms from the CPET the case subject was referred to either ablation or ICD therapy.

2098

A challenging diagnosis

K Kisa Hyde Congo[1]; R Guerreiro[1]; JF Carvalho[1]; D Bras[1]; AR Santos[1]; B Picarra[1]; P Dionisio[1]; J Aguiar[1]
[1]*Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*

Forty-two-year-old male, with a history of lung lobectomy, reports to the emergency department after an episode of syncope at rest. He also referred dyspnea for moderate exertion for the last 2 months. No previous episodes of syncope, chest pain, palpitations, orthopnea, nocturnal paroxystic dyspnea and lower limb edema. The initial ECG showed sinus rhythm with a 1st grade AV Block alternating with 2nd degree AV Block Mobitz II and 3rd degree block. The echocardiogram showed dilated left ventricle with diffuse hypokinesia and severely depressed systolic function. He was admitted at a cardiac ward for further studies and therapy. Viral serologies and autoimmune studies were negative. Coronary angiography showed no lesions. Electromiogram and body CT showed no abnormalities. Endomyocardial biopsy showed advanced fibrosis. Spirometry showed small airway disease. Genetic testing for cardiolaminopathies was negative. Cardiac MRI showed marked dilation and biventricular dysfunction, mid-wall and epicardial late enhancement in septal and inferior segments, respectively. Etiological study didn't arrive at a definitive diagnosis, nevertheless the most likely diagnosis is Cardiac Sarcoidosis. Considering the severe left ventricular dysfunction and advanced AV block with indication for definitive pacemaker, a CRT-D was implanted. At 6 months follow-up the patient showed clinical improvement and NYHA I class.

POSTER SESSION 4

ACUTE HEART FAILURE

P2105

East Asia has a strikingly better survival following acute heart failure compared with Europe

E Akiyama[1]; LNL Van Aelst[2]; M Arrigo[3]; J Lassus[4]; O Miro[5]; J Celutkiene[6]; A Cohen-Solal[7]; AP Maggioni[8]; C Mueller[9]; J Parenica[10]; JJ Park[11]; N Sato[12]; J Spinar[10]; E Gayat[7]; A Mebazaa[7]
[1]Inserm UMR-S 942, Paris, France; *[2]KU Leuven, Leuven, Belgium*; *[3]University Hospital Zurich, Zurich, Switzerland*; *[4]University of Helsinki, Helsinki, Finland*; *[5]University of Barcelona, Barcelona, Spain*; *[6]Vilnius University, Vilnius, Lithuania*; *[7]Hospital Lariboisiere, Paris, France*; *[8]Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy*; *[9]University Hospital Basel, Basel, Switzerland*; *[10]Masaryk University, Brno, Czech Republic*; *[11]Seoul National University Hospital, Seoul, Korea Republic of*; *[12]Nippon Medical School Musashi-Kosugi Hospital, Kawasaki, Japan*

On behalf of: the GREAT (Global Research on Acute Conditions Team) Network
Funding Acknowledgements: This study was supported by a research fellowship from Japan Heart Foundation (E.A.).

Background: Heart failure is a major health problem worldwide and trials to assess novel therapies are increasingly global. However, recent registries suggest that characteristics of acute heart failure (AHF) patients may differ between Asia and Western countries, though direct comparison of mortality after an AHF episode is scarce.
Purpose: This study sought to investigate difference in long-term mortality in AHF patients between East Asia and Europe.
Methods: From the GREAT (Global Research on Acute Conditions Team) registry, patients who were presenting with AHF to the emergency department in East Asia (Japan and Korea) and Europe (Western Europe and Czech Republic) were included in this analysis. Patients were followed up for all-cause mortality at 1-year.
Results: Of 17120 patients, there were 6961 (41%) patients from East Asia and 10159 (59%) patients from Europe. One-year all-cause mortality was lower in East Asia (18%) than in Europe (32%). Furthermore, unadjusted risk of death was lower in East Asia than in Europe (hazard ratio (HR) 0.52, 95%-confidence interval (CI) 0.49-0.56, $P < 0.001$). Long-term risk of death remained lower in East Asia than in Europe after adjustment (HR 0.52, 95%-CI 0.47-0.57, $P < 0.001$), propensity-score matching (unadjusted HR 0.50, 95%-CI 0.42-0.59, $P < 0.001$ and adjusted HR 0.44, 95%-CI 0.37-0.51, $P < 0.001$), or in AHF patients with optimal heart failure therapies (HR 0.40, 95%-CI 0.33-0.49, $P < 0.001$).
Conclusions: In patients presenting with AHF to the emergency department, East Asia has a strikingly better long-term survival compared with Europe. This result will have important impact in the design and choice of recruiting countries in future event-driven AHF trials.

P2106

Comorbidities more than reduced left ventricular ejection fraction correlates with mortality in heart failure patients discharged from internal medicine units

V Valerio Verdiani[1]; P Francesconi[2]; F Profili[2]; G Panigada[3]; A Fortini[4]; R Laureano[5]; G Landini[6]; S Meini[5]; L Masotti[6]; M Alessandri[7]; A Camaiti[8]; S Lenti[9]; C Palermo[10]; R Andreini[11]; R Migliacci[12]
[1]Grosseto Hospital, Internal Medicine, Grosseto, Italy; *[2]Regional Agency for Health of Tuscany, Florence, Italy*; *[3]Pescia Hospital, Internal Medicine, Pescia (PT), Italy*; *[4]New Hospital San Giovanni di Dio, Internal Medicine, Florence, Italy*; *[5]Santa Maria Annunziata Hospital, Internal Medicine, Florence, Italy*; *[6]Hospital of Santa Maria Nuova, Florence, Italy*; *[7]Massa Marittima Hospital, Massa Marittima (Gr), Italy*; *[8]Leghorn Hospital, Leghorn, Italy*; *[9]Arezzo Hospital, Arezzo, Italy*; *[10]Valdelsa Hospital, Poggibonsi (Si), Italy*; *[11]Pontedera Hospital, Pontedera (Pi), Italy*; *[12]Cortona Hospital, Cortona (Ar), Italy*

On behalf of: POST-SMIT Study Group

Background: There is growing awareness that comorbidities frequently accompany Heart Failure (HF) and lead to increased morbidity and mortality. While numerous studies focus on a single comorbidity, only few studies examined the prognosis impact of multiple comorbidities in HF patients. Furthermore, Left Ventricular Ejection Fraction (LVEF) is a powerful predictor of cardiovascular outcome in HF patients, but it is not clear if LVEF maintains its predictive value in old patients with multiple comorbidities.
Methods: We enrolled patients who were discharged by 23 Internal Medical Units of Tuscany, an Italian region of 3,7 million inhabitants, in a period of 30 days (30 Genuary-28 February 2014) with the main diagnosis of HF. We recorded epidemiological, instrumental and clinical data and patients were followed over a 12-months period. We considered 7 comorbidities (diabetes mellitus, hypertension, chronic renal failure, chronic obstructive pulmonary disease, atrial fibrillation, anemia, cognitive deficit) and LVEF during hospitalization. For analysis we distinguished the patients in the three categories used in HF ESC guidelines 2016: HF with reduced, mid-range, preserved ejection fraction (HFrEF, HFmrEF, HFpEF, respectively). The endpoints were: a) correlation between number of comorbidities and all-cause mortality at 1, 6, 12 months; b) correlation between LVEF and all-cause mortality at 1, 6, 12 months when adjusted for > 2 comorbidities.
Results: We recruited 451 patients (M= 44.3%) with a mean age of 83 + 8.4 years. Mean LVEF was 44.2 + 11. Mortality was 9.5%, 25.7%, 38.1% at 1, 6, 12 months respectively. In multivariate analysis mortality was significantly correlated with number of comorbidities (for each increase of one comorbidity RR 1.21 $p = 0.07$; RR 1.19 $p = 0.006$; RR 1.16 $p = 0.008$ at 1, 6, 12 months respectively). Patients with > 3 comorbidities had higher mortality compared with < 3 comorbidities at 1 (RR 2.69 $p = 0.03$), 6 (RR 1.63 $p = 0.04$), 12 (RR 1.43; $p = 0.005$) months respectively. Instead, when adjusted for > 2 comorbidities, LVEF did not correlate with mortality: HFrEF vs HFpEF (RR 1.10 $p = 0.89$; RR 1.81 $p = 0.13$; RR 1.35 $p = 0.41$ at 1, 6, 12 months respectively) and HFmrEF vs HFpEF (RR 0.53 $p = 0.18$; RR 1.03 $p = 0.92$; RR 0.96 $p = 0.86$ at 1, 6, 12 months respectively).
Conclusions: In a cohort of old HF patients discharged from Internal Medicine Units and followed over a 12-months period, mortality was significantly correlated with the number of comorbidities, whereas reduced LVEF did not correlate with mortality when adjusted for two or more comorbidities.

P2107

Liver fibrosis score predicts mortality in heart failure patients with preserved ejection fraction

Y Yasuchika Takeishi[1]; A Yoshihisa[1]
[1]Fukushima Medical University, Fukushima, Japan

Background: Heart failure with preserved ejection fraction (HFpEF) has several pathophysiological aspects, including stiffness and/or congestion of multiple organs. Poor prognosis is expected in heart failure patients with liver stiffness, which has recently been assessed by nonalcoholic fatty liver disease fibrosis score (NFS; based on aspartate aminotransferase to alanine aminotransferase ratio, platelet counts and albumin). We aimed to investigate the impact of NFS on prognosis of HFpEF patients, with consideration for the peripheral collagen markers such as procollagen type III peptide (PIIIP), type IV collagen 7S, and hyaluronic acid.
Methods and Results: We performed prospective observational study. Consecutive 492 hospitalized HFpEF patients were divided into four groups based on their NFS: 1st–4th quartile (n = 123, respectively). The 4th quartile group had the highest levels of PIIIP, type IV collagen 7S, hyaluronic acid, and B-type natriuretic peptide ($P < 0.001$ each). In addition, there were significant positive correlations between PIIIP, type IV collagen 7S, hyaluronic acid, B-type natriuretic peptide and NFS ($P < 0.001$ each). In the follow-up period (mean 1107 days), 93 deaths occurred. All-cause mortality increased in all four quartiles (8.1%, 12.2%, 23.6%, and 31.7%, $P < 0.001$). In the multivariable Cox proportional hazard analysis, NFS was an independent predictor of all-cause mortality in the HFpEF patients.
Conclusion: NFS, a novel indicator of liver stiffness, correlates with circulating systemic markers of fibrosis and congestion, and is associated with higher all-cause

mortality in HFpEF patients. NFS can be calculated simply and may be a useful tool to assess liver stiffness and prognosis in HFpEF patients.

P2109
Incidence and predictors of hyperkalaemia in 1600 patients with chronic heart failure

K Kaoutar Kharbouche[1]; K Kharbouche[1]; I Elhaddad[1]; L Azouzi[1]
[1]*chu ibn rochd, cardiology, casablanca, Morocco*

Background: Heart failure (HF) patients are particularly susceptible to electrolyte abnormalities and especially to hyperkalemia. Potassium (K) balance may be lost both through the neurohormonal mechanisms and through the drugs used in the treatment of this illness. Both hypokalaemia and hyperkalaemia are associated with increased mortality, mainly due to a higher risk of potentially fatal arrhythmia. Our goal was to explore the incidence and predictors of hyperkalemia in a broad population of heart failure patients.
Methods: This was a retrospective study of 1600 consecutive patients admitted to the therapeutic unit for heart failure between May 2010 and September 2014. Patients on dialysis and those with an estimated glomular filtration rate (GFR) < 10ml/min/1,73m^2; were excluded. Complete history on admission, age, sex, body weight, physical findings, comorbidities, and laboratory information were collected.
Results: The mean age of our population was 64.4 years (16-100), with a male predominance (64.6%). In 18 patients (1.3%) K was < 3.0 mmol/L, and in 424 patients (30.9%) K was >5.0 mmol/L. Independent of treatment assignement, patients at highest risk for hyperkalemia were those with age 75 years (28.5%), diabetes (33.9%), male gender (25.5%), high potassium at baseline (24.5%), renal dysfunction (44.5%) (identified by creatinine 2 mg/dl or GFR 30 ml/min/1.73m^2), symptomatic HF (28.1%) and those receiving therapy with angiotensin-converting enzyme (ACE) inhibitors (25.3%) or spironolactone (27.2%).
Conclusion: Changes in potassium ion may cause life-threatening arrhythmias. The risk of hyperkalemia is increased in symptomatic heart failure patients with comorbidities or combined renin-angiotensin-aldosterone system (RAAS) blockade. A favorable balance of benefit and risk requires clinical vigilance and closer laboratory monitoring, articularly among these patients.

P2110
In patients with recent ADHF and hyponatremia on admission, failure to normalize serum sodium is associated with increased risk of all-cause death and rehospitalizations during a 30-day follow-up

C Ariano[1]; R De Vecchis[1]
[1]*Cardiology Unit , Presidio Sanitario Intermedio "Elena d'Aosta", Naples, Italy*

Background: Several studies have shown that hyponatremia is associated with increased risk of rehospitalization and death in patients with heart failure. In these studies, chronic heart failure (CHF) patients with persistent hyponatremia were compared only with CHF patients with a normal sodium level at hospital admission.
Aims: In the present retrospective study, conducted in a cohort of patients with recent acute decompensated heart failure (ADHF), all with hyponatremia ascertained at the time of hospital admission, we aimed to evaluate the effect of the normalization of serum sodium on the composite endpoint of short-term rehospitalization and mortality
Methods: A retrospective study centered on medical records of patients hospitalized for ADHF in the period April 2013 to April 2016 was performed. Data regarding serum sodium measurements had to be collected from medical records of cardiology wards of two hospitals, and were then processed for statistical analysis. As an inclusion criterion for enrollment, patients had to be suffering from heart failure that had required at least one hospitalization. Moreover, they had to be suffering from a state of hyponatremia (serum sodium < 135 mEq/L) at admission on the occasion of the index hospitalization. Patients with hyponatremia at admission were divided into two groups, one comprising patients with hyponatremia that persisted at the time of discharge (persistent hyponatremia) and a second including patients who had achieved normalization of their serum sodium levels (serum Na+ ≥ 135 mEq/L) during hospitalization until discharge. For both groups, the risk of mortality and rehospitalization during a 30-day follow-up was assessed
Results: One hundred and sixty CHF patients with various degrees of functional impairment were enrolled in the study. Among them, 56 (35%) had persistent hyponatremia over the course of hospitalization. At multivariable Cox proportional-hazards regression analysis, the risk of having a 30-day unplanned readmission or death was significantly higher in patients with persistent hyponatremia compared to those who exhibited a sodium level normalized at discharge (adjusted hazard ratio = 3.0743; 95% CI: 1.3981–6.7601; p = 0.0054). Among the other variables included in the Cox regression model, the number of admissions in the last 12 months (p < 0.0001), the length of stay of the index admission (p = 0.0015) and the NYHA class III at discharge (p = 0.0022) were also identified as risk factors associated with the composite endpoint of 30-day unplanned readmission or death.
Conclusions: In the present retrospective study, the risk of 30-day rehospitalization or death was significantly higher in patients with recent ADHF and persistent hyponatremia in comparison with ADHF patients who had had their serum sodium normalized during the hospital stay. This association seemed to be independent of the heart failure severity.

P2111
Prognostic value of right heart catheterization compared with cardiac magnetic resonance in dilated cardiomiopathy

E Eva Rumiz Gonzalez[1]; A Berenguer Jofresa[1]; JV Vilar Herrero[1]; A Cubillos Arango[1]; D Sanmiguel Cervera[1]; P Almela Alcaide[1]; I Lopez Lopez[1]; V Jimenez Cruz[1]; S Morell Cabedo[1]
[1]*Hospital General de Valencia, Valencia, Spain*

Introduction: Cardiac magnetic resonance imaging (CMR) is actually the gold standard technique for the evaluation of dilated cardiomiopathy (DCM). Recently, a new non-invasive model has been proposed to calculate pulmonary vascular resistance (PVR). However, its prognostic role in patients with acute heart failure (AHF) is unknown.
Purpose: Our objective was to evaluate the prognostic role of CMR and RHC in patients with DCM admitted for a first episode of AHF.
Methods: We prospectively included 60 patients who were admitted with a first episode of AHF and in whom a RHC and a CMR were performed the same day. We evaluated PVR, right ventricle ejection fraction (RVEF) and left ventricle ejection fraction (LVEF) using CMR, and mean pulmonary artery pressure, transpulmonary gradient (TPG), cardiac output (CO) and pulmonary wedge pressure were calculated using RHC.
Results: The mean age of our cohort was 64 ± 15 years, 63.3% were males and 35% showed coronary disease. Mean LVEF and mean RVEF were 34 ± 29% and 41 ± 15% respectively. During a median follow-up of 28 ± 5 months, 16 (26.7%) patients suffered a new rehospitalization for AHF and 6 (10%) patients died. After a multivariate analysis, TPG and CO were independly associated with MACE (rehospitalization for HF and/or death) HR: 1.2, CI 95%:1.07-1.54 and HR: 0.45 IC 95%: 0.21-0.93, p = 0.006. PVR assessed by RHC was the unique independent predictor of cardiac death (HR: 1.57 IC 95%. 1.02-2.42, p = 0.040). However, no CMR parameter was independently associated with MACE.
Conclusions: PVR assessed by RHC has shown to be the only independent predictor of rehospitalization for AHF and cardiac death in patients with DCM. Whereas, no CMR parameter was associated with a higher risk of MACE.

P2112
The prognostic value of the clinical presentation with syncope in acute pulmonary thromboembolism

M L Goncalves[1]; LUIS Abreu[1]; BRUNO Marmelo[1]; JULIO Gil[1]; HUGO Antunes[1]; M I Pires[1]; ISABEL Cunha[1]; DAVIDE Moreira[1]; INÊS Almeida[1]; BRUNO Rodrigues[2]; COSTA Cabral[1]
[1]*Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal*; [2]*Centro Hospitalar Cova da Beira, Cardiologia, Covilha, Portugal*

Introduction: Acute pulmonary thromboembolism (APT) has a heterogeneous and nonspecific clinical presentation, which rarely occurs with syncope (S). In fact, S is not included in the currently validated predictive scores (scores Wells and Geneva). Given the discrepancy between the clinical manifestation and the severity of PE, the question arises whether S, when present, is associated with a more unfavorable clinical situation.
Objective: To evaluate the prognostic impact of patients (P) with APT whose initial clinical presentation coincides with S.
Methos: From a total of 185 D hospitalized for APT in a intensive coronary care unit between 2010-2014, clinical, analytical and imaging information (CT and echocardiogram) were collected retrospectively. Division into groups: P whose initial presentation was with S (group S) vs. P with initial presentation without S (NS group). Association analysis (by chi-square method) was performed between the groups and several demographic, analytical and imaging characteristics.
Results: A mean age of 63.5 ± 18.0 years, 58.9% female, 29.7% with initial presentation with S, 50.3% submitted to fibrinolysis, 5.9% with in-hospital death due to the episode. Length of stay with median of 8 days [1-142].
The following statistically significant associations were established:
Group S had a higher prevalence of presentation with shock (33.3% vs. 10.8% p = 0.042) and a tendency for a greater need for treatment with fibrinolysis during hospitalization (60% vs. 40% p = 0.06). At admission they had lower mean arterial pressure (88.6 vs. 101.4mmHg p = 0.002), systolic blood pressure (109.4 vs. 123.7mmHg p < 0.001) and diastolic blood pressure (66.4 vs. 76.7mmHg p < 0.001). They presented lower pO2 / FIO2 ratio (268.6 vs. 272.4 p = 0.041).

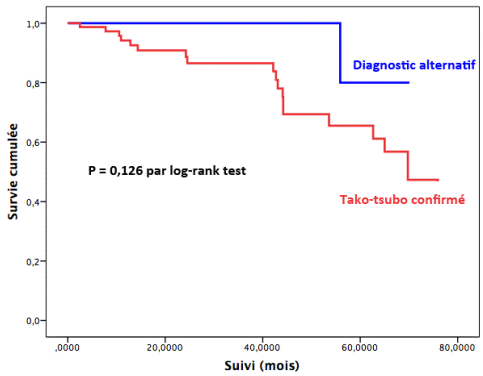
ECG analysis showed a higher prevalence of BCRD (18.2% vs. 7.4% p = 0.033), higher ECGscore (6.3 vs. 3.7 p = 0.001) and higher presence of the S1Q3T3 pattern (36.4% vs. 21.7% p = 0.04).
Angio-CT imaging showed greater reflux of the inferior vena cava (60.6% vs 37.9% p = 0.037), greater interventricular septum bulging (93.9% vs. 72.6% p = 0.013), higher RV / VE ratio (1.62 vs (P < 0.05), greater RV diameter (49.0 vs. 43.8 p = 0.003), lower LV diameter (32.0 vs. 36.9 p = 0.004), higher pulmonary artery / aortic ratio (0.96 vs. 0.88 p = 0.033) and increased angiographic embolic load (Qanadli score 20.5 vs 17.3 p = 0.006).
Analytically, they had a higher prevalence of troponin I values> 0.4 ng / dL (54.5% vs. 34.7 p = 0.013).
Conclusion: P whose initial clinical presentation is with S, are associated with clinical, analytical and imaging characteristics typically associated with a worse prognosis. Thus, the presentation with S should put the hypothesis that we are facing a APT with worse prognosis, with its implications in the approach, monitoring and therapeutic.

P2113

Long-term prognosis in Takotsubo patients: not so benign

C Clement Delmas[1]; G Domain[1]; A Roger[1]; L Marty[1]; C Biendel[1]; M Galinier[1]; D Carrie[1]; O Lairez[1]
[1]*Toulouse Rangueil University Hospital (CHU), Cardiology department, Toulouse, France*

Background: Takotsubo syndrome (TTS) is an improving diagnosis, considered benign despite rare acute complications since its recover in few days or weeks. But although recent large series found 4.1% in-hospital mortality similar to ACS, long-term prognosis is poorly appreciated.
Methods: and results: Between 10.2009 and 03.2016, 113 patients were suspected for TTC according to the Mayo Clinic criteria, and included in a prospective cohort in our tertiary hospital. Patients underwent systematic check up with cardiac MRI, urinary and/or plasma catecholamine, and thyroid balance to differentiate true TTS (n = 91; 80.5%) and alternative diagnosis (n = 22; 19.4%/ myocarditis, spasm, ACS, pheochromocytoma, thyrotoxicosis). 30-days mortality and late mortality were similar with a trends to be more for alternative diagnosis (1.3% vs 0 and 25% vs 5.5%; p = ns). Etiologies of death were shared between cancer (9.1%), heart failure (2.6%), stroke (1.3%) and miscellaneous condition (Table2). Long-term follow-up seems to be similar with more than 60% of NYHA1-2 patients and same re-hospitalisation rate. Moroever long-term medication were similar probably due to same comorbidities.
Conclusion: Patients with confirmed TTS have late complications which seem to be related to older age and comorbidity, and merit special attention. Thus a systematic follow-up seems to be needed.



P2114

Prognosis of pulmonary embolism: risk stratification in non high-risk patients

P Pedro Freitas[1]; AR Santos[2]; M Goncalves[1]; A Oliveira[1]; A Santos[2]; J Oliveira[2]; M Gago[2]; R Mamede[2]; D Correia[2]; N Vale[1]; J Carmo[1]; S Guerreiro[1]; J Brito[1]; J Ferreira[1]; M Mendes[1]
[1]*Hospital de Santa Cruz, Cardiology, Lisbon, Portugal*; [2]*Hospital de Sao Francisco Xavier, Lisbon, Portugal*

Background/Introduction: The prognostic assessment of acute pulmonary embolism (APE) in patients at low or intermediate risk takes into consideration the evaluation of right ventricle dysfunction (RVD) and/or evidence of myocardial injury. Nevertheless, the 2014 ESC guidelines recommendations on risk stratification have not been tested in real-world APE patients.
Purpose: The aim of our study was to compare the PESI classification with the ESC 2014 risk stratification model to predict all-cause mortality at 30-days in non high-risk patients. We also evaluated the role of RVD, elevated troponin and elevated NT-proBNP in the risk stratification of patients with APE.
Methods: We have included 411 patients consecutively diagnosed with APE by computed tomographic angiography (CT-angio) in a single centre, between 2009 and 2015. RVD was evaluated with CT-angio or Echocardiography at admission. The cut-off values for troponin I and NT-proBNP were 0.04 µg/L (99th percentile) and 600 pg/mL. Cardiovascular dysfunction (CVD) was defined as the concomitant presence of RVD, elevated troponin and NT-proBNP. Multivariate analysis was performed using binary logistic regression. Discriminative power was assessed by ROC curves. The studied endpoint was all-cause mortality at 30-days.
Results: Median age was 76 years (IQR 65 – 83), 39% male. All-cause mortality at 30-days was 8.5% (n = 35). RVD was present in 59% (n = 243) of the patients. Troponin I and NT-proBNP were elevated in 50% (n = 205) and 68% (n = 280) of the patients, respectively. CVD dysfunction was present in 30.2% (n = 124). According to the ESC risk stratification strategy, 6.8% (n = 28), 53.8% (n = 221) and 39.4% (n = 162) patients were considered low, intermediate-low and intermediate-high risk, respectively. The PESI score classified 9.5% (n = 44), 13.8% (n = 64), 21.6% (n = 100), 17.5% (n = 81) and 37.6% (n = 174) patients as class I through V, respectively. The discriminative power of the ESC classification was inferior to the PESI classification (AUC = 0.62; AUC = 0.70, respectively; difference between AUC = 0.082; p = 0.07).
Univariate and multivariate analysis are depicted in the table. Only PESI classification and CVD remained independent predictors of all-cause mortality at 30-days. Adding CVD to the PESI classification modestly increased the discriminative power (AUC = 0.73; 95% CI 0.69 – 0.78; p < 0.001) even though AUC difference was not statistically significant (difference between AUC = 0.03; p = 0.16).
Conclusion: In this population, the 2014 ESC risk stratification strategy was not superior to the sole application of PESI classification. The contribution of cardiovascular dysfunction modestly for risk stratification of APE patients was modest.

Table. Univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
Variables	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Elevated Troponin I	2.05 (0.99 – 4.2)	0.053		
Elevated NT-proBNP	6.76 (1.5 – 30.1)	0.012		
RVD	1.36 (0.7 – 2.8)	0.408		
Cardiovascular dysfunction	2.6 (1.3 – 5.3)	0.008	2.2 (1.08 – 4.6)	0.03
PESI classification	2.04 (1.4 – 2.99)	< 0.001	1.99 (1.4 – 2.8)	< 0.001
ESC 2014 model	2.2 (1.2 – 4.2)	0.016		

Cardiovascular dysfunction was defined as concomitant presence of elevated Troponin I, elevated NT-proBNP and right ventricular dysfunction.
Multivariate analysis was first performed considering PESI classification, elevated Troponin I and NT-proBNP and right ventricular dysfunction. Only PESI score remained an independent predictor of mortality. A second multivariate analysis was performed with PESI classification and cardiovascular dysfunction.

Table

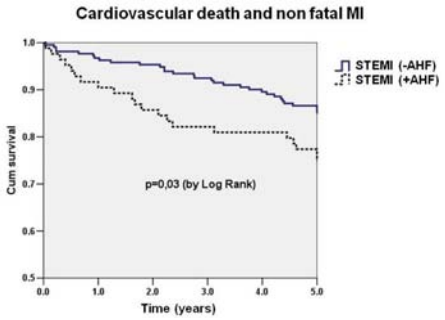
P2115

Long term survival hypertensive patients after ST-elevation myocardial infarction with preserved ejection fraction

S Sergey Kozhukhov[1]; A Parkhomenko[1]; N Dovganych[1]
[1]*NSC "Institute of Cardiology", Kiev, Ukraine*

Purpose: The immediate and long-term mortality after myocardial infarction (MI) in patients (pts) with hypertension is increased. This is likely to be due at least in part to the frequency of complications such as acute heart failure (AHF). AHF with preserved ejection fraction (EF>40%) accounts for almost 45% of heart failure cases. However, prognostic accuracy in those pts is unknown.
The aim of the present study is to focus on hypertensive patients with ACS, in order to better elucidate whether these patients are at higher risk and deserve a tailored approach for management and follow-up.
Methods: Of the 606 pts (age 54.8 ± 9 years, LVEF 49.1 ± 6.1%) who participated in a prospective study, 299 (49.3%) have history of AH. Patients were divided into 2 groups: 1 - with symptomatic AHF (Killip class II/III) during hospitalization (n = 84), 2 - without AHF (n = 215). Main outcomes were cardiovascular death and nonfatal MI with a median follow-up of 5 year.
Results: Pts with AHF were likely to be older, have history of coronary heart disease and have an anterior wall MI. Time from onset symptoms of MI was 3.9 ± 0.3 h and not differ between groups. Reperfusion therapy (TLT or PTCA) performed in 68.7%. On admission AHF pts presented with higher heart rate and glycemia, lower EF. Also AHF patients had a greater degree of LV hypertrophy and diastolic dysfunction. During hospital stay AHF pts has statistically significant ventricular tachycardia/fibrillation (6.0 vs 0.5 %; p < 0.05), early aneurism of LV (17.9 vs 6.5%; p < 0.01). Fig. 1 shows Kaplan Meier estimates of survival in patients with and without signs of AHF during admission and follow-up.

Conclusions: AHF with preserved EF in hypertensive patients is a frequent complication in STEMI and a powerful and independent predictor of 5 year survival. AHF presence is possible because of greater infarct size and more advanced LV diastolic abnormalities highly prevalent among hypertensive pts.



P2116

Comparative analysis of digoxin use among acute heart failure patients during hospital stay: clinical characteristics and outcomes

LCSP Luiz Carlos Passos[1]; TM Trindade[2]; AR Duraes[3]; ACF Queiroz Filho[3]; AGQ Jesus[2]; NRS Silva[2]; SLS Quirino[2]; VRS Souza[4]; YM Lira[5]; EL Garrido[4]; AJS Barbosa[3]; JFO Costa[2]; FV Bulhoes[2]; AOR Sarno[1]; NRS Goes[2]
[1]Federal University of Bahia, Internal Medicine, Salvador, Brazil; *[2]Ana Nery Hospital, Salvador, Brazil*; *[3]Federal University of Bahia, Faculty of Medicine, Salvador, Brazil*; *[4]Federal University of Bahia, College of Nursing, Salvador, Brazil*; *[5]Bahiana School of Medicine and Public Health, Salvador, Brazil*

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Background: The use of digoxin as an effective therapeutic agent in acute systolic heart failure remains controversial mainly because of concerns about its safety and the increased risk of death reported in some groups of patients. Purpose: To describe differences in baseline and outcomes aspects in patients admitted for acute heart failure (AHF) according to the use of digoxin during hospital stay.
Methods: This retrospective cohort study included data from 329 patients admitted in three tertiary cardiac referral centres for AHF management between 2009 and 2016. All the data were collected from medical records. Results: The studied data are shown at the table 1. Conclusion(s): Although digoxin patients had more frequently atrial fibrillation, chronic kidney disease and longer hospital stay, there were no differences regarding outcomes in comparison to non-digoxin group. Digoxin use criteria in acute heart failure need to be further studied.

Baseline Characteristics

	All (n = 329)	Digoxin (n = 177)	Non digoxin (n = 152)	P Value
Patients, %	100	53.8	46.2	-
Male, % (n)	62.9 (207)	56.5 (117)	43.5 (90)	0.2
Age, mean±SD	59.9±14.6	59.17±13.9	60.7±15.3	0.33
LVEF, mean±SD	31.8±9.0	29.9±8.6	34.0±8.9	< 0.001*
Prior Comorbidities, % (n)				
Hypertension	66.3 (214)	63.4 (111)	69.6 (103)	0.24
Atrial Fibrilation (AF)	23.5 (69)	28.3 (45)	17.8 (45)	0.03**
Death among AF patients	4.4 (3)	4.5 (2)	4.2 (1)	0.94
Diabetes	28.2 (91)	28.0 (49)	28.4 (42)	0.94
Chronic Kidney Disease	16.4 (53)	18.9 (33)	13.5 (20)	0.2
>1 Comorbidity	31.6 (102)	30.3 (53)	33.1 (49)	0.59
Heart Failure Etiology, % (n)				
Ischemic	30.0 (96)	24 (42)	37.5 (54)	0.009**
ChagasHeart Disease	24.7 (79)	28.6 (50)	20.1 (29)	0.08
Hypertensive	17.2 (29)	14.3 (25)	20.8 (30)	0.12
Valvular	8.5 (27)	6.3 (11)	11.1 (16)	0.12
Alcoholic	2.8 (9)	4 (7)	1.4 (2)	0.19
Other	10.7 (35)	14.8 (26)	5.9 (9)	0.01**

* T-student test. ** Chi-square test.

P2117

Prognostic significance of left axis deviation in acute heart failure patients with left bundle branch block

KH Ki Hong Choi[1]; GY Lee[1]; JO Choi[1]; ES Ju[1]; YJ Lee[1]; ES Jeon[1]
[1]Samsung Medical Center, Divison of Cardiology, Seoul, Korea Republic of

On behalf of: KorAHF investigators
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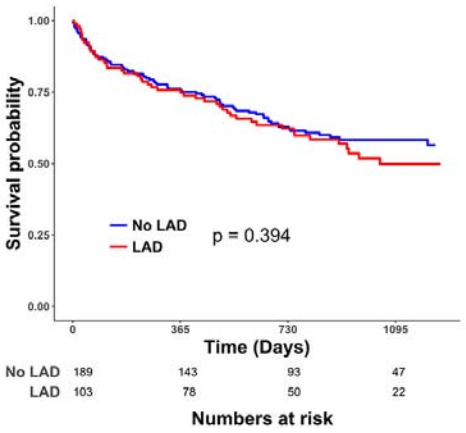
Purpose: The prognostic impact of left axis deviation on clinical outcomes in AHFS with LBBB is unknown. This study aimed to determine the prognostic significance of left axis deviation in patients with acute heart failure syndrome (AHFS) with left bundle branch block (LBBB).
Methods: Between March 2011 and February 2014, 292 consecutive AHFS patients with LBBB were recruited from 10 tertiary university hospitals. They were divided into groups with no left axis deviation (LAD) (n = 189) or with LAD (n = 103) groups according to QRS axis < -30 degree. The primary outcome was all-cause mortality.
Results: The median follow up duration was 24 months (interquartile range 12 to 35 months). On multivariate analysis, the rate of all-cause death did not significantly differ between the normal axis and LAD groups (39.7% vs. 46.6%, adjusted hazard ratio [HR] 1.01, 95% confidence interval [CI] 0.66 to 1.53, p = 0.97). However, on the multiple linear regression analysis to evaluate the predictors of the LVEF, presence of LAD significantly predicted a worse LVEF (adjusted beta -3.25, 95% CI -5.82 to -0.67, p = 0.01). Right ventricle (RV) dilatation was defined as at least two of three electrocardiographic criteria (late R in lead aVR, low voltages in limb leads, and R/S ratio < 1 in lead V5) and was more frequent in the LAD group than in the normal axis group (p < 0.001).
Conclusion: Among the AHFS with LBBB patients, LAD did not predict mortality, but it could be used as a significant predictor of worse LVEF and RV dilatation.

Predictors of lower LVEF

Variables	Unadjusted Slope (95% CI)	p value	Adsjuted Slope (95% CI)	p value
Normal QRS axis (reference)				
LAD	-3.03 (-5.53 to -0.52)	0.02	-3.25 (-5.82 to -0.67)	0.01
RAD	0.45 (-9.47 to 10.36)	0.93	-0.20 (-10.08 to 9.67)	0.97
Age	0.18 (0.07 to 0.28)	0.001	0.16 (0.04 to 0.27)	0.007
Male	-1.31 (-3.69 to 1.07)	0.28	-0.56 (-3.00 to 1.87)	0.65
Ischemic etiology	2.00 (-0.44 to 4.44)	0.11	0.69 (-1.88 to 3.26)	0.60
Hypertension	2.30 (0.90 to 1.88)	0.16	0.98 (0.65 to 1.49)	0.94
Diabetes mellitus	2.64 (0.23 to 5.06)	0.03	1.57 (-1.08 to 4.22)	0.24
Body mass index≥ kg/m^2	0.98 (-1.83 to 3.78)	0.49	0.89 (-1.97 to 3.75)	0.54
QRS duration≥ 150 ms	-0.26 (-2.73 to 2.22)	0.84	-0.26 (-2.73 to 2.22)	0.83
Creatinine≥ 2mg/dL	1.67 (-1.58 to 4.91)	0.31	1.29 (-1.98 to 4.57)	0.44

CI = confidence interval; LAD = left axis deviation; RAD = right axis deviation



Survival curve according to LAD

P2118

Possibility of impedance cardiography in prognosis assessment in hypertensive emergency complicated by acute heart failure

I Darmaeva[1]; E Shavarova[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Objective: impedance cardiography is a noninvasive modality utilized changes in impedance across the thorax to assess hemodynamic parameters. The aim of the study was to evaluate the hemodynamic profile of hypertensive emergencies patients complicated by pulmonary edema.
Design and methods: 27 patients with pulmonary edema due to hypertensive emergencies (55% females, mean age 71,5 ± 10,2 years) were selected from all patients hospitalized with hypertensive crises to emergency care hospital for evaluation of cardiac index, systemic vascular resistance (SVR), thoracic fluid content (TFC) by impedance cardiography (Cardio Screen, Germany). Patients with severe valve dysfunctions, aortic balloon pump were not eligible to the study. All parameters were assessed at baseline, after 2 and 24 hours. 26 (96%) patients had arterial hypertension in the past, 20 (74%) were treated regularly. Blood pressure (BP) was measured at initial contact by first aid doctors, then at hospital just after arrival, after 2, 6, 24, 72 hours. Serum creatinine, urea, potassium and ECG, chest X-ray, neurologic examinations were done for all patients. Fundoscopy, echocardiogram, brain computer tomography were done optionally. All patients were treated with loop diuretic furosemide and alfa1-adrenergic receptor inhibitor urapidil.
Results: mean BP at initial contact in patients with hypertensive emergencies was 209 ± 22/119 ± 17 mm Hg, after 2 hours – 178 ± 18/106 ± 21 mm Hg, after 6 hours – 159 ± 11/91 ± 11, after 24 hours – 147 ± 7/93 ± 5, after 72 hours – 143 ± 9/88 ± 7 mm Hg. So decreasing BP < 160/100 mm Hg after 6 hours was observed in 81%. Baseline, after 2 and 24 hours TFC in woman was 38 ± 7, 33 ± 9, 27 ± 5, in man - 45 ± 11, 38 ± 9, 31 ± 10. Baseline cardiac index 3.01 ± 1,02 l/min/m2, after 2 hours - 2,17 ± 1,06 l/min/m2. Baseline SVR was 3381,9 ± 1012,7 after 2 hours - 2502,2 + 1272,2 dyn × s × cm(-5) × m2. In-hospital mortality was 22% (n = 6). The median cardiac index in nonsurvivors was significantly less than for survivors. The AUC for cardiac index in predicting mortality was 0.76 (95% CI 0.51-0.91, p = 0.033). A cardiac index cut-off value < 2 l/min/m2 had sensitivity of 46% and specificity of 97% in lethal outcomes prediction.
Conclusions: ICG may be a helpful, noninvasive tool in noninvasive monitoring hemodynamic parameters and prognosis evaluation in patients with pulmonary edema due to hypertensive emergency.

P2119

Prognostic value of acute kidney injury and blood urea nitrogen/creatinine ratio in patients with acute heart failure

IR Lala[1]; DA Darabantiu[1]; A Pop-Moldovan[1]; M Puschita[1]
[1]*Vasile Goldis Western University, Cardiology, Arad, Romania*

Purpose: The aim of this retrospective study was to evaluate whether elevated admission blood urea nitrogen/creatinine ratio (BUN/Cr) or acute kidney injury (AKI) during hospitalization is predictive of in-hospital mortality in patients hospitalized with acute heart failure.
Methods: In this study we evaluated consecutive patients from the regional heart failure registry, enrolled during 2015 at our clinical county hospital with a primary diagnosis of acute heart failure. For all patients, BUN/Cr ratio was calculated at admission and correlated with clinical variables and in-hospital mortality. Afterwards patients were divided into two groups: with or without acute kidney injury (defined as an increase of serum creatinine by ≥ 0.3 mg/dl within 48 hours). For statistical analysis we used independent t test for comparison of continuous values, Pearson x ^{2} test for comparison of categorical values, multivariate logistic regression, survival curves and Cox regression for predictors of in-hospital mortality.
Results: A total of 184 consecutive patients with acute heart failure (males and females) were enrolled. Mean age was 69 ± 10 years and mean ejection fraction was 33 ± 10%. The percentage of patients with AKI was 31% and without AKI was 69%. The AKI group presented higher heart rate at admission compared to the non-AKI group (105 b/min vs. 95 b/min, p = 0.012). Higher admission BUN/Cr ratio was associated with lower systolic blood pressure (136 mmHg vs 149 mmHg, p = 0.015) and with the "wet and cold" clinical profile of acute heart failure (p = 0.043). Patients with AKI had a significantly worse survival profile during hospitalization (log-rank test, p < 0.0001) and Cox proportional hazards modelling showed a crude HR = 5.3 (95%CI [2.2.-12.4], p < 0.0001) for in-hospital mortality. Higher admission BUN/Cr ratio proved to be a significant factor for in hospital mortality also, with a crude HR=3 (95% CI [1-8], p = 0.028).
Conclusions: Acute kidney injury during hospitalization in patients with acute heart failure is responsible for worse in-hospital survival rates and is associated with increased heart rate at admission. Elevated BUN/Cr ratio at admission is linked with an increased risk for in-hospital mortality being associated with lower systolic blood pressures and the "wet and cold" clinical profile in patients with acute heart failure.

P2120

Measurement of Circulating endothelial progenitor cell and endothelial microparticles can predict the improvement of ischemic heart failure

YS Yun-Seok Choi[1]; AMI Kwon[1]; CS Park[1]; MY Lee[1]; HJ Youn[1]; WS Chung[1]
[1]*The Catholic University of Korea, Seoul, Korea Republic of*

Introduction: Endothelial microparticles (EMP) are small vesicles shed from activated or apoptotic endothelial cell. We wonder elevated EMP and EPC level is possible to predict the improvement of ischemic heart failure.
Methods: total 354 patients (age 63 ± 11, male 255(72%)) who diagnosed as ischemic heart failure (EF < 45%, three vessel disease) were divided as two group. Group 1 showed improved ejection fraction (mean Δ6.3 ± 1.1%) after optimal medical therapy. Group II did not show improvement of ejection fraction (Δ0.3 ± 0.4%). Mean follow duration was 6.2 ± 2.1 months. EMP and endothelial progenitor cells(EPC) are determined in peripheral blood by anti CD31-PE and anti CD42-FITC. MPs were defined as CD31 + /CD42- particles with a diameter < 1.5μm, being MP size calibrated with flow cytometry size calibrations. The values of EMP, EPC, and EMP/EPC ratio in patients with ischemic heart failure were compared with control group.
Results: Group I (n = 185, mean age 64 ± 11) and Group II (n = 169, mean age 62 ± 10) did not show differences in terms of medication. There were no significant differences in coronary risk factors such as age, DM, HBP, dyslipidemia, smoking between groups. The level of EMP(%) was lower in Group I than Group II [(1.33 ± 0.71) in group I, (1.54 ± 0.96) in Group II, p = 0.03]. But EPC values were similar between two groups. [(0.042 ± 0.016) vs (0.049 ± 0.022, p = 0.11)] and EMP/EPC ratio were significantly different [(49.4 ± 14.3) in Group 1 vs (62.1 ± 22.2) in Group II, p = 0.02]. EMP/EPC ratio had significant predictive value to detect the improvement of ischemic heart failure. (OR, 1.88. 1.32-1.99, p = 0.01)
Conclusion:. Improvement of ischemic heart failure after optimal medical therapy might be predicted by measuring the circulating endothelial microparticle and progenitor cell ratio.

P2121

Serum potassium levels at admission and in-hospital all-cause mortality in patients hospitalised for acute heart failure (insights from RO-AHFS registry).

I Iulian Cosei[1]; L Antohi[1]; R Radu[1]; C Radulescu[1]; M Chivulescu[1]; A Ravasel[1]; AP Ambrosy[2]; C Macarie[1]; SP Collins[3]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; [2]*Duke University Medical Center, Durham, United States of America*; [3]*Vanderbilt University, Nashville, United States of America*

On behalf of: RO-AHFS study investigators

Background: Previous data coming from randomized controlled trials raised some controversies related to the prognostic value of serum potassium levels in patients hospitalised for acute heart failure (AHF).
Purpose: To assess the prognostic value of serum potassium levels at admission in patients hospitalised for AHF regarding in-hospital all-cause mortality in a "real world" national registry.
Methods: RO-AHFS was a prospective, national, multicenter registry that included 3224 consecutive patients admitted for AHF over a 12 month period. This is a post-hoc analysis of 3188 patients who had potassium levels measured at admission. We analyzed in-hospital all-cause mortality in this population stratified by quartiles of serum potassium concentration.
Results: The demographic and clinical characteristics of patients stratified by potassium levels quartiles are shown in Table 1. No linear relationship between in-hospital mortality and serum potassium levels at admission was identified (HR=0.89; CI 95% 0.73-1.26). Also, in-hospital all-cause mortality did not vary significantly across quartiles: the mortality in quartiles Q1, Q2, Q3 and Q4 was 7.9%, 7.2%, 7.8% and 8.1% (p = 0.425) respectively.
Conclusions: In the present analysis we didn't find any relationship between in-hospital mortality and serum potassium levels at admission, finding which may be reflective to the observational nature of the registry.

Table 1

	Q1 n=797	Q2 n=797	Q3 n=797	Q4 n=797	p value
Serum potassium range (mmol/L)	3.1-3.53	3.68-3.97	4.01-4.75	4.88-5.01	
Age (years)	65.7±10.3	68.3±11.3	70.1±9.4	69.7±11	0.031
Gender (male)	61%	65%	64%	63%	0.62
Left ventricular ejection fraction (%)	37.1±9	37.6±8	38.2±10	37.4±9.5	0.13
Atrial fibrillation	39.8%	37.1%	40.0%	39.3%	0.681
Ischemic etiology	60.8%	59.3%	58%	59.4%	0.3101
Diabetes mellitus	39.3%	40.1%	40.8%	38.6%	0.195
Systolic blood pressure (mmHg)	129±21	128±19	131±18	132±16	0.015
Serum creatinine (mg/dL)	1.3±0.7	1.3±0.5	1.43±0.8	1.86±0.6	< 0.001

P2122

Neutrophil-to-lymphocyte ratio: a simple and useful predictor of long term prognosis in patients hospitalized for acute heart failure

J Rigueira[1]; J Agostinho[1]; P Alves[2]; I Ricardo[1]; I Goncalves[1]; T Guimaraes[1]; N Andre[1]; A Nunes Ferreira[1]; R Santos[1]; F Veiga[1]; M Mendes Pedro[1]; FJ Pinto[1]; D Brito[1]

[1]Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Cardiology Department, Lisbon, Portugal; *[2]University Hospital De Santa Maria, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal*

Background/Introduction: The search for risk and/or prognostic markers in acute heart failure (or exacerbation of chronic heart failure) – AHF - has been a constant in the last decades. Inflammation plays a major role in HF and contribute to the occurrence of adverse events. The neutrophil/lymphocyte ratio (rN/L), a simple and easy to perform marker of "inflammation", has been considered promising in small studies including populations affected by diverse cardiovascular diseases, namely in HF.

Purpose: To evaluate the usefulness of rN/L as a predictor of prognosis [rehospitalization (reH) and mortality] in a population hospitalized for AHF.

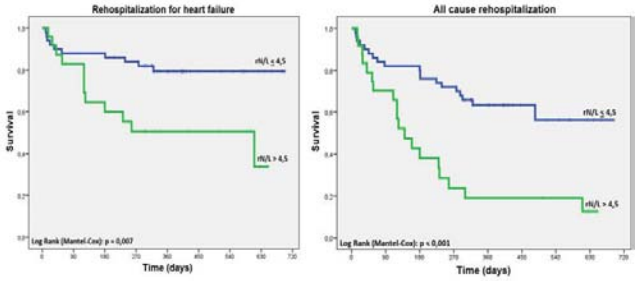
Methods: Discharge notes of 100 patients (pts) consecutively admitted for AHF (cardiology ward, tertiary hospital center), discharged alive and prospectively followed, were analysed. Pts with infection on admission (n = 25) were excluded. Demographic, clinical, laboratorial and echocardiographic data were evaluated and their relation to rN/L was established (Mann-Whitney and Spearman tests). The influence of rN/L on mortality and reH during post-discharge follow-up was determined (Cox regression analysis and Kaplan-Meier survival).

Results: Seventy five pts (58.7% men, 66.7 + 13.3 years) were included in the final analysis. There were no in-hospital deaths. During a mean follow up (Fup) period of 14.1 ± 5.7 months, the reH rate for HF was 29.3% and all cause reH was 57.7%. The mortality rate during the Fup was 13.3%. The median of rN/L on admission was 4 (3-5). The rN/L did not correlate with age, functional class (NYHA) on admission, or in-hospital lenght of stay, and only a weak correlation with plasma NT-proBNP values (Pearson R= 0.27; p = 0.03) or presence of pulmonary congestion on admission (p = 0.036) was observed.

A value of rN/L> 5.5 on admission was a non-independent predictor of long-term mortality (AUC= 0.95, CI= 0.9-0.99, p < 0.01); also NT-ProBNP> 6500 pg/mL on admission did not independently predict mortality during Fup (AUC= 0.79, CI=0.65-0.93, p = 0.014).

A rN/L> 4.5 was an independent predictor of both rehospitalization for HF (HR= 4.16, CI 1.44-11.98, p = 0.008) and all cause rehospitalization (HR= 3.16, CI 1.4-7.14, p = 0.006); NT-ProBNP> 4000pg mL (AUC= 0.68, CI= 0.57-0.79, p = 0.014) was a non-independent predictor of HF rehospitalization.

Conclusion: In patients admitted to hospital with AHF, rN/L on admission revealed prognostic utility given the ability to predict future rehospitalization, although it did not show a significant association with other clinical and laboratorial parameters at admission, namely with NT-proBNP values. The rN/L may be useful as a marker of "fragility" in the identification of AHF patients who may benefit from closer follow-up in the outpatient setting.



P2123

Predictors of prolonged hospitalization in acute heart failure

I Aguiar-Ricardo[1]; J Agostinho[1]; P Alves[1]; J Rigueira[1]; I Goncalves[1]; AR Francisco[1]; T Guimaraes[1]; M Nobre-Menezes[1]; G Lima Da Silva[1]; R Santos[1]; A Ferreira[1]; F Veiga[1]; M Mendes-Pedro[1]; D Brito[1]; J Fauto Pinto[1]

[1]Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Cardiology, Lisbon, Portugal

Background/Introduction: Acute heart failure (AHF) is an increasing cause of hospital admission requiring sometimes prolonged hospitalization. This has an impact on quality of life, it is associated with significant economic burden and may contribute to higher mortality.

Purposes: To identify factors associated with a longer stay in patients admitted for AHF and to assess the possible repercussion of length of stay on the long-term prognosis.

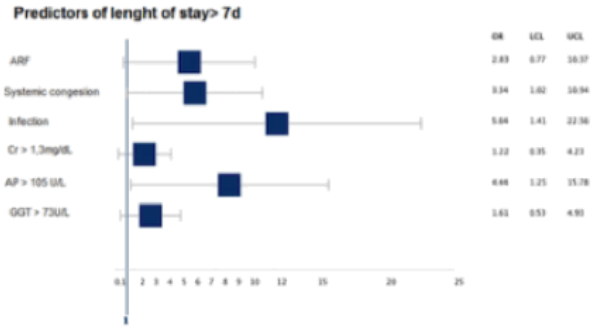
Methods: Retrospective, unicentric study, with 100 consecutive patients (pts) hospitalized for AHF in a tertiary hospital cardiology center. Demographic, clinical, laboratorial and echocardiographic characteristics were evaluated at admission. By logistic regression, the relationship with the length of stay [duration greater than 7 days (LOS> 7d) and greater than 14 days (LOS> 14d)] was analyzed. The relationship between length of stay and the rate of rehospitalization and post-discharge mortality, through Cox Regression and Mann-Whitney test, were evaluated.

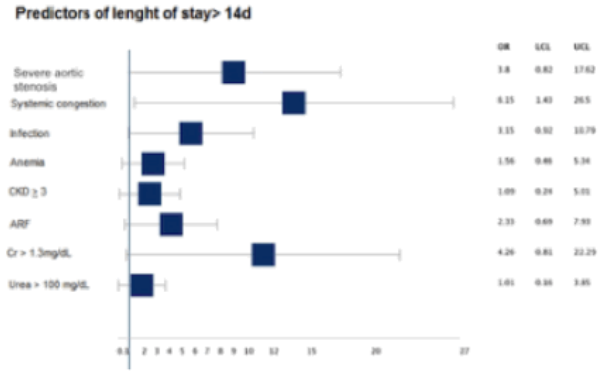
Results: The included population (55% men, 68 ± 13 years) was followed for 14.2 ± 5.5 months after hospital discharge. The median length of stay was 8 days (5-17); 54 pts had LOS> 7d and 28 had LOS> 14d. There was no in-hospital mortality and the post-discharge mortality rate was 14%. The predictors of LOS>7d were: acute renal failure (ARF)(p = 0,003), infection (p = 0,004), systemic congestion (SC) (p = 0,008), creatinine >1,3mg/dL (p = 0,032), alkaline phosphatase (AP)>105mg/dL (p = 0,011) and GGT > 73mg/dL (p = 0,011). By multivariate analysis, the presence of SC (OR = 3.4, CI: 1.0-10.4, p = 0.047), infection (OR=5,6; CI:1,4-22,6; p = 0,015) and AP >105mg/dL (OR=4,4; CI:1,3-15,8; p = 0,021) were independent predictors of LOS> 7d.

The predictors of LOS> 14d were: severe aortic stenosis (p = 0,042), anemia (p = 0,001), chronic kidney disease stage >3 (p = 0,011), ARF (p < 0,001), SC (p = 0,005), infection (p = 0,001), creatinine >1,3mg/dL (p = 0,002) and urea >100mg/dL (p = 0,009). The presence of SC revealed to be an independent predictor of LOS> 14d (OR=6,1; CI:1,4-26,5; p = 0,015).

The length of first hospitalization was not associated with mortality or rehospitalization during follow-up.

Conclusion: The presence of SC was an independent predictor of prolonged hospitalization for AHF, making it imperative to improve strategies for SC control. Infection and PA> 105mg / dL also have the capacity to predict LOS> 7d.





P2124

Prognostic implication of changes in renal function in patients with acute decompensated heart failure

SY Jang[1]; NK Kim[2]; JH Sohn[1]; JH Roh[2]; MH Bae[2]; JH Lee[2]; DH Yang[2]; HS Park[2]; Y Cho[2]; SC Chae[2]

[1]Kyungpook National University Medical Center, Cardiology center, Daegu, Korea Republic of; *[2]Kyungpook National University Hospital, Daegu, Korea Republic of*

Background: There are conflicting data about whether worsening renal function (WRF), as well as improving renal function (IRF), is related to poor prognosis. The purpose if this study was to evaluation the prognostic impact of WRF and IRF on prognosis of patients with acute decompensated heart failure.
Methods: Patients hospitalized for acute decompensated heart failure between January 2009 and June 2015 were retrospectively analyzed. Patients with initial serum creatinine more than 2.5mg/dl were excluded. A total of 846 patients (66.8 ± 15.0 years-old, 430 men) included in the final analysis. WRF and IRF were defined as decrease and increase of >20% from baselines estimated glomerular filtration rate, respectively. The composite event of all-cause mortality and re-hospitalization for heart failure was assessed for the prognosis of the patients.
Results: Among the patients, 135 and 170 patients were included in WRF and IRF, respectiveluy. A total of 193 adverse events (22.8%) were observed during the 1-year follow-up. WRF, IRF and stationary renal function (SRF) group respectively showed 32.6%, 21.8% and 20.7% of adverse event rate. Kaplan-Meier analysis showed significant difference in prognosis among the three groups (p = 0.003). The difference comes from the different prognosis between WRF and SRF (Bonferroni corrected p = 0.002) and there was no significant difference between IRF and SRF (Bonferroni corrected p = 1.000). Cox-proportional hazard model showed WRF was independently associated with poor prognosis (hazard ratio [HR] 1.497 [1.001-2.228], p = 0.047) together with age, ischemic etiology, beta blockers, loop diuretics, natriuretic peptide, and serum hemoglobin level. However, IRF did not showed a distinct prognostic difference compared to SRF group (HR 1.004 [0.678-1.487], p = 0.983).
Conclusion: WRF renal function was associated with poor prognosis in patients with acute decompensated heart failure, whereas IRF was not.

P2125

Clinical characteristics and outcomes of acute heart failure in younger versus very elderly patients

LCSP Passos[1]; TM Trindade[2]; ACF Queiroz Filho[3]; AGQ Jesus[2]; SLS Quirino[3]; VRS Souza[4]; YM Lira[3]; NRS Silva[2]; AR Duraes[3]; AJS Barbosa[3]; JFO Costa[2]; EL Garrido[4]; PPC Camera[2]; FV Bulhoes[2]; GOES Nrs[2]

[1]Federal University of Bahia, Internal Medicine, Salvador, Brazil; *[2]Ana Nery Hospital, Salvador, Brazil*; *[3]Federal University of Bahia, Faculty of Medicine, Salvador, Brazil*; *[4]Federal University of Bahia, College of Nursing, Salvador, Brazil*

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Background: Age has been described as an important prognosis factor in Heart Failure (HF). Nevertheless, the modern approach in pharmacotherapy and quality of care has improved hospital treatment among heart failure individuals and it is not clear if the age, by itself, is associated with worse outcomes among Acute Heart Failure (AHF) inpatients.
Purpose: To evaluate differences in baseline, treatment and prognosis aspects between younger (≤45 years) and very elderly (≥75years) patients admitted for AHF.
Methods: Retrospective cohort study included data from 107 patients admitted in three tertiary cardiac referral centres for AHF management between 2009 and 2016.
Results: All the data are shown at table 1.
Conclusions: Although we noticed some differences among baseline characteristics as higher frequencies of prior comorbidities and higher prevalences of ischemic and hypertensive etiologies among very elderly patients, younger and very elderly patients showed no clinically relevant differences with regard to hospital outcomes.

Baseline and outcomes characteristics

	All (n = 107)	<=45 (n = 56)	>=75 (n = 51)	P Value
Patients. %	100	52.3	47.7	-
Age. mean±SD	59.9±14.5	36.2±7.2	80.8±4.8	< 0.001
LVEF. mean±SD	31.6±8.9	30.3±8.5	35.5±8.0	0.002
Hypertension	59.2 (61)	41.1 (23)	80.9 (38)	< 0.001
Atrial Fibrilation	22.7 (22)	20 (11)	26.2 (11)	0.47
Diabetes	17.5 (18)	3.6 (2)	34 (16)	< 0.001
Chronic Kidney Disease	24.3 (25)	12.5 (7)	38.3 (18)	0.002
Heart Failure Etiology. % (n)				
Ischemic	25.7 (26)	11.1 (6)	42.6 (20)	< 0.001
Chagas Heart Disease	19.8 (20)	29.6 (16)	8.5 (4)	0.011
Hypertensive	18.8 (19)	9.3 (5)	29.8 (14)	0.008
Valvular	7.9 (8)	0 (0)	14.8 (8)	0.007
Lenght of stay median±IQR	13±17	16±19	10±10	0.013
Acute Renal Failure % (n)	44.9 (48)	51.8 (29)	37.3 (19)	0.13
Cardiac surgery. % (n)	14 (15)	19.6 (11)	7.8 (4)	0.08
Electronic Device Implant* % (n)	5.6 (6)	3.6 (2)	7.8 (4)	0.42
Vasoactive amine use. % (n)	27.1 (29)	33.9 (19)	19.6 (10)	0.1
ICU % (n)	40.2 (43)	48.2 (27)	31.4 (16)	0.08
Death during hospital stay % (n)	7.5 (8)	7.1 (4)	7.8 (4)	1

P2126

Multimorbidity and polypharmacy as readmission and mortality factors in acute heart failure

M Mendez[1]; B Chiva-Ballesteros[2]; L De Pedro Alvarez[2]; P Delgado-Paimar[2]; J Marco[1]; FJ Martin-Sanchez[2]; A Esteban[1]; R Bover[1]; E Calvo[1]

[1]Hospital Clinic San Carlos, Madrid, Spain; *[2]Complutense University of Madrid, Medicine, Madrid, Spain*

Introduction and aims: The aim of our study was to evaluate multimorbidity and polypharmacy as factors associated to readmissions and in-hospital mortality in AHF.
Methods: A total of 199 patients with a primary diagnosis of heart failure ICD code, who were discharged from Internal Medicine of our Hospital in 2014 (from January 1 to December 31, 2014), were included. A descriptive analysis was performed. Subsequently, a bivariate analysis was carried out to compare the characteristics of patients who were readmitted or died with respect to those who did not. T-student statistical tests were used for the quantitative variables and Chi-square for the

qualitative ones with a statistical significance $p < 0.05$. Finally, a multivariate logistic regression analysis was performed with the clinical variables that were associated with readmission or in-hospital mortality with the variables of age, sex, associated comorbidity and other variables with statistical significance ($p < 0.05$). The analysis was carried out using the program SPSS version 21.
Results: The study was conducted in a total of 199 patients, with an average age of 82.7 years, of which 61.8% were women. 85% of the patients had a LVEF>40%, with an average NT-proBNP of 9.101.3 pg/ml. 64.3 % of the patients had atrial fibrillation. 30.2 % of the patients were readmitted, with an average of readmissions per year of 1.45 (±0.86). In-hospital mortality during one year of follow-up was 25% of the patients. Regarding the factors associated with in-hospital mortality, older age was the most outstanding variable, OR 1.050 (1.002-1.101) ($p = 0.04$). Polypharmacy 1,137 (1,017-1,272) ($p = 0.024$) and multimorbidity disorders criteria 4,974 (1,396-17,730) ($p = 0,013$) were the most significant factors associated to readmissions.
Conclusions: In our investigation, advanced age was the main factor associated to in hospital mortality. Multimorbidity and polypharmacy have been the factors most associated to hospital readmissions.

P2127
Pre and post hospitalization care pathways for acute heart failure patients

O Olivier Thebault[1]; DG Guijarro[1]; JPG Gueffet[2]; LLG Le Gloan[1]; NP Piriou[1]; BD Delasalle[1]; MP Poilane[1]; JNT Trochu[1]
[1]*University Hospital of Nantes Nord Laennec, Cardiology, Nantes, France*; [2]*Nouvelles Cliniques Nantaises, Nantes, France*

Introduction: Acute heart failure (AHF) is a serious condition with high mortality and a very high rate of early re-admissions. The aim of our study was to analyze the care pathway, general characteristics and 3-month morbidity and mortality of AHF referred to a French tertiary hospital.
Material and Methods: Consecutive patients hospitalized for AHF patients during two 8-week periods, autumn-winter and spring-summer were included. The overall characteristics and data specific to the care pathway were collected. A 3-month follow-up was carried out to study combined total mortality and unplanned cardiovascular re-hospitalizations at 3 months.
Results: 237 patients, mean age 72 ± 13 years old, 43.2 % HFpEF, 39.2 % HFrEF were included and followed. No significant differences were found between the patients' clinical characteristics between the 2 periods of inclusion. Patients were mostly referred to the hospital by a general practitioner (27%) or a cardiologist (27%), 20.3% after an emergency call, 36.2% of the patients reached the cardiology department after an admission in the emergency department, 38.0% were admitted to the intensive care unit. The average length of hospital stay was 10.8 ± 8.1 days, 77% went back home directly, 15.2% were transferred to a rehabilitation center. An outpatient visit with a cardiologist was scheduled upon discharge for 68.9% of patients within an average of 48 ± 37 days, 10 % of the patients entered a cardiovascular rehabilitation program, 6.3% were included in a multidisciplinary management programme. Combined total mortality or unplanned cardiovascular re-hospitalization was 28.9 %. Chronic heart failure (OR = 2.25 ; $p = 0.01$), early re-hospitalization (< 1 year) (OR = 2.18 ; $p = 0.01$), renal insufficiency (OR = 2,77, $p = 0.001$) and cardiogenic shock (OR = 2.49 ; $p = 0.04$) were identified as risk factors for this criterion. Cardiovascular rehabilitation appeared to be a protective factor (OR = 2.14 ; $p = 0.03$).
Conclusion: Heart failure rehospitalization is frequent and cardiovascular mortality high after an index HF hospitalization with a limited access to an organized care plan after hospitalization, underscoring the importance of the implementation of high quality transition care and better identification of high risk patients.

P2128
Characterization of any cause dyspnea in the emergency department and factors predicting the need for mechanical ventilation

C Cristian Militaru[1]; L Antohi[1]; R Radu[1]; M Chivulescu[1]; C Radulescu[1]; R Botea[1]; S Bubenek[1]; C Macarie[1]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*

Background: Dyspnea is the most common symptom of patients presenting with acute heart failure (AHF). Despite this fact, there is no definitive data about how to correctly quantify dyspnea, and whether the parameters currently used are able to predict outcomes or measure treatment efficiency. Mechanical ventilation (MV) has been shown to ameliorate hypoxemia, correct acidosis and alleviate symptoms in patients with significant respiratory distress.
Method: This was a single-center, prospective, observational, cohort study, which enrolled consecutive patients presenting with dyspnea of any etiology to the emergency room (ER). Dyspnea was evaluated clinically and biologically at baseline, at 5 minutes and 30 minutes, by parameters such as respiratory rate, oxygen saturation, pH, lactate, PaO2, and a patient-subjective visual analog scale (VAS). The aim of this paper is to clinically and biologically characterize dyspnea and to determine which acute-phase parameters obtained in the ER could predict the need for mechanical ventilation.
Results: There were a total of 104 patients enrolled, 57.7% male, mean age 66.8 years, with the majority (65.3%) having a history of HF. The clinical profile classification of the dyspnea was: 61% dyspnea at rest, 18% paroxysmal nocturnal dyspnea, and 21% effort induced dyspnea. Mean baseline parameters were: blood pressure 143/81 mmHg, respiratory rate 23.1 bpm, pH 7.39, SaO2 93.4%, PaO2 77.9%, lactate 1.3 mmol/L, NTproBNP 5280 pg/mL, left ventricle ejection fraction 45.8%. The majority of the patients (79%) had a significant improvement of dyspnea at 30 minutes (as derived from the VAS), in contrast to 4.8% who experienced worsening symptoms. Seven patients (6.7%) required mechanical ventilation (invasive or non-invasive). The only parameters that were predictive for mechanical ventilation after multivariate analysis were PaO2<70%, HR=1.72 (CI95% 1.58-2.91) and respiratory rate>29 bpm, HR=1.53 (CI95% 1.19-2.53).
Conclusions: In AHF patients presenting with dyspnea of any etiology to ER, the need for MV can be predicted by baseline PaO2 and respiratory rate.

P2129
Insulin-like growth factor-1 in acute coronary syndrome complicated by acute heart failure

G Guzeliya Kayumova[1]; V Razin[1]
[1]*Ulyanovsk State University, Ulyanovsk, Russian Federation*

Introduction: Coronary heart disease is the leading cause of morbidity and mortality in economically developed countries. For risk stratification and diagnosis of acute coronary syndrome are actively studied new markers, in particular insulin-like growth factor 1 (IGF-I).
Purpose: analysis of IGF-I in plasma in patients with acute coronary syndrome (ACS)
Material and methods: The study included 71 patients with ACS, the mean age was 57 ± 8.5 years. All cases of ACS were classified according to international nomenclature and was allocated 37 patients with Infarction acute phase STEMI, and 34 patients with Infarction acute phase non STEMI. Acute heart failure are divided into groups according to Killip: I – 17 (23.9 per cent), II – 17 (23,9%), III – 32 (45,1%) , IV - 5 (7,1%). In the blood plasma of patients was determined by IGF-I. Blood sampling was performed at the time of admission of the patient to verification of the final diagnosis. The concentration of IGF-I were determined by ELISA using kits company "Diagnostic Systems Laboratories" (USA).
Results: IGF-1 in patients with Infarction acute phase non STEMI had the highest 179,15 ± 41,29. 37 patients with Infarction acute phase STEMI ardent concentrations of IGF-1 was slightly lower 156,05 ± 44,78. Decreased levels of IGF-I in 9 cases of death from acute myocardial infarction - the concentration of IGF-I was 126,06 ± 15,12. Regression of levels of IGF-1 is also observed in groups with acute heart failure: I – 172,45 ± 31,93, II – 182,82 ± 50,76, III – 156,33 ± of 45.90, IV - 144,52 ± 40,64. For all the results, obviously, reduced the plasma concentrations of IGF-1 in patients in a serious condition.
Conclusions: IGF-I is a new highly sensitive biochemical marker of vascular inflammation and damage, can be used in everyday medical practice, as the stratification factor of ACS.

P2130
The difference of benefit of tolvaptan for acute decompensated heart failure within different etiologies

Y Yoriyasu Suzuki[1]; Y Ochiumi[1]; S Kano[1]; S Murase[1]; A Murata[1]; T Ito[1]
[1]*Nagoya Heart Center, Nagoya, Japan*

Background: the benefit of tolvaptan (TLV) for acute decompensated heart failure (ADHF) has been reported, however, the difference of benefit of tolvaptan for ADHF within different etiologies has not been investigated.
Aim; the purpose of this study is to compare the efficacy of TLV for ADHF within different etiologies.
Methods: the consecutive 234 volume-overload ADHF (clinical scenario 2 or 5) was investigated. We divided into 2 groups (TLV (-); n=103. TLV (+); n=131) and compared between both group and different etiologies of ADHF.
Results: the results are shown in figure.
Conclusion: treatment with TLV for ADHF could prevent WRF and shorten the duration of CCU stay. Especially treatment with TLV could be effective in the patients with DCM, IHD, and VHD.

	TLV (+) n=103	TLV (−) n=131	p-value
male gender	54.3%	57.3%	NS
age	76.7±11.2	77.3±12.9	NS
EF, %	41.5±18.8	41.7±18.8	NS
BiPAP, %	5.8	7.6	NS
inotropic, %	47.6	35.1	0.037
previous admission, %	15.4	54.6	0.001
rest stay, day	3.6±1.8	2.2±0.9	<0.001
3day-urine output, ml	4748±2014	6470±2904	0.014
WRF, %	14.6	5.3	0.015

	AF (N=52)	DCM (N=33)	HHD (N=17)	IHD (N=48)	VHD (N87)	p-value
age	76.2±11.4	67.6±16.7	83.0±4.3	76.8±10.6	81.0±10.8	<0.001
male, %	51.9	81.8	52.9	64.6	46.3	<0.05
usage of samsca, %	28.8	69.7	52.9	54.1	64.2	0.001
samsca effective, %	37.1	64.3	54.5	77.4	77.6	<0.001
pre Na	138.9±4.3	138.4±3.9	139.2±3.8	138.1±5.1	136.8±5.6	NS
post Na	139.2±3.8	140.5±2.8	139.2±3.2	136.6±18.5	138.9±3.3	NS
pre Cr	1.10±0.50	1.31±0.69	1.26±0.79	1.36±0.52	1.32±0.68	NS
post Cr	1.11±0.49	1.31±0.65	1.34±0.69	1.32±0.48	1.26±0.68	NS
EF, %	46.9±17.3	21.4±10.0	54.7±14.5	34.2±12.4	45.4±18.5	<0.001
loop, mg	40.4±17.3	36.1±15.5	37.3±16.8	37.1±16.8	37.3±20.7	NS
rest day	3.1±1.7	2.9±1.8	2.9±1.7	3.0±1.9	2.8±1.6	NS
WRF, %	7.7	12.1	23.5	4.2	3.0	<0.05

Table

P2131

Community pharmacists identifying worsening heart failure symptoms, using novel symptom screening tool

R Rocco Hadland[1]; R Lawrance[2]; K Masri[3]; P Ruiz Canela[3]; A Williams[3]; M Oldfield[4]; J Welstand[2]; D Higman James[1]
[1]Cardiff University, Cardiff School of Pharmacy and Pharmaceutical Sciences, Cardiff, United Kingdom; *[2]Betsi Cadwaladr University Health Board, North Wales, United Kingdom*; *[3]Rowlands Pharmacy, North Wales, United Kingdom*; *[4]Johnstown Pharmacy, North Wales, United Kingdom*

Purpose: Early detection and treatment of worsening heart failure (HF) symptoms can reduce the need for hospitalisation. We aimed to utilise a newly developed novel HF symptom screening tool for use by community pharmacists to detect worsening HF symptoms, using a strategy of collaborating with the local HF pharmacist.
Methods: Pilot study. Patients included were prescribed, loop diuretics, beta blockers, angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and mineralocorticoid receptor antagonists (MRAs). At the time of inviting patients to participate the community pharmacist had no prior knowledge of whether the participant had a diagnosis of HF. The screening tool was designed to identify worsening symptoms during the previous month. and included six questions pertaining to breathlessness, nocturnal breathlessness, signs of oedema, tiredness and weight gain. Participants with suspected worsening HF symptoms were referred to the local HF pharmacist who acted as triage to the general practitioner (GP) referrals.
Results: 28 patients participated out of 40 that were invited to participate, across 5 community pharmacies in North Wales over a 2-month period. 6 patients were identified with suspected HF symptoms and were all referred to their GP by the HF pharmacist. All 6 participants that were referred to a GP resulted in an intervention by the GP. The GPs interventions were: 2 patients required changes to HF therapies, 1 patient required a change to a non-HF treatment, 3 patients were referred to a cardiologist, with 1 participant subsequently diagnosed with HF with preserved ejection fraction. Retrospective review of the participants' medical notes indicated that 16/28 had a confirmed diagnosis of HF. The screening tool had a sensitivity of 65% and the specificity of 73%.
Conclusion: The community pharmacy HF screening tool identified worsening HF symptoms in existing HF patients and also lead to the eventual new diagnosis of HF with preserved ejection fraction. A larger randomised trial is required to fully assess the outcomes of the screening tool.

P2132

Diuretic resistance in a population of acutely decompensated chronic heart failure patients

I Ilir Sharka[1]; S Myftiu[1]; A Quka[2]; J Rustemaj[1]; A Duka[1]; A Kristo[1]; I Balla[1]
[1]University Hospital Center Mother Theresa, Department of Cardiology & Cardiac Surgery, Tirana, Albania; *[2]University Hospital Center Mother Theresa, Tirana, Albania*

Purpose: Loop diuretics represent one of the mainstay of therapy in acutely decompensated chronic heart failure (ADCHF) patients (pts), but despite increased doses a proportion of pts represents diuretic resistance (DR) manifested with persistence of systemic congestion with important respiratory, hepatic and renal dysfunction and poor prognosis. The aim of the study was to investigate diuretic resistance in ADCHF population, and to explore a prediction model for DR development.
Methods: we prospectively analyzed clinical and laboratory data of 637 consecutive ADCHF pts on previous chronic loop diuretics therapy from January 2014 to November 2016. The MELD score evaluation was performed on a daily basis. A logistic regression model was used to determine independent predictors of DR, ROC curves were used for evaluation of prediction models of DR entering consecutively independent variables. A MELD score > 7 was considered abnormal. Primary liver disorders were excluded. DR was identified on clinical criteria.
Results: DR was identified in 116 (18,2%) pts.: between DR and non DR pts there were no significant differences in age (67.4 ± 0.3 vs 65.8 ± 0.7, NS), sex (males) (62% vs 59.7%, NS), diabetes (31.7% vs 30.1%, NS), but there were significant differences in MELD score (38.2 ± 7.7 vs 16.3 ± 9.5, $p < .0001$), hyponatremia (132 ± 2.7 vs 128 ± 9.3 mEq/L, $p < .001$), Charlson Comorbidity index (CCI) = 4 (68.1% vs 47.2%, $p < .001$), right ventricular function (TAPSE 21.5 ± 3.7 vs 12.3 ± 6.8 mm, $p < .001$), presence of metabolic alkalosis (89.7% vs 41.5%, $p < .0001$), rehospitalisations for AHF 4 (2 to 6) vs 2 (0 to 3), $p < .05$. Independent predictors of DR in multivariate analysis were an abnormally high MELD score HR 2.94 (95%CI: 1.36 to 5.62), low RV function HR 2.36 (95%CI: 1.28 to 4.37), hyponatremia HR 1.83 (95%CI: 1.13 to 3.5), metabolic alkalosis HR 1.67 (95%CI: 1.09 to 3.12). From ROC curve analysis for MELD score model AUC was 0.84 (95%CI: 0.73 to 0.91), when entering the model the presence of low RV function, hyponatremia and metabolic alkalosis AUC reached 0.91 (95%CI: 0.85 to 0.97) indicating a good ability to discriminate patients at risk of DR.
Conclusions: despite advances in AHF treatment, DR remains an ominous sign of the overall prognosis, hence a reliable prediction model of DR development would be an important diagnostic tool in clinical practice. We suggest from our study that an improved model incorporating simple clinical and laboratory values could help to stratify better patients at risk.

P2133

Metabolic therapy impact on the manifestation of heart failure in patients with acute myocardial infarction presented with ST-segment elevation

T Svanidze[1]; T Saralidze[1]
[1]Tbilisi State Medical University (TSMU), Department of Internal Medicine N 1, Tbilisi, Georgia Republic of

Mild heart failure (HF) usually accompanies acute myocardial infarction presented with ST-segment elevation (STEMI), but in some cases its severity increases in the first week of infarction. It is well known, that spectrum of myocardial injury depends not only on the intensity of impaired myocardial perfusion but on the existing metabolic state as well.
Our aim was to diminish the onset of HF in the course of acute myocardial infarction. For this aim we used metabolic therapy with Mildronat and Trimetazidine just from the first day of STEMI.
Evaluation of the functional condition of heart was based on ECG and echocardiographic data received before and after treatment. We observed 40 patients with STEMI who did not undergo reperfusion therapy because of different reasons. These patients did not have diabetes mellitus and HF did not exceed Killip class II. 20 patients were treated routinely, but without metabolic therapy (control group) and 20 were treated in addition with Sol. Mildronat 10% - 5 ml/day i.v. and Trimetazidine MR 35 mg twice a day.
Our research showed that in patients with STEMI treated with metabolic therapy normalization of S-T segment elevation was begun on the second day (in 40% of patients), on the 5th day it was observed in 70% and its normalization ended on the 7th day of treatment. In control group normalization of S-T segment elevation was begun on the second day in 20% of patients, on the 5th day it was revealed in 50% and it ended on the 10th day of treatment. Investigation of echocardiographic data in dynamic (before treatment and after a week) showed improvement of ejection fraction (EF) by 5,6% and stroke volume (SV) by 8,6% in patients with STEMI treated with metabolic therapy while in control group EF increased by 2,5% and SV by 4,5%. In patients treated with metabolic therapy end diastolic diameter (EDD) was decreased by 2,8%, end systolic diameter (ESD) - by 3,5%, end diastolic volume (EDV) - by 5,5% and end systolic volume (ESV) - by 7,8% while in control group EDD was decreased by 0,9%, ESD - by 1,4%, EDV - by 1,8% and ESV - by 2,6%. The received data make it relevant to include the complex metabolic therapy for effective treatment of HF in patients with STEMI. Metabolic therapy not only improves the course of disease, but diminishes rehabilitation period as well.

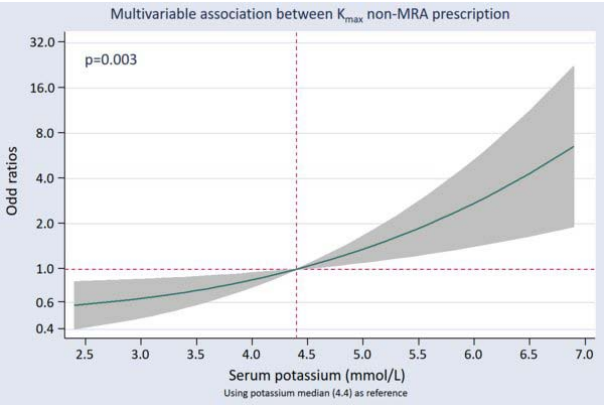
P2134

non-prescription of aldosterone receptor blocker following acute heart failure: high serum potassium levels during admission as a determinant factor

R Farcasan[1]; J Gummel[1]; J Parra[1]; A Paya[1]; R Heredia[1]; G Minana[1]; I Cardells[1]; A Mollar[1]; E Santas[1]; S Garcia-Blas[1]; E Valero[1]; F Chorrro[1]; J Sanchis[1]; J Nunez[1]
[1]University Hospital Clinic of Valencia, Valencia, Spain

Background: Mineralocorticoid receptor antagonists (MRA) constitute one of the cornerstones of the treatment for heart failure and reduced left ventricular ejection fraction (HFrEF). However, despite its proven efficacy, they are often underused. In this work, we aimed to evaluate whether high serum potassium levels found during hospitalization for acute heart failure (AHF) are determinant of MRA prescription at discharge.
Methods: We prospectively included 584 consecutive patients discharged after an episode of AHF and left ventricular ejection fraction ≤40%. The maximum level of potassium (Kmax) along the hospitalization was selected as the exposure. Independent factors related with the odds of prescribing MRA at discharge were evaluated by multivariate logistic regression analysis.

Results: The mean (SD) of age, minimum estimated glomerular filtration rate (eGFR) and maximum potassium during admission were 71 ± 12 years, 55 ± 22 ml/min/1.73m2 and 4.5 ± 0.6 mmol/L, respectively. The proportion of males, ischemic heart disease and MRA prescription upon discharge were 67.1%, 42% and 56.2%, respectively. Patients with potassium >5.0 mmol/L (17.5%) showed lower prescription of MRA (45.1% vs. 58.5%, p = 0.001). In multivariate analysis, adjusting for age, ischemic heart disease, systolic blood pressure < 100 mmHg, (eGFR) and left ventricle ejection fraction, Kmax showed to be independently associated with the odds of non-prescribing MRA. Functional form of Kmax revealed a positive and non-linear gradient of risk, with a greater magnitude of risk above 5 mmol/L as is shown in the figure below. Compared to patients with Kmax ≤5mmol/L, those with Kmax >5.0 mmol/l were about two-fold increase odds of non-MRA prescription (OR=1.83; CI 95%: 1.13-2.98, p = 0.015).
Conclusion: In patients with AHF and reduced LVEF, high serum potassium levels during hospitalization predict lower prescription of MRA at discharge. Potassium lowering strategies in selected patients may increase the use of MRA following the episode of AHF.



P2135
patient engagement improvement following implementation of a remote monitoring system

E Berry[1]; A Silvera[1]; W Whitney Downer[1]; D Agar[1]; S Beske Radford[1]; N Chiromeras[1]; M Bogart[1]; N Bonnet[1]
[1]*Morristown Medical Center, The Heart Success Program, Morristown, United States of America*

On behalf of: The Heart Success Program
Funding Acknowledgements: Verizon

Introduction: The rising prevalence and cost of heart failure (HF) has increased the desire to improve self-care management skills and behaviors. This program aimed to document an improvement in patient engagement and compliance through the integration and implementation of three disparate remote monitoring systems.
Purpose: High HF readmission rates reflect patient vulnerability in the 30 days post-discharge. The inability to effectively manage and influence patient behavior, and patient's inability to identify signs of worsening HF are major hurdles to improving outcomes and minimizing readmissions. This study was designed to utilize remote monitoring technologies to foster patient self-care management skills. This is a model of supported, low touch/high tech care to bridge patients to home and help keep them out of the hospital.
Methods: Patients admitted with acute decompensated HF were enrolled over a 13 month period beginning November 2015, and agreed to be monitored for 30 days post-discharge. All patients wore a wireless cutaneous telemetry sensor. Those discharged to home performed daily health check-ins using a telehealth scale, blood pressure cuff, and pulse oximeter. Questions regarding symptoms and HF education where included in these check-ins. Patients discharged to a nursing facility performed daily health check-ins using a mobile monitoring application on a tablet. Arrhythmia data was monitored, and study staff notified if data met specific parameters. Telehealth check-in data was sent wirelessly, and reviewed by a nurse in a web portal. Clinically significant biometrics prompted a phone call or home visit for additional assessment and intervention. Patient surveys were administered at enrollment, and upon completion of the 30 day program. ER visits and hospital readmissions were tracked.
Results: 31 patients participated in the program with a mean age of 78.5 years, 58% being 80 years old or older. Of the participants, 7 withdrew prematurely. The readmission rate of patients that did not withdraw early was 20.8%. 100% of the patients who completed the program found it helpful based on patient surveys. Post program follow up reflected patient plans to continue monitoring activities, based on improved self-confidence and learned self-care management skills. In addition, twelve program participants and caregivers became involved in an outpatient HF support group, which led to continued engagement in disease management.
Conclusion: The use of mobile monitoring tools can be an effective way of improving HF patient engagement, ownership of disease management, and deliver strengthened partnerships between patients and healthcare providers.

P2136
Are the risk stratification's methods effective to diagnose pulmonary embolism in patients with heart failure?

A Attila Pandur[1]; B Banfai[1]; B Radnai[1]; J Betlehem[1]
[1]*University of Pecs, Institute of Emergency Care and Pedagogy of Health , Pecs, Hungary*

Background/Aims: Pulmonary embolism is connected with high morbidity and mortality. Prognostic assessment is important for the management of patients with pulmonary embolism. Pulmonary embolism often has a nonspecific clinical presentation. The use of diagnostic testing in an attempt to avoid missing the potentially life-threatening diagnosis increases both cost and use of medical resources. Various score systems exsist to evaluate the probability of pulmonary embolism, which can be used for risk stratification, to get the most accurate diagnosis. The aim of our study was to review the evidence for existing prognostic models in acute pulmonary embolism and determine validity and usefulness for predicting patient outcomes.
Materials and Methods: We performed a retrospective analysis of pulmonary embolism in three hungarian emergency departments. Data from 519 patients were included for this retrospective analysis. The Wells, Geneva, Padua score systems were used to reevaluate retrospectivly the risk of pulmonary embolism. The diagnosis of pulmonary embolism was accurate, when the CT verified it. We allowed the weighted probability of the score systems. We analyzed which score system is the most specific for the risk stratification of pulmonary embolism in our cases. Data were analyzed with a SPSS 20.0 statistical software. In our study, chi-square test, Independent-Samples T-test, ANOVA, korrelation interpretation were performed. P values of < 0.05 were considered to be statistically significant.
Results: 238 (45,8 %) men and 281 (54,2 %) women patient-documentation were participated in the study. 156 patients got into the ED due to heart failure. In 68 cases (43,5 %) the CT verified pulmonary embolism. Padua score indicated in 16 cases (p = 0,2), Geneva score in 29 cases (p = 0,05) and Wells score in 6 cases (p = 0,1) a high probability of pulmonary embolism, from the 68 cases, where the CT is positive for PE.
Conclusions: Our study showed that Genfi score(which was calculated from the patients complaints, medical history and physical examination) had the closest correlation with the diagnosis. Finally we can conclude that risk-evaluation is indispensable in acute heart failure because pulmonary embolism can be in the backround as the root cause.

P2137
Acute Heart Failure and cardiogenic shock are independent predictor for in-hospital mortality in patient admitted with ST-elevation myocardial infarction

B Bambang Widyantoro[1]; I Firdaus[1]; SS Danny[1]; D Zamroni[1]; I Irmalita[1]; DPL Tobing[1]; DA Juzar[1]
[1]*Dept of Cardiology and Vascular Medicine, Universitas Indonesia-NCVC Harapan Kita Hospital, Jakarta, Indonesia*

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 the in-hospital outcomes predictors of patients with ST-elevation MI (STEMI).
We examined 1590 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 1590 patients, 910 (57.2%) were STEMI and 680 patients were UA/NSTEMI. Most of them are male (82.4%), below 65 years old and had hypertension (59.6%). Overall in-hospital mortality for STEMI were 6.6% (60 of 910). Revascularization with primary percutaneous intervention (Primary PCI) were performed in 521 (57.2%) of STEMI patients, with median door to device time 83 (65-103) minutes. Fifty two (5.71%) patients received fibrinolytics treatment with door to needle time 24 (18-42) minutes with successful rate of 84.6%. Those with failed fibrinolytics underwent rescue PCI. The other 14 patients underwent urgent CABG. Among patients treated with PPCI, 89.3% achieved TIMI 3 flow, while 5 (1%) patients have no-reflow due to high grade thrombus. About 245 (26.9%) patients were not revascularized

due to very late onset of presentation. Most of STEMI patients who failed to survive during hospitalization more likely to have diabetes, more late presentation (>9 hours), suffered from acute heart failure (AHF, 32.6%) and cardiogenic shock (7.4%). After multivariable risk adjustment, 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).
In conclusion, we observed acute heart failure and cardiogenic shock as predictors for in-hospital mortality among STEMI patients.

P2138

Impact of the potassium concentration in drug titration of heart failure patients

G M Gustavo Miguel Rocha Rodrigues[1]; AT Tralhao[1]; NV Vale[1]; MC Castro[1]; JM Mesquita[1]; CA Aguiar[1]; AV Ventosa[1]; MM Mendes[1]
[1]Hospital Santa Cruz, Cardiology, lisboa, Portugal

Heart failure patients have multiple comorbidities which hamper the titration of drugs with proven impact on clinical outcomes. The renin angiotensin aldosterone system (RAAS) blockage is crucial in these patients, but hiperkalemia often troubles the use of recommended drugs and dosages. New potassium lowering drugs are being evaluated in order to allow the recommended titration of the RAAS blockage. We aimed to assess the possible usefulness of these new drugs in a population of heart failure patients. We reviewed the records of 196 outpatients followed in a specialized HF clinic between January 2013 and December 2014. We excluded 108 patients with left ventricular ejection fraction (LVEF) >35%. Of the 88 patients with HF-REF (LVEF<35%), median age was 65 ± 13.8 years, 73 (82%) are male, 33 (37%) are diabetic, 51 (57%) are hypertensive, 39 (44%) have dislipidemia, 43 (48%) have chronic kidney disease and 25 (28%) have atrial fibrillation. Median LVEF was 28.5 ± 5.2%, median [K+] was 4.7 ± 0.44 mmol/L and 66% of the patients had the RAAS blockage titrated. 34% were not on a titrated dosage of angiotensin-converting-enzyme inhibitors (ACEI) or angiotensin II receptor blocker (ARB) and 43 (49%) patients weren't on a titrated mineralocorticoid receptor antagonist (MRA). Of the patients without titrated ACEI/ARB, 2 were hypotensive (ST≤95 mmHg), 10 had [K+] ≥5 mmol/L and 8 had GFR ≤ 30 ml/min/1.73 m2. Most of those with high [K+] (n = 8), were not hypotensive or had severe chronic kidney disease (CKD). 16 of the patients without titrated MRA had [K+] ≥5 mmol/L, 4 had hypotension and 7 had severe chronic kidney disease (GFR ≤ 30 ml/min/1.73m2). Most of the patients with [K+] ≥5 mmol/L (N=14) were not hipotensive or had severe CKD. (table1) In this cohort, a high level of [K+] was the most probably cause to the lack of titration of the RAAS system blockage. This aspect highlights the possible clinical benefit of potassium lowering drugs on heart failure patients.

P2139

Intra-aortic balloon pump and dose of amiodarone in post-operative atrial fibrillation

K Kevin Domingues[1]; A Kontogeorgis[2]; TC Aw[2]; S Price[2]
[1]Hospital of Santarem, Cardiology, Santarem, Portugal; *[2]Royal Brompton Hospital, London, United Kingdom*

Introduction: Atrial fibrillation (AF) is the most common arrhythmia in the post-operative period of cardiac surgery, with amiodarone being the most frequently used drug for its control. However, its use is widely heterogenous, and it is unknown which factors demand higher doses in critical patients in this context. The intra-aortic balloon pump (IABP), still frequently used after cardiac surgery, is preferably ECG-triggered, and arrhythmias are potentially a cause of inferior effectiveness.
Aim: To determine if the use of intra-aortic counter pulsation influences amiodarone doses during hospital admission in critical patients with AF after cardiac surgery.
Methods: Retrospective study of patients admitted to a level III cardiothoracic intensive care unit in the post-op period after cardiac surgery, between September 2012 and February 2015, which were medicated with amiodarone because of AF. Demographic and clinical data were analysed.
Results: We included 177 patients, predominantly male (68.6%), with mean age of 67,3 ± 12,5 years. The surgery involved more than one procedure in 50.3% of the cases and, in total, 49.7% had revascularization surgery (CABG), 28.2% aortic valve surgery and 25.4% mitral valve surgery. The most frequent main diagnosis of admission to the unit were arrhythmic complications (31.1%), haemorrhagic complications (25.4%) and left and/or right ventricular dysfunction (20.3%), with 20.3% of the patients having the need of IABP during their stay.
The median total dose of amiodarone was 2275 mg, with a median of 102 mg per day in hospital. Patients who had IABP had significantly higher total doses of amiodarone (4981 vs 1610 mg; p = 0.016) and higher doses of amiodarone per day in hospital (183 vs 87 mg; p < 0.001).
In the multivariate analysis, with age, sex, type of surgery and main diagnosis of admission, the use of IABP was independently associated with a need of an average amiodarone dose of >200 mg per day (p = 0.025). There was also a positive correlation between the total amiodarone dose and the time with IABP (r=0.409, p = 0.025).
Conclusion: In this population of critical patients, those who required IABP also required higher doses of amiodarone, possibly due to the need of rhythm stability for mechanical optimization.

P2140

Screening for the Improve Management of heart failure with Procalcitonin (IMPACT)-study

A Anna Slagman[1]; M Bolanaki[2]; J Frick[2]; F Holert[2]; M Mazelka[2]; H L Neumeier[2]; S Rabsch[2]; F Ruggaber[2]; J Searle[2]; C Thomas[2]; S Toro[2]; C Werk-Wenzel[2]; M Mockel[1]
[1]Charite - Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany; *[2]Charité - Universitätsmedizin Berlin, Division of Emergency Medicine (CVK, CCM); Department of Cardiology (CVK), Berlin, Germany*

Funding Acknowledgements: This study was sponsered by Thermo Fisher Scientific

Background: The IMPACT-study evaluates an advantage of PCT guided antibiotic treatment over established treatment practice in patients with acute decompensated heart failure. The primary endpoint is 90-day all-cause mortality.
Purpose: To investigate the proportion of successfully screened patients and the main reasons for non-enrollment.
Methods: Patients who present to the Emergency Department (ED) with leading symptom dyspnea and suspected or known heart failure are eligible for the study. These patients were screened in two EDs of the Universitätsmedizin between March 2015 and December 2016. Inclusion criteria: 1. MR-proANP>300 pmol/L, BNP>350 ng/L or NT-proBNP>1800 ng/L; 2. Patient has given written Informed consent within study timelines to allow antibiotic treatment within 8 hours; 3. Adult patients (i.e. >18 years of age); 4. Hospitalization for at least 1 overnight stay planned. Exclusion criteria: 1. Patient participates in any other interventional clinical trial; 2. Trauma related shortness of breath; 3. Patient diagnosed with lung or thyroid cancer; 4. Known terminal disease with life expectancy of less than 6 months, e.g. advanced metastasized cancer disease; 5. Organ transplant requiring immunosuppression; 6. Abdominal, vascular or thorax surgery within the last 30 days; 7. End stage/advanced HF – defined by planned heart transplantation, or cardiogenic shock; 8. Female patients who have given birth within 3 months before study enrolment; 9. Current use of antibiotics or requirement of immediate antibiotic therapy before randomization and measurement of PCT; 10. End stage renal failure requiring dialysis; 11. Patient is not willing, or it is not possible or advisable for the patient, to follow the study schedule, including antibiotic therapy and 90 days follow up; 12. Patient has already participated in the clinical trial previously; 13. Pregnant or lactating women; 14. Patients who are institutionalized by official or judicial order; 15. Dependants of the sponsor, the CRO, the study site or the investigator
Results: Overall, 1,918 patients were screened for the IMPACT study within 22 months. Of these, 7.5% (n = 143) were enrolled. The proportion of enrolled patients differed between both study centres: 8.5% of all screened patients were enrolled at the Campus Virchow Klinikum (CVK; 112 out of 1,212) and 5.1% at the Campus Charité Mitte (CCM; 31 out of 605). The main reason for non-enrollment were low values of natriuretic peptides (26% at CVK and 30% at CCM). Other reasons for non-enrollment differed only slightly between both EDs and are depicted in figure 1.
Conclusions: The IMPACT study is the first study to evaluate the concept of PCT-guided antibiotic treatment applying a randomized design in this specific setting. Despite the high number of patients with dyspnea in the investigated EDS, many patients cannot be included especially due to low natriuretic peptide values.

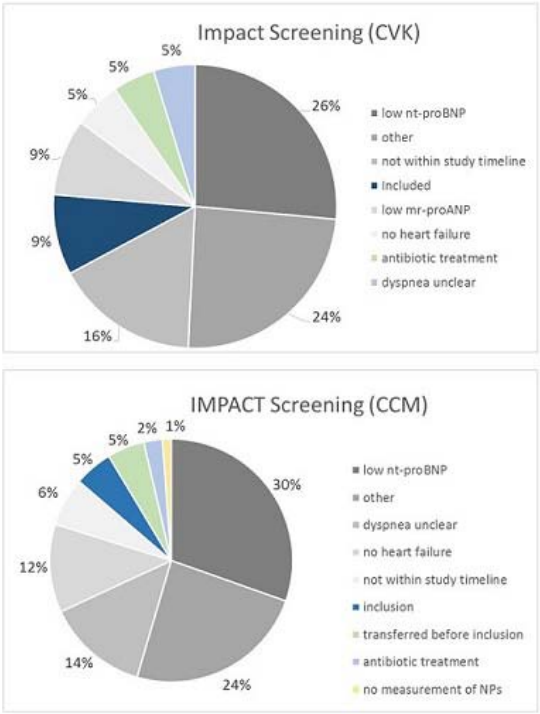


Figure 1: Results of IMPACT-Screening at both Campi of the Charité Universitätsmedizin Berlin (CVK and CCM)

P2141

Lung echocardiography in the initial evaluation of acute respiratory failure using a pocket ultrasound device: what is wrong the heart or the lungs?

M Manuel Lobo Gonzalez[1]

[1]*University Hospital of Virgen Macarena, Cardiology, Seville, Spain*

Background and purpose: Acute respiratory failure (ARF) is a very common cause of illness in the emergency department, sometimes, it is difficult to elucidate its etiology. A rapid diagnosis that allows to differentiate between the cardiac or extracardiac origin is fundamental to begin an early managed treatment. The aim of this study is to evaluate the ability of lung ultrasound with pocket device (PD) to classify patients with respiratory failure in cardiac origin (heart failure) or not.
Methods: 46 patients with ARF (dyspnea and oximetry below 90%) admitted to our emergency 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; according to the ultrasound analysis, the patients were classified into heart failure or not. The management of patients and the final diagnosis was made according to the clinical presentation, personal history, physical examination and the rest of complementary tests.
Results: 30 of 46 patients included were women, the mean age was 62 ± 17 years. According to findings in pulmonary ultrasound, 21 patients (45,65%) were classified as heart failure and 25 patients as non cardiac ARF. After clinical exams and the others complementary test, 22 patients (47,82%) had a final diagnosis of heart failure. The pulmonary ultrasound classified correctly as cardiac failure at 20 patients, with 1 false positive (sensitivity of 90%). In the non-cardiac failure group, 2 false negatives were generated by the test (specificity of 95%). Although not the objective of this study, lung echography identified 3 pneumotorax, 5 consolidative pneumonies, and 3 pleural effusions in the non-cardiac group.
Conclusion: Our results are consistent with those previously reported. Lung ultrasonography assessed with a PD may represent a fast and reliable diagnostic tool in ARF, Allowing to classify the cause as cardiac or non-cardiac, and thus instituting an early managed treatment.

P2142

Acute heart failure in the elderly: which are the main precipitating causes of heart failure? Real world evidence from the ATHENA registry

AC Baroncini[1]; F Orso[1]; A Pratesi[1]; C Tozzetti[2]; F Bacci[2]; A Herbst[1]; S Parlapiano[1]; A Cortese[2]; G Baglioni[1]; C Nozzoli[2]; L Gabbani[1]; L Poggesi[2]; A Moggi Pignone[2]; N Marchionni[3]; S Baldasseroni[1]

[1]*Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy*; [2]*Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; [3]*Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA study group

Background: Heart failure (HF) is very common in the elderly population, and is characterized by frequent re-hospitalization which worsen prognosis. In clinical trials precipitating causes leading to hospitalisations are mainly cardiovascular. In cardiological clinical registries precipitating causes are also more frequently cardiovascular, even if the percentage of hospitalisations due to non-cardiovascular causes grows significantly. On the contrary, "real world" administrative data suggest that precipitating causes may be mainly non-cardiovascular.
Purpose: to compare precipitating causes in elderly patients hospitalised for acute HF in the settings of care of most frequent management: cardiology, internal medicine and geriatrics.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (≥ 65 years) admitted with diagnosis of acute HF (worsening or de novo) to the emergency department (ED) of a tertiary University teaching-hospital and transferred to the above described settings of care in the period 01.12.2014-12.01.2015. We evaluated the main precipitating causes of HF reported in literature comparing cardiology, geriatrics and internal medicine wards.
Results: 342 patients composed the study population; 17.8% were hospitalised in cardiology, 17.3% in geriatrics and 64.9% in internal medicine. Mean age was 83.7 years, females were 54.1%. In the attached table we report the main precipitating causes of HF.
Conclusions: In geriatric and internal medicine wards the main precipitating causes are non-cardiovascular, as pneumonia and sepsis. In cardiology, cardiovascular causes, such as ACS, are prevalent. Precipitating causes seem to be a criteria for admittance to different setting of care in elderly HF patients.

Precipitating causes of HF

	Total N=342	Cardiology N=61	Geriatrics N=59	Internal Medicine N=222	P Value
Pneumonia (%)	39.7	20	52.1	42.6	0.001
Sepsis (%)	5.9	0	4.2	8.1	0.001
AKI (%)	3.6	3.3	8.3	2.5	0.001
ACS (%)	6.2	21.7	2.1	2.5	0.001
AF (%)	9.2	3.3	4.2	12.2	0.001
Poor Compliance (%)	3.3	1.7	2.1	4.1	0.001

AKI, acute kidney injury; SCA, acute coronary syndrome; AF, atrial fibrillation

P2143

Value of systolic time intervals in the diagnosis of heart failure in the emergency department patient with undifferentiated dyspnea

ZW Zhani[1]; ZZ Ezzina[1]; EM Malek Echeikh[1]; AN Azaiez[1]; BAA Ben Abdallah[1]; BK Beltaief[1]; MMA Msolli[1]; DZ Dridi[1]; BH Boubaker[1]; GMH Grissa[1]; BW Bouida[1]; NS Nouira[1]

[1]*university of monastir, monastir, Tunisia*

On behalf of: great network

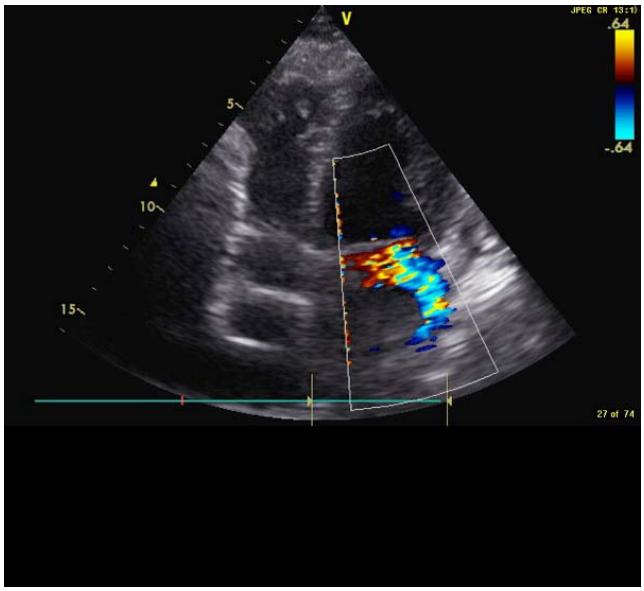
Background: The diagnosis of heart failure in the emergency department (ED) is challenging. Our objective is to determine if systolic time intervals (STI) can predict heart failure (HF) in ED patients with dyspnea.
Methods and Results: A total of 658 patients with suspected HF were prospectively enrolled. They underwent echocardiographic measurements of left ventricular ejection fraction (LVEF), B-type natriuretic peptide (BNP) testing and computerized phonoelectrocardiography to assess STI including electromechanical activation time (EMAT), left ventricular ejection time (LVET) and their ratio (EMAT/LVET). Diagnostic accuracy was calculated including sensitivity, specificity, likelihood ratio and receiver operating characteristic (ROC) curve.
Patients with HF (n = 402) had significantly higher EMAT and lower LVET compared to no HF patients. ROC curve c-statistic was 0.74, 0.72, and 0.78 respectively for EMAT, LVET, and EMAT/LVET. Sensitivity and specificity of EMAT/LVET at a cut-off=40%

were 64% and 82%. EMAT/LVET had the highest correlation with LVEF(r = -0.48). Patients with preserved LVEF (≥50%) had STI values not significantly different from those of patients without HF. In patients with intermediate BNP(n = 107), EMAT/LVET increased positive likelihood ratio from 1.8 with BNP alone to 3.6 with combined parameters.
Conclusion: STI provide rapid and useful information that assist noninvasively prediction of HF in ED patients with dyspnea especially when BNP values are in the gray zone and echocardiography not readily available.

P2144
Pulmonary edema as a manifestation of an acute mitral insufficiency in a woman in puerperium the unthinkable cause of pulmonary edema

M J Maria Juliana Rodriguez Gonzalez[1]; LA Medina Lopez[1]; MM Botia Osorio[1]
[1]*Fundación Cardiovascular de Colombia, Santander, Bucaramanga, Colombia*

Mitral insufficiency is not a common cause of pulmonary edema during pregnancy or the puerperium. The principal etiologies are preexisted congenital heart defect, valvular conditions not previously diagnosed, pregnancy related conditions poorly understood as peripartum cardiomyopathy and finally coronary heart disease.
Coronay heart disease has increased by incidence because of the reproductive tecniques and the women advanced age. The Acute coronary syndrome during pregnancy and puerperium has a high mortality range from 5- 37%. The principal etiology is not the same to the observed in other situations.
In previous case series it has been reported coronary artery disease (43%), thrombus (21%), normal epicardial vessels (29%), coronary artery disection (16%).
Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome. The condition affects women more commonly than men, with 70% of cases occurring in young women of childbearing age. The relationship between SCAD and gestational and puerperal period varies among populations, ranging from 0 to 18%. occurring predominantly in late pregnancy or the early postpartum period. The etiology of SCAD is poorly understood, it is interrelated with other factors including connective tissue disorders, vasculitis, extreme physical and emotional stress, and cardiac stress.
The most common coronary artery affected is the left anterior descending (LAD) branch, but there are some case series where they describes RCA, left circunflex , Obtuse marginal; most of them single vessel disease.
There is not consensus in its management, some of them are managed in a conservative way and some of them with stents or CABG. We report a single case that it presented in the emergency department as an acute pulmonary edema in the puerperium with an ST inferior acute myocardial infarction. She is a pleasant 32 female patient who was admitted at cardiology Ward; coming from the gynecology service. She was admitted with pre- eclampsia. She was in her 4th day after Caesarean section and presented an intense chest pain, 30 min duration, severe dyspnea with some electrocardiographic changes (st elevation in inferior leads no right ventricular extensión; these changes were intermittent). Positive troponin (2797 ng/l) , Chest X-ray with interstitial edema. At that time we decided to take an echo which was informed with severe mitral insufficiency and segmentary contractility alterations (inferior Wall), she was taking to the cath lab and the findings were spontaneous coronary artery disection of a single vessel (right coronary artery), having an IVUS with 100% vessel lumen compromised ant the heart team decided to implant 2 medicated stents; proximal and distal trying to seal the disection with a good angiographic result.
Conclusions: SCAD can be a cause of acute mitral insufficiency knowing the anatomical issues of its papillary muscles irrigation.



mitral insufficiency

P2145
Patterns of dyspnoea onset, clinical characteristics and the outcomes in patients with acute heart failure- implications for clinical trials

JM Krzysztofik[1]; M Sokolski[1]; R Zymlinski[2]; J Biegus[1]; P Siwolowski[2]; S Nawrocka- Millward[2]; W Banasiak[2]; EA Jankowska[3]; P Ponikowski[1]
[1]*Wroclaw Medical University, Department of Heart Diseases, Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland*; [2]*Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland*; [3]*Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland*

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Background and purpose: Dyspnoea is the most common presenting symptom related to hospital admission for acute heart failure (HF). We investigated whether the patterns of dyspnoea onset are associated with clinical characteristics and the outcomes.
Methods: We investigated 137 patients (mean age– 65 years, 110 [80%] men) hospitalized for acute HF, whose major reported symptom was orthopnea. Patients were divided according to the time of onset of orthopnea into 3 groups: rapid (n = 26), acute (n = 72) and subacute onset (n = 39) – i.e. within 24 hours, 2-7 days and > 7 days preceding hospital admission, respectively.
Results: On admission, patients with a rapid onset of orthopnea had higher systolic blood pressure (154 ± 38 vs. 132 ± 29 vs. 121 ± 32 mmHg, P < 0.001), faster heart rate (101 [80-140] vs. 88 [75-100] vs. 90 [72-103] beats/min, P < 0.05), more moderate-severe pulmonary congestion (69 vs. 19 vs. 8 %, P < 0.05), less moderate-severe peripheral oedema (23 vs. 58 vs. 62 %, P < 0.001), ascites (4 vs. 10 vs. 28 %, P < 0.01) and lower level of serum bilirubin (0.73 [0.59-1.14] vs. 1.13 [0.82-1.72] vs. 1.27 [0.87-2.06] mg/dL, P < 0.01) (rapid vs. acute vs. subacute onset of orthopnea, respectively). There were no differences in the history chronic HF, the presence of co-morbidities, LVEF, and serum NT-proBNP levels between groups. Those with a rapid onset received lowest dose of iv furosemide within first 48 hours (100 [60-160] vs.120 [80-200] vs. 200 [80-240] mg, P < 0.05), and were treated more often with iv vasodilators (65 vs. 33 vs. 36 %, P < 0.01) (rapid vs. acute vs. subacute onset of orthopnea, respectively). Patients with a rapid onset of orthopnea reporter greater dyspnea relief after 6, 24 and 48 h (P < 0.001 in all time points vs. remaining groups) and there were less worsening HF during hospital stay in this group (8 vs. 15 vs. 39 %, P < 0.01). During one year follow-up, cardiovascular mortality was highest in patients with subacute onset (23 vs. 19 vs. 41 %, P < 0.05), but the rate of hospital re-admissions due to acute HF was marginally higher in those with rapid onset (46 vs. 24 vs. 36 %, P=0.08) (rapid vs. acute vs. subacute onset of orthopnea, respectively).
Conclusion: In patients admitted with acute HF, pattern of dyspnoea onset is associated with significant differences in clinical characteristics, in-hospital response to standard treatment and the long-term outcomes. This is relevant information for planning clinical trials in acute HF.

P2146

The incidence and profile of cardiotropic viruses in the myocardium in patients with decompensated chronic heart failure with systolic dysfunction of ischemic origin

EV Kruchinkina[1]; VV Ryabov[2]; YU V Rogovskaya[3]; TR Ryabova[1]; RE Batalov[1]; MS Rebenkova[1]; SV Popov[1]; RS Karpov[1]
[1]*Cardiology Research Institute, Tomsk National Research Medical Center, Tomsk, Russian Federation*; [2]*Siberian State Medical University, Tomsk, Russian Federation*; [3]*National Research Tomsk State University, Tomsk, Russian Federation*

Background: Tremendous evidence has emerged over the past decades that HF is associated with inflammation. However, anti-inflammatory therapy widely lacks positive outcomes. No reports on exploration of the molecular and cellular phenotypes of myocardial inflammation (viral, viral and autoimmune, and autoimmune types of inflammation) in patients with acute decompensated chronic heart failure (ADHF) and ischemic cardiomyopathy.
The purpose of study to determine the frequency of occurrence of inflammation and the profile of cardiotropic viruses in the myocardium by immunohistochemistry.
Methods: This open-label, nonrandomized, single-center, prospective trial — NCT02649517. This trial includes ADHF patients with ischemic systolic dysfunction underwent percutaneous coronary intervention/coronary artery bypass graft with optimal results not earlier than 6 months after surgery and acute coronary syndrome. Patients receive standard treatment of ADHF according to ESC guidelines. All patients undergo invasive coronary angiography to exclude the progression of coronary heart disease as the cause of ADHF. Endomyocardial biopsy (EMB) and following immunohistochemical analysis were performed to determine type of inflammation in the myocardium. The following parameters are assessed during hospitalization: inflammatory infiltrate in the myocardium.
Results: The subanalysis of the 12 patients (8% female, 92% men, left ventricular ejection fraction 29.17 ± 9.4%) with ADHF hospitalized from January 2015 to August 2016. The average age of our patients was 61.08 ± 7.84 years. All of the patients underwent endomyocardial biopsy which revealed signs of myocarditis in 7 patients (58.33%) and no myocarditis in 5 patients (41.67%). Viruses in the myocardium were determined in 9 cases (81.82%). The most common combinations were Enterovirus with Epstein-Barr virus in 4 patients (36.36%) and Enterovirus with Human herpesvirus 6 in 4 patients (36.36%). The correlation between the inflammatory infiltrate in the myocardium and Enterovirus, and Epstein-Barr virus ($p < 0.05$, $r = 0.62$ and $r = 0.58$ respectively). At the moment, the results showed that 7 patients hospitalized for ADHF had signs of myocarditis 58.33%.
Conclusion: The results showed the frequency of occurrence of myocardial inflammation 58.33% and cardiotropic viruses 81.82% in myocardium in patients with ADHF. The most encountered viruses in myocardium were Enterovirus and Human herpesvirus 6.

CHRONIC HEART FAILURE

P2147

Cardiac coherence by breathing in heart failure patients during cardiac rehabilitation

L Simone[1]
[1]*University Hospital of Strasbourg, Strasbourg, France*

Background: Heart rate variability (HRV) represents the fluctuations in heart rate (HR) from beat-to-beat, measured in milliseconds. HRV is a non-invasive measure of the autonomic nervous system by assessment of the balance between sympathetic and parasympathetic influences on the intrinsic rhythm. Low HRV related to autonomic dysfunction, which is frequent in chronic heart failure (CHF) patients, is associated with increased cardiac morbidity and mortality. Since the HRV can be influenced by many situations, like decreased with smoking or hypertension, HRV could be improved by deep breathing, as demonstrated in heart coherence training. By breathing 6 times per minute, with a respiratory frequency at 0,1 Hz, heart is synchronized with breath (state of cardiac coherence), which lead to an amplified HRV curve.
Objective: Explore the relationship between heart coherence training (HCT) and cardiac coherence ratios (low, medium, high) in CHF patients, and factors associated with high ratios.
Method: Patients with ventricular dysfunction < 45% were randomly separated in 2 groups: one into conventional cardiac rehabilitation (no HCT group) and other into cardiac rehabilitation plus HCT (HCT group) sessions consisting of daily abdominal breathing practice, 3 sessions of 5 minutes a day, during 3 weeks. Patients with atrial fibrillation, diabetes, chronic kidney failure and depression were excluded. Coherence ratios and spectral density power were measured with a biofeedback software before and after program.
Results: 18 patients were included (10 in HCT group). Baseline characteristics were similar for both. The HCT group show a significant increase in medium or high coherence ratios (90% vs 20%, p = 0,012). Analyze of spectral density power showed an increased in high frequencies in HCT patients, which can be considered as a reflect of parasympathetic component. In HCT group, patients had a significatively lower HR (p = 0,004), lower brain natriuretic peptid > 30% (p = 0,023) and blood sodium was higher by 3 mmol/L (p = 0,011). No differences occurred with quality of life, ejection fraction, or dyspnea.
Conclusion: In CHF patients with autonomic dysfunction, cardiac coherence by breathing exercises seems to improve coherence ratios, and as a consequence, could have a positive effect on HRV amplitude.

P2148

Cardiopulmonary exercise testing, right heart catheterization and etiology of heart failure

M Dudek[1]; MI Marta Izabela Kaluzna-Oleksy[1]; J Migaj[1]; E Straburzynska-Migaj[1]
[1]*Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland*

Introduction: Heart failure (HF) is a clinical condition with a miscellaneous background. The most prevalent cause of HF in Europe is coronary artery disease (CAD). Depending on etiology of HF, its natural history may vary. In evaluation of HF patients there are used as well noninvasive as invasive diagnostics methods.
Aim: Characterization of patients with heart failure with reduced ejection fraction (HFrEF) qualified to the heart transplantation. Evaluation the role of noninvasive and invasive procedure in assessment of HF patients related to the etiology of HF.
Methods: This was a prospective analysis of 211 patients (both genders) with HFrEF (left ventricular ejection fraction < 40%), with ischemic (ICM) and non-ischemic cardiomyopathy (NICM), hospitalized at a tertiary health care center, undergoing qualification process for heart transplantation. The epidemiological data, laboratory test results (including BNP), and chosen parameters obtained in echocardiography, cardiopulmonary exercise testing (CPET) and RHC (thermodilution method) were analyzed related to the etiology of HF.
Results: Mean age of analyzed population was 51.7 ± 10.3 years. Most patients were men (88%), 73% were in NYHA class 3 and 4. Patients with ICM were significantly older (55 vs. 49, p = 0.005) and without any gender differences (males 94% vs. 89%, NS). Had lower BNP level (721 vs. 1253, p = 0.005) and higher mean aortic pressure measured invasively (40 vs. 36, p = 0.036). The RHC parameters like PAPm and TPG were higher in ICM without any significant differences in echocardiography or CPET.
Conclusions: Ischemic etiology of HF is associated with lower level of BNP but with worse result of RHC, and there are no differences between ICM and NICM in echocardiography or CPET. PH occurred with the same frequency in ICM and NICM group.

P2149

Determinants of cardiovascular death risk in dialysis patients.

M Merita Rroji[1]; S Seferi[1]; N Spahia[1]; M Cafka[1]; M Barbullushi[1]
[1]*University Hospital Center Mother Theresa, Department of Nephrology, Cardiology, Tirana, Albania*

Background: Dialysis patients have a higher risk of morbidity and mortality related to cardiovascular disease (CVD) than the general population. The aim of the current study was to characterise the role of traditional and uraemia-specific CV risk factors in this patient population.
Methods: In this prospective case study we enrolled all adult patients who were on long-term dialysis (hemodialysis and peritoneal dialysis) for more than 3 months. Cardiovascular mortality was assessed during a 2-year follow-up period. Factors predictive of cardiovascular mortality were identified by a logistic regression model. P values less than. 05 were considered significant.
Results: There were 129 participants, of whom 86 (66%) were on hemodialysis. Cardiovascular mortality during the follow-up was 15.5% (19 events). The main causes of cardiovascular death were sudden deaths (31.5%) followed by deaths from ischemic heart disease and stroke (26.3%). In 15.7% of the patients, heart failure was found the cause of death. We didn't found difference in CV mortality between patients in two dialysis modalities (log rank (Mantel- Cox) p = 364. Multivariable analysis showed that C-reactive protein (OR, 1.06; 95% CI, 1.01 to 1.10; P = .01), pulse pressure (OR, 1.01; 95% CI, 1.0 to 1.26; P = .046), Phosphate (OR,1.11; 95% CI, 1.01 to 1.26; P = .033) and left ventricular mass index (OR, 1.03; 95% CI, 1.01 to 1.21; P = .03) were independent risk factors for cardiovascular mortality.
Conclusions: We found Inflammation, arterial stiffness, Phosphate and LVH as independent risk factors in Cardiovascular mortality. These factors are interrelated and both contribute to increase mortality and cardiovascular death risk of dialysis patients.

P2150

The effects of ferrous sulfate supplementation on left ventricular intrinsic function by global longitudinal strain in systolic heart failure patient with iron deficiency anaemia

RS Sagita[1]; LD Suryani[1]; BB Siswanto[1]; LD Liastuti[1]; NH Hersunarti[1]; RS Soerarso[1]
[1]National Cardiovascular Center Harapan Kita, cardiology and vascular medicine , Jakarta, Indonesia

Background: Iron deficiency is common in heart failure (HF) and associated with impairment of myocardial functional parameters and dimension of the left ventricle (LV).Speckle tracking echocardiography assesses myocardial deformation and LV systolic function by measuring global longitudinal strain (GLS). But the improvement of intrinsic LV function using GLS in systolic HF patient with iron deficiency anaemia (IDA) due to oral iron treatment is not yet known.
Objectives: To evaluate improvement in intrinsic LV function measured by GLS after oral Ferrous Sulfate (FS) treatment.
Methods: This is a single center, randomized controlled trial that enrolled HF (LVEF < 50%), IDA (Ferritin < 100ng/mL or 100-300 ng/mL with Tsat < 20%) and Hb < 13 g/dl) patients at outpatient clinic of Harapan Kita Hospital between January to November 2016. Patients were randomized 1:1 to treatment with FS or placebo for 12 weeks. Echocardiography was performed before and after treatment to measure GLS.
Results: We performed analysis of 37 patients that complete follow up period, Treatment Group (n = 21) and Control Group (n = 16). There was no significant improvement in GLS in treatment group compared to control group (-9,17 ± 3,71 vs -8,83 ± 4,07;p = 0,876). Interobserver variability for GLS was small with mean of difference of 0,32(CI95%: -0,09-0,75;p = 0,106).
Conclusions: There was no significant improvement in GLS after oral FS treatment in systolic HF patient with IDA.

Comparison of GLS between groups

	Group	Pre-Treatment	Post-Treatment	P value
Apical 4 Chamber (%)	FS	-8,42± 3,82	-8,79± 4,03	0,588
Control		-8,16± 3,45	-8,08± 3,81	
Apical3 Chamber(%)	FSC ontrol	-7,20 (-14,10-0) -8,05 (-21,70-(-4,00)	-8,40(-14,00-(-3,10) -8,70 (-20,70-(-3,70)	0,783
Apical2 Chamber(%)	FS Control	-8,76 ± 4,70 -8,68 ± 3,32	-9,86 ± 4,44 -9,1 ± 4,01	0,592
GLS(%)	FS	-8,19 ± 3,73	-9,17 ± 3,78	0,876
Control		-8,67 ± 3,56	-8,83 ± 4,07	

FS: Ferrous Sulfate; GLS: Global Longitudinal Strain

P2151

Body composition in heart failure and chronic obstructive pulmonary disease patients

AG Navarrete-Penaloza[1]; A Orea-Tejeda[2]; D Gonzalez-Islas[2]; L Verdeja-Vendrell[2]; A Jimenez- Cepeda[2]; GK Perez-Cortes[2]; R Sanchez-Santillan[2]; V Pelaez-Hernandez[2]; B Robles-Uribe[2]; A Figueroa-Herrera[2]; S Torres-Montiel[2]
[1]Autonomous University of Puebla, Puebla, Mexico; [2]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Distress Respiratory Clinic , Mexico City, Mexico

Background: Heart Failure (HF) and Chronic Obstructive Pulmonary Disease (COPD) patients present an endothelium function imbalance. This populations presents a pro-catabolic metabolism which is associated with the progression disease. Both population present a high cachexia prevalence characterized by loss skeletal muscle and and fat mass. There also exists a dismish in phase angle which is a marker of nutritional status and cell membrane. Cachexia and phase angle are associated with a worse prognosis in HF and COPD patients. However, ther exists few body composition evidence related with HF and COPD. Objective: To evaluate body composition in subjects with HF and COPD compared with COPD subjects.
Methods: A Cross – sectional study, 77 subjects older than 18 years olds, with confirmed HF and / or COPD diagnosis, and those who attend to outpatient visits were included. Asthma subjects were excluded. Body composition were assessed by BIVA, endothelial function by photopletysmography. Results: 77 were randomized, mean age 71.2 ± 11.57 years, 69.43% with COPD and 30.57% HF and COPD. Subjects with HF and COPD had high prevalence of diabetes (21.6 vs 9.5, p = 0.07), pulmonary hypertension (29.7 vs 9.5, p = 0.005), obstructive sleep apnea syndrome (35.1 vs 10.7, p = 0.001) compared to subject which present only COPD. There were not significative difference in other variables. In body composition the prevalence of cachexia were 57.1% in both groups, 20.8% obesity and normal composition 22.1%. Subjects with HF and COPD presented a lower phase angle (4.15 ± 1.2 vs 4.73 ± 0.89, p = 0.05) and higher endothelial dysfunction (0.361 ± 0.086 vs 0.325 ± 0.064, p = 0.035) than COPD subjects. Respect to fluid corporal distribution subjects with HF and COPD reported low total corporal water (46 ± 8.23 vs 51.06 ± 8.64, p = 0.019) and high extracellular water (3.12 vs 3.03, p = 0.006) compared to COPD subjects. Conslusions: Body composition with HF and COPD subjcets showed a high deterioration which can benefit a worse diagnosis.

P2152

Association of diastolic dysfunction and cognitive function in heart failure

MS Mi-Seung Shin[1]; JS Kim[2]; MJ An[3]; SH Kim[4]; JL Shim[4]; JK Park[5]
[1]Gachon University Gil Medical Center, Incheon, Korea Republic of; [2]Gachon University, College of Nursing, Incheon, Korea Republic of; [3]Chonnam National University College of Nursing, Gwangju, Korea Republic of; [4]Hanyang University, College of Nursing, Seoul, Korea Republic of; [5]Hanyang University, Department of Internal Medicine, Seoul, Korea Republic of

Background and purpose: Poor cognitive function is a common comorbid condition in heart failure (HF) associated with progressive deterioration of cardiac function and prolonged cerebral hypoperfusion. The relevance of cardiac functional markers to the cognitive performance was primarily focused on systolic functional markers, such as ejection fraction (EF) or cardiac output, while specific diastolic functional influence on cognitive declines in HF are lacking. To examine whether systolic and concomitant diastolic dysfunction were associated with poor cognitive performance in memory, attention, and executive function among patients with HF.
Methods: Using a correlational study design, 90 persons with HF completed face-to-face interviews for neuropsychological testing for cognitive evaluation and echocardiographic evaluation for systolic and diastolic function.
Results: Sixty one patients (67.8%) and 29 patients (32.2%) had mild-to-moderate and severe systolic dysfunction, using cutoff values of EF≥30% and < 30%, respectively; 22 (26.8%) had severe diastolic dysfunction using a cutoff value of peak velocity of early mitral inflow/early mitral annular velocity ratio>15. Those who had severe systolic dysfunction had significantly lower scores for attention (Digit Span Test [DST] backward, t=2.54, p = .013); those with a concomitant severe diastolic dysfunction had significantly lower attention (DST backward, t=2.01, p = .048), verbal fluency (t=3.13, p = .002) and executive function (Korean-Trail Making Test Part B) (t=-2.38, p = .02), compared with those without severe diastolic dysfunction. After controlling for age and education, HF patients with a concomitant presence of systolic and severe diastolic dysfunction had poorer cognitive function in verbal fluency than those free of severe diastolic dysfunction (F=4.45, p = .038, partial eta=.057).
Conclusions: Poor cognitive performance, particularly executive function was more substantial in HF with systolic dysfunction when diastolic dysfunction concomitantly presented. Monitoring and surveillance of diastolic dysfunction and cognitive screening are warranted in routine clinical practice of HF management.

P2153

Interventions to enhance medication adherence in older heart failure patients, a systematic review

RL Roberta Fulton[1]; T Kroll[2]; MET Mcmurdo[1]; G Molloy[3]; MD Witham[1]
[1]University of Dundee, Ageing & Health, Dundee, United Kingdom; [2]University College Dublin, Dublin, Ireland; [3]National University of Ireland, School of Psychology, Galway, Ireland

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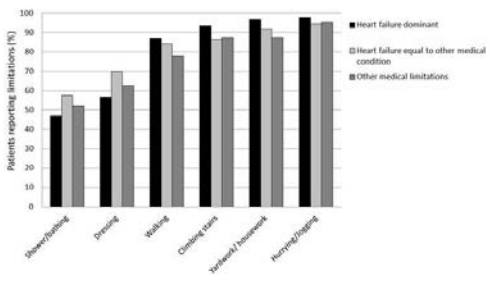
Introduction: While there is clear evidence that pharmacotherapy improves survival and reduces hospitalisation due to heart failure, medication adherence is sub-optimal. With increasing numbers of effective self-administered treatments available, there is a need for better understanding and management of non-adherence to medication. The purpose of this systematic review was to establish which interventions are effective in enhancing medication adherence in heart failure patients
Methods: We conducted a systematic review of randomised controlled trials (RCTs) searching for all-language publications in electronic databases (Medline, CINAHL, Embase, Cochrane Central Register of Controlled Trials and PsychINFO) up to the end of April 2015. We included RCTs where an intervention was compared to usual care or a clearly justified comparison group and where the intervention strategy clearly had a primary or secondary aim of increasing adherence to heart failure medication. Included trials required to have enrolled patients'≥ 18years, with a clinical diagnosis of heart failure, who did not have their daily medication administered by a healthcare professional. Two independent reviewers examined

lists of retrieved articles extracting study characteristics and results for adherence. Methodological quality was examined using the Cochrane Collaboration risk of bias tool. Studies were critically reviewed and assessed for validity of their findings.
Results: From the initial 1,801 identified papers 21 trials, containing data on 4346 patients (mean ages 56 to 85 years), were included. The median sample size was 148 patients (range 50 to 902); the median follow-up time was 9 months with 9 of the 21 (43%) trials having follow-up times of ≤6 months. Medication adherence improvement was reported in 8 of 21 trials. 5 of these 8 were categorized as intensified patient care, with these studies specifically designed to increase the contact time between participant and health care professional. Heterogeneity of interventions and outcome measures precluded meta-analysis of results.
Conclusions: While it is possible to improve medication adherence in heart failure patients, the current litetrature does not allow reliable conclusions to be drawn as to the best intervention. Heterogeneity in both intervention techniques and measurement methodology leave us unable to identify reliable and efficacious intervention approaches. Future studies should aim to build on the methodologically stronger studies so that a cumulative set of findings can emerge.

P2154
Patients in nyha III report substantial limitation to routine daily activities which may not be related to heart failure

R R T Castro[1]; E Joyce[2]; M Givertz[1]; GC Stewart[1]; NK Lakdawala[1]; E Lewis[1]; LW Stevenson[1]
[1]Brigham and Women's Hospital, Boston, United States of America; *[2]Cleveland Clinic Foundation, Cleveland, United States of America*

Background: Left ventricular assist devices (LVADs) are effective in improving survival and patient-reported outcomes in refractory heart failure (HF). Although LVAD implantation is not currently indicated in patients labeled as NYHA Class III, this physician designation may not always capture patient-reported limitations in specific activities. Furthermore, these activities may be limited by conditions other than HF. This study aimed to analyze how often patients labeled as NYHA Class III describe limitations to routine daily activities, and to determine how often these patients ascribe the major limitation of their quality of life (QOL) to HF or to combination with other medical conditions.
Methods: During routine HF clinic visits, ambulatory pts completed questionnaires including a graded scale for self-perceived limitations to daily activities, QOL on a visual analog scale (0-100), and their impression of whether their limitation was due mostly to HF or to other medical conditions. This analysis was restricted to those patients labeled by their HF physicians as having NYHA class III symptoms. Results between groups were compared by Student's T test or chi-square test.
Results: Patient symptoms were described by physicians as NYHA Class III in 162 patients. Patients who rated HF as a dominant limitation to QOL (n = 97) had similar QOL (46 ± 25 vs. 51 ± 29, p = 0.138) to the ones who rated limitation as due equally to HF and other medical condition (n = 40), and the ones whose major limitation was not HF (n = 25; QOL=57 ± 28). Limitation was described for bathing for 50.3% of patients and 60.9 % for dressing. There was no difference of daily activities' limitations between groups.
Conclusion: Patients in NYHA III have substantial limitations to daily activities and to QOL. When these limitations are due to HF, it may be reasonable to consider advanced therapies. However, it is important to identify those patients with HF that have other conditions limiting their daily activity, which would not improve with HF advanced therapies.



Limitations reported by NYHAIII patients

P2155
Predictors of 6- and 12-month mortality in chronic heart failure

N Nataliya Tkach[1]; L Voronkov[1]
[1]NSC Institute of Cardiology M.D. Strazhesko, Heart Failure department, Kiev, Ukraine

Background: Despite good knowledge about predictors of long-term mortality in chronic heart failure (CHF) the comparable value of them in dependence of patients follow-up duration is still non-well investigated.
Aim: The purpose of study was to identify the predictors of 6- and 12-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 6- and 12-month mortality were determined in stepwise multiple logistic regression model.
Results: Table 1.
Conclusion: HOMA index is an important predictor of CHF patients as 6 and 12 months. "Hemodynamic-linked" predictors (low LVEF, high LVEDVI) are valuable only in relation to 6-month mortality prognosis. The predictive value of elevated plasma UA and level blood lymphocyte < 21% is the more important to 6-months mortality; according to follow-up duration, the predictive value of low BMI, HR > 75 beats p.m. and LA size > 49 mm. are increased

Predictors of 6- and 12-month mortality

6 month	OR	12 month	OR
UA>450μmol/l	7.86	HOMA>2,65	8.48
HOMA>2,65	6.18	HR>75 beats p.m.	7.9
Blood lymphocyte <21%	5.15	SAP<100mmHg	5.4
LVEF <30%	3.4	BMI<22kg/m^2	3.59
BMI<22kg/m^2	3.33	UA>500μmol/l	3.125
LVEDVI	3.23	Blood lymphocyte <21%	2.69
6 min walk distance <360m	2.66	6 min walk distance <360m	2.43
		LA>49mm	2.18

* Only significant predictors are included (p < 0.05). 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.

P2156
The role of hibernation in potential recovery of ischemic myocardium in chronic heart failure as a manifestation of coronary artery disease

E Elena Stefanovic[1]; P Otasevic[1]; L Lausevic-Vuk[1]; P Milojevic[1]; M Jovic[2]; V Kanjuh[3]; P Seferovic[3]
[1]Institute for Cardiovascular Diseases Dedinje, Belgrade, Serbia; *[2]Military Medical Academy of Belgrade, Belgrade, Serbia*; *[3]University of Belgrade, Belgrade, Serbia*

Background: The aim of this study was to investigate the morphologic characteristics of the hibernating human myocardium and ,thrue the correlation its with dobutamine stress echocardiography (DSE), to study the potential for myocardial recovery in coronary artery disease.
Methods and Results. We evaluated 15 patients with coronary disease (58 + /-12 years old, ejection fraction 38 + -/14%) with a corresponding wall motion abnormality on DSE (up to 10 micrograms kg (-1) min(-1) before coronary bypass surgery. During surgery, transmural myocardial biopsies from hypokinetic or akinetic area were perfomed (n = 37). The samples of myocardium were analyzed by histopathology and immunohistochemestry to investigate the extent of interstitial fibrosis, intracellular and interstitial proteins. Among the 15 patients included in the study, 7 recovered function as assessed with an echocardiography, one month after bypass surgery, 8 with DSE viability showed less fibrosis and less vimentin expression,more glycogen, a higher ration of alpha-smooth muscle actin, actin and desmin then those without recovery. The degree of severity of the morphological changes (three stages) correlated well with the demonstration of inotropic reserve during DSE and with the extent of postoperative functional recovery (wall-motion score index, NYHA).
Conclusion: Myocardial hibernation as the adaptation to a reduced oxygen supply in coronary artery disease, have an important role in potential recovery of ischemic myocardium after coronary artery bypass surgery, as shown by more favourable histopathologic features.

P2157

Metabolic treatment elderly patients with congestive heart failure with preserved systolic function and non severe aortic stenosis

OV Olena Soya[1]; OV Kuryata[1]
[1]*Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine*

Background: Calcific aortic stenosis (AS) is the most common valvular abnormality in the geriatric age group. Like the AS, the prevalence of congestive heart failure (CHF) with preserved systolic function increases with age. Meldonium is cardioprotective drug with anti-ischemic and stress-protective effects in treating various cardio-vascular diseases and other pathologies. The aim of this study was to assess effect of meldonium treatment on cardiovascular function and exercise capacity in elderly patients with non severe AS and CHF with preserved systolic function.
Methods: In study were included 112 patients (male 61, female 51, age 79.8yrs+/-1.8) with non critical AS (mean gradient 31.1+/-5.1 mmHg) and with NYHA II-III functional class CHF due to ischemic heart disease or arterial hypertension. All patients have had left ventricular ejection fraction>45%. Patients were divided in two groups: in 1-st group – 58 patients got a standard combined CHF therapy, in 2-nd group – 54 patients got standard CHF therapy in combination with meldonium 1,0 g daily. Plasma level of insulin was measured before and after 4 months treatment with meldonium or placebo. RESULTS: There were no differences in baseline characteristics including hemodynamic parameters between 2 groups. After 4 months the elderly patients with AS and meldonium treatment demonstrated improved CHF functional class (50.1% vs 27.3%, $p < 0.01$) and exercise capacity by 6 minute walk test (39.3% vs 24.7%, $p < 0.01$) compared with standard therapy group. Patients receiving placebo demonstrated increasing insulin level (263/-31 pmol/l vs 381+/-39 pmol/l, $p < 0.01$). In contrast, in patients receiving meldonium, plasma level of insulin did not change.
Conclusion: Metabolic treatment with meldonium could have positive effect on cardiohemodynamic and exercise capacity in elderly patients with non severe aortic stenosis and CHF with preserved systolic function. Besides, meldonium prevents increasing plasma insulin level which could be significant negative prognostic marker.

P2158

Rheumatoid arthritis and congestive heart failure

TH Theodoros Michailidis[1]
[1]*General Hospital of Veria, Department Of Internal Medicine, Veria, Greece*

Introduction: It is widely accepted that Congestive Heart Failure (CHF) and Rheumatoid Arthritis (RA) are associated. There are studies that have examined the importance of RF and the anti – TNF treatment in the development of CHF in RA.
Purpose: Our purpose was to examine Greek women with RA and CHF and determine whether RF(+) women were at greater risk of developing CHF than those who were RF(-) independently of the presence of other cardiovascular risk factors.
Methods: We studied two groups of women with RA. Group A included 22 women from 55 to 74 years old, non-smokers, suffering from hypertension and dyslipidemia, who were RF positive and anti-ccp positive, receiving DMARDs treatment per os. Group B included 21 women, with similar age (55-75 years old) and history of CV risks, who were anti-ccp(+) and RF seronegative and were receiving similar to group A DMARDs treatment. All of the women were submitted to CMR (cardiovascular magnetic resonance).
Results: The results have shown that 17 women from group A suffered from stage A to stage D CHF whereas only 5 group B women had CHF compatible CMR imaging. Having ruled out the possible role of anti TNF treatment in CHF development (some women had pastly received anti-CD 20 and abatacept, adalimumab, anakinra and golimumab therapy when none of them received etanercept), the difference of the presence of CHF in the two groups was statistically important ($p < 0,01$)
Conclusion: Therefore, although the population sample examined was not huge, we have concluded that RF(+) Greek women, older than 55 years and suffering from RA have a much greater risk at developing CHF than RF(-) Greek women with RA. The determination of RF seropositivity in such women should always concern the cardiologist involved.

P2159

Heart failure development and rs2274273 in the vicinity of LGALS-3 locus, LGALS-3 relative mRNA expression in patients with first myocardial infarction

MD Dekleva[1]; AD Djordjevic[2]; MZ Zivkovic[2]; AS Stankovic[2]; NM Markovic Nikolic[1]; TD Djuric[2]
[1]*University Clinical Center Zvezdara, Department of Cardiology, Belgrade, Serbia*;
[2]*Insitute for Nuclear Science "Vinca", Belgrade, Serbia*

Background: Previous research has shown an association between circulating galectin-3 and fibrosis, apoptosis, cardiac dysfunction and heart failure (HF) after first myocardial infarction (MI)
Aims: Authors investigated an association of the genetic variant potentially affecting galectin-3 levels-rs 2274273 (C>T) as well as LGALS-3 mRNA with adaptive or maladaptive LV remodeling, functional LV dynamics and heart failure occurrence.
Methods: The prospective study enrolled 166 patients with first acute MI. Clinical, laboratory, ECG echocardiographic and angiographic data were obtained at admission time and after 6 months follow up. Rs 2274273 and LGALS-3 mRNA expression were detected by real time PCR.
Results: T allele according to dominant model was significantly associated with LV enlargement (diameter and volume) ($p = 0.037$, $p = 0.034$), global radial strain ($p = 0.003$) and LV spherical index ($p = 0.032$). LGALS-3 mRNA expression was significantly higher in: patients with maladaptive remodeling ($p = 0.045$), apical LV dilatation and remodeling (0.046) and in patients who developed HF after six month follow up ($p = 0.021$).
Conclusions: Our exploratory results suggested that rs 2274273 T allele and LGALS-3 mRNA could bear the risk for more severe post MI LVR and HF development. Further replication and validation in a larger group of patients is inevitable.

P2160

The relationship between blood pressure, heart rate and clinical status in patients with chronic heart failure with reduced left ventricular ejection fraction

M Michal Bohdan[1]; A Kowalczys[1]; M Gruchala[1]
[1]*Medical University of Gdansk, 1st Dept of Cardiology, Gdansk, Poland*

Introduction: The effects of increased heart rate (HR) and blood pressure (BP) on cardiovascular mortality have been thoroughly studied for many years. The impact of BP on clinical status and prognosis of patients with CHF still needs further investigation.
Purpose: The aim of the study was to assess the relationship between BP as well as HR and clinical status including: major adverse cardiac events (MACEs), left ventricular ejection fraction (LVEF), brain natriuretic peptide (BNP) and six-minute walk test (6MWT) distance in stable patients with CHF.
Methods: There were 80 patients: 73 (91%) men and 7 (9%) women (mean age: 59 ± 12 years) with stable CHF and mean NYHA class 2.15 ± 0.57, with reduced LVEF recruited for the study. Coronary artery disease (CAD) was the main CHF cause. The majority of patients were nondiabetic ($n = 56$, 70%). All patients underwent following examinations: medical history, physical examination, laboratory tests including BNP, 12-lead electrocardiogram, echocardiogram, six-minute walk test (6MWT). We obtained: BP, systolic and diastolic (SBP, DBP) and HR as determined in 24-hours ECG and blood pressure monitoring (50% of patients) or telemetry monitoring and BP measurements 5 times a day (in the rest of the group). All patients were treated according to ESC guidelines. Most of them received β-blockers ($n = 71$, 89%). The median follow-up period was 6 months. MACEs were defined as: death of all causes, cardiovascular death, hospitalization due to the heart failure exacerbation.
Results: There was sinus rhythm in the majority of patients (55%) while atrial fibrillation was found in 16 (22%) patients. The LVEF $\leq$35% (mean 23 ± 6%) was confirmed in all patients as well as elevated BNP level (742 ± 701 pg/ml). Median 6MWT distance was 351 ± 110 m. Median heart rate was 75 ± 14.3/min. Median SBP was 114 ± 14mmHg and DBP: 70 ± 9.5mmHg. The percentage of patients with heart failure exacerbation was 13% at 3 months and 24% at 6-month follow-up. The mortality rate was 4% at 3 months and 6% at 6-month follow-up. We found positive correlations between SBP and: LVEF (R=0.4, $P = 0.0002$), 6MWT distance ($R = 0.33$, $P = 0.0056$) and negative between SBP and BNP ($R = -0.03$, $P = 0.0068$). We also revealed positive correlation between DBP and EF ($R = 0.26$, $P = 0.0182$). Although there was no relationship between HR and EF, BNP, 6MWT, we confirmed negative correlation between HR and LVEF ($R = -0.35$, $P = 0.0089$) in the subgroup of patients with atrial fibrillation. After 3-month but not 6-month follow-up there was a significant correlation between DBP and all-cause mortality ($P = 0.048$) as well as CHF decompensation ($P = 0.0004$) in the whole group. We have not found any significant relationship between HR or SBP and MACEs.
Conclusions: Blood pressure is strongly associated with clinical status of patients suffering from CHF. Moreover, DBP may be helpful in prediction of heart failure exacerbations in stable patients with CHF with reduced ejection fraction in short-term observation.

P2162

Liver dysfunction at chronic heart failure patients

K Kaoutar Kharbouche[1]; I Elhaddad[1]; K Kharbouche[1]; L Azouzi[1]; R Habbal[1]
[1]*chu ibn rochd, cardiology, casablanca, Morocco*

Introduction: Comorbid conditions such as anemia. Liver and renal dysfunction are significantly influence on chronic heart failure (CHF) prognosis.
Objectives: To studying of a liver function at patients with CHF.
Methods: 1600 patients from 22 to 58 yrs (mean 44,21,8, males/females 61/21) are included. CHF has been caused by ischemic (n25) and idiopathic dilated cardiomyopathies (DC, n56). The hepatic function was assessed by determination of

aspartate (AsT) and alanine transaminase (AlT), total bilirubin (TB), and albumin plasma concentration. After initial investigation all patients are divided on two: I (with liver abnormalities, n28; 43,72,1 yrs) and II (without hepatopathy, n54, 41,41,9 yrs) groups.
Results: Apparently, the prevalence of liver dysfunction characterized by increasing of TB and/or transaminase levels was 37,2% and at 6 (5,8 %) from them had cirrhosis signs. The most typical markers of hepatic damage at our patients was hyperbilirubiemia, registered at 25 (89%) pts of I gr. At the same time, increase of transaminase was less expressed (at 18 pts). It is noticed, that at I gr patients decreasing of plasma albumin (3,30.12g/l vs 3.80,15g/l) and total cholesterol (allocated as adverse predictor at CHF patients) levels was more expressed (123,89,7mg/dl vs 147,36,8mg/dl, both p0.05). Comparative analysis of diseases severity showed that differences of NYHA class was non significant, but I gr pts characterized by reduction of distance by 6 minute walking test on 16.3% (168.79.3m vs 20210.2m accordingly, p0.04).
Conclusion: The 37.2% pts with various etiology CHF had signs of hepatic dysfunction, including cirrhosis. It is noticed, that the hyperbilirubiemia is frequent display of hepatopathy. Increasing of liver markers associated by hypoalbuminemia, hypocholesterolemia and physical tolerance worsening.

P2163
Cardiac resynchronization therapy in heart failure patients

R Kallel[1]; R Hammami[1]; M Akrout[1]; J Jedidi[2]; N Mallek[1]; L Abid[1]; S Kammoun[1]; J Dammak[2]
[1]Hedi Chaker Hospital University, Department of cardiology, Sfax, Tunisia; *[2]Hedi Chaker Hospital University, Departement of Epidemiology and community Medicine, Sfax, Tunisia*

Background: Patients with symptomatic heart failure and severe depression of left ventricle ejection fraction despite optimal medical treatment can benefit from cardiac resynchronization.
However, the increase use of implantable cardiac electronic devices was associated with an increase in complications and mortality.
Purpose: Our goal was to determinate the rate and the predictors of complications in patients with cardiac resynchronization therapy (CRT) in a real-world study.
Methods: Patients who received CRT-D/P between January 2009 and December 2013 were included in the study. We identified all complications during the follow up. Appropriate statistical tests were applied to identify the rate and the predictors of complications. We are particularly interested with the subgroup of patients with cardiac resynchronization therapy.
Results: 64 complications in 53 patients were noted over the period of the study, in fact 11,5% of patients receiving an implantable cardiac device (n = 462) experimented complications. Twenty six patients received a cardiac resynchronization therapy; just ten ones got defibrillation function. Patients with CRT experienced outcomes with higher rates (9 cases, 34%) compared to other implanted patients (13%). Infectious complications were registered in 11,5% of patients with CRT versus 1,37 % in patients with non CRT devices (p = 0,03). Independent risk factor of infections were heart failure (OR= 9) and diabetes (OR=4). Only one patient (3,8%) presented with left ventricle's lead dislodgement. The same patient had coronary artery dissection and then failure of resynchronization. Neither pocket hematoma nor complication linked to route access was noted in CRT patients over the study period. Mortality linked to complications of cardiac stimulation reached 13,2% especially with infectious outcomes (p = 0,04). However heart failure (p = 0,25) and resynchronization therapy (p = 0,95) were not directly associated to mortality due to complications.
Conclusion: Patients receiving cardiac resynchronization devices are subject to experience higher rates of complications compared to other types of implantable cardiac devices. Heart failure is an independent risk factor of complications. Comorbidities especially diabetes are an additional risk factor. Nevertheless, centers with low volume of implantation have particularly a high complication rate.

P2164
Myopathy and iron deficiency in chronic heart failure: dynamic 31P MR spectroscopy study of the skeletal muscle

K Katerina Hlavata[1]; P Sedivy[2]; M Dezortova[2]; M Hajek[2]; J Kautzner[1]; V Melenovsky[1]
[1]Institute for Clinical and Experimental Medicine (IKEM), Cardiology Department, Praque, Czech Republic; *[2]Institute for Clinical and Experimental Medicine (IKEM), Magnetic Resonance Imaging, Praque, Czech Republic*

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Introduction: The effect of sideropenia on myopathy due to chronic heart failure (CHF) is unclear.
Purpose: determine whether CHF leads to disruption of energetic metabolism of skeletal muscle, whether the abnormalities are affected by presence of sideropenia and whether these abnormalities disappear after correction by intravenous administration of ferric-carboxymaltose (FCM).
Methods: 25 healthy volunteers (49 ± 15y, 28 ± 4kg/m2, 70%) and 44 CHF patients (55 ± 16y, BMI 27 ± 6kg/m2, 75% men) underwent blood sampling and 31P MR spectroscopy of gastrocnemius muscle at rest and during exercise. In13 sideropenic patients examination was repeated 1 month after administration of FCM.
Results: HF was associated with reduction of high-energy phosphates content, acidosis and slower recovery of PCr after exercise, corresponding to CHF myopathy (table). The factors with highest impact on PCr-tau in CHF were: age, diabetes and male sex. Iron deficient HF patients had lower peak muscle strength, significant decrease of PCr during exercise and trend toward slower PCr recovery.
Conclusion: The administration of FCM led to a correction of sideropenia, improved functional capacity and muscle strength, but did not influence on energy metabolism in skeletal muscle, or redistribution of iron into skeletal muscle requires a longer period than 1 month.

P2164 Results

	control (n = 25)	HF (n = 44)	p	non-sideropenic HF (n = 12)	sideropenic HF (n = 32)	p	pre Fe HF (13)	post Fe HF (n = 13)	p
NYHA	-	2.7 ± 0.7	-	2.8 ± 1.0	2.6 ± 0.7	0.7	2.5 ± 0.5	2.2 ± 0.6	0.04
Hgb, (g/L)	-	134 ± 18	-	146 ± 13	129 ± 17	0.002	125 ± 13	133 ± 15	0.01
Ferritin, (ug/L)	-	131 ± 127	-	273 ± 155	77 ± 55	0.001	83 ± 61	403 ± 309	0.003
Transferrin sat, (%)	-	21 ± 13	-	31 ± 9	17 ± 13	0.0004	12 ± 6	18 ± 12	0.004
Muscle metabolism rest									
PCr (Phosphocreatine)/total signal	0.51 ± 0.02	0.50 ± 0.04	0.09	0.51 ± 0.04	0.50 ± 0.03	0.7	0.50 ± 0.03	0.50 ± 0.02	0.6
Pi (inorganic phosphate)/total signal	0.06 ± 0.01	0.07 ± 0.01	0.005	0.07 ± 0.02	0.08 ± 0.01	0.09	0.08 ± 0.01	0.08 ± 0.01	0.6
ATP/total signal	0.09 ± 0.007	0.08 ± 0.01	0.0006	0.08 ± 0.01	0.08 ± 0.01	0.7	0.08 ± 0.01	0.08 ± 0.01	0.7
Excercise									
peak isometric force, (N)	-	356 ± 143	-	439 ± 125	325 ± 139	0.03	360 ± 115	406 ± 127	0.03
PCr drop, %	24 ± 13	28 ± 16	0.2	19 ± 7.9	31 ± 17	0.01	37 ± 22	35 ± 17	0.6
PCr-tau, (s)	43 ± 17	66 ± 48	0.01	50 ± 15	71 ± 54	0.06	81 ± 72	76 ± 45	0.6
V-PCr, (mmol/s)(initial speed of PCr recovery)	0.27 ± 0.18	0.24 ± 0.12	0.4	0.20 ± 0.04	0.26 ± 0.13	0.04	0.28 ± 0.16	0.28 ± 0.17	0.9
Q-max, (mmol/s)(mitochondrial capacity)	0.55 ± 0.23	0.49 ± 0.21	0.3	0.44 ± 0.05	0.50 ± 0.2	0.3	0.53 ± 0.27	0.52 ± 0.28	0.7
Final pH	7.02 ± 0.03	7.0 ± 0.15	0.05	7.04 ± 0.06	6.95 ± 0.17	0.03	6.90 ± 0.20	6.93 ± 0.17	0.4

P2165

Assessment of causes of increased myocardial fibrosis, left ventricular dysfunction and poor prognosis after valve replacement for acquired heart disease

Il Irina Averina[1]; OL Bockeria[1]; SA Aleksandrova[1]; MU Mironenko[1]; LG Geletsian[1]
[1]*Bakoulev Center for Cardiovascular Surgery RAMS, Cardiosurgical , Moscow, Russian Federation*

Background: Despite technically successful operations postoperative complications as heart failure, sudden death are still observed. Dynamic contrast-enhanced MRI with gadolinium-based contrast and 2D speckle tracking echocardiography (Echo) can be reliable tools for evaluating fibrosis, LV dysfunction and possible poor prognosis after valve replacement.
Aim: Assessment of reasons for increased or maintained myocardial fibrosis, left ventricular dysfunction and poor prognosis after valve replacement based on the dynamic contrast-enhanced MRI with gadolinium-based contrast and 2D speckle tracking echocardiography
Methods: 144 (99 men, 45 women; age 47 ± 15) patients with aortic and mitral valve disease were included. In all cases 2D speckle tracking Echo was performed. 28 patients also underwent pre- and post-op MRI with gadolinium. Prognostic groups were considered: 0–no complications, 1–arrhythmia, 2–heart failure, 3–death. MRI fibrosis score was used: A–none, B–moderate, C–moderate-severe, D–severe. The global longitudinal, circumferential strain (LSt, CSt), strain rate (SR), rotation rate and torsion were obtained with Echo. Statistical analyses were done. Remodeling was considered as positive with reduced volume, increased ejection fraction, as negative with increased volume, decreased ejection fraction.
Results: The prognostic factors of high risk of heart failure: increased left ventricular systolic volumes index before surgery (IESV=45 ml/m2, AUC=0,84 ± 0,05), diminished basal septum motion (LSR = −0.4 c-1, AUC=0,7 ± 0,1), decreased apex rotation rate (37°/c, AUC=0,88 ± 0,1), diminished circular function of LV basal part (CStav= −14 %, AUC=0,8 ± 0,1).
Reverse remodeling was observed in 26% of pts. with moderate fibrosis. It was positive, but with persisted moderate-severe fibrosis in 62%, and negative with increased fibrosis in 12%. In persistent fibrosis LV IESV fell from 45 ml/m2 to 34 ± 15 (p = 0.001) With fibrosis increasing residual LV volume was higher (43 ± 8), despite its reduction from the initial (p = 0.001). LV LSt, CSt did not improve in persistent or increased fibrosis occurrence. Focal fibrosis was the most discernible at the junction of the septum with LV and RV free walls
Conclusion: Initial irreversible stretching LV is the main cause of incomplete remodeling and the heart failure in the postoperative period. Pointed values, shown incomplete reverse remodeling, fibrosis and preservation of the heart failure after surgery were: IESV–45 ml/m2, IEDV–99.89 ml/m2, LSt La–26.8%. Initial IESV ≥ 59 ± 8.9 ml/m2 was the reason for the increase of fibrosis in the postoperative period. Initial IESV ≥ 45.3 ml/m2 ± 14.9 was the cause of persisted myocardial fibrosis. The valve/ventricular approach may be needed to counteract.

P2166

Predictors of left ventricular function recovery in patients followed in a heart failure clinic

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

Background: Chronic Heart Failure (HF) remains a major worldwide problem with high prevalence and incidence. It is the end stage of many diseases. The recovery of left ventricular systolic function (LVSF) is important for the prognosis of these patients (pts), with relevance in the morbidity and mortality associated with HF.
Purpose: To evaluate the factors with impact on the recovery of LVSF (rLVSF) in pts with chronic HF and reduced ejection fraction (EF).
Methods: Retrospective study where were including 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. Pts with follow-up (FU) of less than 12 months were excluded. The rLVSF was measured by echocardiography and defined as an increase of ≥ 10% with respect to the initial value. The pts were divided into 2 groups: rLVSF (G1) and not rLVSF (G2). The groups were compared as to their clinical and echocardiographic characteristics and occurrence of hospitalization for HF (hHF), hospitalization for acute coronary syndrome, cardiovascular mortality and non-cardiovascular mortality. To analyze the relationship of the qualitative variables we used Fisher's exact test, while the Student t test was used to analyze the influence of the quantitative variables. It also appealed to the Cox regression model for multivariate adjustment (SPSS 22.0)
Results: Included 290 pts, mean age 60.6 ± 13.3 years. 75.1% were male. 41% had ischemic etiology, 34.1% permanent AF and 63.8% severe depression of LVSF. The mean initial EF was 29.2 ± 10.8%. Mean FU time was 39.9 months ± 18.5 months. 86 pts (29.7%) presented rLVSF (initial EF 25.3 ± 10.8% vs current EF 44.7 ± 12.5%). There were no significant differences in the composition of the two groups. In the univariate analysis, rLVSF was more common in patients with non-ischemic etiology (p = 0.007), sinus rhythm (p = 0.023), lower left ventricular end-diastolic diameter index (LVEDDi) at the end of the follow-up (30.4mm/m2 vs 34.4mm/m2, p < 0.001), lower prevalence of chronic kidney disease (defined as glomerular filtration rate ≤ 60mL /min/1.73m2, p < 0.001), less hHF (p = 0.008), lower functional class (≤2, p = 0.004), higher percentage of patients receiving angiotensin converting enzyme inhibitors / angiotensin receptor blockers (ACEi/ARB, 94.2% vs 85.3%, p = 0.034) and less with diuretics (64.0% vs 76.5%, p = 0.034). When used logistic regression, the non-ischemic etiology (p = 0.011), LVEDDi (p < 0.001), hHF number (p = 0.047) and ACEi/ARB therapy (p = 0.035) were significantly associated with rLVSF.
Conclusion: In this study, the non-ischemic etiology, lower LVEDDi, less hHF and ACEi / ARB therapy were predictors of rLVSF.

P2167

Heart failure as predictor of sudden death in patients with myocardial infarction after prior CABG; 27-year experience

P Predrag Mitrovic[1]; B Stefanovic[1]; M Radovanovic[1]; N Radovanovic[1]; G Matic[2]; D Rajic[2]; I Subotic[2]; N Mitrovic[2]; N Mijic[2]
[1]*University Institute for Cardiovasculari Diseases, CCS, School of Medicine, University of Belgrade, Belgrade, Serbia*; [2]*Clinical Center of Serbia, Institute for Cardiovascular Diseases, Belgrade, Serbia*

On behalf of: The POP Study Group
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To elucidate the clinical predictors of death, 1080 patients (pts) with acute myocardial infarction (AMI) after prior coronary artery bypass grafting (CABG) have been selected from the pts consecutively submitted from April 1990 to January 2017.
Methods: In this group of patients with AMI after prior CABG mean age was 59.4 ± 6.4 yrs. There were more males (79.6%). The pts with early perioperative AMI were excluded from the study. The average time interval from CABG to AMI was 94.8 ± 11 months. The average number of grafts was 3.3 grafts/pts. All pts were divided in 3 groups: pts died from sudden cardiac death, pts died from cardiac causes of death and pts died from non-cardiac causes of death. The mean interval of survival was 12.4 ± 5.2 months.
Results: In 180-months follow-up period 220 (20.4%) pts died after AMI and previous CABG. One hundred and forty-three pts (65%) died in first five years after AMI and the more often cause of death in these pts was sudden cardiac death (132/143 pts, 92.3%). Seventy-nine total of 220 pts (35.9%) died from cardiac causes of death. The most frequent cause of death in this group of pts was congestive heart failure (64/79 pts, 81%). Fifteen pts (19%) died from reinfarctus. In twelve pts (5.5%) the cause of death was non-cardiac. One hundred and thirty patient (59.1%) died from sudden cardiac death. Analyze of events which might be causes of death in pts died from sudden cardiac death shown that: angina pectoris was present in all 132 pts, atrial fibrillation was present in 60/132 (45.5%) pts and congestive heart failure in 105/132 (79.5%) pts. Conclusion: the most frequent cause of death in 220 patients died after AMI and previous CABG was sudden cardiac death; congestive heart failure is one of very important predictor of sudden cardiac death in this patients.

P2168

ST2 in HFpEF and HFrEF, similarities and differences

E Emil Najjar[1]; LH Lund[1]; UL Faxen[2]; C Hage[1]; E Donal[3]; J Daubert[3]
C Linde[1]; [1]*Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden*; [2]*Karolinska University Hospital, Department of Anesthesia and Intensive Care, Stockholm, Sweden*; [3]*University Hospital of Rennes, Département de Cardiologie & CIC-IT U 804, Rennes, France*

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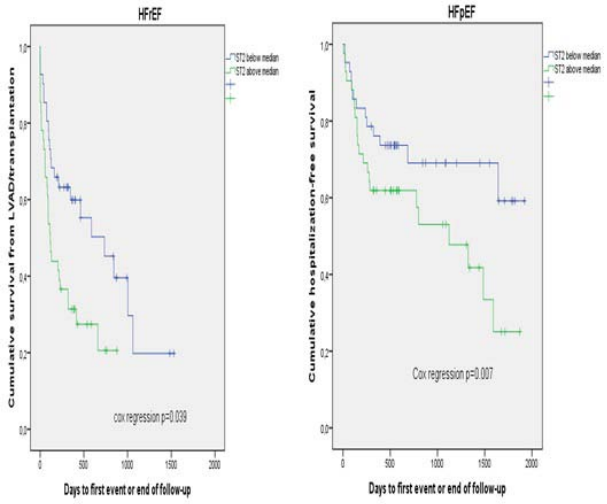
Background: Soluble suppression of tumorigenecity 2 (ST2) reflects myocardial stress, ventricular remodeling and fibrosis. It is prognostic in heart failure with reduced ejection fraction (HFrEF) but poorly studied in HF with preserved EF (HFpEF).
Purpose: To evaluate ST2 concentrations, correlations with biomarkers and associations with outcome in HFpEF compared to HFrEF, and associations with echocardiographic measures of diastolic function in HFpEF.
Methods and Results: Eighty-six patients with HFpEF from the prospective KaRen cohort (median age 73 [67-80] years, 51% women), 86 patients with HFrEF (median age 63 [52-68] years, 19% women) and 21 controls (median age 67 [59-70] years, 57% women) were included.
Concentrations of ST2 were lower in HFpEF (median and interquartile range); 23 (17; 31) μg/L and controls 25 (21; 32) μg/L, compared to HFrEF; 35 (23; 52) μg/L, overall p < 0.001. NT-proBNP was also lower in HFpEF; 1000 (465; 2335) ng/L vs.

HFrEF, 3290 (1405; 6115) ng/L, p < 0.001.
In both HFpEF and HFrEF, ST2 showed a significant positive correlation with NT-proBNP (HFpEF r = 0.36, p = 0.001 and HFrEF r = 0.453, p < 0.001) but not with eGFR in HFpEF or HFrEF. In HFpEF, ST2 correlated to indexed left atrial volume (r = 0.27, p = 0.020) but not to E/E′, nor to left ventricular mass index.
ST2 was significantly associated with survival free from hospitalization for HF in HFpEF and survival free from heart transplant or left ventricular assist device in HFrEF (Figure); hazard ratio (HR) per log increase in ST2 10.04, 95% confidence interval (CI) 1.89-53.44, p = 0.007, and 3.28, 95% CI 1.06-10.16, p = 0.039, respectively. In HFpEF, but not in HFrEF the association persisted after adjustment for NT-proBNP and age, HR 7.2, 95% CI 1.1-43.28, p = 0.032.
Conclusions: We confirm previous studies that ST2 is prognostic in HFrEF but this may not be independent of covariates. We show that ST2 is independently prognostic in HFpEF.

Figure: Kaplan-Meier estimates of survival free from hospitalization for HF in HFpEF and survival free from heart transplant or left ventricular assist device in HFrEF.



P2169

Increasing the efficiency of treatment of patients with chronic heart failure through the changes of control systems of patients.

N Nabil Kraiem[1]; I Fomin[1]; NG Vinogradova[1]; M Zhirkova[2]; S Allahverdiyeva[2]; A Krylova[2]; A Subbotin[2]; A Kozlova[2]; N Anyutochkina[2]
[1]Nizhny Novgorod State Medical Academy, Department of internal medicine, Nizhny Novgorod, Russian Federation; *[2]Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russian Federation*

Introduction: It was proved that treatment of chronic heart failure (CHF) is less effective on the ambulatory period; therefore, it is important to consider some methods to make ambulatory treatment more effective.pgtaghb**Purpose:** To compare the treatment efficiency of patients with CHF in specialized center of CHF treatment and in real clinical practice.
Methods: Patients, after being discharged from hospital for acute decompensated heart failure (ADHF) were under observation in a specialized center of CHF treatment (group1, n=244) in period of 8 months and patients (group2, n = 243) under observation in real practice conditions. Hemodynamic parameters, frequency of recommended treatment use and outcomes (total and cardiovascular death) were identified in both groups. In specialized center, the nurse made structured calls to patients from group 2 one time every month.
Results: Mean age of patients was 70.1 ± 10.4 years in group 1 and 72.5 ± 11.8 in group 2 (p = 0.006). Quantity of patients according to NYHA classification was comparable in both groups: 15.4% and 7.1% in first class, 30.2% and 39.3% in second, 41.6% and 46.4% in third, 12.8% and 7.2% in fourth for group 1 and group 2 respectively. Results, depending of ejection fraction (EF) were comparable: 68.6% and 68.6% of patients had conserved EF, 18.5% and 21.6% with mid-range EF, 12.9% and 9.8% with reduced EF in group 1 and 2 respectively.Hemodynamic parameters (Systolic blood pressure, Diastolic blood pressure, Heart rate) were similar. After 8 months, administration frequency of Renin Angiostensin Aldosteron system blockers, Beta Blockers and Mineralocorticoid Receptor Antagonist in group 1 increased from 84.3% to 93.8% (p < 0.001), form 78.5% to 87.4% (p = 0.01) and from 63.1% to 70.3% (p = 0.09) of patients respectively. In group 2, there was a decrease from 86.4% to 50.5% (p < 0.001), from 79.6% to 54.9% (p < 0.001), and from 64.5% to 24.1% (p < 0.001). After 8 months, 70.5% of patients continue to use loop diuretics in group 1 (p < 0.001), in group 2 only 38.5% (p < 0.001). Total mortality during 8 months was 1.9% and 13.9% in group 1 and 2 respectively (OR=8.5 CI 95% 2.7-26.6, p < 0.001). In group 1, causes of cardiovascular mortality were ADHF, sudden cardiac death and pulmonary embolism (PE). In group 2, ADHF was in 58.3% of cases, PE in 16.7%, stroke in 16.7% and myocardial infarction in 8.3% of cases.
Conclusion: during the period of observation, the recommended treatment was less used among patients under observation in conditions of real clinical practice comparing with patients under observation in specialized center of CHF. After ADHF, patients are having bad prognosis, that's why, in Russian Federation, there is a big need in changing the strategy of treatment and observation of patients with CHF and developing of a specialized health care system.

P2170

Utilization of evidence based therapies in patients hospitalized for worsening heart failure

CI Radulescu[1]; L Antohi[1]; R Radu[1]; M Chivulescu[1]; I Cosei[1]; A Covaliov[1]; G Tatu-Chitoiu[2]; D Vinereanu[3]; D Dobreanu[4]; O Chioncel[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; *[2]Emergency Clinical Hospital Floreasca, Cardiology, Bucharest, Romania*; *[3]University Emergency Hospital of Bucharest, Cardiology, Bucharest, Romania*; *[4]Institute of Cardiovascular Diseases of Targu Mures, Cardiology, Targu Mures, Romania*

Background: In real world setting, the rate of use of evidence based heart failure therapies (EBHFT) is lower than guidelines recommendations, suggesting the unmet need of further improving of medical education.
Aim: To evaluate the pattern of in-hospital use of EBHFT in patients hospitalized for worsening HF (WHF).
Methods: Romanian National Observational Study of In-Hospital Heart Failure (SONIC-RO) enrolled 1222 consecutive patients, over one month period, admitted with a primary diagnosis of WHF, from 41 hospitals (9 academic and 32 community), representative for the Romanian cardiological network. The rate of prescription and the doses of EBHFT (beta blockers (BB), ACE inhibitors/sartans and aldosterone antagonists (AA)) were collected at admission and discharge. A multivariate logistic regression model was developed to identify baseline clinical variables predictive for the utilisation of EBHFT.
Results: The proportions of BB, ACEI/sartans and AA prescription on admission were 63%, 51%, and 43%, respectively; only 18% were prescribed all 3 medications. At discharge proportions were 74%, 57%, and 54%, respectively, and only 26% of patients had been prescribed all three classes. We identified the following variables that influence the rate of prescription for these medications – for BB use: age (HR = 1.21, 95% CI 1.14-1.33), admission in a community hospital rather than an academic one (HR = 1.24, 95% CI 1.09-1.30), the presence of chronic obstructive pulmonary disease (HR = 1.32, 95% CI 1.14-1.53), and NYHA IV functional class (HR = 1.94, 95% CI 1.75-2.31); for ACEI/sartans use: age (HR = 1.02, 95% CI 1.01-1.05), NYHA IV functional class (HR = 1.22, 95% CI 1.10-1.31), chronic kidney disease (HR = 1.65, 95% CI 1.41-1.82), and systolic blood pressure < 100mmHg (HR = 2.21, 95% CI 1.94-2.53); and for AA use: chronic kidney disease (HR = 1.35, 95% CI 1.21-1.56), and systolic blood pressure < 100mmHg (HR = 1.52, 95% CI 1.34-1.73) respectively.
Conclusion: In present study, patients with higher cardiovascular risk at admission are less likely to receive optimal EBHFT. Distinct to clinical severity, non-academic clinical setting seems to influence in-hospital utilization of EBHFT, which should be considered by future educational programs.

P2171

B-natriuretic peptide and its prognostic value in coronary patients with heart failure, irrespectively of renal function; the interaction with heart failure phenotype; hellenic heart failure study

M Kouvari[1]; C Christina Chrysohoou[2]; H Kosyfa[1]; G Kalogirou[1]; P Aggelopoulos[1]; I Kotsiopoulou-Xaritou[1]; G Georgiopoulos[1]; S Iosifidis[3]; A Filippou[3]; E Tsiamis[1]; D Tousoulis[1]
[1]University of Athens, First Cardiology Clinic, School of Medicine, Athens, Greece; *[2]University of Athens, Athens, Greece*; *[3]Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

On behalf of: Hellenic Heart Failure study

Background/Introduction: Although important advances have been performed in the interpretation and understanding of the pathophysiology behind heart failure,

this chronic disease remains a challenge in the area of prognosis stratification. In this context, renal function and B-natriuretic peptide (BNP) remain predictors of much interest. Purpose: to evaluate the role of renal function, through glomerular filtration rate (GFR) and BNP on the 10y ACS mortality of coronary patients with heart failure.
Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, the 10y follow-up (2006-2016) was performed in 745 participants. GFR was evaluated through the MDRD formula. Heart failure phenotype was defined according to baseline ejection fraction (EF); heart failure with reduced EF (i.e. < 40%) (HFrEF), preserved EF (i.e ≥50%) (HFpEF) and mid range EF (i.e. 40-49%) (HFmrEF). Results: 10y ACS mortality was 21%. Patients who suffered from a new fatal episode within the decade had significantly lower GFR and higher BNP values at baseline, compared with their alive counterparts (all ps < 0.001). In multivariate logistic regression analysis, GFR remained an independent predictor for the incidence of ACS death within the decade, after adjusting for potential confounders (OR=0.98 95%CI (0.97, 1.00), p = 0.04). Additionally, since BNP levels were strongly associated with both the primary outcome and the GFR (p < 0.001 from Spearman's correlation test), BNP was forced included in the multivariable model as a covariate with possible mediating effect. After adjusting for baseline BNP, GFR lost its significance whilst BNP levels (expressed per 2 fold increase) independently predicted ACS mortality (OR=1.39 95%CI (1.15, 1.67), p = 0.001). What is more a significant interaction was observed between EF and BNP levels on the tested outcome (p for interaction < 0.001). In stratified analysis the aforementioned significant predictive value of BNP retained only in HFmrEF (OR=1.43 95%CI (1.01, 2.03), p = 0.04) and in HFpEF (OR=1.80 95%CI (1.15, 2.82), p = 0.01).
Conclusion: BNP values were highlighted as an important predictor in long term prognosis of coronary patients with heart failure, namely those with better performance of left ventricle for whom further investigation is highly demanded.

P2172

Red cell distribution width change during hospitalisation and 1-year mortality in chronic heart failure

P Lazarev[1]; E Kotova[1]; A Shavarov[1]; YU Karaulova[1]; G Kiyakbaev[1]; V Moiseev[1]
[1]*RUDN University, Moscow, Russian Federation*

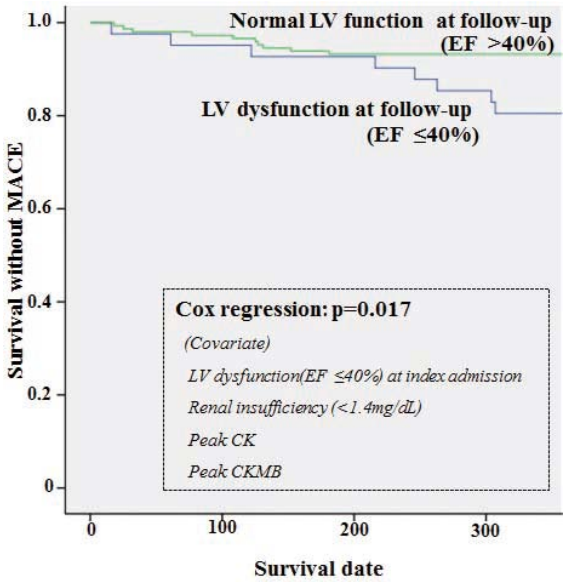
Background: Red cell distribution width (RDW) is considered to be one of the novel predictors of adverse events in chronic heart failure (CHF) patients. However, the role and significance of RDW change during hospital stay has not been completely identified.
Purpose: We aimed to evaluate the influence of in-hospital RDW change on 1-year mortality in CHF patients.
Methods: Our study included 351 consecutive hospitalised CHF patients [46% male, mean age 72 ± 11 years old, mean left ventricular ejection fraction (LVEF) 53 ± 14%, 24% anemic]. RDW measurements were obtained at least twice during hospitalisation: within 24 hours of admission and on discharge, respectively. The association between in-hospital RDW change and 1-year total mortality was tested with ROC-curve analysis and logistic regression, with further adjustment for possible confounders (routine clinical, laboratory and instrumental findings). If no cut-off value was established in the ROC-curve analysis, RDW change of > or < 1% was considered to be significant. Correlation was estimated with the use of Spearman's rank correlation coefficient (rho).
Results: On admission 118 (34%) patients had NYHA class II heart failure, 115 (50%) – class III and 58 (16%) – class IV disease. Association between in-hospital RDW change and 1-year total mortality was not found to be significant both in ROC-curve and linear trend analysis (p = 0.364). An increase in RDW was noted in 92 (26%) patients and conferred a higher risk of the negative outcome [odds ratio (OR) 2.07, 95% confidence interval (CI) 1.02-4.18, p = 0.046] compared to 185 (53%) patients with insignificant RDW change. This increased risk lost statistical significance after adjustment for other risk predictors (OR 3.56, 95% CI 0.80-5.97, p = 0.097), among which the measures of kidney function and echocardiographic parameters reflecting left and right ventricular function were the most potent. No correlation was found between changes in RDW and hemoglobin (rho=0.093, p = 0.206) or MCH (rho=-0.029, p = 0.692) values. However, weak positive association was present between changes in RDW and MCV readings during hospitalisation (rho=0.177, p = 0.015).
Conclusion: RDW increase during hospitalisation in CHF patients is a weak predictor of 1-year mortality in comparison to other risk factors.

P2173

Left ventricular dysfunction and cardiac outcomes one year after successful percutaneous coronary intervention in patients with acute ST elevation myocardial infarction

H-J Hwang[1]; C-B Park[1]; IS Sohn[1]; J-M Cho[1]; C-J Kim[1]
[1]*Kyunghee University East-West Neo Medical Center, Cardiology, Seoul, Korea Republic of*

Background: Preferred treatment for patients with ST-segment elevation acute myocardial infarction (STEMI) is primary percutaneous coronary intervention (PCI). However, some patients after successful PCI have suffered several attacks due to heart failure.
Purpose: We investigated predictors related to left ventricular (LV) dysfunction at follow-up echocardiography within one year and the association between LV dysfunction and one-year major adverse cardiac events (MACE) (composites of all cause of death, non-fatal myocardial infarction, and revascularization) in patients who underwent primary PCI successfully in diagnosis of STEMI.
Methods: A prospective cohort of 1736 consecutive patients who were successfully received primary PCI following a diagnosis of STEMI between January 2008 and March 2012, and underwent follow-up echocardiography from 30-days to one year was analyzed from Korea Working Group on Myocardial Infarction (KorMI) registry.
Results: Among 1736, 243 (14%) patients had LV dysfunction [LV ejection fraction (EF) ≤40%] at follow-up echocardiography. In multivariate analysis, independent predictors of LV dysfunction at follow-up were LV dysfunction at index admission, renal insufficiency (creatinine ≥ 1.4mg/dL), peak creatine kinase (CK), and peak CKMB. Independent predictors for the deterioration of LVEF at follow-up (absolute 5% decrease less than LVEF at index admission) were dyslipidemia, LVEF at index admission, peak CK, and peak troponin I, whereas independent predictors for the improvement of LVEF at follow-up (absolute 5% increase more than LVEF at index admission) were the male, no history of coronary artery disease, pre-TIMI flow, LVEF at index admission, peak CKMB, and peak troponin I. One-year major adverse cardiac events (MACEs) were significantly increased in patients with LV dysfunction at follow-up on Cox-regression analysis (Figure).
Conclusions: Persistent LV dysfunction after successful primary PCI was related with poor clinical outcomes at one-year clinical follow-up. We should evaluate post-infarction patients more meticulously for selection of the possibility of persistent LV dysfunction and to facilitate more appropriate treatment.



MACE by LV dysfunction

P2174

Heart failure with mid-range ejection fraction: clinical profile and mid-term outcome.

MA Miguel Antonio Lopez Garrido[1]; A De Vicente-Ortega[2]; AI Molina-Ramos[1]; V Garcia-Ruiz[1]; VM Becerra-Munoz[1]; A Ruiz-Salas[1]; L Morcillo-Hidalgo[1]; M Jimenez-Navarro[1]; JJ Gomez-Doblas[1]; E De Teresa-Galvan[1]; JM Garcia-Pinilla[1]
[1]*University Hospital Virgen de la Victoria , Department of Cardiology, Malaga, Spain*; [2]*Faculty of Medicine, University of Malaga, Malaga, Spain*

Background: The ESC Heart Failure (HF) Guidelines of 2016 introduce the term HF with mid-range ejection fraction (HFmrEF) as a separate group with characteristics between HF with reduced and preserved ejection fraction. This is a population that probably has primarily mild systolic dysfunction, but with features of diastolic dysfunction. We conducted this study in order to know the the clinical characteristics and mid –term outcome of this population.
Methods: We studied all the patients with HFmrEF at follow-up in the HF Unit of our Hospital in the years 2010-2014, recording their clinical characteristics,

comorbidities and adverse events during follow-up (mortality, functional class worsening, HF hospitalization, coronary acute syndrome and arrhythmias).
Results: Of the 114 patients (68 years, 24.6% women), 57 (50%) had ischemic etiology, 18 (15.8%) dilated cardiomyopathy and 17 (14.9%) valvular disease as etiology of the HF. 35 (30.7%) had previous hospitalization for HF and 17 (14.9%) had severe systolic dysfunction. In terms of cardiovascular risk factors, 81 (71.1%) had high blood pressure, 52 (45.6%) diabetes mellitus, 63 (55.3%) dyslipidemia, 25 (21.9%) had smoking habits, being the mean BMI 28.1 ± 4.8 kg/m2. Analyzing the comorbidities, 25 (21.9%) had atrial fibrillation, 29 (24.4%) chronic kidney disease, 25 (21.9%) anemia and 12 (10.2%) protein malnutrition, being the mean Charlson Index 5.7 ± 2,4. In the echocardiogram, 29 (25.4%) had dilated left ventricle, 34 (29.8%) left ventricular hypertrophy, 45 (39.%) dilated left atrium and 22 (19.3%) hemodynamically significant mitral regurgitation. 105 (92.1%) were treated with ACE inhibitors or ARBs, 95 (83.3%) with beta-blockers, 44 (38.6%) with MR antagonists and 74 (64.9%) with other diuretic treatment. The median follow-up was 39 months (IQR 29-52), presenting recovery of ejection fraction 23 patients (20.2%). In 3 years of follow-up, the global mortality was 15.7%. 23.4% of the patients presented decompensation of HF, 18.8% HF hospitalization, 14.5% acute coronary syndrome, 8.9% atrial fibrillation and 3.9% ventricular tachycardia or sudden cardiac death.
Conclusions: 1. The most frequent etiology in HFmrEF was ischemic heart disease. 2. There is a high prevalence of comorbidities in this population. 3. Echocardiogram showed both signs of systolic and diastolic dysfunction. 4. In our series this group had a high percentage of adverse events in the follow-up.

P2175
Precipitants of ADHF in era of disease management programs

F Faizan Rathore[1]; K Mcdonald[1]; R O'hanlon[1]; P Campbell[1]; C Keane[1]; F Ryan[1]; M Walsh[1]
[1]*St Vincent's University Hospital, Department of Cardiology, Dublin, Ireland*

Background/Introduction: Disease Management Programs (DMP) have been shown to improve prognosis in heart failure with significant reduction in hospitalizations. Insight into how to further improve this intervention will be helped by understanding the precipitants of admission in patients enrolled on these programs. To date,analysis of precipitants have been confined to general population. The aim of the study was to identify the precipitants of hospitalization in patients enrolled on a DMP. As a comparison we look at patients presenting for first time as Denovo diagnosis, who have not yet been enrolled on a DMP.
Methods: In an ongoing study we are prospectively enrolling patients admitted with ADHF to our unit. Patients are classified as being enrolled on a DMP or Denovo Heart Failure determined by history. Possible precipitants of decompensation are defined as follows; Infection, Arrhythmia (documented on ECG & clinically felt to be contributing),Ischemia(presence of suggestive symptoms & significant new ECG changes , with or without typical pattern of troponin release), Medication Alteration (reduction in diuretics) ,Medication Adherence (assessed using Morisky 8 point,MMAS8 scale, defining Low Adherence as score < 6) & Unknown. Adherence to immunisation advice (defined as receipt of influenza vaccine in the preceding year & receipt of pneumococcal vaccine at all in the past) was also analyzed.
Results: To date we have enrolled 46 patients (65.2% males, mean age 75.3 years, 54.35% Denovo HF). Infection was noted to be the major precipitant in both groups (Denovo 40%,DMP 28.6%).In Denovo category higher prevalence of Arrhythmia (Denovo 32% DMP 4.8%) & Ischemia (Denovo 16% DMP 9.5%) was noted.In DMP category higher prevalence of Medication Alteration (Denovo 4%, DMP 23.8%) was noted.Failure to identify a precipitant was noted in 4% Denovo & 33.3% DMP population. MMAS8 scoring classified 9.5% of the DMP group as Low Adherence.Adherence to immunisations was marginal for Influenza vaccine (Denovo 52%, DMP 71.4%) & low for Pneumococcal vaccine. (Denovo 16%, DMP 19%).
Conclusions:
Results: so far demonstrate that Infection, predominantly Respiratory, was the major precipitant of hospitalization in both groups, followed by Arrhythmia and Ischemia in Denovo & Medication alteration in the DMP group.It is encouraging to see medication adherence is not a major issue in the DMP group, reflecting good insight to HF self care, however continued under utilizations of vaccines need to be addressed through improved education and reinforcement.

P2176
Sleep disordered breathing (SDB) in heart failure with preserved ejection fraction (HFpEF) the tip of the iceberg

MA Barandiaran Aizpurua[1]; VPM Van Empel[2]; BLM Schroen[3]; M Van Bilsen[1]
[1]*Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands*; [2]*Maastricht University Medical Centre (MUMC), Cardiology , Maastricht, Netherlands*; [3]*Maastricht University, Cardiology , Maastricht, Netherlands*

Background: The prevalence of sleep disordered (SDB) in heart failure is high and is related to a poor prognosis, higher prevalence of hypertension, arrhythmias, specially atrial fibrillation, coronary artery disease and worse diastolic left ventricular function. However, there is very little known about the prevalence and effects of SDB in heart failure with preserved ejection fraction (HFpEF).
Purpose: This study aims to investigate the prevalence of SDB in the HFpEF population and the influence on the objective exercise tolerance.
Methods: From January 2015 to December 2016, 115 patients were included in the HFpEF cohort of our dedicated HFPEF out-patient clinic. SDB was screened using an ApneaLink tool. 9 patients were already diagnosed with SDB. 40 patient underwent a ApneuLink test without polisomnography (PSG), 46 patients got both, ApneuLink test and PSG and 11 patients got directly a PSG. We classified the severity of the SDB using the Apneu - Hypopneu Index (AHI): No SDB if AHI < 5 per hour, mild SDB if AHI ≥ 5, but < 15 per hour, moderate SDB if AHI ≥ 15, but < 30 per hou and severe SDB if AHI ≥ 30 per hour. We preferively used the AHI results of the PSG, but if it was not conducted we used the results of the ApneaLink test. We compared the basaline characteristics of a total of 94 patients: 53 without or with a mild SDB versus 41 patients with a moderate or severe SDB. We measured the objective exercise tolerance using the six minute walking test (6MWT).
Results: We observe that SDB patients are more frequently men (46,3% vs 20,8% p = 0,008) and have a higher body mass index (BMI) (31 vs. 28,6 p = 0,01). There are not any significant differences in the rest of co-morbidities, echocardiographic characteristics of exercise capacity.
This is the first study using ApneaLink Plus in a HFpEF population to determine the prevalence of SDB. We measured a high prevalence SDB (65,2%) in a general outpatient HFpEF population in a Dutch academic hospital. Also, this is one of the few studies investigating the influence of moderate to SDB on objective exercise tolerance in HFpEF patients. SDB is highly prevalent in a HFpEF population, but so far SDB does not seem to affect objective exercise tolerance.

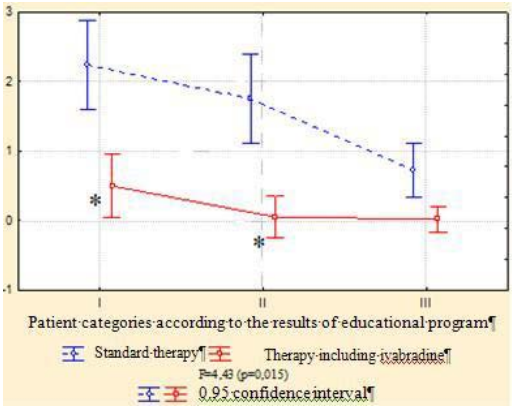
Baseline characteristics

	Totaal (n = 115)	no/mild SDB (n = 53)	moderate/ severe SDB (n = 41)	p-value
Age (years/mean)	76,1 (±6,5)	75,7 (± 7,5)	77,3 (±5,1)	0,38
Sex (% female)	78 (67,8%)	42 (±79,2%)	22 (±53,7%)	0,008
Body mass index (BMI) (kg/m^2) (mean ±SD)	30,02 (±5,3)	28,6 (±5,3)	31 (±4,07)	0,01
6MWT percentage walked (%) (median-IQR)	63,2 (44,7-75,5)	64 (54-78)	58 (45-73)	0,59

P2177
Management of patients with chronic heart failure and mid-range left ventricular ejection fraction

A K Alena Kurlianskaya[1]; T L Denicevich[1]
[1]*Research & Practical Centre "Cardiology", Minsk, Belarus*

Aim: To evaluate the effect of drug therapy including ivabradine and structured education on rates of hospitalization due to chronic heart failure (CHF) in patients with mid-range left ventricular ejection fraction (LVEF).
Methods: The study population of 93 patients with CHF I-IV NYHA and LVEF 40-49% was divided into group 1 – standard drug therapy (19 patients) and group 2 – drug therapy including ivabradine (74 patients). The intervention also included structured education of the patients. Learning capability (LC) was rated on a 4-point scale (1=poor to 4=excellent). LC and need for hospitalization due to CHF (expressed per 10 people) were investigated over 12 months.
Results: The cluster analysis specified 3 categories of patients with different LC: Category I – LC lower than 3 points at the hospital and outpatient stages of education (13 patients), Category II – LC 3-4 points after structured education (22 patients), Category III – LC 3-4 points at the hospital stage with a long learning capability of knowledge (58 patients). The average number of rehospitalizations due to CHF was lower in group 2 than in group 1 (0.8 and 9.0, respectively, P=0.028). Drug therapy including ivabradine reduced the number of readmissions of patients in Category I (Figure). The lowest need for rehospitalization was seen in Category III patients in groups 1 and 2, as well as in Category II patients in group 2: 0.7, 0.2, and 0.3 rehospitalizations due to CHF per 10 people, respectively.
Conclusions: The dynamic education of CHF patients in combination with drug therapy including ivabradine has a positive influence on the course of the disease, as evidenced by a significant decrease in the number of hospital readmissions due to CHF within 12 months.



Dependence of hospital readmission

P2178

Initial experience from a novel service for the initiation and uptitration of sacubitril/valsartan

R Richard Crawley[1]; K Guha[1]; P R Kalra[1]; G Morton[1]
[1]*Portsmouth Hospitals NHS Trust, Cardiology, Portsmouth, United Kingdom*

Background: The current ESC guidelines recommend that sacubitril/valsartan (SV) is considered for patients with ongoing symptomatic heart failure (HF), and an ejection fraction persistently ≤ 35% despite first line medical therapy. In England & Wales, SV was recently approved for use by the National Institute for Health and Clinical Excellence (NICE) after a health technology appraisal (TA388).
Purpose: We developed a novel trainee-led service to deliver SV therapy in the setting of limited resources and large numbers of potentially eligible patients.
Methods: Suitable candidates were identified by heart failure consultant cardiologists. Subsequent SV optimisation clinics were delivered by a cardiology registrar under remote supervision. Patients were optimised as per recommendations every 2-4 weeks. At every clinic visit symptomatic status, physical examination, biochemistry and clinical progress were documented. Once patients had been established on the optimal tolerated dose, their SV prescribing care was transferred to their primary care physician. The data reflect an evaluation of the service to date.
Results: 86 patients (mean age 63.1 ± 11.1 years) were initiated on SV. Mean LVEF 27.8 ± 6.5%; mean baseline eGFR 66 ± 22 ml/min/1.73m^2. Prior to initiation of SV, mean baseline ACEi/ARB dose was equivalent to 16.7 ± 6.5 mg enalapril daily. Overall 85/86 (98.8%) prescriptions of SV were compliant with ESC and NICE guidelines. 11 patients (12.8%) stopped the medication due to adverse effects (PARADIGM-HF 17.8%), whilst another 5 patients (5.8%) were down titrated to a tolerable lower dose. 15.1% of all patients experienced symptomatic hypotension (PARADIGM-HF 14.0%). No episodes of angioedema, nor significant deterioration in renal function (≥50% reduction in eGFR) were observed. Only 2 (2.3%) patients were hospitalised with decompensated heart failure symptoms, whilst 4 (4.6%) patients were admitted with syncope resulting from orthostatic hypotension.
A total of 46 patients were discharged to primary care, with a median follow up time of 42 days (IQR 25) from commencement to stable discharge dose – each requiring 1 initiation consultation and a mean of 2.3 ± 1.1 follow-up consultations. The majority of patients (33; 71.7%) were discharged at the highest dose - 97/103 mg BD. 32 (69.6%) of those discharged reported a subjective improvement in symptoms and quality of life.
Conclusions: The data support the creation of a novel trainee-led (with consultant supervision) clinical service to deliver this new added component of HF services. Cautious real-world application of the guidelines leads to many patients being safely established on high doses of SV with similar tolerability to that seen in PARADIGM-HF. However, the lower mean age within this particular population, who were carefully selected, may indicate that such findings are not representative of the entire heart failure population.

P2179

Does allopurinol have any benefit in heart failure patients without hyperuricemia?

M M Ansari-Ramandi[1]; M Maleki[1]; N Naderi[1]; A Alizadehasl[1]; A Amin[1]; S Taghavi[1]; MJ Alemzadeh-Ansari[1]; N Hadavand[1]; M Noori[1]
[1]*Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of)*

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Introduction: Heart failure (HF) is a devastating syndrome leading to hemodynamic abnormality and neuroendocrine activation which affects multiple organs. It has been shown that allopurinol, a xanthine oxidase inhibitor, may improve vascular endothelial and myocardial dysfunction. However, data are still lacking regarding the precise effects of allopurinol on HF patients without hyperuricemia.
Purpose: In this study we sought to assess whether allopurinol could improve biochemical and functional parameters of HF patients without hyperuricemia.
Methods: Thirty five patients with a diagnosis of chronic heart failure were consecutively enrolled according to the following inclusion criteria; Severe left ventricular systolic dysfunction (Ejection Fraction ≤35%), New York heart association functional class I-III, absence of hyperuricemia (above 6mg/dl for women and 6.8mg/dl for men) and presence of guideline directed medical therapies for at least 3 preceding months. Moreover, patients were kept on the same medical regimen during the study period. Patients were excluded if they had; Glomerular filtration rate of less than 60ml/min; severe hepatic failure; use of azathioprine or warfarin; known sensitivity to allopurinol. Allopurinol was administered with a dose of 300mg per day for a week and then was up titrated to 600mg per day and continued for 3 months. Study participants were asked to contact the research team whenever they had any adverse effects.
Results: Finally in this study 30 HF patients with a mean age of 49.37 ± 14.44 years old were evaluated (46.7% male and 53.3% female). No adverse effects were reported except for one case of skin rash after 4 days treatment which was excluded from the study. Four patients were also excluded from the study due to need for drug dose changes. Patients showed significant improvement in six minute walk test, average global longitudinal peak strain and laboratory parameters which are summarized in the table.
Conclusions: It can be concluded that allopurinol could be of great benefit in patients with severe LV systolic dysfunction not having hyperuricemia without significant adverse effects. Randomized clinical trials are needed in future to confirm the results.

Data at baseline and after treatment

Index	Value at baseline	Value after treatment	P value
Uric acid, mg/dl, mean (SD)	5.91 (1.34)	3.15 (0.91)	< 0.001
High sensitivity C reactive protein , mg/l, median (IQR)	4.85 (4.7-5.2)	5.05 (4.1-5.4)	0.71
N-terminal pro b-type natriuretic peptide, pg/mL, median (IQR)	979.33 (522.75-1000)	810.30 (405-895.75)	< 0.001
Average global longitudinal peak strain , %, mean (SD)	-9.38 (3.29)	-10.96 (4.4)	< 0.001
Six minute walk test, meters, mean (SD)	384.5 (81.52)	402.8 (89.61)	< 0.001

SD: Standard deviation, IQR: Interquartile range

P2180

Patient reported outcomes, health service utilisation and place of care/death for advanced heart failure patients attending a palliative cardiology clinic or receiving usual care: a feasibility study

MJ Miriam Jane Johnson[1]; P Mcskimming[2]; C Geue[2]; Y Millerick[3]; K Hogg[2]
[1]*University of Hull, Hull, United Kingdom*; [2]*University of Glasgow, Glasgow, United Kingdom*; [3]*Glasgow Caledonian University, Glasgow, United Kingdom*

Funding Acknowledgements: British Heart Foundation

Background: Trials show benefit for advanced heart failure (HF) patients receiving specialist palliative care, but is unknown if cardiology-led models of palliative care are cost-effective.
Purpose: To assess the feasibility of conducting a randomized controlled trial (RCT) testing cost-effectiveness of a palliative cardiology clinic.
Methods: A feasibility study with baseline and 4 month measures from two unmatched patient groups from: G1) cardiology-run palliative assessment and management service, G2) HF liaison service. At enrolment, G1 recruits had been seen at least once in the service.
Eligible patients had HF (LVSD/non-LVSD) and persistent symptoms. Study measures included: symptoms (Edmonton Symptom Assessment Score [ESAS]), HRQoL (KCCQ12; EQ-5D-5L), performance, understanding of disease, anticipatory care planning (ACP), health service costs and survival. Feasibility outcomes; recruitment, retention, data quality, variability/sample size estimation.
Results: 77 (G1=43; G2=34) enrolled over 8 months (53% men; mean age 77 [33 to 100]). Average G1 clinic prior attendance was 8 months. At baseline: fewer in G1

had LVSD (50% vs 97%) than G2; G1 had worse ESAS (43.5 vs 35.2) & KCCQ (35.4 vs 39.9) scores; fewer admissions/past 6 months (32.6% vs 47.1%); G1 understood their care better ($p = 0.003$); more had ACP ($p < 0.001$). All were on optimal cardiac treatment. G2 had a higher screen/consent ratio (1: 2.8 vs 1:1.7) and more 4 month attrition than G1 (29% vs 25%). Data quality was good. Estimated sample size for a future trial: 141 to detect a 1 point clinically important change in ESAS shortness of breath (80% power, 0.05 alpha).
At 4 months ESAS and KCCQ improved in G1 and G2 (change from baseline) but by more in G2, reaching statistical significance for ESAS scores, (G1: -1.5 (14.8) vs G2: -5.6 (16.6), $p = 0.046$), although between group differences were not statistically significant in a repeated measures model.
Documentation of ACP and understanding of care remained better in G1 ($p < 0.001$). There was no difference in survival between the two groups. G1 average NHS costs were lower (£785 cost saving/patient) with fewer nights in hospital, fewer nurse contacts, lower drug costs, but more GP and out-patient contacts and an average decrease in QALYs of 0.012388 (0.01235). Cost savings are likely to be underestimated given the duration of G1 clinic attendance at baseline, reflected in baseline differences in admission. The uncertainty around the findings is too great to draw definitive conclusions and must be seen as exploratory.
Conclusions: This exploratory study shows that a trial in advanced HF patients, to test the cost-effectiveness of a cardiology-driven palliative care assessment and management service using patient-report data as a primary outcome is feasible in terms of recruitment and data quality. An adequately powered trial is warranted.

P2181
Reducing hospital readmissions in heart failure patients: preliminary data from Azienda USL Toscana Centro heart failure pathway

F Grossi[1]; F Zerauschek[1]; L Zampini[1]; A Fornaro[1]; A Giomi[1]; P Francesconi[2]; F Orso[3]; M Milli[1]
[1]*Hospital of Santa Maria Nuova, Cardiology and Electrophysiology Unit, Florence, Italy*; [2]*Regional Health Agency, Florence, Italy*; [3]*Careggi University Hospital, Florence, Italy*

Background: Hospital readmission of patients suffering from heart failure (HF) is a well known problem and it requests new organizational challenges. Such patients are often elderly, with many comorbidities, poor compliance to optimal medical therapy (OMT), social issues. Data from our Regional Health Agency registry (Tuscany – Italy) shows that the percentage of HF patients that are taking OMT is still around 50%. Only 16.1% of patients receive a follow-up evaluation within 30 days after hospital discharge. Mortality from all causes at one year after discharge is to date of 12.1%.
Objectives: With the aim of reducing hospital readmissions we have identified three targets to propose improvement actions.
- Out-of-hospital setting: FAST-TRACK path (cardiology consultancy delivered within 24/72 hours).
- Hospital setting (Emergency Department): stratification of medium-high risk vs low risk HF patients according to a checklist; direct discharge for low risk patients, hospital admission in the appropriate clinical setting only for medium-high risk patients.
- Discharge and follow-up: creation of a web-based score (TAV Centro HF SCORE) to identify patients at high risk for readmission (score>15) that will receive personalized home care. We tested this program in a pilot group of Cardiology and Internal Medicine Units of our Department.
Results: Preliminary data (May-December 2016) showed: 137 consecutive patients discharged with a primary diagnosis of HF, mean age 80.95 ± 11.01 years, weight at admission 72.43 ± 14.13 kg, weight at discharge 69.02 ± 12.53 kg, NT-proBNP at admission 5343.90 ± 6237.42 pg / mL, average TAV Centro HF SCORE at discharge 9.57 ± 2.95. Only 2% of patients were identified at high risk for hospital readmission. Mean lenght of hospital-stay was 8.96 ± 7.30 days. The percentage of hospital readmission in the observation period amounted to 21.4%.
Conclusions: Preliminary results show that the improvement actions taken to reduce hospital readmissions are effective when compared to data found in literature (50% of readmissions at 12 months in EuroHeart Survey II and 30% readmissions at 12 months in IN-HF registry ANMCO). A greater sample size and the involvement of all the Cardiology and Internal Medicine Units of our Department will allow a more meaningful analysis of the clinical and managing impact of such an innovative organizational project.

P2182
Factors of improvement of physical ability after exercice training program in heart failure patients with reduced ejection fraction

E George[1]; J Costa[1]; HT Bui[1]; L Simone[1]; P Nazeyrollas[1]; D Metz[1]
[1]*Robert Debré Hospital, Reims, France*

Background: Exercice training is a fundamental part of heart failure with reduced ejection fraction (HF-REF) treatment. It reduces mortality and hospitalizations and improves functional capacities. The aim of this study was to find predictive factors of improvement of physical ability in HF-REF patients after completion of an exercise training program.
Methods: Functional, clinical, biological and echocardiographic data, were retrospectively analyzed in 50 HF-REF patients who underwent an exercice testing.
Results: Patients were 53.3 +/-12.1 years old with a mean ejection fraction of 34 +/-10% and an average of 18.7 sessions over a 4 month period was performed. Mean pre and post training MET were retrospectively 4.9 +/-1.6 and 6.1 +/-2.3 ($p < 0.001$). At the end of the training period, 22 patients displayed an improved exercise testing. Exercise testing improvement was associated with the absence of arterial hypertension (57% vs 23% $p = 0.04$), and a tendency was seen with lower furosemide daily intake (25.7mg vs 84.3mg $p = 0.05$), and lower Heart Failure Risk of Death at 1-year score (7.02% vs 10.22%). Pre-training exercice capacity was not associated with post-training improvement (4.6 +/-1.5 MET vs 5.2 +/-1.8 MET $p = 0.17$).
Conclusions: HF-REF patients without previous arterial hypertension had more chance to improve physical capacities after exercise training program. A lower furosemide daily dosage, and a lower Heart Failure Risk of Death at one-year score tend to be associated with improvement of physical abilities, so the sooner the better.

P2183
Heart failure virtual consultation - a mixed methods evaluation

J Gallagher[1]; S James[1]; C Keane[1]; A Fitzgerald[1]; B Travers[1]; E Quigley[1]; C Hecht[1]; S Zhou[1]; C Watson[1]; M Ledwidge[1]; K Mcdonald[1]
[1]*University College Dublin, Dublin, Ireland*

Background: A number of studies have identified difficulties in accessing specialist expertise and diagnostics for patiens with heart failure in the community. Modern technologies may help overcome these barriers.
Purpose: We undertook a mixed methods evaluation of a web based conferencing service (heart failure virtual consult -HFVC) between general practitioners and cardiologists in managing patients with heart failure in the community to determine its effect on use of specialist heart failure services and acceptability to general practitioners.
Methods: All cases from June 2015 to October 2016 were recorded using a standardized recording template which recorded patient demographics, medical history, medications and outcome of the virtual consult for each case. Quantitative surveys and qualitative interviewing of 17 participating GPs were also undertaken.
Results: During this time 142 cases were discussed – 68 relating to a new diagnosis of heart failure, 53 relating to emerging deterioration in a known heart failure patient and 21 relating to therapeutic issues. Only 17% required review in outpatient department following the virtual consultation. GPs reported increased confidence in heart failure management, a broadening of their knowledge base and a perception of overall better patient outcomes
Conclusion: These data from an initial experience with HFVC present a very positive impact of this strategy on the provision of heart failure care in the community and acceptability to users. Further research on the implementation and expansion of this strategy is warranted.

P2184
Rationale and design of PREFER: a prospective evaluation of natriuretic peptide based referral of chronic heart failure patients in primary care

FDR Hobbs[1]; C Vitale[2]; H Bueno[3]; B Lequeux[4]; M Pauschinger[5]; Y Pinto[6]; RI Rizwan Iqbal Hussain[7]; F Gustafsson[8]
[1]*University of Oxford, Nuffield Department of Primary Care Health Sciences, Oxford, United Kingdom*; [2]*Dermopatic Institute of the Immacolata (IRCCS), San Raffaele Pisana, Rome, Italy*; [3]*University Hospital 12 de Octubre, Department of Cardiology, Madrid, Spain*; [4]*Centre Hospitalier Universitaire, Service de Cardiologie, Poitiers, France*; [5]*Paracelsus Medical University, Department of Cardiology, Nuremberg, Germany*; [6]*Academic Medical Center of Amsterdam, Departments of Cardiology and Experimental Cardiology, Amsterdam, Netherlands*; [7]*Novartis Pharma AG, Basel, Switzerland*; [8]*Rigshospitalet - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark*

Background: Heart failure (HF) is a chronic syndrome that affects 1–2% of the population with a high mortality rate and major impact on quality of life (QoL), despite available effective treatments. In many European countries, the daily management of stable HF patients is primarily the responsibility of primary care physicians (PCPs) in collaboration with specialist consultants; however, despite well-defined guidelines for the treatment of HF, adherence to recommendations is often below par leading to sub-optimal management of patients. For this reason, strategies to improve adherence to evidence-based therapies are needed. Here, we report the rationale and design of PREFER, an international, low-interventional study in patients with

chronic HF with reduced ejection fraction (HFrEF) managed in the primary care setting across Europe.
Purpose: The primary objective of PREFER is to assess whether biomarker-guided (≥600 pg/mL N-terminal pro B-type natriuretic peptide [NT-proBNP]) referral of clinically stable HFrEF patients from PCP to a cardiologist improves treatment, as defined by increased adherence to ESC HF management guidelines. Secondary objectives include the assessment of baseline characteristics (demographic, clinical and treatment, NT-proBNP levels, and health-related QoL) of HFrEF patients managed by PCPs across Europe; the impact of patient baseline characteristics on prescribed treatment; the effect of treatment optimisation on NT-proBNP levels; and the proportion of HFrEF patients considered to be clinically stable, defined as requiring no change in HF treatment for ≥3 months prior to baseline visit.
Methods: PREFER will enrol consecutive HFrEF patients ≥18 years with left ventricular ejection fraction ≤40% attended in the PCP setting. Main exclusion criteria are primary management by a cardiologist; co-morbidities including severe renal insufficiency (estimated glomerular filtration rate [eGFR] < 25 mL/min/1.73 m^2 since severely decreased eGFR is known to increase NT-proBNP, thus avoiding this specific confounder), cerebral trauma or cancer; and major surgery, cerebrovascular incident or acute exacerbation of chronic obstructive pulmonary disease within the previous three months. The study comprises three visits over a maximum period of 10 months with patient and disease characteristics and NT-proBNP concentrations documented at Visit 1. Patients assessed as clinically stable by the PCP with NT-proBNP ≥600 pg/mL will be referred to a cardiologist. Treatment changes, health status, and vital signs will be recorded over subsequent visits; QoL will be assessed by means of EuroQol EQ-5D and Kansas City Cardiomyopathy Questionnaire (KCCQ) and NT-proBNP will also be assessed at Visit 3.
Conclusion: To conclude, we report the rationale and design of the PREFER study. Recruitment will begin in June 2016. It is expected that the study will recruit approximately 4,000 patients from a total of ˜20 European countries.

P2185

Reliability of peripheral arterial tonometry for assessment of endothelial function in patients with heart failure with preserved and reduced ejection fraction, diabetic nephropathy and arterial hyper

F Weisrock[1]; M Fritschka[2]; S Beckmann[1]; S Litmeier[1]; J Wagner[1]; D Djawid Hashemi[1]; E Tahirovic[1]; S Radenovic[1]; C Zelenak[1]; A Busjahn[3]; T Krahn[4]; B Pieske[1]; W Dinh[4]; HD Duengen[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; *[2]German Heart Institute of Berlin, Department of Cardiology, Berlin, Germany*; *[3]Health Twist, Berlin, Germany*; *[4]BAYER Pharma AG, Wuppertal, Germany*

Aims: Endothelial dysfunction plays a major role in cardiovascular (CV) diseases and pulse amplitude tonometry (PAT) offers a non-invasive way to assess endothelial dysfunction. However, data about the reliability of PAT in CV patient populations are scarce. Thus, we evaluated the test-retest reliability of PAT using the natural logarithmic transformed reactive hyperaemia index (LnRHI).
Methods and Results: Our cohort (figure 1) consisted of 92 patients (mean age: 65 ± 9.7 years, 32 % female), who were divided into four groups: those with heart failure with preserved ejection fraction (HFpEF) (n = 25), heart failure with reduced ejection (HFrEF) (n = 24), diabetic nephropathy (n = 20), and arterial hypertension (n = 23). All subjects underwent two separate PAT measurements at a median interval of 7 days (range 4-14 days). LnRHI derived by PAT showed good reliability in subjects with diabetic nephropathy (intra-class correlation (ICC) = 0.864) and satisfactory reliability in patients with both HFpEF (ICC = 0.557) and HFrEF (ICC = 0.596). However, in subjects with arterial hypertension, reliability was poor (ICC = 0.125) (figure 4).
Conclusion: We demonstrated that PAT is a reliable technique to assess endothelial dysfunction in adults with HFpEF, HFrEF or diabetic nephropathy. In subjects with arterial hypertension, we did not find high reliability, possibly related to the greater daytime and heart rate variances in this group of patients.

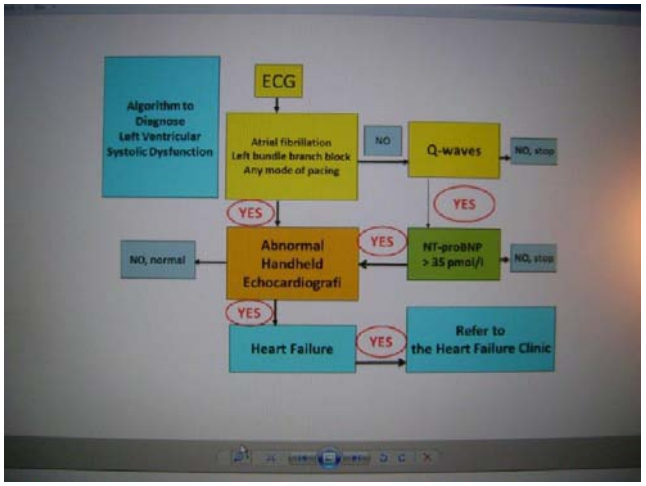
P2186

An algorithm to screen for left ventricular systolic dysfunction in the elderly, based on specific ECG-changes, NT-proBNP and handheld echocardiography

LL Olesen[1]
[1]Zealand University Hospital, Cardiology, Roskilde, Denmark

Funding Acknowledgements: The Region Zealand Research Fundation of Cross-Sectional Health Projects

Background and Introduction: Elderly 75+ are under-represented in the Danish National Heart Failure Registry, which suggests under-diagnosing and under-treatment of Left Ventricular Systolic Dysfunction (LVSD) in the elderly, especially elderly women.
LVSD may be asymptomatic or with non-specific symptoms.The clinical diagnosis is not reliable, especially in the elderly with comorbidities, and there should be looked for effective ways to screen for LVSD in the vicinity of the elderly.
Purpose: To develop a reliable objective method to screen for LVSD in the high-risk and growing geriatric population, in cooperation between the primary and the secondary health care system, to improve diagnosis and treatment of LVSD.
To extract an algorithm to screen for LVSD from previously published studies about this topic.
Methods and Results: A study performed to find a way to screen for LVSD, included 260 elderly (80 years of age (75-92)) from the community and from the local heart failure clinic. In everyone a handheld (HE) and a standard echocardiography (SE) were performed. Even though HE has limited options, HE was comparable to SE (gold standard) in diagnosing LVSD.
Sixty had LVSD and 200 did not have LVSD, and in a case-control study, LVSD was correlated with specific ECG-changes with sensitivity > 90 % and specificity > 80 %. These ECG-changes, atrial fibrillation (AFIB), left bundle branch block (LBBB) and any mode of pacing, were all associated with elevated NT-proBNP. In addition, LVSD was correlated with Q-waves combined with elevated NT-proBNP.
On this background, was evolved the illustrated algorithm to screen for LVSD.
Conclusions: LVSD seems to be under-diagnosed and under-treated in the elderly 75+, with serious consequences not only for the patients, but also for society and the health care systems.
Screening for LVSD in the growing geriatric population should have high priority, because correct diagnosis is the cornerstone of effective treatment, which can reduce symptoms, morbidity and mortality and the overall societal burden of this serious disorder.
The present study suggests a new LVSD-screening-algorithm.
This algorithm recommends that, when LVSD is under suspicion, due to AFIB, LBBB or pacing, or Q-waves combined with elevated NT-proBNP, a handheld echocardiography should be performed. In case of LVSD, the local heart failure clini c should treat the patient and find the cause of LVSD, including a standard echocardiography.
Further studies are needed to validate this algorithm.



Algorithm to screen for LVSD

P2187

Association of serum ADAM-10 with cognitive function in patients with stable chronic heart failure

S M Sonja Maria Wedegaertner[1]; S Selejan[1]; J Karbach[2]; M Boehm[1]; I Kindermann[1]
[1]Saarland University Hospital, Department of Internal Medicine III, Cardiology, Angiology and Intensive Care Medicine, Homburg, Germany; *[2]JW Goethe University, Department of Psychology, Frankfurt am Main, Germany*

Background/Purpose: Patients with stable heart failure show cognitive impairments associated with adverse events like higher mortality rates, worse quality of life, poorer drug adherence, and increased hospitalization rates. Possible pathophysiological causes are cerebral hypo-perfusion and multiple cardiogenic emboli, however the underlying mechanisms are still not fully understood. ADAM-10 (A Disintegrin and Metalloproteinase-10) prevents the generation of neurotoxic amyloid ß peptide and has been described to be reduced in patients with Alzheimer´s Disease. The purpose of the study is to investigate the relation of serum circulating ADAM-10

to the cognitive functioning in patients with chronic heart failure.
Methods: In a cross-sectional study (patients with stable chronic heart failure, n=13, mean age=66.77 years, SD=9.87, 15.4 % females, 54 % ischemic cardiomyopathy, left ventricular ejection fraction ≤ 45 %, NYHA classification II-III), serum levels of ADAM-10 were assessed by Western blot and densitometric analysis and compared to healthy age-matched controls (n = 13). Cognitive abilities (attention, processing speed, executive control, working memory, and intelligence) were assessed in heart failure patients using validated psychological instruments (Frankfurt Attention Inventory [FAIR], Digit Symbol Substitution Test, Stroop Test, Digit Span, Corsi Block Tapping Task, Matrix Reasoning [Wechsler Adult Intelligence Scale]).
Results: Serum ADAM-10 activity was decreased in patients with chronic heart failure as compared to healthy controls (-44 % decrease). Additionally, ADAM-10 protein levels showed a negative correlation (p = 0.03; r=-0.6) with cognitive abilities like attention as assessed by the FAIR in patients with chronic heart failure.
Conclusion: A reduction of ADAM-10 activity might promote neurotoxic processes in patients with chronic heart failure resulting in further cognitive deterioration in these patients.

P2188
Assessment of syndecan-4 expression in the hearts of mice and human subjects with chronic chagas cardiomyopathy

C Macedo[1]; TF Larocca[1]; BS Souza[1]; CM Azevedo[1]; JF Vasconcelos[1]; DC Portella[1]; F Tavora[2]; JD Lima[2]; RR Santos[1]; MBP Soares[1]
[1]Sao Rafael Hospital, Center for Biotechnology and Cell Therapy, Salvador, Brazil; *[2]Hospital de Messejana Dr Carlos Alberto Studart Gomes, Fortaleza, Brazil*

Background: The hallmark of chronic Chagas cardiomyopathy (CCC) is the presence of a multifocal inflammatory reaction, which leads to myocardial fibrosis, often followed by ventricular dysfunction and arrhythmias. The expression of syndecan-4, a transmembrane protein, is increased in the hearts of mice chronically infected with Trypanosoma cruzi, suggesting a role of this protein in the pathogenesis of CCC.
Purpose: Here we aimed to evaluate the pattern of expression of syndecan-4 in heart tissue of mice and subjects with Chagas cardiomyopathy and to correlate with the degree of inflammation and fibrosis.
Methods: First we evaluated the expression of syndecan-4 in the hearts of mice at different time points after infection. C57BL/6 mice (n = 5 per group) were infected by intraperitoneal route with Colombian strain T. cruzi and the heart tissue was evaluated and compared to uninfected controls. We also compared the expression of syndecan-4 in sixty samples of explanted human hearts of subjects with CCC, idiopathic dilated cardiomyopathy (idDCM) and ischemic cardiomyopathy (ICM). Samples were analyzed by confocal microscopy to determine the expression pattern of syndecan-4. Inflammation and fibrosis were evaluated by morphometric analysis.
Results: Syndecan-4 expression was increased after the acute infection and was sustained during the chronic phase, and did not correlate with the intensity of inflammation or fibrosis. Confocal microscopy analysis showed syndecan-4 expression mainly by vascular smooth muscle cells. Confocal microscopy analysis of fragments of explanted human hearts showed a similar pattern of syndecan-4 expression. No correlation between syndecan-4 expression and inflammation or fibrosis was found in the hearts from subjects with CCC. We also compared the expression of syndecan-4 of subjects with CCC, idiopathic dilated cardiomyopathy (idDCM) and ischemic cardiomyopathy (ICM). No differences in the number of syndecan-4 positive vessels/mm2 were found comparing the three subject groups (P=0.466), whereas a statistically significant difference in inflammation was seen (P=0.035). Additionally, no correlation between syndecan-4 and fibrosis or inflammatory cells was found.
Conclusion: We conclude that there is no evidence of correlation between either the degree of myocardial fibrosis or the number of inflammatory cells and syndecan-4 expression. Additional studies are required to determine its role in Chagas disease.

P2189
Analysis of mirna alterations in subjects with chronic chagas disease cardiomyopathy

C Carolina Macedo[1]; CK Nonaka[1]; TF Larocca[1]; BS Souza[1]; MN Rabelo[2]; LC Correia[2]; MI Moreira[2]; A Caldas[2]; JA Torreao[2]; RR Santos[1]; MBP Soares[1]
[1]Sao Rafael Hospital, Center for Biotechnology and Cell Therapy, Salvador, Brazil; *[2]Sao Rafael Hospital, Salvador, Brazil*

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Background: Chagas disease is an anthropozoonosis caused by the flagellate protozoan Trypanosoma cruzi and is considered to be one of the major causes of death due to heart failure in Latin America. To date, there is no effective treatment for chronic Chagas disease. The biological role of microRNAs in the mammalian cardiovascular system has become a rapidly evolving field of research. Several studies in humans and animal models have shown that microRNAs are differentially expressed in heart failure and play a critical role in the pathogenesis of the disease.
Purpose: The objective was to evaluate the expression of different microRNAs in Chagas disease subjects and to investigate possible associations with clinical evaluation.
Methods: This study investigated the expression of 88 microRNAs in serum obtained from eight Chagas disease subjects, selected from a database of the outpatient clinics at Hospital (Brazil). As controls, four healthy subjects, with negative serology for Chagas disease, were selected. The Pick-&-Mix Custom microRNA qPCR Panels (Denmark) was used. MicroRNAs were selected based on the clinical profile of Chagas disease cardiopathy, characterized by inflammation and fibrosis. The 7500 Fast Real-Time PCR (ThermoFisher) was used under standard thermal cycling conditions. Data was analysed using threshold cycle (2-ΔΔCt) method and STATA statistical software.
Results: Of the analyzed microRNAs, 28 presented statistical significance ($p < 0.05$) in relation to healthy individuals. Of these, 22 miRNAs were down-regulated and 6 of them amplified only in the control group. We performed analysis of correlations between the miRNAs and clinical and imaging parameters, such as standard two-dimensional and strain by speckle tracking echocardiography, myocardial fibrosis by nuclear magnetic resonance, NT-ProBNP and galectin levels and Rassi score. Analysis miR-29b and miR-29c showed a negative association with longitudinal global strain only for miR-29c ($r = -0.7553$, $p < 0.05$). In the miR-30 family, miR-30d showed a tendency of a negative association with fibrosis ($r = -0.7115$, $p < 0.07$), whereas miR-30c had a negative association with longitudinal global strain ($r = -0.8308$, $p < 0.05$). We did not find any correlations between miRNAs the other clinical and imaging parameters.
Conclusion: Preliminary data suggest the correlation of miR-29c and miR-30c with longitudinal global strain measurement in Chagas disease. The investigation of the expression from these miRNAs in a larger group of chronic chagasic subjects, as well as in subjects with the indeterminate form is currently being performed in order to expand and validate the results.

P2190
Sex-related differences in the systolic function in the setting of acute coronary syndrome

N Semerdzieva[1]; S Denchev[2]; S Dimitrov[3]; M Gospodinova[2]; J Hristova[4]; A Kundurdziev[5]
[1]University Hospital Alexandrovska, Clinic of Cardiology, Sofia, Bulgaria; *[2]Medical Insitute of the Ministry of Internal Affairs, Clinic of Cradiology, Sofia, Bulgaria*; *[3]Second MHAT, Department of Invasive Cardiology, Sofia, Bulgaria*; *[4]Medical University of Sofia, Central Clinical Laboratory, Sofia, Bulgaria*; *[5]Medical University of Sofia, Faculty of Public Health, Sofia, Bulgaria*

Sex-related characteristics of acute coronary disease may contribute to the contrast in heart failure incidence between men and women. We examined the relation of severity of coronary atherosclerosis and inflammatory response to sex-related differences in the myocardial contractile function during acute coronary syndrome (ACS) and after six-month follow-up. Three hundred and twenty one patients (48% women) with ACS were included. They had their acute and chronic phase left ventricular ejection fractions (EF1; EF2), end-systolic and end-diastolic indexed to body surface area volumes (ESVI1; EDVI1; ESVI2; EDVI2) assessed with 2D-echocardiography. Echocardiography at the sixth month - available in 147 (45.8%). Other methods used: immunoturbidimetry - for high-sensitive C-reactive protein, hsCRP; coronary angiography with SYNTAX score calculation - performed in 282 (87.6%). Men had worse systolic function in the acute phase ($55.3 \pm 10.3\%$ vs $58.8 \pm 10.9\%$, $p = 0.001$ for EF1; 29.6 ± 14.9 ml vs 24.5 ± 11.7 ml, $p < 0.0001$ for ESVI1; 65.9 ± 19.1 ml vs 60.6 ± 14.7 ml, $p = 0.013$ for EDVI1) and at the sixth month (33.8 ± 18.8 ml vs 27.1 ± 13.3 ml, $p < 0.0001$ for ESVI2). Inflammatory markers correlated positively with all enzymes of myocardial necrosis. Higher SYNTAX scores of men had a closer association with the myocardial necrosis severity and the contractile function deterioration in acute and chronic phase compared to women. Higher WBC were significantly related to lower EF regardless of sex and increased hsCRP levels - to worse EF and ESVI at the time of ACS and during follow-up only among men (table 1). The severity of coronary atherosclerosis and of the acute inflammatory response contribute in lesser degree among female than among male patients to the systolic function decline after ACS.

P2191
A study of coronary flow response to nitroglycerin in patients with slow coronary flow syndrome and other types of non-obstructive coronary disease having diastolic dysfunction

N Semerdzieva[1]; S Denchev[2]; S Dimitrov[3]; M Gospodinova[2]
[1]University Hospital Alexandrovska, Clinic of Cardiology, Sofia, Bulgaria; *[2]Medical Insitute of the Ministry of Internal Affairs, Clinic of Cradiology, Sofia, Bulgaria*; *[3]Second MHAT, Department of Invasive Cardiology, Sofia, Bulgaria*

P2190						
Group	Male patients	Female patients				
Indices	hsCRP	WBC	SYNTAX score	hsCRP	WBC	SYNTAX score
CPK	r=0.305,p = 0.004	r=0.356,p < 0.0001	r=0.202,p = 0.025	r=0.262,p = 0.025	r=0.363,p = 0.001	r=0.038,p = 0.708
CPK-MB	r=0.377,p < 0.0001	r=0.422,p < 0.0001	r=0.168,p = 0.064	r=0.208,p = 0.077	r=0.350,p = 0.001	r=0.064,p = 0.002
hsTnT	r=0.307,p = 0.004	r=0.376,r < 0.0001	r=0.271,p = 0.004	r=0.299,p = 0.011	r=0.332,p = 0.002	r=0.304,p = 0.002
EF1	r= - 0.257,p = 0.012	r= - 0.236,p = 0.014	r= - 0.441,p < 0.0001	r= -0.145,p = 0.209	r= - 0.290,p = 0.005	r= - 0.452,p < 0.0001
ESVI1	r=0.217,p = 0.044	r=0.154,p = 0.131	r=0.304,p = 0.001	r=0.252,p = 0.697	r=0.155,p = 0.632	r=0.394,p = 0.050
EDVI1	r=0.193,p = 0.077	r=0.231,p = 0.169	r=0.465,p = 0.001	r=0.052,p = 0.001	r= - 0.057,p = 0.697	r=0.372,p = 0.050
EF2	r= - 0.334,p = 0.018	r= - 0.294,p = 0.036	r= - 0.407,p = 0.002	r= - 0.267,p = 0.116	r= - 0.331,p = 0.040	r= - 0.317,p = 0.032
ESVI2	r=0.292,p = 0.057	r=0.188,p = 0.232	r=0.186,p = 0.038	r=0.056,p = 0.755	r=0.048,p = 0.789	r=0.243,p = 0.008
EDVI2	r=0.175,p = 0.293	r=0.231,p = 0.169	r=0.271,p = 0.004	r=0.392,p = 0.011	r=0.026,p = 0.889	r=0.247,p = 0.141

Backgroud: Nitroglycerin (NTG) induces extremely slow coronary flow and angina in patients with microvessel dysfunction and normal coronary angiograms. The coronary slow flow syndrome (SCFS) is an angiographic finding characterized by delayed distal vessel opacification in the absence of significant epicardial coronary and myocardial disease.

Purpose: The object of our study was assessment of the response of coronary blood flow to intracoronary injection of NTG in patients with non-obstructive coronary atherosclerosis (including SCFS) with diastolic dysfunction.

Methods: The study included 143 patients: 66 - with SCFS and other 77 – with non-obstructive coronary disease, NCAD (coronary plaques causing < 50% stenoses). The following myocardial perfusion indices defined during selective coronary angiography, SCA (at baseline and after intracoronary administration of 100-200 μg of NTG) were employed: corrected TIMI frame count (cTFC) – assessed in 140 (97.9%) patients; propagation of contrast medium in coronary artery in systole (CPs – 63.6%, n=91) and propagation velocity of contrast in systole (Vcps – 62.9%, n=90). Diastolic dysfunction was defined based on Doppler echocardiographic evaluation of mitral flow and tissue Doppler imaging.

Results: Diastolic dysfunction of impaired relaxation type was found with nonsignificant difference between NCAD and SCFS patients (15.6 % (n = 12) versus 9.1% (n = 6), p = 0.061).

At baseline coronary flow in SCFS was impaired compared to other patients with NCAD (cTFC 37.7 ± 11.9 vs 28.2 ± 13.6 frames, p < 0.0001; a trend for CPs 18.4 ± 9.4 vs 22.6 ± 12.3, p = 0.077). Additional analysis demonstrated impairment of coronary flow after NTG (considerable for Vcps; a trend for CPs) only in the group with non-obstructive coronary disease (including SCFS) having diastolic dysfunction (table 1).

Conclusion: NTG reduces myocardial blood supply in non-obstructive coronary disease with diastolic dysfunction. It should not be given for angina relief to patients without proven on angiography significant coronary stenoses.

SCFSNCAD	No diastolic dysfuntion	With diastolic dysfunction	P value
cTFC, frames (n = 58/18)	31.1±14.0	31.0±10.4	0.982
CPs, mm (n = 52/15)	21.3±10.7	19.5±10.1	0.557
Vcps, mm/s (n = 52/15)	61.3±30.7	52.2±31.2	0.317
After i.c. NTG	No diastolic dysfunction	With diastolic dysfunction	P value
cTFC, frames (n = 59/18)	32.0±16.8	30.7±9.0	0.765
CPs, mm (n = 52/15)	20.3±13.3	13.2±11.7	0.069
Vcps, mm/s (n = 52/15)	58.9±40.9	34.5±36.0	0.040

ATRIAL FIBRILLATION

P2192

The adequacy of antithrombotic therapy in patients with atrial fibrillation in Uzbekistan

NU Zakirov[1]; RD Kurbanov[1]; TZ Tohir Ganiyev[1]; DB Irisov[1]

[1]*Specialized Cardiology Center of the Republic of Uzbekistan, Cardiac arrhythmia, Tashkent, Uzbekistan*

Background: Epidemiological studies on atrial fibrillation (AF) and prevention of thromboembolism have not been conducted in Uzbekistan (Central Asia).

Objective: To assess the pre-hospital antithrombotic therapy (ATT) in patients with AF, according to the ESC recommendations.

Material and Methods: We retrospectively analyzed the medical data of patients, who were discharged from specialized center of cardiology between 01.10.15 and 30.11.15. The thromboembolic events and bleeding risks were assessed by CHA2DS2-VASc and HAS-BLED scores, respectively.

Results: Among 1298 patients, AF was detected in 161 (12.4%, mean age 65.3 + 8.7 years), of these 75(44.6%) men. In 129 (80.1%) patients were identified non-valvular and in 32 (19.9%) valvular AF. Paroxysmal AF was detected in 45 (28%), persistent in 19 (11.8%) and permanent in 97 (60.2%) patients. Hypertension 1-3 degree was detected in 67.1% of patients (n = 108), heart failure 2-4th FC by NYHA in 69.6% (n = 112), diabetes in 14.9% (n = 24). History of thromboembolism or TIA were present in 9.3% patients (n = 15) and peripheral vascular disease identified by ultrasonography of artery (major and peripheral vessels) in 54.6 % (n = 88). At the time of admission HAS-BLED score > 3 were identified in 13.7 % (n = 22) of patients and the mean HAS-BLED score was 1.7 + 1.2 and CHA2DS2-VASc score was 4.1 + 1.5. At pre-hospital period, ATT was indicated to 157 (97.5%) patients, (125 patients according to CHA2DS2-VASc score). It was found that 28% (n = 45) of patients did not take any ATT. There weren't any patients treated with new oral anticoagulants (NOACs). Only 31.7% (n = 51) of patients received warfarin. Compliance of anticoagulant therapy in patients with valvular AF were superior to non-valvular AF patients (50% vs 21.7%, respectively, p < 0.037). Only 2.5% (n = 4) of patients received aspirin and clopidogrel in combination. 37.9% (n = 61) of patients received antiplatelet agents as a monotherapy. Among patients receiving warfarin INR control from 2.0 to 3.0 revealed only in 7 (13.7%), at the same time 7 (13.7%) patients had an INR > 3 at the time of admission.

Conclusion: Despite, high risk of thromboembolic events and low bleeding risk, 28% of patients with AF did not take any ATT at the time of admission. There weren't any patients treated with NOACs. Only 31.7% of patients requiring anticoagulation, receive warfarin regularly and compliance to anticoagulant therapy was significantly superior in patients with valvular AF. Totally, 4.4 % of patients who had indicated ATT, receive warfarin in selected dose (INR 2.0-3.0) for optimal prevention of thromboembolic events according to ESC recommendations.

P2193

Predictive markers of atrial remodeling and role of PA-TDI duration and NT-proBNP in the assessment of atrial fibrillation reccurences

T Tea Gegenava[1]; M Gegenava[1]

[1]*Tbilisi State Medical University, Tbilisi, Georgia Republic of*

Introduction: Total atrial activation time has been identified as an independent predictor of new-onset atrial fibrillation (AF). Echocardiographic assessment of PA-TDI duration provides an estimation of total atrial conduction time.Recently total atrial conduction time (Total atrial conduction time measured by tissue doppler (PA-TDI duration) has been shown to be predictive marker of atrial remodelling. Pre-procedural assessment of the extent of atrial remodelling could be used to identify patients with a high risk of AF recurrence. Purpose of the present study was to measure and identify new predictors of AF occurrence: PA-TDI duration, also left atrial (LA) volumes, LA function in patients after radiofrequency catheter ablation and with heart failure and elevate level of Natriuretic peptid- NT-proBNP who had undergone ICD implantation.

Methods: we assessed n=80 patients, among them n=65 patients with atrial fibrillation-AF paroxysmal and persistent forms of AF without structural changes and normal NT-proBNP in pre- and post- operative periods of RFCA and electrical and pharmacological cardioversion and n=15 patients with AF with structural

heart disease and elevated level of NT-proBNP with mild to severe heart failure symptoms scheduled for ICD implantation. The PA-TDI duration was assessed by measuring the time interval between the onset of the P-wave in lead II of the surface ECG and the peak A-wave on the tissue Doppler tracing. A long PA-TDI duration corresponded to a long total atrial conduction time. In all patients we performed 24h holter monitoring. Results: an increased total atrial conduction time (PA-TDI > 119ms, mean PA-TDI 139-189) was associated with poor outcome and complications such as symptoms of heart failure $P < 0.001$ and reccurences after RFCA $p < 0.001$ and reccurences after cardioversion in all subgroups -in patients with atrial fibrillation with or without structural heart changes. Increased PA-TDI duration also correlated with NT-proBNP level in patients with heart failure symptoms. It was found correlation between LA size and PA-TDI duration $p < 0.001$, but In 35% of the patient without LA enlargment and prolonged PA-TDI duration we also found AF Reccurences.
Conclusions: An increased PA-TDI duration can be independently associated with AF reccurrence in heart failure patients with history of AF who had undergone ICD implantation and this parameter correlates with elevated NT-proBNP.

P2194
long term outcome of pulmonary vein isolation for atrial fibrillation in patient with left ventricular dysfunction.

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

Pulmonary vein isolation (PVI) is one of the effective option of atrial fibrillation (AF) treatment. The effectiveness of PVI for AF patient with left ventricular dysfunction was reported, but mid to long term outcome is still unidentified. The purpose of this study is to evaluate the mid to long term effectiveness of PVI for AF patient with left ventricular dysfunction.
Methods: Total 828 sessions of PVI for 609 cases were performed in our institute since 2003 to 2015, left ventricular dysfunction, which was defined as left ventricular ejection fraction (LVEF) under 50%, was complicated with in 96 cases. We retrospectively analyzed the patient's characteristics and outcomes in those cases. Results: The average observation period after PVI was 32.7 +/- 25.0 months, longest term was 93 months. The maintenance rate of sinus rhythm was 93.7% (87 cases), 36.8% of those (32 cases) was still under rhythm control treatment. Left atrium dimension (LAD) and left ventricle end systolic volume (LVESV) at least three years after PVI reduced significantly in comparison with pre-procedure (LAD 43.9 + /-7.7 to 40.8 + /-6.3mm ; $p = 0.01$, LVESV 66.8 + /-34.0 to 51.7 + /-27.3ml ; $p = 0.0001$), and LVEF was significantly improved, too(38.9 + /-9.8 to 57.5 + /-14.6 ; $p < 0.00001$). Conclusions: The PVI for AF patient with left ventricular dysfunction contributes to left atrial and left ventricle remodeling, and outcomes are excellent.

P2195
Relation between ventricular-arterial coupling parameters, left atrial remodeling and recurrences of atrial fibrillation in hypertensive patients with preserved left ventricular systolic function

A Shavarov[1]; EV Kokhan[2]; GK Kiyakbaev[1]; VS Moiseev[1]
[1]*RUDN University, Moscow, Russian Federation*; [2]*Lomonosov Moscow State University, Moscow, Russian Federation*

Background: Deterioration of the left ventricular-arterial coupling (VAC) might play a key role in the development of diastolic dysfunction and therefore structural and functional changes of the left atrium (LA). But the data concerning the relationship between VAC parameters and atrial fibrillation (AF) is scarce.
Purpose: To evaluate the relation between VAC parameters, structural and functional changes of the LA and their predictive value for AF recurrence in hypertensive patients with paroxysmal or persistent AF and preserved left ventricular systolic function.
Methods: The study included sixty hypertensive patients [45% male, median age 65 (61; 72) years] with recurrent non-valvular AF and preserved left ventricular systolic function. A group of 30 patients received 200 mg of amiodarone + 50 mg of metoprolol daily, while another group, also consisting of 30 patients, received 160 mg of sotalol daily. All the patients underwent conventional and speckle tracking echocardiography. Global peak LA longitudinal strain (PALS) and strain rate (PALSR) in the reservoir (r) and contractile (c) phases were assessed using 6 segments in the 4-chamber and 2-chamber views. To estimate VAC EaI, EesI, Ea/Ees and also systemic vascular resistance index and total arterial compliance (TAC) were calculated. Follow-up period was 3 months.
Results: Significant relation between EaI and LA size ($r=0.38$, $p = 0.003$), LA end diastolic volume ($r=0.33$, $p = 0.009$) and PALSc ($r=-0.31$, $p = 0.02$) were found. Other VAC parameters were not associated with changes of the LA. 35 (58%) patients maintained sinus rhythm (group 1) throughout the follow-up period, whereas 25 (42%) patients (group 2) experienced at least one AF recurrence. Despite having comparable LA volume index, the patients of group 1 had significantly higher PALSr (15.7 vs 12.6, $p = 0.004$), PALSc (-16.2 vs -13.9, $p = 0.008$), PALSRr (2.44 vs 1.76, $p < 0,001$), PALSRc (-2.4 vs -1.66, $p < 0.001$), TAC (1.26 vs 1.08, $p = 0.04$), whereas Ees corrected by left ventricular mass was higher in group 2 (619 vs 803, $p = 0,004$). Stepwise multiple regression analysis showed a significant association between PALSRc and the efficacy of antiarrhythmic therapy (β=0.38, $p = 0.04$).
Conclusion: Despite the fact that TAC and Ees corrected by left ventricular mass were significantly different between the two groups, they had no predictive value in AF recurrence. PALSRc was the only independent parameter associated with AF recurrence.

P2196
Russian observational survey of heart failure patients with atrial fibrillation (RIF-CHF): clinical characteristic of patients

N Romanova[1]; IV Zhirov[1]; SN Tereshchenko[1]; YUF Osmolovskaya[1]; SP Golitsyn[1]
[1]*Cardiology Research and Production Center, Moscow, Russian Federation*

Background: Atrial fibrillation and heart failure frequently coexist. Both conditions are risk factors for stroke, systemic embolism, and when combined have much worse outcomes. Data on clinical characteristic and compliance with clinical guidelines for heart failure patients with atrial fibrillation in Russian Federation is limited.
Methods: We conducted a registry of consecutive in- and outpatients with heart failure and atrial fibrillation from 38 medical centers in different regions of the Russian Federation. All patients had ECG-documented diagnosis of atrial fibrillation and heart failure. Patients with preserved ejection fraction (≥40%) were eligible for study if they had level of BNP or NT-proBNP larger then100 pg/ml or 300 pg/ml, respectively.
Results: A total of 1003 patients (57% men, mean age 67 years) with heart failure and atrial fibrillation were included in this study between February and December, 2015. Ejection fraction more than 40% was present in 54,8% of patients. In our registry 45,4% of patients had NYHA Class II, 45,7% had NYHA Class III and 8,9% - NYHA Class IV. The commonest associated comorbidities were coronary heart disease (68,9%), hypertension (65%), diabetes mellitus type 2 (26%), previous stroke or TIA (23%) and chronic kidney disease (12,9%). Of the whole cohort, 56,8% of patients had permanent atrial fibrillation, 27 and 9,4 % had paroxysmal and persistent atrial fibrillation, respectively. Of the whole cohort, the mean CHA2DS2-VASc score was $4,2 \pm 1,74$ and the mean HAS-BLED was $1,68 \pm 1,12$. High risk of thromboembolism (CHA2DS2-VASc score ≥ 3) had 77,6% of patients. Oral anticoagulants were used in 81% of patients with CHA2DS2-VASc = 1; 69% patients with CHA2DS2-VASc = 2 and only 58% in CHA2DS2-VASc score ≥ 3.
Conclusions: Based on current guidelines, oral anticoagulation is recommended for the vast majority of patients with heart failure and atrial fibrillation. Compliance with the treatment guidelines for patients with higher stroke risk scores remains suboptimal.

P2197
Management of atrial fibrillation in heart failure

AL Gamez Lopez[1]; JL Bonilla Palomas[1]; MC Lopez Ibanez[1]; M Moreno Conde[1]; Y Pimentel Quezada[1]; A Villar Raez[1]
[1]*Hospital San Juan de la Cruz, Úbeda, Spain*

Background: There are no specific recommendations for the management of patients with heart failure (HF) and atrial fibrillation (AF), not knowing if the management of these patients is similar to that done in patients without HF diagnosis.
Purpose: Describe the characteristics and management of AF in patients with or without HF.
Methods: Observational and prospective study on patients with AF, analyzing differences in the diagnostic and therapeutic approach among patients with or without HF. Sociodemographic, clinical, analytical and echocardiographic variables were collected, and a comparative analysis of the same was performed between both groups.
Results: A total of 915 patients were analized, 144 with HF (15,7%) and 771 without HF (84,3%). No differences between groups were observed in: age, sex, CHADSVASC, HASBLED, renal function, hemoglobin, hypertension or previous bleeding events. The percentage of diabetic patients was higher in the group of patients with HF (39.6% vs 21.9%, $p < 0.001$), with these patients having a larger left atrium size (left atrial area in apical four chamber view: 30,9 vs 26,9 cm2, $p = 0,045$). The rhythm control was used less frequently in patients with HF (2.2% vs 12.6%, $p < 0.001$). Beta-blockers (78.3% vs 58.3%, $p < 0.001$) and digoxin (23.4% vs 12.7%, $p = 0.002$) were more frequently used in patients with FH, with less use of antiarrhythmic drugs in this group (5,7% vs 13,4%, $p = 0,008$). When antiarrhythmic drugs were employed, amiodarone was used in 100% of patients with HF. The most frecuent antiarrhythmic drug in AF without HF was flecainide (46%) followed

by dronedarone (26%) and amiodarone (25%). No differences between anticoagulated patients (90,6% vs 91,7% p = 0,387) or type of anticoagulation prescribed (AVK: 65,7 vs 67%; NOAC :34% vs 33%, p = 0,765) were observed.
Conclusions: Patients with AF and HF are more frequently diabetic and have a larger atrial size. In them the rhythm control strategy is used less frequently, being the antiarrhythmic of choice amiodarone with a greater use of beta-blockers and digoxin.

HYPERTROPHIC CARDIOMYOPATHY

P2198
Predictors of ICD-related adverse events in patients with hypertrophic cardiomyopathy

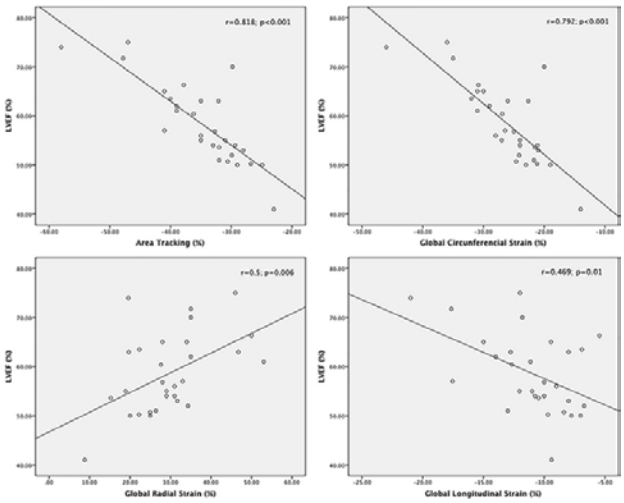
C Cedric Klein[1]; A Duva Pentiah[1]; D Klug[1]; C Marquie[1]; S Ninni[1]; H Blangy[2]; PC Flechon[2]; N Sadoul[2]; P De Groote[1]
[1]Lille University Hospital, Institut Cœur Poumon, Lille, France; *[2]Hospital Brabois of Nancy, Vandoeuvre les Nancy, France*

Background: Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac death in young patients. Implantable cardioverter-defibrillator (ICD) therapy may be considered in HCM patients at high risk of ventricular arrhythmia.
Aims: To determine predictive factors of transvenous ICD-related adverse events in HCM patients.
Methods: All patients with HCM referred for ICD implantation in two French tertiary centres between May 1992 and August 2016 were retrospectively included. Clinical, electrocardiographic and echocardiographic data were obtained from electronic medical records. 'ICD-related adverse event' was defined as the combination of inappropriate shock and/or other complication related to the device (infection, access-, generator- or lead-related complication).
Results: A total of 177 patients were included. Median follow-up was 45.6 months. One hundred and fifty-six patients received a transvenous-ICD (TV-ICD) and 21 a subcutaneous-ICD. Among the whole cohort, 46 patients (26%) experienced at least one appropriate therapy. Among TV-ICD group, inappropriate shocks occurred in 27 patients (17%) and 41 patients (26%) experienced a total of 51 complications including 14 lead fractures and 7 infections. In multivariate analysis, history of atrial flutter (HR=12.5 [2.3-67.2], p = 0.003), unexplained syncope (HR=5.5 [2.0-15.4], p = 0.001) and young age (HR=0.956 [0.930-0.983], p = 0.001) were associated with TV-ICD-related adverse event. Among S-ICD group, inappropriate shocks occurred in 2 patients (8%) during a follow-up of 12.0 months. After adjusting for year-implantation, no difference was found between TV-ICD and subcutaneous-ICD in terms of device-related adverse events.
Conclusion: We identified three simple and readily available variables that are associated with TV-ICD-related adverse events in HCM patients at high risk of SCD. Considering the model performance in this population, it should be validated in a larger cohort.

P2199
Impact of hypertrophy in left ventricular ejection fraction and myocardial strain: application of three-dimensional wall-motion tracking technology in hypertrophic cardiomyopathy

L Marques[1]; N Moreno[1]; H Guedes[1]; R Santos[1]; A Pereira[1]; D Seabra[1]; R Sousa[1]; P Pinto[1]
[1]Centro Hospitalar do Tâmega e Sousa, EPE, Cardiology Department, Penafiel, Portugal

Introduction: Hypertrophic cardiomyopathy (HCM) is morphologically characterized by a thickened, non-dilated, left ventricle (LV). Myocardial mass seems to be related to deformation parameters, and some authors suggest that circumferential strain, as assessed by three-dimensional (3D) techniques, may be the major component in the maintenance of a normal systolic function in HCM. However, more data are needed to confirm the reliability and reproducibility of 3D strain evaluation in HCM.
Purpose: Using three-dimensional wall-motion tracking (3DWMT) echocardiographic technique, we aimed to assess the impact of indexed myocardial mass in LV ejection fraction (LVEF) and in deformation parameters in a cohort of HCM patients. We also aimed to assess the impact of individual deformation components in LVEF, as assessed by 3DWMT
Methods: Thirty-five (35) HCM patients underwent standard bi-dimensional (2D) echocardiography, followed by 3DWMT evaluation. Using Toshiba Artida echocardiography equipment (Toshiba Medical System), global strain values were obtained for each component [global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), area tracking (AT)], as well as LV indexed mass and LVEF. Six patients (17%) were excluded from LVEF analysis. Statistical analysis was performed using Statistics Version 22; the correlations between continuous variables were established by linear regression.
Results: We found no significant correlation between LV indexed mass and LVEF (p = 0.497). Only GLS exhibited a significant correlation with LV indexed mass (r=0.375, p = 0.029). All strain components were correlated with LVEF (AT: r=0.818, p < 0.001; GCS: r=0.792, p < 0.001; GRS: r=0.500, p = 0.006; GLS: r=0.469, p = 0.01) (Figure 1). The strongest correlations were found with AT (r=0.818, p < 0.001) and GCS (r=0.792, p < 0.001)
Conclusion(s): In HCM patients, increased myocardial mass is associated with a decreased GLS, but not with a decreased LVEF. Global circumferential strain and AT exhibited a strong correlation with LVEF, and seem to be important components in LV function preservation. Three-dimensional wall motion tracking technology appears to be a useful tool in evaluation of HCM patients, allowig detection of subclinical dysfunction and providing new insights into LV mechanics.



P2200
Assessment of left ventricular strain by three-dimensional wall-motion tracking technology: a study in hypertrophic cardiomyopathy

L Marques[1]; N Moreno[1]; H Guedes[1]; R Santos[1]; A Pereira[1]; D Seabra[1]; R Sousa[1]; P Pinto[1]
[1]Centro Hospitalar do Tâmega e Sousa, EPE, Cardiology Department, Penafiel, Portugal

Introduction: Hypertrophic cardiomyopathy (HCM) is a genetic disease with an autosomal dominant pattern of transmission. It is histologically characterized by cardiomyocytes hypertrophy, fibre disarray and interstitial fibrosis. These microscopic abnormalities translate into functional abnormalities, not always recognized by conventional cardiac imaging assessment. Thus, quantitative assessment of myocardial dysfunction caused by hypertrophy and heterogeneous fibrosis in HCM remains a challenge.
Purpose: Using three-dimensional wall-motion tracking (3DWMT) echocardiographic technique, we aimed to characterize the left ventricle (LV) global mechanics in a HCM group of patients, and to compare morphological and strain parameters with a group of healthy controls.
Methods: Thirty five (35) HCM patients (HCM group) and 27 healthy controls (control group) underwent standard bi-dimensional (2D) echocardiography, followed by 3DWMT evaluation. Using Toshiba Artida echocardiography equipment (Toshiba Medical System), global strain values were obtained for each component [global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), area tracking (AT)], as well as, twist and torsion angle, and LV ejection fraction (LVEF).
Results: We found no age (61.5 ± 10.3 vs 57.5 ± 7.2 years, p = 0.097), gender (p = 0.384) or LVEF (63 ± 9 vs 65 ± 13%, p = 0.437) differences among HCM and control groups. Regarding strain parameters, we found a statistically significant decrease in GLS (-10.6 ± 3.1 vs -16.5 ± 4.3%, p < 0.001) and GCS (-24.4 ± 8.1 vs -28.8 ± 7.3%, p = 0.032) in HCM group. A non-significant trend to lower GRS values was also observed in this group (27.9 ± 11.2 vs 31.0 ± 1 0.7%, p = 0.275). Furthermore, a significant decrease was observed in AT values (-32.9 ± 9.1 vs -39.8 ± 9.8%, p = 0.007). No diferences were verified in twist angle values (5.7 ± 2.9 vs 5.5 ± 2.7°, p = 0.889), nor torsion (1.8 ± 1.1 vs 1.6 ± 0.9°/cm, p = 0.399).
Conclusion(s): Patients with HCM and preserved LVEF exhibit abnormal myocardial

deformation parameters. In the analysed cohort, a significant decrease was found in GLS, GCS and AT values. Three-dimensional wall-motion tracking proved to be a useful and practical tool in the assessment and characterization of LV global mechanics, allowing a better comprehension of HCM pathophysiology, and allowing the detection of subclinical dysfunction.

P2201

Brain natriuretic peptide level in patients with hypertrophic cardiomyopathy

AE Demkina[1]; NS Krylova[1]; NG Poteshkina[1]; EA Kovalevskaya[2]; FM Hashieva[2]
[1]The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation; *[2]City Hospital 52, Moscow, Russian Federation*

In clinical practice, most patients with hypertrophic cardiomyopathy (HCM) have an increased levels of brain natriuretic peptide (BNP) despite of preserved global systolic function of the left ventricle (LV). The relationship of BNP level and clinical-instrumental parameters in patients with HCM is of great interest of investigators.

Purpose: To assess BNP level and its relationship with clinical status and instrumental parameters in HCM patients.

Materials and methods: 55 patients with HCM were examined (13 men (33%), average age 58.0 ± 15.5 years). All patients were treated with bisoprolol (5.5 ± 1.8 mg). In 15 patients (27.2%) obstructive form of the disease was identified. All patients underwent clinical examination, echocardiography with tissue doppler imaging (TDI) and brain natriuretic peptide (BNP) estimation.

Results: 52 HCM patients (94.5%) had an elevated BNP level with average mean 150 (83; 300) pg/ml. There was a significant correlation between BNP level and functional class (FC) of chronic heart failure (CHF) by NYHA (r=0.37, p = 0.04), left ventricular interventricular septum (r=0.40,vp = 0.04), size of the left atrium (r=0.93, p = 0.001), mitral regurgitation (r=0.60, p = 0.006), E/A (r=0.37, p = 0.04) and IVRT of transmitral flow (r=0.30, p = 0.04). There was a correlation between BNP level and right ventricle (RV) Tei index (r=0.48, p = 0.01), tricuspid annulus lateral s' (r=-0.79, p = 0.01), and basal lateral RV wall s' (r=-0.94, p = 0.002), medium lateral RV wall s' (r=-0.73, p = 0.02).

CONCLUSIONS. BNP levels was elevated in 94.5% HCM patients. Increased BNP level was associated with higher functional class of CHF by NYHA, myocardial hypertrophy, increased left atrium size, left ventricle diastolic disfunction and RV longitudinal systolic disfunction.

P2202

Myosin heavy chain and MAP-kinase activating death domain-containing gene polymorphisms in adults with hypertrophic cardiomyopathy

AA Poliakova[1]; VG Davydova[1]; EN Semernin[1]; SA Pyko[2]; AA Kostareva[1]; AYA Gudkova[3]; EV Shlyakhto[1]
[1]Almazov Federal Medical Research Centre, Saint-Petersburg, Russian Federation; *[2]St.Petersburg Electrotechnical University "LETI", Saint-Petersburg, Russian Federation*; *[3]St.Petersburg State Pavlov Medical University, Saint-Petersburg, Russian Federation*

Background and Purpose: Hypertrophic cardiomyopathy is the most common inherited cardic disorder. Phenotypic manifestation of the disease, especially in the adult and eldery group, depends on many inviromental and genetic factors, including co-existing genetic variants such as SNPs. Our aim was to study the genotype and allele distribution in rs2290149, rs10838692, rs7124958, rs753992 of MADD gene and rs2069542 of MYH7 gene in adults with hypertrophic cardiomyopathy (HCM).

Methods: The study group included 154 patients with HCM at the age 45 - 91 years (57,69 ± 11,19 years, men - 48% women - 52%). The diagnosis of HCM was established according to the guideline of the European society of cardiology on the diagnosis and treatment of HCM, 2014. The control group included 257 healthy donors without cardiovascular diseases and other severe pathologies, matched by age and sex with the studied group. Genotyping for rs2290149, rs10838692, rs7124958, rs753992 of the MADD gene and rs2069542 of the MYH7 gene was performed using real time PCR.

Results: We observed a significant increase in frequency of TT genotype of rs10838692 of the MADD gene in patients with HCM compared to healthy group (55.2% vs. 45.3%, p < 0.05). A trend although not reaching a statistical significance was detected towards the predominance of the TT genotype in rs2290149 of the MADD gene in patients with HCM compared to healthy donors (82.5% vs. 73%, p = 0.055). The allele frequency also differs for rs2290149 (T:C = 89.9%:10.1% in HCM and 83.3%:16.7% in control group, p = 0.007) and for rs10838692 (T:C=72.4% : 27.6% in HCM and 63.6%: 36.4% in control, p = 0.008), respectively. We did not detect any difference in genotype and allele distribution for rs7124958, rs753992 of MADD gene and for rs2069542 of MYH7 gene.

Conclusion: In older adults with HCM the T allele of SNP rs2290149 and SNP rs10838692 and TT genotype of rs10838692 of the MADD gene are prevailing compared to control healthy individuals, while polymorphic variants rs7124958, rs753992 of the MADD gene and rs2069542 of the MYH7 gene had no association with HCM.

P2203

The role of soluble st2 and galectin-3 in hypertrophic cardiomyopathy assessed by cardiac magnetic resonance

M Monika Gawor[1]; M Spiewak[2]; M Marczak[2]; K Kozuch[3]; J Janas[4]; J Grzybowski[1]
[1]Institute of Cardiology, Department of Cardiomyopathies, Warsaw, Poland; *[2]Institute of Cardiology, CMR Unit, Warsaw, Poland*; *[3]Institute of Cardiology, Department of Congenital Heart Diseases, Warsaw, Poland*; *[4]Institute of Cardiology, Department of Clinical Biochemistry, Warsaw, Poland*

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Background: Soluble ST2 (sST2) and galectin-3 (Gal-3) are useful biomarkers for prognosis of heart failure. Both of them are involved in cardiac fibrosis and remodeling. Myocardial fibrosis identified on cardiac magnetic resonance (CMR) imaging is present in approximately 70% of patients with hypertrophic cardiomyopathy (HCM) and may play an important role in predicting sudden cardiac death in this population.

Purpose: The aim of this study was to evaluate sST2 and Gal-3 as potential biomarkers in HCM.

Methods: Serum sST2 and serum Gal-3 concentrations were measured in 60 patients with HCM and 20 healthy controls with normal physical examination. The patients with HCM underwent routine evaluation including 12-lead electrocardiography (ECG), two-dimensional (2D) echocardiography, 48-hour Holter ECG monitoring, NT-proBNP and high-sensitivity Troponin T measurements. Additionally, CMR examination was performed in this group to calculate left ventricular (LV) mass, LV mass indexed for the body surface area (LVMI), LV ejection fraction (LVEF), and maximal wall thickness (MWT). The control group underwent 12- lead ECG, 2D echocardiography and NT-proBNP measurements to exclude asymptomatic heart disease.

Results: Concentrations of sST2 and galectin-3 were significantly higher in patients with HCM than in control group (15.0 [9.8 - 18.9] vs. 12.9 [9.4 - 14.8] p = 0.04 and 8.4 [6.8 - 10.0] vs. 6.1 [5.5 - 7.6] p = 0.003, respectively). We observed positive correlations between sST2 levels and CMR-derived parameters: LV mass (r=0.296, p = 0.023), LVMI (r=0.290, p = 0.026) and MWT (r=0.334, p = 0.010). Gal-3 levels were associated only with hs-cTnT concentrations (r=0.257, p = 0.046). We confirmed positive correlations between NT-proBNP levels and LV mass (r=0.328, p = 0.0098), LVMI (r=0.458, p = 0.0002) and MWT (r=0.438, p = 0.0004). There were also positive correlations between hs-cTnT levels and LV mass (r=0.598, p < 0.00001), LVMI (r=0.518, p < 0.00001), MWT (r=0.337, p = 0.008), and negative correlation between hs-cTnT levels and LVEF (r= -0.355, p = 0.005). Patients with non-sustained ventricular tachycardia (nsVT) had higher levels of sST2 (19.0 [9.6 - 22.8] vs. 13.7 [9.2 - 17.4] p = 0.027) and hs-cTnT (24.2 [10.2 - 31.2] vs. 11.5 [7.4 - 22.9] p = 0.039).

Conclusions: Our study confirmed that NT-proBNP and hs-cTnT are valuable biomarkers in HCM. Gal-3 levels were higher in patients with HCM than in control group, but there were no correlations between Gal-3 levels and CMR-derived LV dimensions. We demonstrated a significant correlations between serum sST2 levels and LV mass, LVMI and MWT assessed by CMR in HCM patients. Levels of sST2 were also higher in patients with nsVT. These findings suggest that sST2 may have a potential as a biomarker for better risk stratification in HCM.

Figure1. Correlations between sST2 levels (ng/ml) and CMR-derived parameters: (A) MWT (mm), (B) LVMI (g/m2), and (C) LV mass (g) in HCM patients. Levels of sST2 in patients with nsVT (D).

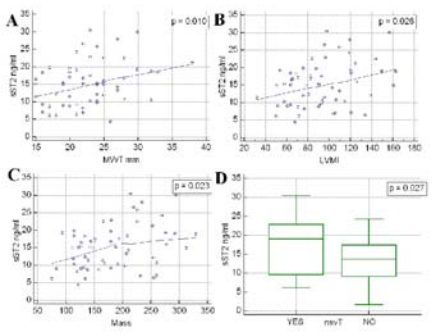


Figure 1

COMORBODITIES

P2204

Valve calcification is associated with parameters of central pulse wave in patients with end-stage renal disease on hemodialysis

N Manukhina[1]; M Trukhanova[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: Arterial stiffness is known marker of poor cardiovascular prognosis. Associations of valve calcification and arterial stiffness in patients with end-stage renal disease (ESRD) are not well studied. The aim if the study was to assess the incidence of valve calcification in patients with and its associations with clinical parameters and markers of arterial stiffness.
Methods: In 68 adults with end-stage renal disease on maintenance hemodialysis for >3 months (45.6% males, median age 58.3 (interquartile range (IQR) 54.6; 61.6) years, dialysis duration 62.7 (47.8;77) months, body mass index 26.8 [25.3;28.3] kg/m2, arterial hypertension 94%, stable angina 26.5%, heart failure 28%, diabetes mellitus 21%, glomerulonephritis 35%, pyelonephritis 25%, multicystic dysplastic kidney 13%, urolithiasis 10%) echocardiography and applanation tonometry was performed. Calcification in mitral, aortic or both valves and parameters of arterial stiffness and central pulse wave were assessed. Mann-Whitney test was performed. $P < 0.05$ was considered significant.
Results: Calcification of the aortic, mitral and both valves was revealed in 46 (67.6%), 34 (50%) and 33 (48.5%) of patients respectively. 20 (29%) patients had no signs of calcification of valves. Patients with vs without calcification of aortic valve were older (65.1 ± 9.5 vs $41.4 \pm 11,9$ years, $p < 0.001$), had higher dialysis duration (51 (8;252) vs 21 (10;38) months, $p < 0.01$), left atrium volume (LAV) (44 (40;70) vs 42 (40;44) ml, $p < 0.05$), right atrium volume (RAV) (44 (39;62) vs 42 (40,5;43) ml, $p < 0.05$), lower stroke volume (SV) (74 (48;108) vs 80 (71;86,5) ml, $p < 0.05$). Patients with vs without calcification of aortic valve had lower peripheral diastolic blood pressure (DBP) (76 ± 17 vs 84 ± 12 mmHg, $p < 0.05$), central DBP (75 ± 15 vs 82 ± 11 mmHg, $p < 0.05$), lower reflected wave transit time (RWTT) (131 ± 17 vs 137 ± 15 ms, $p < 0.05$). Patients with vs without calcification of mitral valve were older (67.8 ± 8.2 vs $47.9 \pm 13,5$ years, $p < 0.001$), had higher dialysis duration (51 (34;111) vs 36 (14;57) months, $p < 0.01$), LAV (45 (43;56) vs 42 (40;44) ml, $p < 0.05$), RAV (44 (43;45) vs 42 (42;43) ml, $p < 0.05$), systolic pulmonary artery pressure (33 (29;37) vs 29 (27;30) mmHg, $p < 0.01$), lower stroke volume (71.9 ± 10.2 vs 78.4 ± 13.6 ml, $p < 0.05$). Patients with vs without calcification of mitral valve had higher carotid-femoral pulse wave velocity ($10.1 \pm 2.$ 7 vs 8.9 ± 3.5 m/s, $p < 0.05$), lower peripheral DBP (73 ± 17 vs 84 ± 14 mmHg, $p < 0.01$), central DBP (72 ± 13 vs 83 ± 13 mmHg, $p < 0.001$), higher central pulse pressure (52 ± 13 vs 45 ± 16 mmHg, $p < 0.05$), lower RWTT (133 (120;130) vs 135 (132;142) ms, $p < 0.05$).
Conclusion: High prevalence of valve calcification (71%) was revealed in patients with ESRD on maintenance hemodialysis. Patients with vs without valve calcification were older, had higher duration of dialysis and more pronounced arterial stiffness.

P2205

control of uric acid in the blood - A new lever quality of life of patients with rheumatoid arthritis and chronic heart failure

D Dmitrii Bublikov[1]; D Anchugina[1]
[1]*Altay State Medical University, Barnaul, Russian Federation*

Increased uric acid levels in patients with chronic heart failure and in patients with rheumatoid arthritis - the spread in the clinic. The impact on quality of life of hyperuricemia in patients with chronic heart failure, as well as ways of correction of elevated levels of uric acid in patients by different ways until plasmapheresis and prednisone - study topic. Today, however, it is not clear whether there is a relationship between the level of hyperuricemia in patients with rheumatoid arthritis and chronic heart failure with quality of life. Purpose of the study. To study the effect of hyperuricemia on the quality of life of patients with rheumatoid arthritis and chronic heart failure
Materials and methods: We examined the patients ($n = 79$), including 46 women and 33 men, average age - $55.6 \pm$ 7.2 years, with verified diagnosis of rheumatoid arthritis by ACR criteria (1988). Chronic heart failure and its functional class (for NYHA) exhibited on the basis of complex clinical and laboratory, instrumental methodics that included physical examination of the patient, with the six-minute walking test, echocardiogram, pro-BNP. 77% of patients had hypertension, 23% angina pectoris. 16% had a combination of these diseases. All of the patients at the time of inclusion in the study were 1st functional class of angina and well-controlled blood pressure. Quality of life was assessed by the SF-36 questionnaire.
Results: Found korrelation communication medium strength between the level of uric acid in the group of men surveyed and functional class chronic heart failure ($p = 0.54$). In the subgroup of women this correlation goes missing ($p = 0.12$). In addition, if not statistically different functional class of heart failure, patients with higher levels of uric acid had statistically lessnes indicators by questionnaire SF-36, such as the role functioning ($p = 0.008$), role physical functioning ($p = 0.005$), physical pain ($n = 0.003$), social functioning ($p = 0.002$). Also found a correlation of medium strength, positive between uric acid levels and an indicator on the questionnaire SF-36 mental health.
Conclusion: The results show the effect of hyperuricemia on the functional class of chronic heart failure in men with rheumatoid arthritis. Also, the findings suggest a direct effect of hyperuricemia on the quality of life parameters in patients with rheumatoid arthritis and chronic heart failure and reverse its impact on the mental quality of life parameters.

P2206

Cognitive impairment in heart failure

E Elnur Smajic[1]; M Isabegovic[1]; L Dizdarevic- Hudic[1]; M Avdagic- Piric[1]; D Loncar[1]; D Mrsic[1]; N Mesanovic[1]
[1]*University Clinical Center Tuzla, 75000 Tuzla, Bosnia and Herzegovina*

The early features of brain failure are deterioriation of intellectual capabilities, especially loss of concentration and memory. Cognitive impairment (CI) and dementia are increasing globally. It is one of the primary causes of loss of autonomy and institutionalization of elderly patients in many countries.
The prevalence of CI is higher among patients with Heart Failure (HF) than in those without. CI is often recognized in conjunction with heart failure, but the reported prevalence has varied ranging from 25% to 75%. In the literature, the reported prevalence of cognitive impairment in heart failure patients is at least 15-fold higher. Studies have shown up to a fivefold increase in mortality in HF patients when cognitive impairment is present.
HF and CI share several common pathological processes and risk factors, and cause or consequence. The pathophysiological mechanisms that like it is hypoperfusion and/or micro-emboli seem to play an important role. Atrial fibrillation is independently associated with the onset of cognitive impairment and Alzheimers disease. Another important determinant of cognitive impairment is the presence of cerebral white matter lesions, abnormality of hippocampus, such as reduction in gray matter and cerebral blood flow. Cerebral blood flow is much lower in the posterior part of hippocampus. The hippocampus is one of the regions of the brain most vulnerable to cerebral hypoxia. HF patients showed the loss of gray matter in the different brain regions (cortical and subcortical) than patients with ischemic heart disease. HF patients display more widespread and extensive brain changes than adults with ischemic heart disease.
The spectrum of CI in HF is similar to that observed in the general population and range from delirium to isolated memory or non-memory-related deficits to dementia. The path leading to dementia is often long with a wide spectrum of subclinical and clinical presentation. Vascular dementia is the most prevalent type with 36%. Both HF with reduced ejection fraction and HF with preserved ejection fraction have been associated with defects in different domains of cognition. The main type of heart failure is with preserved ejection fraction, which is more prevalent in those of greater age. No relationship could be demonstrated between type of dementia and type of heart failure. Studies have shown a rise in CI in HF patients with higher New York Heart Association classification.
CI in HF has been associated with higher rates of disability and impairment in self-care activities that increase healthcare cost, hospital readmission and mortality. Morphologic and functional changes in HF patients with CI may be detected at an early stage using cardiovascular and brain imaging techniques. Early detection of CI and appropriate management strategies in HF may help to reduce CI and improve clinical outcomes in HF patients.
Key words: Cognitive impairment, Heart failure, Older age

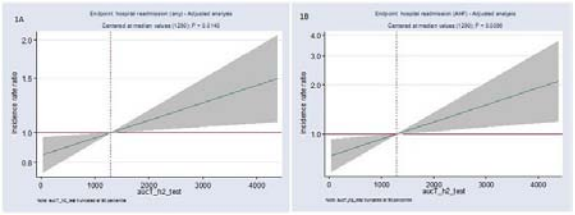
P2207

Intestinal bacterial overgrowth assessed by lactulose breath test and adverse outcomes in heart failure

A Anna Mollar Fernandez[1]; MP Villanueva[2]; G Minana[1]; A Villaescusa[1]; D Escribano[1]; E Santas[1]; P Palau[1]; A Bayes-Genis[3]; J Lupon[4]; M Minguez[5]; F Mora[5]; E Nunez[1]; J Sanchis[1]; J Nunez[1]
[1]*University Hospital Clinic of Valencia, Cardiology, Valencia, Spain*; [2]*University Hospital Clinic of Valencia, clinical biochemistry, Valencia, Spain*; [3]*University Hospital Trias i Pujol, Cardiology, Barcelona, Spain*; [4]*University Hospital Vall d'Hebron, Cardiology, Barcelona, Spain*; [5]*University Hospital Clinic of Valencia, Gastroenterology, Valencia, Spain*

Background: Some evidence endorses the role of gut microbiome in the pathophysiology of heart failure (HF). Indeed, intestinal bacterial overgrowth has been postulated to play a crucial role in the progression of the disease. In this work, we aimed to evaluate whether small intestinal bacterial overgrowth syndrome (SIBO) assessment by measuring the hydrogen (H2) and methane (CH4) exhaled by lungs and measured in breath after a lactulose breath test is associated with the risk of repeated unplanned hospitalizations.

Methods: This is an observational prospective study that enrolled 102 patients with the following inclusion criteria: a) advanced HF (stage C-D as per the ACC/AHA classification); b) at least one previous decompensating episode, c) non-clinical signs of active infection. In all of them, we performed a lactulose breath test collecting breath samples at baseline and every 20 minutes for 2 hours. Negative binomial regression method was used to determine the association between the area under the receiving operator curve of H2 and CH4 (AUC-H2 and AUC-CH4, respectively) and the risk of recurrent hospitalizations. Estimates of risk were reported as incidence rate ratios (IRR).
Results: Median (interquartile range) of AUC-H2 and AUC-CH4 were 1290 (520-2430) and 985 (450-2120), respectively. SIBO prevalence was up to 65.69% of the sample. At a median (interquartile range) follow up of 203 (80-369) days, 100 all-cause readmissions in 49 patients and 51 AHF-readmissions in 26 patients were recorded. In multivariate setting, AUC-H2 was significant, positive and linearly associated with an increased risk of recurrent all-cause (IRR=1,14; CI 95%:1,03-1,27; p = 0,014) and AHF-hospitalizations (IRR=1,27; CI 95%:1,06-1,52; p = 0,010) as is shown in figure 1a and 1b.
Conclusions: In this preliminary study, exhaled H2 and CH4 after a lactulose breath test were independently associated with higher risk of recurrent admissions in patients with HF.



P2208

Prevalence of comorbidities and one-year prognosis based on ejection fraction findings: understanding heart failure with mid-range ejection fraction.

MA Miguel Antonio Lopez Garrido[1]; AI Molina-Ramos[1]; A De Vicente-Ortega[2]; V Garcia-Ruiz[1]; VM Becerra-Munoz[1]; A Ruiz-Salas[1]; L Morcillo-Hidalgo[1]; M Jimenez-Navarro[1]; JJ Gomez-Doblas[1]; E De Teresa-Galvan[1]; JM Garcia-Pinilla[1]
[1]*University Hospital Virgen de la Victoria , Department of Cardiology, Malaga, Spain*; [2]*Faculty of Medicine, University of Malaga, Malaga, Spain*

Background: The ESC Heart Failure (HF) Guidelines of 2016 introduce the term HF with mid-range ejection fraction (HFmrEF) as a separate group with characteristics between HF with reduced and preserved ejection fraction (HFrEF and HFpEF, respectively). We conducted this study in order to know the the differences in the prevalence of comorbidities and events at one-year follow-up in the groups of HF according to their ejection fraction.
Methods: We studied all the patients with HFmrEF at follow-up in the HF Unit of our Hospital in the years 2010-2014, recording their clinical characteristics, comorbidities and adverse events during follow-up. Subsequently we compared its characteristics with patients with HF with preserved and depressed ejection fraction included in the ESC HF Registry in our Hospital during the same period.
Results: The group of patients with HFmrEF had a lower percentage of women than the group of HFpEF (24.6% vs 52.2%, p < 0.001), presenting no differences with HFrEF (24.6% vs 20%, p = 0.56). There were also no significant differences in age compared to HFpEF (69 vs 69 years, p = 0.91) or HFrEF (68 vs 66 years, p = 0.24). The ischemic etiology was the most frequent in the groups of HFmrEF and HFrEF (50% and 41.8%, respectively) and the hypertensive etiology in HFpEF (39.1%). The Charlson Index was higher in HFmrEF than in HFpEF (5.7 vs 4.6, p = 0.003), not existing significant differences with HFrEF (5.7 vs 5.2, p = 0.22). In comparison with the group of HFpEF, HFmrEF patients presented higher prevalence of diabetes (45.6% vs 27.5%, p = 0.019) and peripheral artery disease (19.3% vs 1.4%, p < 0.001), and lower prevalence of atrial fibrillation (21.9% vs 36.2%, p = 0.041). In term of comorbidities there were no differences with respect to the HFrEF group, except in the hypertension that was more prevalent in HFmrEF (71.1% vs 45.5%, p = 0.002). There were no significant differences in the three groups with respect to overall mortality (HFmrEF 6.6%, HFpEF 3.3%, HFrEF 4%, p = 0.59), nor with respect to hospitalization for HF at one-year of follow-up (HFmrEF 11.7%, HFpEF 1.4%, HFrEF 7.5%, p = 0.07), although a higher percentage was observed in HFmrEF patients.
Conclusions: 1. The ischemic etiology was common in the three groups of HF. 2. HFmrEF and HFrEF present similar clinical characteristics in terms of comorbidities. 3. Diabetes and arterial disease was more frequent in HFmrEF with respect to HFpEF. 4. HFmrEF had a higher percentage of mortality and hospitalizations for HF at one-year follow-up, although without statistically significant differences.

P2209

Chronic kidney disease in heart failure is associated with higher CA 125 and hsCRP levels

Y Yuksel Cavusoglu[1]; ME Altinbas[1]; F Mutlu[1]; S Eraslan[1]; K Isgendarov[1]; E Babayigit[1]
[1]*Eskisehir Osmangazi University, Eskisehir, Turkey*

Purpose: Chronic kidney disease (CKD) is a common comorbid condition in heart failure (HF). Plasma levels of carbohydrate antigen 125 (CA-125) have been shown to correlate with clinical, hemodynamic, and echocardiographic parameters in HF. However, less is known with regard to CA-125 levels in patients with HF and CKD. Inflammatory activation has also been shown to involve in the pathophysiological process of HF and elevated level of hsCRP is demonstrated to be present in HF. The aim of this study was therefore to assess possible associations between CKD and plasma levels of CA-125 or hsCRP in patients with HF.
Methods: A total 446 patients with the diagnosis of HF, NYHA II-IV, LVEF < 40% and >18 years of age were included in this study. CKD was defined as an eGFR < 60 mL/min/1.73 m2. Plasma levels of CA-125 and hsCRP levels have been measured from the blood samples. Patients were classified into two groups: patients with CKD (n = 227) and patients without CKD (n = 219).
Results: Mean age of study population was 67 ± 12 years. Mean EF was 25.4 ± 7.9%, NT-proBBNP was 7667 ± 9876 pg/mL, creatinine level was 1.41 ± 0.88 and hemoglobin level was 12.4 ± 2 gr/dL. Median plasma levels of CA-125 were found to be significantly higher in patients with CKD as compared to those without CKD (46.9 [20.9-125.5] U/mL vs 25.4 [13.5-77.7] U/mL, p < 0.002, respectively). hsCRP levels were also found to be significantly higher in patients with CKD as compared to those without CKD (18.2 [6.0-46.3] mg/L vs 8.43 [3.48-19.3] mg/L, p < 0.001, respectively). As expected, NT-proBNP levels were higher in patients with CKD as compared to those without CKD (6634 [2723-15898] pg/mL vs 1482 [554-3665] pg/mL, p < 0.001 respectively). Furthermore, a significant correlation was found between eGFR and CA-125 (r=-,172, p < 0.001), eGFR and hsCRP levels (r=-,253, p < 0.001), eGFR and NT-proBNP (r=-,558, p < 0.001), eGFR and hemoglobin levels (r=,399, p < 0.001), and also eGFR and sodium levels (r=,153, p < 0.001).
Conclusions: The results of this study showed that impaired kidney functions in HF is associated with higher CA-125 and hsCRP levels, suggesting an inflammatory activation and worse clinical status of the disease in HF patients with CKD.

P2210

Plasma ferritin and transferring saturation in chronic heart failure: relation to clinical variables

L Voronkov[1]; A Lyashenko[1]; V Gorbachova[1]
[1]*NSC Institute of Cardiology M.D. Strazhesko, Heart failure, Kiev, Ukraine*

Background: According to FAIR-HF and CONFIRM-HF approach, both plasma ferritin (F) and transferrin saturation (TSAT) are considered to be an iron deficiency (ID) criteria in chronic heart failure (CHF). Nevertheless, it is still a question whether the obligate measurement of both F and TSAT is really necessary in detection of ID in CHF.
Purpose: To establish the relation of F and TSAT to clinical variables in CHF.
Methods: 45 stable CHF patients (pts), NYHA class II-IV, with left ventricular ejection fraction (LVEF) < 40% were examined. Plasma F and TSAT were determined by chemiluminescent immunoassay and colorimetric method, respectively. Beside routine clinical and laboratory examination, 6 min walk test, standardized endurance leg test and flow-mediated vasodilation (FMD) of the brachial artery were performed.
Results: Abnormal levels of F (< 100 ng/mL) were observed in 16 pts (35.5%), while abnormal levels of TSAT (< 20%) - in 31 pts (68.9%). Both F and TSAT levels didn't show significant differencies in regard to the age (< 60 or >60), sex, comorbidities (hypertension, diabetes), atrial fibrillation and hemoglobin level. In contrast to F, TSAT was lower in pts with LVEF <= 30%: 15 (2-37)% vs LVEF > 30%: 21 (8-37)%, p = 0.017; and in hyperuremic pts 15 (2-65)% vs 21 (6-48) % in non-hyperuremic pts, p = 0.022.
Plasma F demonstrated no significant correlations with numerous clinical and laboratory variables. Simultaneously, TSAT demonstrated the significant direct link with endurance leg test (r=0,27, p = 0.033), FMD (r=0.3, p = 0.046) and borderline link with 6 min walk test distance (r=0.27, p = 0.06), as well as with LVEF (r=0.26, p = 0.08).
Conclusions: In contrast to plasma F, TSAT in CHF is related to some important clinical variables that can reflect ID state. Possibly, TSAT alone is a relevant marker of ID, which requires guideline-recommended iron therapy.

P2211

Anaemia is associated with development of acute heart failure in patients with acute coronary syndrome: propensity-score matched study

RA Rui Azevedo Guerreiro[1]; J Pais[1]; K Congo[1]; D Bras[1]; J Carvalho[1]; M Carrington[1]; D Neves[1]; AR Santos[1]; B Picarra[1]; A Caeiro[1]; J Aguiar[1]
[1]*Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*

Introduction: Anaemia is a prevalent comorbidity in patients with heart failure (HF), associated with worse prognosis as highlighted by 2016 ESC guidelines of HF, which reinforced the importance of its treatment to improve HF patients' outcomes. However, the role of anaemia in the development of acute HF in patients with acute coronary syndrome (ACS) is not well characterized.
Purpose: Authors pretend to evaluate if anaemia at admission for ACS is associated with in-hospital development of acute HF.
Methods: Observational retrospective study, with a sample of 594 consecutive patients admitted for ACS. Patients were divided in two groups: with anaemia, defined as haemoglobin at admission less than 12 g/dL, and without anaemia. Propensity-score was calculated to each patients taking into account age, sex, previous history of smoking, arterial hypertension, diabetes mellitus, hyperlipidaemia, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, heart failure, significant valvular disease, stroke, peripheral artery disease, cancer, chronic obstructive pulmonary disease, dementia, family history of coronary artery disease, type of acute coronary syndrome justifying admission, severity of coronary artery disease, degree of revascularization and value of creatinine at admission. Each patient with anaemia was matched with a patient without anaemia with similar propensity-score. Outcome of acute HF was defined as evolution in Killip-Kimball classes 3 (acute pulmonary oedema) and 4 (cardiogenic shock) during hospitalization. The association of anaemia with acute HF was accessed in the matched-pairs with logistic regression and $p < 0.05$ was considered statistically significant.
Results: From the study sample of 594 patients, 120 (20.2%) patients had anaemia at admission. Matching each patient with anaemia with a patient without anaemia with similar propensity-score resulted in 120 matched-pairs of patients and a study sample of 202 patients, due to multiple matching of controls. Matched-pairs on propensity-score were similar in every variable used in the construction of the propensity-score, proving the correct pseudo-randomization. Anaemia at admission was associated with the development of in-hospital acute HF with an odds ratio (OR) of 1.11 (95% CI 1.04 – 1.19, $p = 0.003$).
Conclusion: Patients with anaemia at admission for ACS had in our propensity-score matched study a 11% greater probability of developing acute HF during hospitalization.

P2212

Do we properly treat iron deficiency with intravenous ferric carboxymaltose in clinical practice?

A Esteban Fernandez[1]; M Gonzalez Barja[1]; M Perez Serrano[1]; M Mendez Bailon[2]; C Ramirez[1]; M Garcia[1]; S Ortega[3]; A Travieso Gonzalez[3]; T Luque Diaz[3]; C Olmos Blanco[3]; D Vivas Balcones[3]; J Higueras Nafria[3]; I Vilacosta[3]; C Macaya Miguel[3]; R Bover Freire[1]
[1]*Hospital Clinic San Carlos, Heart Failure Unit, Madrid, Spain*; [2]*Hospital Clinic San Carlos, Internal Medicine Service, Madrid, Spain*; [3]*Hospital Clinic San Carlos, Cardiology Service, Madrid, Spain*

Introduction: Iron deficiency, with or without anemia, is a common finding in patients with heart failure (HF), and its intravenous correction with ferric carboxymaltose has been shown to improve the functional status and quality of life of the patients, according to FAIR-HF and CONFIRM-HF trials. However, there is less data about its effectiveness in clinical practice and the analytical follow-up of these patients.
Methods: We considered the patients in chronic follow-up in the HF Unit of our center in whom iron deficiency was detected in a routine analysis, according to 2016 ESC HF clinical practice guideliens criteria. The analytical and clinical characteristics of the patients were collected. Intravenous ferric carboxymaltose was administered, adjusting the dose according to patient weight and analytical parameters (500 or 1000 mg in a single dose, 15 minutes time infusion in daily hospital of the HF Unit). Then, clinical and analytical reevaluation was performed at 3 months after infusion.
Results: Ferric carboxymaltose was infused in 122 patients, and 80 (62% men) completed the follow-up with control at 3 months. Only one patient presented an adverse effect consisting in local allergic reaction. The mean age was 86 ± 8.4 years old. 7.4 % of the patientes was in NYHA I, 70.4% in NYHA II and 22.2% in NYHA III. The cause of his heart disease was: ischemic 42.3%, valvular 25.6 %, hypertensive 5% and other ones 27.1%. The mean left ventricular ejection fraction was 45.2 ± 17.3 %. The analytical parameters were (baseline-3 months post): Hemoglobin (Hb) 12.2 ± 1.6 vs. 12.8 ± 1.6 (ns); HCM 29.1 ± 2.9 vs. 30.0 ± 2.5 (ns); VCM 90.9 ± 6.9 vs. 93.9 ± 5.6 (ns); Iron 52.9 ± 26.9 vs. 75.2 ± 30.3 ($p = 0.03$); Ferritin 74.7 ± 126.1 vs. 322.8 ± 560.4 ($p = 0.02$); Transferrin 287.3 ± 66.5 vs. 236.7 ± 67.5 (ns); IST% 13.4 ± 6.6 vs. 22.1 ± 10.5 ($p = 0.04$) and NT-proBNP 4845.9 ± 8931.0 vs. 3627.2 ± 4301.1 ($p = 0.04$).
Conclusion: According to our results, the intravenous administration of ferric carboxymaltose in patients with iron deficiency and heart failure is safe and improves the analytical parameters of the ferric profile even 3 months after infusion. The impact on hemoglobin is lower, due to the multifactorial origin of anemia. In addition, there was a significant decrease in cardiac biomarkers.

P2213

Comparison of diagnostic criteria for iron deficiency in heart failure

LNLC Van Aelst[1]; M Abraham[2]; M Sadoune[3]; T Lefebvre[4]; P Manivet[3]; D Logeart[2]; JM Launay[3]; Z Karim[4]; H Puy[4]; A Cohen-Solal[2]
[1]*Catholic University of Leuven, Department of Cardiovascular Diseases, Leuven, Belgium*; [2]*Hospital Lariboisiere, Department of Cardiology, Paris, France*; [3]*Inserm UMR-S 942, Paris, France*; [4]*University Paris Diderot , INSERM U1149, Centre de Recherche sur l'inflammation, Paris, France*

Background: Iron status assessment in routine clinical care of heart failure (HF) patients is mainly based on circulating levels of ferritin and transferrin saturation (TSAT), with ferritin < 100 µg/L being diagnostic for absolute ID and ferritin 100–299 µg/L with TSAT < 20% meaning functional ID. Recently, hepcidin < 14.5 ng/mL and/or soluble transferrin receptor (sTfR) ≥ 1.59 mg/L were proposed to diagnose ID.
Purpose: We compared the diagnostic performance and concordance between ferritin/TSAT and hepcidin/sTfR for ID diagnosis in acutely decompensated and stabilized HF.
Methods: Data derive from a single center study, investigating the evolution of biomarkers upon presentation with ADHF and 30 days of follow-up (FU).
Results: Ferritin/TSAT levels at admission and 30 days of FU were available for 47 patients. At admission, twenty-seven patients fulfilled criteria for absolute ID (57%) and twelve patients for functional ID (26%). At 30 days of FU, 5 patients (11%) and 27 patients (57%) had absolute and functional ID respectively. Circulating levels of hepcidin and sTfR were available for 41 patients at admission. Thirty-four patients (83%) were ID. Twenty-seven patients (66%) were identified as ID by ferritin/TSAT and hepcidin/sTfR. Seven patients (17%) were considered ID based on hepcidin/sTfR yet not based on ferritin/TSAT. Six patients (15%) were considered ID based on ferritin/TSAT but not based on hepcidin/sTfR. There was no significant difference in the sensitivity of ferritin/TSAT and hepcidin/sTfR to detect ID at admission; yet there was only a weak association between both tests ($p = 0.78$, phi coefficient 0.04). Levels of hepcidin and sTfR were available for 46 patients after 30 days of FU; 36 patients were ID (78%) and 10 (22%) were non-ID. When comparing hepcidin/sTfR and ferritin/TSAT to diagnose ID at 30 days of FU, 63% of patients was similarly identified as either ID or non-ID in both assays, 24% was ID using hepcidin/sTfR yet not using ferritin/TSAT; 13% was ID using ferritin/TSAT yet not using hepcidin/sTfR. These differences did not reach statistical significance ($p = 0.2253$; phi coefficient 0.18). Comparing the detection rate of ID using either hepcidin/sTfR at admission and ferritin/TSAT at 30 days of FU, 24 patients (59%) were identified as ID in both assays. Three patients (7%) would be considered false negatives and 10 patients (24%) would be considered false positives using hepcidin/sTfR during ADHF if compared with ferritin/TSAT at 30 days of FU. The difference in ID detection using ferritin/TSAT at 30 days and hepcidin/sTfR at admission was borderline significant ($p = 0.05$), with a moderate measure of association (phi coefficient 0.30).
Conclusion: There is only a moderate correlation at most between ferritin/TSAT and hepcidin/sTfR to assess ID, urging for additional research to adequately detect ID using circulating biomarkers.

P2214

Prevalence of iron deficiency in acute decompensated and stabilized chronic heart failure

LNLC Van Aelst[1]; M Abraham[2]; M Sadoune[3]; T Lefebvre[4]; P Manivet[3]; D Logeart[2]; JM Launay[3]; Z Karim[4]; H Puy[4]; A Cohen-Solal[2]
[1]*Catholic University of Leuven, Department of Cardiovascular Diseases, Leuven, Belgium*; [2]*Hospital Lariboisiere, Department of Cardiology, Paris, France*; [3]*Inserm UMR-S 942, Paris, France*; [4]*University Paris Diderot , INSERM U1149, Centre de Recherche sur l'inflammation, Paris, France*

Background: In clinical studies, the reported prevalence of iron deficiency (ID) varies remarkably. Estimates range between 30-50% in patients with stable chronic heart failure (CHF), whereas 60-80% of patients are reported to be ID in acute decompensated HF (ADHF). We hypothesised that the timing of its assessment influences the reported prevalence of ID.
Purpose: We aimed to depict the spontaneous evolution of biochemical parameters of iron metabolism following presentation with ADHF and ensuing treatment; secondly, we wanted to unravel the pathophysiological processes explaining changing iron status.

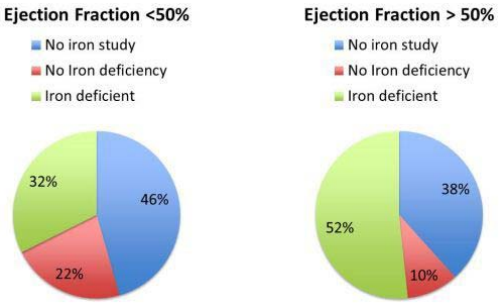
Methods: Data derive from a prospective, observational, single center study, investigating the evolution of biomarkers upon presentation with ADHF and 30 days of follow-up (FU). ID was defined as ferritin <100 μg/L or ferritin 100–299 μg/L with transferrin saturation <20%.
Results: We included 47 patients in the final analysis with a mean age of 70.4 years (y; SD 13.7 y), median ferritin of 93 μg/L (IQR 76 – 107 μg/L) and median brain natriuretic peptide (BNP) of 1004 pg/mL (IQR 652 – 1676 pg/mL) at baseline. At 30 days of follow-up, ferritin levels significantly increased (median: 159 μg/L, IQR 134 – 190 μg/L; $p < 0.0001$), BNP significantly decreased (median: 261 pg/mL, IQR 176 – 462 pg/mL; $p < 0.0001$). Whereas 57%, 26% and 17% of patients had absolute, functional and no evidence of ID respectively at admission, these respective percentages changed to 11%, 57% and 32% at 30 days of FU ($p = 0.00001$). There was only a moderate association between ID status at baseline and 30 days of FU using ferritin/TSAT (phi-coefficient 0.26). Changing ferritin levels between 0 and 30 days correlated with circulating soluble ST2 ($r^2 = 0.1152$; $p = 0.0278$) and TNFα ($r^2 = 0.0950$; $p = 0.0351$), but not with changing levels of mid-regional pro-adrenomedullin, BNP, procalcitonin, interleukin 6, CRP, growth differentiation factor 15, galectin-3, fibrinogen nor myeloperoxidase. Our results implicate systemic inflammation, not dilution, as one causative factor of increased ID prevalence in ADHF compared to CHF.
Conclusion: During ADHF, ID diagnosis based on ferritin levels and transferrin saturation is unreliable: indices of iron metabolism vary and only reach a steady state several weeks after remission of ADHF. Systemic inflammation, not dilution, may be one of the causative factors of altered iron status between admission and steady state. These results suggest that ID diagnosis and correction should only be undertaken at distance of an ADHF episode.

P2215

Assessment and treatment of iron deficiency in patients hospitalised for heart failure

S L Su Ling Tee[1]; N B Leonardo[2]
[1]Queen Elizabeth Hospital, Cardiology, Adelaide, Australia; *[2]Lyell McEwin Hospital, General Medicine, Adelaide, Australia*

Introduction: Iron deficiency (ID) is common in patients with heart failure (HF). Despite current guidelines and existing evidence stating the importance of ID as a co-morbidity in patients with chronic HF, ID has continued to remain under-diagnosed and under-treated by physicians in clinical practice, including in patients hospitalised for acute decompensation.
Purpose: To investigate whether hospitalised patients with HF were screened routinely for ID within 12 months of their admission, and whether they were managed according to the latest recommendations.
Methods: This retrospective observational study included 154 patients who were admitted over a 6-month period with a primary diagnosis of decompensated HF. Anaemia was defined as haemoglobin <13g/dL for men and <12g/dL for women. ID was defined as either serum ferritin <100μg/mL, or serum ferritin 100-299μg/mL and transferrin saturation <20%.
Results: Out of the 154 included patients, 68 patients had an ejection fraction (EF) of <50%, while 60 patients had heart failure with preserved ejection fraction (HFpEF). The other 26 patients' EF was unknown. Slightly more than half (82; 53.25%) of all patients had had a recent iron study. Of the 82 patients who had iron studies performed, 60 (38.96%) had ID. However, only 22 (36.67%) received iron replacement therapy. 100 patients (64.94%) were found to be anaemic, with only 66 of them being investigated for ID. 52 out of the 66 patients (78.79%) were later found to be iron-deficient but only 20 (38.46%) of them were treated. In patients with no evidence of anaemia, iron parameters were only assessed in 15 (27.78%) of them. 7 non-anaemic patients were iron-deficient, but only 1 patient was treated. One patient with HFpEF who had ID and anaemia was treated with blood transfusion only. Patients with ID were more likely to get treated when they were admitted under General Medicine rather than Cardiology (39.13% versus 18.92%).
Conclusion: Although the prevalence of ID in our study was consistent with that described in current literature, we suspect the actual prevalence could be higher, as many patients did not have an assessment of their iron status. Despite its small patient sample, this retrospective study demonstrated that assessment of iron status has continued to remain overlooked in patients with HF, and that strategies to reinforce awareness in treating physicians are necessary.



Assessment of ID based on EF

P2216

Anaemia is associated with higher mortality risk in patients presenting to the emergency department with acute dyspnoea

K Cerlinskaite[1]; G Ziubryte[2]; I Jonauskiene[3]; D Rimkeviciute[3]; L Badgonaite[4]; A Mebazaa[5]; A Kavoliuniene[3]; J Celutkiene[4]
[1]Faculty of Medicine of Vilnius University, Vilnius, Lithuania; *[2]Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[3]Department of Cardiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[4]Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; *[5]U942 Inserm, Hospital Lariboisière, Université Paris Diderot, Paris, France*

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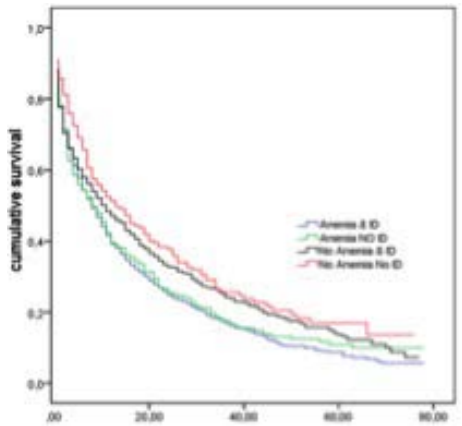
Introduction: Acute dyspnoea or shortness of breath is one of the chief complaints occurring among patients in Emergency Department (ED). Prognosis of the patients often remains uncertain, therefore accurate risk stratification would be of benefit. The AHEAD score is a recently developed simple prognostic scoring system evaluating the role of important co-morbidities in patients with acute heart failure (AHF). We performed a pilot investigation on whether the AHEAD score or any of its independent variables would be valuable in predicting outcomes in broader ED patients' population with acute dyspnoea of any cause.
Purpose: To examine the prognostic value of AHEAD score and its separate parameters in patients with acute dyspnoea presenting to the ED.
Methods: Prospective two-centre observational cohort study enrolled consecutive patients admitted to the ED with acute dyspnoea due to acute heart failure (AHF), exacerbation of chronic obstructive pulmonary disease (COPD), pneumonia, pulmonary embolism (PE) and other conditions. Parameters for AHEAD (A- atrial fibrillation (AF), H – haemoglobin <130 g/l for men and 120 g/l for women (anaemia), E – elderly (age>70 years), A – abnormal renal parameters (creatinine>130 μmol/l), D – diabetes mellitus (DM), each counted as 1 point) score were obtained at the time of admission. Patients (N=266, mean age 68 ± 13 years, 61.3% male) were followed-up after 1, 3 and 12 months. Main outcome was one year all-cause mortality, which was measured by performing logistic regression on AHEAD score and on its five parameters to determine mortality risk and odds ratios (ORs). Data was analysed using SPSS v22 statistical package.
Results: AHF was the main cause of dyspnoea among our patients (47% of the cases), PE was present in 8% of the cases, COPD exacerbation – in 6%, pneumonia – in 5%, while others were less common. The AHEAD score variables were frequent in study population: 48.9% of the patients were >70 years old, AF was present in 47.7% of the cases, anaemia in 35.7%, abnormal renal parameters in 23.7% and DM in 22.9%. The mean AHEAD score was 1.79 ± 1.3. One year mortality rate was 29.3%. There was no statistically significant one year all-cause mortality risk associated with AHEAD total score. When analysing its parameters in logistic regression, anaemia was associated with significantly increased mortality risk with OR 1.83 (95% confidence interval (CI): 1.05 to 3.19, $p = 0.032$) with no other parameter showing statistically significant results. Unadjusted OR for anaemia was 1.87 (95% CI: 1.09 to 3.22, $p = 0.023$).
Conclusions: AHEAD scoring system based on the analysis of the co-morbidities did not prove to be useful in this broad patients' cohort with acute dyspnoea of any cause. Nonetheless, anaemia was associated with significantly higher mortality risk at one year for patients presenting to the Emergency Department with acute dyspnoea. This finding may have a therapeutic implication in this patient population.

P2217

Impact of anemia and iron deficiency on long-term mortality and heart failure hospital re-admissions among patients hospitalized for heart failure: a regional population-based investigation from italy

P Lesizza[1]; MD Tinti[1]; A Cherubini[1]; G Barbati[1]; G Russo[1]; S Tolone[1]; D Del Sindaco[1]; L Tarantini[1]; G Cioffi[1]; G Pulignano[1]; A Di Lenarda[1]
[1]*Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy*

Background: In Registries on acute heart failure (HF), anaemia (AN) and iron deficiency (ID) are common, particularly in patients hospitalized with severe HF, women, elderly and with renal impairment. AN and ID showed in some studies a negative independent prognostic value. Aim of the present study was to analyze the frequency and prognostic relevance of AN&ID in patients admitted in 2009-2014 for acute HF in the area of our city in Northern Italy.
Methods: Data were retrieved from the Cardiovascular Observatory of our city. Different databases were linked: hospital records with discharge diagnosis, cardiological chart, laboratory tests, registry of death. 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). Patients were include in the analyses if hemoglobin (Hb), ferritin and TSAT were available. AN was defined as Hb <12 g/dl in females and <13 g/dl in males; ID as ferritin <100 ug/L or ferritin 100-300 ug/L and TSAT $<20\%$. "Worsening" HF (WHF) was classified in presence of at least one HF hospitalization in the 5 years preceding the index admission.
Results: Out of 7466 hospital admissions, 3046 (40.8%) were available for evaluation. AN&ID was present in 49.8% of cases, Only ID in 6.2%, only AN in 10.3%, NO AN & NO ID in 33.7%. Patients with AN&ID vs NO AN & NO ID showed an older age (82.5 vs 79 yo, $p<0.001$), more frequent female gender (61.9% vs 40.5%, $p<0.001$), worsening HF (47.1% vs 34.7%, $p<0.001$), Charlson index ≥ 3 (76.4% vs 62.1%, $p<0.001$), HFpEF (61.2% vs 47.4%, $p<0.001$) and CKD-EPI <60 ml/min (77% vs 56.3%, $p<0.001$). Follow-up was 33 months. KM curves were significantly different among the 4 groups ($p<0.001$). At multivariate analysis age (HR 1.02; 95% CI 1.01-1.03; $p<0.001$), male gender (1.15; 1.01-1.31; $p=0.028$), Charlson index ≥ 3 (1.42; 1.22-1.65; $p<0.001$), worsening HF (1.69; 1.49-1.93; $p<0.001$), BNP ≥ 450 pg/ml (1.36; 1.20-1.55; $p<0.001$) were independently associated to all-cause mortality. AN&ID showed a trend of correlation (HR 1.25; 95% CI 0.96-1-64; $p=0.098$).
Conclusions: AN&ID are frequent in acute HF particularly in elderly female patients, with worsening HF, HFpEF and multimorbidity (specifically renal impairment). AN&ID are less strongly related to mortality. The correlation with symptoms and re-hospitalizations may improve our understanding of the clinical impact of AN&ID on quality of life of HF patients.



AN and/or ID and survival

P2218

Prognostic impact of different trends of renal function before, during and after hospitalization for acute decompensated heart failure: cardio-renal interactions and 180-days cardiac mortality

L Ludovico Lazzari[1]; A Faggioni[2]; D Bovelli[1]; G Ambrosio[3]; E Boschetti[4]
[1]*Az. Osp. "S. Maria", Cardiology Department, Terni, Italy*; [2]*Nottingham University Hospitals NHS Trust, Cardiology Department, Nottingham, United Kingdom*; [3]*Hospital Santa Maria Della Misericordia, Cardiology and Cardiovascular Pathophysiology Division \ University of Perugia, Perugia, Italy*; [4]*Az. Osp. "Santa Maria" Terni \ University of Perugia, Cardiology Department, Terni, Italy*

Background: In the setting of acute decompensated heart failure (ADHF) worsening renal function (WRF) has been associated inconstantly with a poor prognosis; even less is known on improved renal function (IRF) and the association between the two phenomena.
Purpose: to better characterise WRF and IRF (prior, during and after hospitalization) and their associated risk of 180 days cardiovascular (CV) mortality.
Methods: Consecutive patients with a discharge diagnosis of ADHF were reviewed. IRF was defined as a reduction of $\geq$ 0,3 mg\dl in serum creatinine and an improvement by $\geq 20\%$ in glomerular filtration rate (GFR), whereas a worsening in creatinine and GFR by the same cut-offs defined WRF. Patients who received renal replacement therapy, contrast medium or transfusions were excluded from this study. Mortality was judged as CV unless a clear non-cardiac cause was identifiable. Pre-admission and post-discharge lab test within a six-month period of time were collected; chronic renal failure (CRF) was defined as GFR $<$ 60 ml\min for at least three months prior hospitalization.
Results: In a six month period,121 patients were eligible. During hospitalization, 23.9% of them experienced IRF whilst 42.1% WRF. Differently from the in-hospital WRF group, those undergoing IRF had an increased risk of short-term CV mortality (HR = 4.3, 95% CI 1.6–11.6, $p=0.004$; $p<0.05$ even after adjustment for baseline characteristics, in-hospital and discharge medications; for any level of GFR at discharge and for GFR $>$ 30 ml\min on admission). IRF patients showed no difference in the prevalence of signs of venous congestion or medications used; however, they needed more diuretics to obtain a similar diuresis ($p=0.04$) and had a greater neuro-hormonal activation on admission, with a higher BUN\creatinine ratio (56 ± 19 vs 44 ± 15, $p=0.001$) and lower levels of sodium (134.9 ± 5 vs $136.9\pm 3,8$ mEq\L, $p=0.02$). IRF-patients, compared to the WRF group, had a lower GFR on admission (35.1 ± 14.5 vs 64.8 ± 23.6 ml\min, $p<0.001$) but no different values at discharge (58.9 ± 22.2 vs 55.3 ± 21.2 ml\min, p = NS); moreover, the prevalence of CRF was similar (p = NS), thus suggesting a pre-admission WRF in the IRF group. In fact, we found an association between in-hospital IRF, pre-admission WRF (OR = 15, 95% CI 4.6-48, $p<0.001$) and post-discharge WRF (OR = 3.6, CI 95% 1.1-11.6, $p=0.03$). After adjustment for any level of admission GFR, a pre-admission WRF was found to be an independent predictor of CV mortality (adjusted HR=5.9, 95% CI 2–17.4, $p=0.02$).
Conclusion: pre-admission WRF, in-hospital IRF and post-discharge WRF are associated phenomena with an higher risk of CV mortality. We agree with other authors that IRF may represent the resolution of a pre-admission WRF, induced by venous congestion. This trend, together with a marked neuro-hormonal activation, may signify a more advanced stage of heart failure.

P2219

Interrelationship between renin-angiotensin-aldosterone system and oxidative stress in chronic heart failure patients with impaired renal function

M Reina Couto[1]; T Sousa[1]; M Morato[2]; J Afonso[1]; J Carvalho[1]; L Morgado[3]; FB Fernandes[4]; VP Leite[4]; D Casarini[4]; P Bettencourt[3]; A Albino-Teixeira[1]
[1]*University of Porto, Faculty of Medicine, Porto, Portugal*; [2]*University of Porto, Faculty of Pharmacy, Porto, Portugal*; [3]*Sao Joao Hospital, Porto, Portugal*; [4]*Univ. Federal de São Paulo, Dep. Medicina, São Paulo, Brazil*

Introduction: The coexistence of kidney and heart failure (HF) is increasing and represents a major clinical challenge nowadays defined as cardiorenal syndrome (CRS). Chronic activation of the renin-angiotensin-aldosterone system (RAAS) can increase oxidative stress which in turn can lead to renal injury and to a vicious cycle of more sodium and water retention in CRS type 2. Furthermore, accumulating evidence indicates that reactive oxygen species also regulate the activation of RAAS.
Purpose: To evaluate oxidative stress and RAAS in patients with chronic HF and to compare the relationship between these systems in patients with normal (nRF) or impaired (iRF) renal function (estimated glomerular filtration rate $>$ or $<$ 60 mL/min per 1.73 m2, respectively).
Methods: Sixty CHF patients from the Heart Failure Clinic of our hospital consent to participate according to the principles of the Declaration of Helsinki of the World Medical Association. Urinary H2O2 (U-H2O2), plasma and urinary isoprostanes (P- and U-Isop), plasma total antioxidant status (P-TAS), plasma and urinary angiotensinogen (P- and U-AGT), plasma renin activity (PRA), angiotensin converting enzyme (ACE) activity, angiotensin I (Ang I), angiotensin II (Ang II) and angiotensin 1-7 (Ang 1-7), biomarkers of cardiac dysfunction/injury (B-type natriuretic peptide, BNP; troponin I) and renal parameters were evaluated.
Results: Severe CHF patients (New York Heart Association, NYHA, classes III and IV) had higher levels of U-Isop (3.9 ± 0.7 vs 2.6 ± 0.3 ng/mg creatinine, $p<0.01$) and lower levels of ACE activity (11.0 ± 2.7 vs 12.4 ± 3.0 U/L, $p<0.05$) but no differences in other oxidative stress or RAAS parameters. Patients with iRF had higher U-AGT than those with nRF (58 ± 16 vs 15 ± 3 μg/g creatinine, respectively) and presented positive correlations between oxidative stress and RAAS markers (U-H2O2 vs P-AGT, U-Isop vs P-AGT, U-H2O2 vs U-AGT, U-H2O2 vs PRA, U-Isop vs ACE activity, PRA vs aldosterone). In contrast, in CHF patients with nRF, we mainly observed negative correlations between oxidative stress and RAAS parameters

(U-H2O2 vs Ang II; P-Isop vs P-AGT). Of note, we only found positive correlations of oxidative stress or RAAS markers with biomarkers of cardiomyocyte dysfunction/injury (U-Isop vs BNP; U-Isop vs Troponin I; PRA vs Troponin I) or with biomarkers of renal dysfunction (U-Isop vs urinary protein-to-creatinine ratio) in patients with impaired renal function.
Conclusions: CHF patients with renal dysfunction have higher intrarenal RAAS activation, evidenced by increased U-AGT. Furthermore, positive correlations between RAAS and oxidative stress were mainly observed in patients with renal dysfunction. This suggests that the addition of antioxidant treatment to these patients could exert renoprotection in the setting of CRS where no specific therapy was shown to be beneficial until now.

P2220
State of kidney in patients with chronic heart failure

SI Elmurodov[1]; AA Madaliyev[1]
[1]*Tashkent Medical Academy, Cardiology, Tashkent, Uzbekistan*

Background. Chronic heart failure (CHF) is currently one of the main problems of modern cardiology and public health.
Purpose: To study changes in renal function and their relationship with the severity of clinical symptoms and quality of life in patients with chronic heart failure.
Material and methods: The study group included 27 patients with chronic heart failure (CHF), different functional classes with left ventricular ejection fraction less than 40% (LVEF $<40\%$) held in-patient treatment in coronary care and cardiology departments. As a control group examined 25 patients with coronary heart disease (CHD), (stable angina functional class (FC) II-III, postinfarction cardiosclerosis (PICS)), held in-patient treatment in the department of cardiology.
Results: In the study group, 14 patients had serum creatinine concentration within the normal range (71-115 umol / L), 10 patients increased slightly (norm: 123 mmol / l for women and 132 mmol / l for men). When calculating GFR, GFR normal levels (> 90 ml / min) were detected in 4 (13.3%) patients, a decrease in GFR to 60-89 ml / min was observed in 13 (46.6%) ($p \leq 0.05$) of patients to 30-59 ml / min, in 12 (40.0%) ($p \leq 0.05$ in the control group of patients with a creatinine concentration was normal in 27 (90.0% serum) ($p \leq 0.05$) patients and slightly elevated in 3 (10.0%) patients. It highlights the need for calculation of GFR for the timely diagnosis of renal dysfunction in patients with CHF.
Conclusion: The growth of FC in CHF leads to more frequent cases of chronic kidney disease. When FC I and II of heart failure, according to GFR, chronic kidney disease was significantly less, than in patients with chronic heart failure FC III and IV. Reduction of hemodynamic parameters associated with reduced glomerular filtration rate, which indicates the necessity of their correction to reduce the incidence of chronic kidney disease and improve the quality of life in patients with severe FC of CHF.

P2221
Predictors of acute kidney injury in acute cardiorenal syndrome

M Dankova[1]; Z Minarikova[2]; V Hricak[3]; J Gergel[4]; B Zitny[5]; P Pontuch[2]
[1]*The National Institute of Cardiovascular Diseases, Department of Heart Failure and Heart Transplant, Bratislava, Slovak Republic*; [2]*University Hospital, 4th Department of Internal Medicine, Bratislava, Slovak Republic*; [3]*The National Institute of Cardiovascular Diseases, Department of Emergency Cardiology, Bratislava, Slovak Republic*; [4]*Medirex OJSC, Bratislava, Slovak Republic*; [5]*STUVITAL s.r.o., Bratislava, Slovak Republic*

Aim: Aim of the study was to identify independent predictors of acute kidney injury (AKI) in patients with acute heart failure (AHF).
Methods: We analysed clinical, echocardiographic parameters and selected biomarkers in 74 consecutive patients admitted to intesive care unit due to AHF. Mean age of the patients was $69 \pm 10{,}3$ years, with gender distribution 48/26 (M/W). Majority of patients were admitted with de novo diagnosed AHF (55,4%). HFrEF/HFmrEF/HFpEF was in 34/24/16 patients. Mean value of systolic blood pressure (BP) was $140{,}6 \pm 30$ mmHg. Renal damage was defined according to KDIGO guidelines based on creatinine levels and daily diuresis. Patients were divided into two groups AKI + (with renal injury, n=20) and AKI- (without renal injury, n=54). Age, BMI, systolic BP, urinary NGAL, s-NTproBNP, hemoglobin, LVEF were included into the multivariate regression analysis.
Results: The development of AKI was recorded in 27% of patients. These patients were older (median age: 76 vs. 64 years, $p = 0{,}007$), with lower BMI (median: 27 vs.29 kg/m2, $p = 0{,}02$), particularly in HFrEF group (45,8%, $p = 0{,}002$). Urinary NGAL at admission was significantly higher in the AKI + compared to AKI – group (154 vs. 19,5 ng/ml, $p = 0{,}0001$). Except BMI, parameters as age (OR 2,3: 95% CI 1,7-3,7, $p = 0{,}03$), systolic BP (OR 3,0: 95% CI 1,0-5,6, $p = 0{,}02$), u-NGAL (OR 0,97: 95% CI 0,95-0,99, $p = 0{,}0001$) , s-NTproBNP (OR 1,03: 95% CI 0,94-0,98, $p = 0{,}001$), s-hemoglobin (OR 1,4: 95% CI 0,99-1,8, $p = 0{,}04$) and LVEF (OR 1,1: 95% CI 1,02-1,22, $p = 0{,}007$) significantly identified development of AKI.
Conclusions: The predictors of AKI in the AHF patients were age, systolic BP, elevated levels of cardiac failure markers and also renal injury markers together with determination of LVEF and s-hemoglobin at admission.

P2222
Cardiotoxicity in breast cancer patients receiving trastuzumab - assessing the clinical need for a structured cardio-oncology service

A Mcinerney[1]; D Hughes[1]; P Morris[1]; B Mcadam[1]
[1]*Beaumont Hospital, Dublin, Ireland*

Introduction: Trastuzumab has revolutionised the management of HER2 positive breast cancer. However, cardiotoxicity is a well recognised complication. Many patients also receive anthracyclines which can increase this risk. We reviewed the incidence of left ventricular ejection fraction (LVEF) reduction in patients who received trastuzumab in our hospital to assess the need for a structured Cardio-oncology service.
Methods: Review of charts and all echocardiograms (ECHO) for patients who received trastuzumab therapy between 2010 and 2015.
Results: Between 2010 and 2015, 134 patients completed trastuzumab treatment for breast cancer. Follow up data were available on 109. All were female. The average age at first dose was 52 years (SD 12.8). Ninety nine (91%) were invasive ductal carcinoma with 6 (5.5%) being lobular. Eleven (10%) had metastatic disease, 51 (46.8%) had node positive disease and 47 (43.1%) were node negative. Cardiovascular (CV) comorbidities included six (5.5%) with ischaemic heart disease, twenty-two (20.1%) with hypertension, seventeen (15.5%) with dyslipidaemia, three (2.75%) with type II diabetes mellitus and five (4.6%) with atrial fibrillation. Thirty eight (34.9%) had a smoking history. Prior to chemotherapy, 16 (14.7%) were taking either an ACE inhibitor or an ARB, 12 (11%) a beta blocker, 11 (10%) a calcium channel blocker, 5 (4.6%) a loop diuretic and 5 (4.6%) a thiazide diuetic. Fifteen (13.7%) patients were taking an antiplatelet or an anticoagulant. The average number of trastuzumab doses per patient was 17.87. Thirty four (31.2%) received an anthracycline. Seventy five (68.8%) had chest wall radiotherapy: forty (36.7%) to the left chest. Seven (88.9%) had tumour resection. The average number of ECHO's per patient was 5.7. Four had LVEF of less than 50% pre-chemotherapy. Valvular disease was common (16 patients (14.5%)). Twelve (11%) patients had an EF drop by >10%. Of these, two were being treated for metastatic disease. CV risk factors were identified in eight (66.7%). Two had inadequately controlled hypertension. One of these also had atrial fibrillation and dyslipidaemia. One patient had a left bundle branch block on baseline ECG. Six had a smoking history. Seven patients had received an anthracycline, four had left sided radiotherapy. Two had their trastuzumab discontinued and one had a dose reduction. Seven (59%) patients did not have full recovery of their LVEF. Two patients had a Cardiology referral. Both had assessments for other causes and had evidence based therapies commenced or titrated. The remainder did not.
Conclusion: LVEF reduction occurred in 11% in keeping with previously reported figures. The lack of LVEF recovery was unexpected. This may be due to other causes of LVEF dysfunction which were not investigated. Many had known CV risk factors which were not adequately controlled. This demonstrates the need for a more structured Cardio-oncology service within our institution.

P2223
The effect of cardiovascular risk factors and tumor histologic grade in the risk of cardiotoxicity

AC Ana Catarina Gomes[1]; LR Lopes[1]; AG Ferreira[1]; M Correia[1]; I Rangel[1]; K Congo[2]; P Fazendas[1]; H Mansinho[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*; [2]*Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*

Introduction: Cardiotoxicity can be a side effect of chemotherapy (CT) including anthracyclines and taxanes for whom the presence of cardiovascular risk factors also impact. The effect of cancer itself in the risk of developing cardiotoxicity remain to be clarified.
Aim: Prospective study including cancer patients submitted to anthracyclines ± taxanes ± radiotherapy (RT) ± trastuzumab and referred to echocardiographic monitoring during treatment: T0 – before CT, T1 – after the first cycle, T2 – after third cycle, T3 – at the end of CT and T4 - 1 year after the end of CT. The effect of cardiovascular risk factors and the histologic grading of cancers in the risk of developing cardiotoxicity was studied as well as the cardioprotective effect of some drugs, used for other indications.
Results: 108 patients, 79.6% females, age 52.47 ± 12.2 years. Breast cancer 69.4% (29.4% right, 23.9% left and 1.8% bilateral breast cancer; tumor grade: G1 3.7%, G2 48.6%, G3 14.7%), lymphoma 22.2%, gastric cancer 8.3%. Epirrubicine 52.3% and doxorrubicine 47.7%: cumulative dose 506 ± 222 mg/m2. Docetaxel 57.8% and Paclitaxel 2.8%: cumulative dose 511 ± 111 mg/m2. Diabetes Mellitus (DM)

7.3%, hypertension 27.5%, dyslipidaemia 20.2%, obesity 40.4%, smoking 15.6% and alcohol intake 14.6%. 50.5% submitted to Radiotherapy (RT) – median 50GY. Left ventricle ejection fraction (LVEF) and global longitudinal strain (GLS) at baseline: 64.14 ± 4.63% e 20.73 ± 2.68%. 22.9% of patients were taking beta-blocker, calcium channel blocker, ACE inhibitors/ARBs or spironolactone due to hypertension and/or statin for dyslipidemia. The hypertensive patients had a higher LVEF variation between T0-T3 (p = 0.02), although similar GLS, TAPSE and tricuspid S' values in the same interval. GLS at T2 and LVEF at T3 in DM patients were significantly lower (p = 0.018 and p = 0.036, respectively). DLP patients had lower lateral and septal e' values at T1 (p = 0.022 e p = 0.020, respectively). The obese patients had significantly lower lateral e' at T1 (p = 0.008), and a trend for higher TAPSE values – reaching statistically significant value at T3 (p = 0.036) and lower GLS variation in T0-T3 (p = 0.026). At T1, GLS was significantly better in G1 tumors versus G2 (p = 0.001). Lateral S' was lower in G2 tumors versus G3 (p = 0.767). T3: TAPSE was superior in G1 tumors versus G3 (24.0 ± 2.65 versus 19.9 ± 1.6, p = 0.008). There was no difference in LVEF, GLS, TAPSE, tricuspid S' variation in T0-T4, between patients with or without cardioprotective drug and/or statins: p = 0.915, p = 0.599, p = 0.268, p = 0.767 respectively.

Conclusion: Hypertension and dyslipidemia were associated with higher left ventricular dysfunction. Obesity seems to be a protective factor in the risk of developing systolic biventricular dysfunction. The tumor differentiation grade also impacted in systolic biventricular dysfunction. The use of cardioprotective therapy previous to systolic dysfunction didn't seem to have benefit in preventing cardiotoxicity.

P2224

Evaluation of routine use of global longitudinal strain for the early detection of subclinical left ventricular dysfunction in cancer patients

LM Michal Laufer-Perl[1]; A Milwidsky[1]; B Sadeh[1]; D Ravid[1]; N Amrami[1]; M Derakhshesh[1]; J Sherez[1]; G Keren[1]; Y Arbel[1]; Y Topilsky[1]
[1]*Tel Aviv Sourasky Medical Center, Cardiology, Tel Aviv, Israel*

Background: Cardiac toxicity from cancer therapy has become a leading cause of morbidity and mortality in survivors, reaching mortality rate as high as 60% in two years. The most commonly used definition is a reduction in left ventricular ejection fraction (LVEF). However, according to the recent American and European Society of Echocardiography Expert Consensus, global longitudinal strain (GLS) is the optimal parameter for early detection of subclinical LV dysfunction.
Objectives: To evaluate the frequency of GLS reduction in cancer patients and its correlation to LVEF reduction and other echocardiography parameters.
Methods: A retrospective, single-center observational study that included 62 consecutive patients evaluated in the Cardio-oncology clinic from February to December 2016. All patients performed at least two echocardiography exams, including GLS. All exams were performed with the same vendor, technician and interpreting cardiologist. Excluded were patients with reduced LV function (Ejection Fraction < 55%) at baseline. We evaluated the frequency of GLS reduction (once by ≥10% and then by ≥15% relative reduction), its correlation to LVEF reduction and if there are other predicting echocardiographic parameters.
Results: Among 62 consecutive patients, 14 patients (23%) had ≥15% relative reduction in GLS, of which 71% had no concomitant EF reduction. Moreover, 22 patients (32%) had ≥10% relative reduction in GLS, of which 68% had no EF reduction. There were no significant differences in the baseline characteristics; however, exposure to chest radiation was significantly correlated to GLS reduction. No other echocardiography parameters (including diastolic parameters, right ventricular function or systolic pulmonary artery pressure) were significant predictors for GLS reduction.
Conclusions: Early identification of cardiac dysfunction is essential for the prevention of symptomatic heart failure. Our study demonstrates that GLS reduction is frequent among cancer patients and precedes the LVEF reduction and cannot be anticipated by other echocardiography parameters. Using GLS routinely during cancer treatment may lead to an early cardio protective treatment and prevention of irreversible LVEF reduction and heart failure.

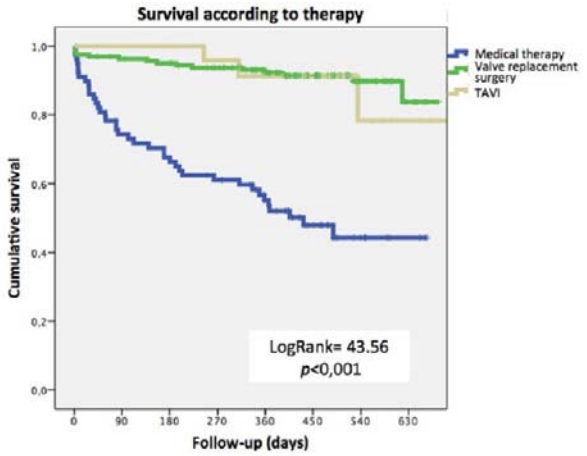
VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

P2225

Severe aortic stenosis: experience and outcomes of a tertiary center

J Agostinho[1]; I Goncalves[1]; I Ricardo[1]; J Rigueira[1]; A Ferreira[1]; R Santos[1]; T Guimaraes[1]; G Lima Da Silva[1]; A Francisco[1]; M Meneses[1]; FJ Pinto[1]; A Almeida[1]
[1]*Hospital Universitário de Santa Maria/CHLN, CAML, CCUL,Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

Introduction: Aortic stenosis continues to be the most prevalent valvulopathy, conditioning high morbidity and mortality. Transcatheter aortic valve implantation (TAVI) remerged as a revolutionary therapy in patients (pts) with high surgical risk, and it may alter the paradigm in the treatment of severe aortic stenosis (sAS). This study aims to characterize the population of pts from a tertiary center with diagnosed sAS during the year 2015 and its therapeutic approach.
Methods: retrospective unicentric study, with inclusion of consecutive pts with sAS (excluding low-flow low-gradient and paradoxical aortic stenosis) diagnosed during 2015 in a tertiary center. Clinical, laboratory and echocardiographic parameters were collected at the time of diagnosis and the type of therapy (medical, surgical, percutaneous) and mortality were evaluated.
Results: A total of 278 pts were included (54% women and 46% men, mean age 74 ± 9 years). The most frequent found comorbidities were hypertension (83.3%), dyslipidemia (67.4%), chronic kidney disease > 3 (34.4%), coronary artery disease (33%), diabetes (32.5%) and smoking (13.7%). Concerning echocardiographic evaluation, the mean left ventricular ejection fraction was 58 ± 11.14% and the peak aortic jet velocity was 4.58 ± 0.5 m/s, conditioning a mean gradient of 52.2 ± 12.7 mmHg. The valve area was 0.75 ± 0.2 cm2 (0.43 cm2/m2 when indexed to body surface area- BSA). The left ventricular mass/BSA mean value was 149.69 ± 41.2 g/m2. 33% of the pts also had significant aortic and/or mitral regurgitation. The majority of the pts was symptomatic, with angor being the most reported symptom (79%) and 43% of pts were in functional NYHA class II. The mean value of NTproBNP was 6911pg/mL.
In this population,167 pts (60.3%) underwent valvular replacement surgery, 4(1.4%) had aortic percutaneus valvuloplasty and 24 underwent TAVI (8.7%). The remaining patients (29.6%, n=82), were maintained under optimized medical therapy and follow-up. The overall mortality rate was 22.1%, and it was significant higher when conservative strategy was adopted (50% vs. 9.3% in pts undergoing surgery vs. 12.5% in pts undergoing TAVI).
Conclusions: This sample, composed of elderly pts with several cardiovascular comorbidities, shows the experience of a tertiary center in the post-TAVI era and reinforces the unequivocal superiority of aortic valve intervention (surgical and/or TAVI) versus conservative medical therapy. TAVI thus emerges as a safe option, comparable to surgery, in this real-life population.



P2226

Epidemiological characteristics; clinical and echocardiographic evaluation of rheumatic mitral stenosis in men

A Abir Abardazzou[1]; S Oummou[1]; A Raouah[1]; S El Karimi[1]; D Benzeroual[1]; M El Hattaoui[1]
[1]*Marrakech University Hospital, the cardiology department , Marrakech, Morocco*

Introduction: In most developing countries, the rheumatic mitral stenosis, sequelae of acute rheumatic fever, is one of the first affections of the young adult. According to the published series, the proportion of women affected mitral stenosis is twice as high as that in men population.
Material and Methods: We report the results of a retrospective study, over 3 years (January 2014 - January 2017), and collected from 300 files of patients with rheumatic mitral stenosis, followed in the cardiology department of University Hospital, MOROCCO.
The objective of our work is to identify the particularity epidemiological; Clinical and echocardiographic of rheumatic mitral stenosis in men.
Results: The series consists of 130 men and 170 women; The average age of women was 38 years compared with 45 years for men; The majority of men (70%) are diagnosed after the age of forty.

The Clinical presentation shows no specificity between the two sexes.
Heart failure and complete atrial fibrillation arrhythmias are the most frequent complications in both sexes; With a clear predominance of the complete atrial fibrillation arrhythmias in women (80%) against 60% of men.
The calcifications of the mitral valve and the shortening of the device under valvular are found in 82% of the men against 52% of the women.
The mitral stenosis was very tight in women (68%) and tight in men (50%).
Associated aortic valvulopathy was more common in men with 80% versus 64% in women.
The left atrial dilation and intra-auricular thrombus were more common in women, whereas that men had more dilated cavities.
Conclusion: Through this study we concluded that in man, the diagnosis of rheumatic mitral stenosis arises later; The rheumatic lesions are more severe and the aortic valvular involvement is more frequently associated.
The repercussion on the right cavities is more frequent, whereas that, the passage in complete atrial fibrillation arrhythmias as well as the intra-auricular thrombus are less observed in the man.

P2227
Predictors and long-term outcomes after transcatheter aortic valve replacement in high-risk patients with severe aortic stenosis

E Munoz-Garcia[1]; M Munoz-Garcia[1]; AJ Antonio Jesus Munoz Garcia[2]; AJ Dominguez-Franco[2]; F Carrasco-Chinchilla[2]; JM Garcia-Pinilla[2]; L Morcillo-Hidalgo[2]; JH Alonso-Briales[2]; JJ Gomez-Doblas[2]; MF Jimenez-Navarro[2]; JM Hernandez-Garcia[2]; E De Teresa-Galvan[2]
[1]Department of Cardiology , Malaga, Spain; *[2]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

Few data exist on the clinical impact of Transcatheter Aortic Valve Replacement (TAVR) in patients with symptomatic aortic stenosis and a high surgical risk. The aim of this study was to determine the survival and the factors predicting mortality after TAVR with the Auto-expandable prosthesis.
Methods: From April 2008 to December 2016, the CoreValve prosthesis was implanted in 582 patients with symptomatic severe aortic stenosis with deemed high risk.
Results: The mean age was 79.4 ± 6.9 years. The logistic EuroSCORE and STS score were 17.5 ± 12% and 7.3 ± 5%, respectively. The implantation success rate was 98.9%. In-hospital mortality was 3.4%, and the combined endpoint of death, vascular complications, myocardial infarction or stroke had a rate of 14%. The late mortality (beyond 30 days) was 32.1%. Survival at 1, 2, 3, 4 y 5 years were 83.3%, 78.3%, 71.8%, 60.7% and 50.3%% respectively, after a mean follow-up of 36.5 ± 25 months. The NYHA functional class improved from 3.1 ± 0.6 to 1.77 ± 0.7 in the follow-up. The predictors of cumulative mortality were: Charlson index [HR 1.2 (95% CI 1.08-1.336), p = 0.001], Acute Kidney Injury [HR 1.94 (95% CI 1.203-3.141), p = 0.007], Frailty [HR 2.33 (95% CI 1.43-3.817), p = 0.001] and protective factors were a higher Karnosfky index [HR 0.987 (95% CI 0.976-0.998) p = 0.002] and Ejection Fraction [HR 0.372 (95% CI 0.203-0.681), p = 0,001]
Conclusions: TAVR is associated with significant survival benefit throughout 2.59 years of follow-up. Survival during follow-up depends particularly among patients with associated comorbidities.

P2228
Redo-MVR operations: a 11-year single center experience

A Artan Bajraktari[1]; I Bytyci[2]; E Prifti[1]
[1]University Hospital Center Mother Theresa, Division of Cardiac Surgery, Tirana, Albania; *[2]University Clinical Centre of Kosovo (UCC), Clinic of Cardiology, Pristina, Kosovo Republic of*

Background and Aim: Major advances have been made in mitral valve (MV) surgical technique, prosthesis design and perioperative care for patients undergoing MV replacement (MVR). Improved survival has inevitably meant that more patients will require redo-MVR during the follow-up. Patients undergoing redo-MVR are a diverse population. The aim of this study was to investigate the indications, clinical and epidemiological data of the patients who underwent the redo-MVR.
Methods: A retrospective review of hospital records was performed for 116 patients with age 49 ± 11 years (20-76 years), who underwent redo-MVR operations between 2004 and 2014. We described proper indications, clinical and epidemiological, preoperative, operative, and postoperative data of the study patients.
Results: Of study patients, 84% were female, 86% in NYHA III and 12% in NYHA IV class. Re-interventions were done for the first time in 89%, for the second time in 7.8 % and for the third time in 3.5 % of the patients. Mean time of the re-intervention was 11 ± 7.5 years from the previous intervention. Planned operation was done in 68%, whereas in 32% of patients it was an emergency. Previous MVR had 44% of patients, 40% were patients after commisurotomy, 2% after mitral valve reparation and 15% of them had concomitant interventions. From study patients, 54% had mitral stenosis, 33% had mitral regurgitation, whereas 13% had combined mitral valve disease (stenosis and regurgitation). Indications for in redo-MVR were: valvular structural degeneration (40%), thrombosis of MV prosthesis (17%), residual MV stenosis (14%), paravalvular fistulas and mitral valve regurgitation (11%, for both). Mechanical MV prosthesis was implanted in 77%, whereas biological MV prosthesis in 12% of patients. Concomitant heart intervention was performed in 40% of operated patients (6 patients had aortic valve replacements, 4 had tricuspid valve replacements, 11 underwent tricuspid valvuloplasty and 3 patients had aorto-coronary by-pass). The prosthetic dimensions were 28.6 ± 1.8 mm. Aortic cross-clamping time was 22 ± 13 minutes, length of stay in intensive care unit was 91 ± 14 hours, whereas the duration of hospitalization was 22 ± 13 days.
Conclusions: Female gender dominates and valvular structural degeneration is the most common indication for redo-MVR operation. The MV prosthesis thrombosis, emergency rate of redo-MVR and the hospital stay remain high in these patients.

P2229
Changes over time in infective endocardites disease

A Ana Marques[1]; I Cruz[1]; I Joao[1]; AL Broa[2]; S Alegria[1]; AC Gomes[1]; G Morgado[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal; *[2]Hospital Garcia de Orta, Internal Medicine, Almada, Portugal*

Background: Epidemiologic profile of patients (pts) with infective endocarditis (IE) has changed in recent years with fewer cases associated with rheumatic disease and a higher incidence in elderly due to degenerative valvular disease and health-care associated procedures.
Purpose: To analyze the main differences between 2006-2010 and 2011-2015 IE pts relative to epidemiology, microbiologic profile, outcomes during hospitalization and in-hospital death rate.
Methods: Retrospective study including consecutive pts with IE admitted to our centre during a 10 year period (2006-2015). Data on demographics, past medical history, clinical presentation, isolated microorganisms and echocardiogram findings were evaluated, as well as hospitalization outcomes. The differences between 2006-2010 and 2011-2015 IE pts were analyzed.
Results: We included 134 pts, 98 (73%) males, mean age 61 ± 16 years.53 pts were diagnosed with IE during 2006-2010 period and 81 pts during 2011-2015 period.
The pts diagnosed between 2011-2015 had a significantly lower median age (59 vs 73 years, p = 0.037), more previous hepatic disease (37% vs 14%, p = 0.001) and HIV infection (23% vs 7%) and fewer past history of arterial hypertension (32 vs 63%, p < 0.001) and coronary artery disease (6 vs 20%, p = 0.022). At admission, comparative to 2011-2015 pts, the 2006-2010 IE pts had less anaemia (9 vs 43%, p < 0.001) and embolization symptoms (11 vs 28%, p = 0.032). The infection was significantly more considered to be nosocomial/health-care associated in 2011-2015 pts (9 vs 31%, p = 0.004).
The right-side valves were more affected in 2006-2010 pts (23 vs 7%, p = 0.007). The mitral and aortic valves, as well as the prevalence of prosthetic and native valve IE weren´t significantly different.
Relative to microbiology, it was observed more IE due to viridans streptococci (4 vs 17%, p = 0.018) and less due to Streptococcus milleri (6 vs 0%, p = 0.03) during 2011-2015 period.
We didn´t observed significantly differences between the two groups relative to echocardiographic findings, mean length of hospital stay, adverse events during hospitalization, number of pts submitted to cardiac surgery and in-hospital death rate.
Conclusion: The IE profile pts had changed during the 10 years period, with more elderly pts, with more cardiovascular risk factors like arterial hypertension and coronary artery disease, more anemia and embolization symptoms at presentation, and more nosocomial/health-care associated infective endocarditis during 2010-2015 period. In this group, the right-side valves were less affected as well as isolation of Streptococcus milleri. On the other hand, the infection due to viridans streptococci was higher.
Unfortunately, we didn´t observed a decrease in length of hospital stay, adverse events during hospitalization and in-hospital death rate.

P2230
Safety and effectiveness of percutaneous mitral commissurotomy for rheumatic mitral stenosis

M Majed Hassine[1]; M Boussada[1]; I Mechri[1]; M Mahjoub[1]; M Ben Massoud[1]; Z Dridi[1]; F Betbout[1]; H Gamra[1]
[1]Cardiology A Department – Fattouma Bourguiba University Hospital, monastir, Tunisia

Background: Percutaneous mitral commissurotomy (PMC) has become the reference treatment for mitral stenosis in patients with favorable valvular anatomy.

Purpose: We sought to evaluate the safety and effectiveness of PMC for patients with mitral stenosis.
Methods: Late results of PMC were assessed in 1035 consecutive patients at our institution. A good immediate result was defined as valve area ≥ 1.5 cm^2 without mitral regurgitation > 2/4. PMC are using a double balloon or the Inoue balloon.
Results: The average age in our population was 35 ± 12 years. Good immediate results were obtained in 92.4%.
The 20-year rate of good functional results (survival without cardiovascular death, mitral surgery, or repeat percutaneous mitral commissurotomy and in New York Heart Association class I or II) was 47.6 ± 2.4%.
A multivariable Cox model identified 3 predictive factors of poor late functional results: Prior commissurotomy ($p = 0.014$), Wilkins score>8 ($p < 0.0001$) and final mitral valve area < 1.8 cm^2 ($p < 0.0001$).
The scoring system was derived from the final multivariable model in the derivation cohort of 987 patients, corresponding to predicted good functional results in the validation cohort.
Conclusions: Twenty years after percutaneous mitral commissurotomy in a population of patients with varied characteristics, 47% still had good functional results. Prediction of late functional results is multifactorial and strongly determined Wilkins score and the quality of immediate results. A simple validated scoring system is useful for estimating individual patient outcome.

P2231
Short-term mortality is not influenced by aminoglycozide decrease in renal function during treatment of prosthetic valve endocarditis

MM Monica Mariana Baluta[1]; E Panaitescu[2]; MM Vintila[3]
[1]*Carol Davila University of Medicine-St Pantelimon Clinical Emergency Hospital-Cardiology Department, bucharest, Romania*; [2]*Carol Davila University of Medicine and Pharmacy , Medical Informatics and Biostatistics, Marketing, Medical Technology , Bucharest, Romania*; [3]*St. Pantelimon Emergency Hospital, Cardiology, Bucharest, Romania*

Introduction: Antibiotic therapy (AT) for prosthetic valve endocarditis (PVE) is standardized by guidelines and depends on the etiology and on the type of PVE. Aminoglycosides (AGs), especially Gentamicin is often included in the antimicrobial combination for the management of PVE.
Purpose: The objective of our study is to quantify the potential nephrotoxic effect of AGs and to verify those speculations from literature about their relationship with mortality and about the safety and efficacy of single dose administration in PVE patients.
Methods: Retrospective analysis of 56 patients admitted with PVE in two university hospitals over 5 years (2000-2004). We divided our patients in two groups: early and late PVE related to time of surgery for valve replacement. We evaluate the influence of antimicrobial therapy with AGs on renal function. Kidney function abnormalities were determined by blood creatinine (Cre). We defined renal injury as low (LRI: Cre < 2 mg/dl), moderate (MRI: cre≥2and < 3 mg/dl) and severe (SRI:cre≥3mg/dl). We analyzed (uni- and multivariate analysis) if the absence of AGs or presence of AGs administered once or multiple doses influenced the renal function. AGs were used according to the antibiogram or with infectious specialist decision. AGs duration was individualized according to renal function and guidelines.
Results: We found 52% patients with early vs 48% late PVE with high rate of negative blood cultures 55.2 % in early vs 48.2% late PVE. Patients outcome: responders to antibiotics: 71%, in-hospital death 2%, transferred due to complications 27%. AT was frequently changed due to side effects but the type of combinations did not influence the overall efficacy of AT. Amikacin was frequently used according to antibiogram but also for negative blood culture endocarditis. LRI was observed fifth times higher in patients with multiple dose AGs compared with those without AGs ($p = 0.01$, $\chi 2 = 6.25$, RR=2.3, OR= 5.56) and similar with them with single dose ($p = 0.2$, $\chi 2 = 3.81$). MRI was observed seventh times higher in patients with multiple dose AGs compared with those without AGs ($p = 0.01$, Fischer, RR=3.6, OR=7.5) and similar with them with single dose ($p >> 0.05$). MRI was more frequent with Imipenem-Amikacin association ($p = 0.008$). SRI was not influenced by type of administration (single dose $p = 0.2$, $\chi 2 = 3.81$; multiple doses $p = 0.1$, Fischer).There was no statistical correlation between mortality and renal impairment determined by AGs.
Conclusions: Multiple dose AGs administration determines more renal function impairment than in patients treated without AGs. Nevertheless, in-hospital mortality was not influenced by AGs decrease in renal function. Single dose AGs does was safe without significant renal function impairment. Amikacin was safe and effective including in negative blood culture PVE. Study limitation: small number of patients and lots of negative blood cultures PVE.

P2232
Relation of frequency and severity of mitral regurgitation to clinical and paraclinical features among patients with heart failure

AN Anass Inchaouh[1]; A Hadadi[1]; R Habbal[1]
[1]*Ibn Rochd University Hospital, Casablanca, Morocco*

Introduction: Mitral regurgitation (MR) is a common finding in patients with heart failure(HF), and it often develops during progressive remodeling and dilation of the left ventricle. However, the association between the presence of varying grades of MR, clinical, paraclinical features and symptoms in patients with HF has not been well characterized. The purpose of this analysis was to determine the frequency of MR in patients with LV systolic dysfunction and clinical HF, and to explore the relations between the presence and severity of MR and cardiovascular profile.
Methods: This is a retrospective study of all patients with HF in combination with MR registered in the therapeutic Unit of Chronic Heart failure in the cardiology department over a period of 3 years. Patients were diveded to 3 groups following the MR grades wich was defined according to the european society of cardiology guidelines into : mild, moderate and severe MR.
Results: The study was conducted in 893 patients with a mean age of 67.9 years and male predominance (56,2%). The group with mild MR was the most presented(52,1%) and was charcterized by older age(70.7 years old), higher prevalence of hypertension, dyslipidemia, stroke, myocardial infarction, renal failure and anemia ; the most prescription of β-blockers and ischemic HF was the most frequent etiology. The group with moderate MR was charcterized by higher prevalence of diabetes, smoking history, number of hospitalization and right ventricular dysfunction; the lowest ejection fraction(EF) and the most prescription of angiotensin-converting enzyme (ACE) inhibitors. The group with severe MR was the younger group, the most symptomatic with frequent class III of NYHA and was characterized by the lowest Cardiovascular risk factors, higher prevalence of left ventricular dilation and the highest EF.
Conclusion: Our study shows that mild and moderate MR is common in patients with HF. Physicians should consider the early management of MR to be a therapeutic target that could favorably affect clinical status and outcome of patients with systolic HF.

DEVICES/CRT/ICD/SURGERY

P2233
How does pulmonary arterial pressure improve after mitral valve surgery in patients with preoperative pulmonary hypertension?

F Lopez Valdiviezo[1]; J Joffrey Eduardo Lujan Valencia[1]; J Hernandez Campo[1]; MA Gutierrez Martin[1]; C Velazquez Velazquez[1]; O Araji Tiliani[1]; JM Barquero Aroca[1]
[1]*Virgen Macarena University Hospital, Sevilla, Sevilla, Spain*

Introduction and objectives: Left heart pathology, including mitral valve disease, causes damage on the pulmonary vasculature and, therefore, the development of pulmonary hypertension. The aim was to compare the reduction of preoperative pulmonary pressures with respect to one year control in patients who underwent mitral valve surgery with diagnosis of pulmonary hypertension.
Methods: We reviewed all patients diagnosed with pulmonary hypertension who underwent any mitral surgery from January 2010 to June 2015. A total of 61 patients were included. Clinical and echocardiographic data both pre and postoperative were collected and compared changes in pulmonary pressure at one year follow up. In addition, a subdivision according to the type of surgery was performed.
Results: Of 61 patients, 36 (59%) were women with a mean age of 66 ± 2.17 years. 72% were in functional class III-IV. Mean preoperative pulmonary arterial pressure was 53.74 ± 3,44mmHg. A perioperative mortality of 18 % was observed. At follow-up, mean pulmonary arterial pressure was 34.44 ± 3,81mmHg (difference of 19.33 ± 4,12mmHg $p < 0.0001$). In the subdivision according to type of surgery the reduction was: 22.2 ± 8,88mmHg for mitral repair, 5,57 ± 18.43mmHg for mechanical prosthesis and 10.75 ± 9,4mmHg for biological prosthesis.
Conclusion: Mitral valve surgery improves pulmonary arterial pressure in patients with preoperative pulmonary hypertension, being more evident with valve repair. Perioperative mortality is high; but patients who are discharged, have excellent survival follow-up.

P2234
Effect of hemodynamic status on postoperative outcome in infective endocarditis: a literature overview

WP Mistiaen[1]
[1]*Artesis-Plantijn University College, Health and Social Care, Antwerp, Belgium*

Purpose: Infective endocarditis (IE) is a serious condition with a high 30-day mortality. Surgery is needed in many patients. The preoperative hemodynamic status

(congestive heart failure or CHF, need for emergent surgery, need for mechanical support, NYHA functional class III/IV) could have an impact on postoperative outcome. Each of these parameters is an indication for the inadequacy of the left ventricle to maintain an adequate circulation.
Methods: A literature search was performed using "endocarditis AND hospital mortality OR outcome AND predictor" and "International Collaboration on Endocarditis – Prospective Cohort Study" in Web of Science database, (2010 to 2016). Manuscripts were excluded if no logistic regression was available or if hemodynamic status was not included in the analysis. This resulted in nine manuscripts. The predictors were ranked according the odd ratios (numerator: place of the parameter, denominator: total of identified predictors).
Results: Most studies are coming from one tertiary center and are retrospective, with different designs. Recruitment periods are long with small patient populations. Definitions of hemodynamic status are not uniform. Need for emergent surgery is mostly labeled as "needed within 24h". Thirty-day mortality varies between 10 and 50%. In almost all papers, the hemodynamic status is ranked as first, according to the odds ratio.
Conclusions: A compromised hemodynamic status is the dominant predictor for 30-day mortality after surgery for IE. However, IE is a heterogeneous condition. In spite of these limitations (listed above), development towards a compromised hemodynamic status could be prevented by timely surgery.

ranking of the hemodynamic status

Author (year)	hemodynamic status	rank	OR	95%CI	p-value
Caes 2014	emergency	1/7	11.8	2.8-50.3	0.001
Chirouze 2015	CHF	2/3	2.0	1.1-3.5	0.016
Gaca 2011	emergency	1/14	3.2	3.0-3.3	0.001
Garcia 2013	CHF	1/17	2.4	1.8-3.1	0.001
Grubitzsch 2014	mechanical support	1/3	3.8	1.7-8.4	0.001
Kiefer 2011	NYHA III/IV	1/6	3.4	2.5-4.6	-
Musci 2010	mechanical support	1/5	4.3	3.1-5.9	0.001
Ohara 2012	CHF	1/3	7.4	1.8-30.7	0.01
Sambola 2010	CHF	1/4	19.5	3.5-108.2	0.001

CHF: congestive heart failure; NYHA: New York Heart Association; OR: odds ratio; 95%CI: 95% confidence interval; p: probability

P2235
Value of clinical information from cardiac stimulation devices in the heart failure program: the hf + ep team

C I Clara Ines Saldarriaga[1]; H Pino[2]; YA Vasquez[2]; JD Ramirez[1]; JF Agudelo[1]
[1]Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia; *[2]medtronic, heart and rhythm, bogota, Colombia*

Cardiac stimulation devices have clinical information that can be useful in the follow up of heart failure patients.
Objective: to identify the frequency of events detected by cardiac stimulation devices in a cohort of patients from a Colombian heart failure program and the impact of the knowledge of this information in clinical decisions.
Methodology: Prospective cohort study. All patients had a cardiology evaluation plus device interrogation (atrial fibrillation, FV/VT episodes, optivol index, impedance, and hour of daily activity).
Results: 101 patients were included during 4 months; 43.7%% were women with a mean age of 65 years (IR 24 – 89). The types of devices are listed in table 1. 27.7% of the patients had at least 1 alert in the device. 67% were due to arrhythmia, 28% were optivol alerts, and 10% were changes in impedance. In 96.4% of the cases, this information was important and changed medical decision. 42.8% of the patients had a change in medications (increase in beta-blocker dosage or start antiarrhythmic), 42.85% had an increase in diuretic dose, and 14.28% required reprogramming of the device. Hospitalizations of this population during the next three months were 13.8%.
Conclusion: Clinical information from cardiac devices is important for the HF + EP team in detecting predictors of decompensation in heart failure. This provides an opportunity for remote monitoring programs in Colombia.

table 1: type of devices

Device	Percentage
Pacemaker	16.84%
CRT + P	5.94%
CRT + D	27.72%
ICD	49.5%

type of devices

P2236
VitD Calc a mobile application for patients with heart failure and significant mitral regurgitation which helps to identify those at risk for vitamin d deficiency.

O Mozenska[1]; J Bil[2]; A Segiet[3]; P Podziemski[4]; DA Kosior[1]
[1]Clinical Hospital of the Ministry of Internal Affairs, Cardiology and Hypertension, Warsaw, Poland; *[2]Clinical Hospital of the Ministry of Internal Affairs, Invasive Cardiology, Warsaw, Poland*; *[3]Medical University of Warsaw, 1st Medical Faculty, Warsaw, Poland*; *[4]Maastricht University, Physiology, Maastricht, Netherlands*

Introduction: Vitamin D deficiency is increasingly attracting attention in the field of cardiovascular research. For patients with heart failure (HF) is it a known morbidity and mortality risk factor. At the same time cardiology is one of the fastest and receptive areas of medicine to utilize new and emerging technologies.
Purpose: We aimed for equipping cardiologists in their everyday busy practice with a simple tool to identify amongst patients with HF and significant mitral regurgitation (MR) those at risk for vitamin D deficiency.
Methods: 99 consecutive patients hospitalized in our Department between July and September 2013 were included in the study. Inclusion criteria were: age>18, HF and significant MR assessed with transthoracic echocardiography (TTE) (vena contracta>3mm, effective orifice area (ERO)>0.2 cm2, MR volume>30ml/s). We used uni-and multivariate analysis to look for vitamin D deficiency classifier.
Results: We included 39 patients with severe MR and 60 with moderate MR (39.9% and 60.6% accordingly, median age 75 yrs [Q1-Q3 66.0-81.5], 35.4% were female). Median left ventricular ejection fraction (LVEF) was 50% [Q1-Q3 29.00-62.00], median LV diastolic diameter was 56 mm [Q1-Q3 49.5-65]. Median 25(OH)D3 was 14.8 ng/ml [Q1-Q3 9.93-20.12]. Using multivariate analysis, we found a classifier for vitamin D deficiency in population with HF and significant MR (including radius of PISA, left atrium area in apical 2-chamber view and posterior wall diastolic diameter) with AUC of 89.1% (85.7% specificity and 78.6% sensitivity). We further used the formula and developed VitD Calc – a mobile application available in the Play store (link) which allows clinicians in 3 simple steps to predict probability of vitamin D deficiency in their patients.
Conclusions: Mobile technology and telemedicine are already present in our everyday medical practice. Answering the need for practical implementation of our research results we developed a mobile tool that helps cardiologists in identifying patients at risk for vitamin D deficiency. Further studies are needed to validate our application.

P2238
Cardiac kinematic parameters computed from video of in situ beating heart during coronary artery bypass grafting

G Giacomo Rozzi[1]; L Fassina[2]; S Rossi[3]; S Scacchi[2]; M Galletti[4]; P Colli Franzone[2]; G Petrilli[1]; G Faggian[1]; M Miragoli[3]
[1]University of Verona, Scienze chirurgiche odontostomatologiche e Materno-infantili, Verona, Italy; *[2]University of Pavia, Pavia, Italy*; *[3]University of Parma, Medicina Clinica e Sperimentale, Parma, Italy*; *[4]Italian Workers' Compensation Authority (INAIL), CERT Research Center, Parma, Italy*

Mechanical function of the heart during open-chest cardiac surgery is monitored by transesophageal echocardiographic techniques (TEE). However, little is known about local kinematics, particularly for the reperfused region after an ischemic event. We reported a novel imaging modality, which extracts local and global kinematic parameters from recorded videos of in-situ beating cardiac tissue, displaying live data of the contraction events. A custom algorithm tracks the movement of a circular video-marker positioned ad hoc onto the selected area and analyses, during the entire recording, frequency, contraction trajectory, displacement, velocity, contraction force, and kinetic energy. Furthermore we implemented our algorithm with particles image velocimetry tool (PIV), showing difference for global epicardial tissue vorticity and velocity during systolic and diastolic phases.
After validation in-silico and in ischemic/reperfused rat hearts we applied our technique on beating human hearts, i.e. ten patients underwent coronary artery

bypass graft (CABG, >75% coronary occlusion), and faced the results with the conventional gold-standard TEE approach. While both ejection fraction (EF) and fractional shortening (FS) showed global left-ventricle recovery in all patients (EF: from 37.7 ± 6.2 to 52.4 ± 5.6; FS: from 25.0 ± 5.2 to 40.5 ± 2.6) our technique precisely detected an average improvement for kinetic energy (from 37190 ± 5216 to 40240 ± 7617) and contraction force (from 26260 ± 2862 to 32730 ± 4612) but not for all patients, plausible due to the level of local myocardial stunning. Particle image velocimetry showed an average improvement for velocity (from 1.96 ± 1.16 to 2.58 ± 1.61) after CABG but not for those patients who did not display a recover of the aforementioned kinematic parameters.
Our functional imaging technique adds important kinematic values on cardiac outcomes and supports the intervention in contact-free and non-invasive mode by detecting the level of myocardial stunning. Moreover, it can be easily adopted in the cardiac theater with TEE and does not require particular operator-dependent skills.

P2239

Four years of baroreflex activation therapy in advanced heart failure: 3rd long-term follow-up report of a proof-of-concept study

E Gronda[1]; G Costantino[1]; A Alberti[1]; B Baronio[1]; T Staine[1]; G Grassi[2]; G Seravalle[3]; E Vanoli[1]
[1]IRCCS Multimedica, Cardiovascular Departement, Sesto San Giovanni, Milan, Italy; [2]Università Milano-Bicocca, Clinica Medica, Monza, Italy; [3]Istituto Auxologico, Milan, Italy

Funding Acknowledgements: The study was sponsored by CVRx, Inc., Minneapolis, Minnesota, USA.

Background and Purpose: In a proof-of-concept study of eleven heart failure patients with reduced ejection fraction (HFrEF), Baroreflex Activation Therapy (BAT) effectively reduced sympathetic activity in the peroneal nerve (MSNA) at 6 and 22 average months of follow-up. Hospitalization rate was also significantly lower during these follow-up periods relative to pre-implant baseline. The objective of the present study is to extend the long-term follow-up data on this patient cohort over 42 months.
Methods: and Results: Eleven patients were enrolled in the study who presented with optimized, stable, guideline-directed medical therapy, NYHA Class III HFrEF with left ventricular ejection fraction (LVEF) ≤ 40%, and no indication for cardiac resynchronization therapy. For the present report, MSNA, baroreflex sensitivity data and hospitalization rate together with standard clinical data were collected at 6, 21.5 ± 4.2 and 42.5 ± 3.5 months following BAT activation. Four patients died during long-term follow-up. The remaining seven patients (two with ischemic heart disease) maintained the improvements observed at 6 months, including reduced sympathetic activity, reduced hospitalization rate and improved clinical variables as addressed in Table 1. Blood pressure and heart rate did not change over the course of follow-up.
Conclusion: BAT provides chronic reductions in sympathetic activity and restrains utilization of hospital resources in patients with HFrEF. Patient clinical presentation, quality of life and functional capacity are consistently improved and maintained. The temporal association of BAT with sympathetic drive diminution and improvement in objective clinical measures suggests a cause-and-effect relationship that is currently under investigation in a randomized, controlled outcomes trial.

Table 1. BAT long-term follow-up data

	Baseline	21.5 ± 4.7 months	41.5 ± 3.5 months	P-value
MSNA (bursts/min)	41 ± 6	31 ± 8	26 ± 3	< 0.001
Minnesota living with heart failure score	31.3 ± 26.0	17.7 ± 9.2	16.9 ± 7.7	< 0.005
Six-minute walk distance (m)	306 ± 31.4	365 ± 36.2	425 ± 116	0.001
LVEF (%)	31.1 ± 6.0	35.1 ± 3.6	37.1 ± 9.1	< 0.02
Hospitalization rate (days/year/patient)	17.18	0.93	0.87	< 0.001

P2240

The effects of haemoglobin and doxycycline in response to non-physiological shear stress in bovine and human blood

C Christian Robinson[1]; I L Pieper[1]; V Kanamarlapudi[1]
[1]Swansea University, Swansea, United Kingdom

Background: The effects of non-physiological shear stress were evaluated by measuring the activity and integrity of platelets and von Willebrand factor (vWF) in the presence of haemoglobin and doxycycline in human and bovine blood.

Purpose: Left ventricular assist devices (LVADs) exert high levels of non-physiological shear stress on the blood components. However, little is known of the relationship between haemoglobin, doxycycline and vWF.
Methods: Bovine and human whole blood, platelet-rich plasma and platelet-poor plasma containing haemoglobin, doxycycline, both or none were subject to shear stress in vitro. Platelet function and vWF activity and integrity was analysed using ELISA, immunoblotting and ristocetin-induced platelet aggregometry.
Results: Shear stress leads to reduced vWF activity and integrity. However, these effects can be minimised with doxycycline or haemoglobin. Immunoblotting and ELISA indicate that collagen binding activity is preserved. This study suggests that haemoglobin enhances ristocetin-induced platelet aggregation.
Conclusions: Shear stress results in vWF degradation and reduced platelet function, which may be contributing to gastrointestinal bleeding in LVAD patients. Furthermore, haemoglobin seems to be protective of vWF degradation and enhances platelet aggregation. As such, vWF may be lost in platelet aggregates. Thus, haemoglobin levels could reduce the risk of gastrointestinal bleeding, but contribute to the development of thrombosis in LVAD patients.

P2241

The predictive value of proteinuria for mortality or renal failure in patients receiving left ventricular assist devices.

R Rahat Muslem[1]; K Caliskan[1]; S Akin[1]; A Constantinescu[1]; DA Hesselink[2]; G Whitman[3]; RJ Tedford[4]; AJJ Bogers[5]; SD Russell[4]; OC Manintveld[1]
[1]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; [2]Erasmus Medical Center, Nephrology, Rotterdam, Netherlands; [3]Johns Hopkins University of Baltimore, Cardiothoracic Surgery, Baltimore, United States of America; [4]Johns Hopkins University of Baltimore, Cardiology, Baltimore, United States of America; [5]Erasmus Medical Center, Cardiothoracic Surgery, Rotterdam, Netherlands

Purpose: This study evaluated the predictive value of proteinuria before Left Ventricular Assist Device (LVAD) implantation in relation to renal failure and mortality during the first-year.
Methods: A retrospective multicenter cohort study was conducted, evaluating all LVAD patients (n = 241) implanted in the two participating centers with age ≥18 years and minimal survival >48 hrs. A urinary dipstick was available in 201 (83%) patients within a 7-day period before LVAD implantation. Proteinuria was defined as ≥trace (≥1 +) and renal failure as the need for renal replacement therapy. Exclusion criteria were; positive for microscopic haematuria (>3 RBC/hpf or positive dipstick for haematuria), 28 patients were excluded.
Results: Overall, 173 patients met the inclusion criteria (mean age 52.3 ± 13.3, 78% male, mean eGFR at baseline 60.1 ± 25.9 mL/min per 1.73 m2), of who 42 (24%) had significant proteinuria (mean age 54, 76% male, mean eGFR 60 ± 32.3 mL/min per 1.73 m2). During the first-year 32% of the patients with proteinuria vs. 16% without proteinuria developed severe renal failure (adjusted HR 2.47, 95% CI 1.18 to 5.15, p = 0.016). The 1-year survival was 52% in patients with proteinuria vs. 78% in patients without proteinuria (Log-rank p < 0.001). In multivariate analysis proteinuria was identified as an independent predictor of 1-year mortality (HR 2.09, 95% CI 1.14 to 3.84, p = 0.017).
Conclusion: Proteinuria in patients undergoing LVAD implantation was highly associated with renal failure and mortality.

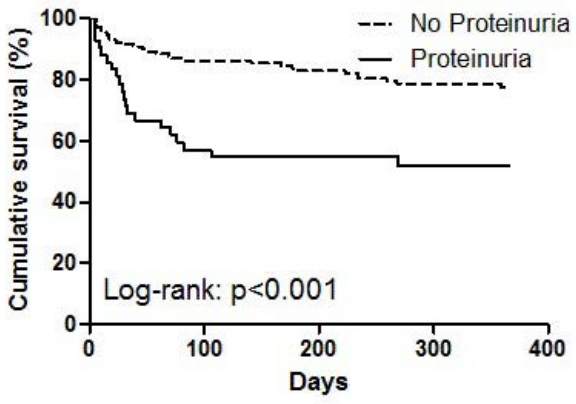


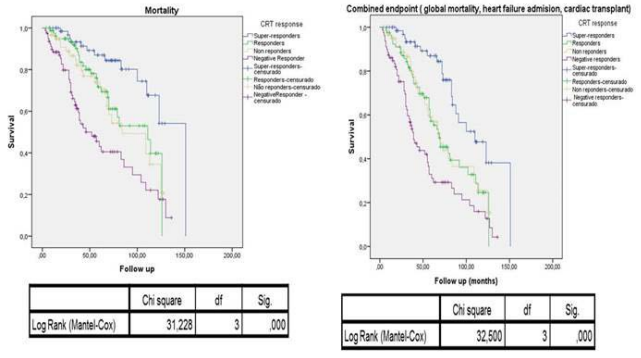
figure 1. survival

P2242

Long term outcome of different responses to cardiac resynchronization therapy

V Vera Marinho[1]; J Milner[1]; P Alves[1]; M Santos[1]; C Domingues[1]; N Antonio[1]; M Ventura[1]; J Cristovao[1]; L Elvas[1]; F Goncalves[1]; M Pego[1]
[1]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*

Introduction: There is strong evidence that Cardiac Resynchronization Therapy (CRT) reduces mortality and hospitalization, and improves cardiac function in heart failure (HF) patients. However, response to CRT may vary widely (from negative-responders to super-responders). Aim: The aim of this study was to evaluate de long-term prognosis of patients with different responses to CRT.
Population and Methods: Retrospective single-centre study that included all patients submitted to CRT therapy between January 2006 and December 2015. Super-responders were defined as patients with at least a duplication of baseline left ventricular ejection fraction (LVEF) or a LVEF >45% at 6 months echo. Responders included all patients with an increase of LVEF > 25%, without super-response criteria. Non-responders were defined as patients with an increase in LVEF from baseline ≤ 25% and negative-responders as patients with a decrease in LVEF. During a median follow-up of 57 months (IQR=31-78), we evaluated all-cause mortality, transplantation and admission for heart failure. Survival curves were compared using the log rank test.
Results: In this cohort of 431 patients, 103 (23.9%) were submitted to CRT-P and 328 (76.1%) to CRT-D. There were 23.4% super-responders, 28.9% responders, 20.6% non-responders and 27.1% negative-responders. Regarding baseline characteristics, super-responders were more frequently female (48.5% vs 29.8 vs 25.0 vs 19.9%, respectively, p = 0,001), had less ischemic etiology (16.2 vs 29.8 vs 37.3 vs 38.0%, respectively, p = 0.019). The QRS duration was proportion to CRT response (152.3 ± 39.0 in super-responders vs 148.8 ± 30.5 in responders vs 144.3 ± 24.7 in non-responders vs 135.7 ± 27.0 ms in negative-responders, p = 0.045). The were no significant differences in baseline echocardiographic parameters or other baseline characteristics between groups.
During long-term follow-up, there were significant differences in global mortality, heart transplantation and readmission due to heart failure, with a continuum worsening of outcomes from super-responders to negative-responders. The global mortality ranged from 11.8% in super-responders, 25.0% in non-responders to 39.2% in negative-responders (p = 0.002). Heart transplantation rate ranged from 1.5% in super-responders, to 4.8% in responders to 6.7% in non-responders and 13.9% in negative-responders (p = 0.021). The same continuum was observed for the rate of hospitalization for heart failure (19.1% vs 31.3% vs 39.0% vs 55.7%, respectively, p < 0.001). Survival curves comparing the 4 profiles of response to CRT also show this continuum from super-responders to negative-responders (figure 1).
Conclusions: In our study population, the long-term prognosis of super responders was excellent. This study confirms the importance of wide QRS and also suggests non-ischemic etiology as predictors of a positive response to CRT.



	Chi square	df	Sig.
Log Rank (Mantel-Cox)	31,228	3	,000

	Chi square	df	Sig.
Log Rank (Mantel-Cox)	32,500	3	,000

Figure 1

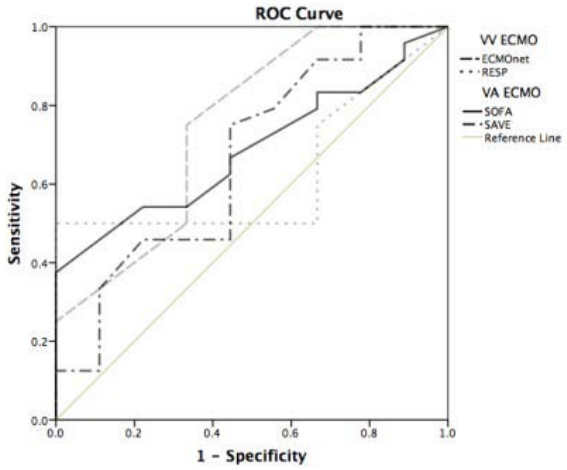
P2243

External validation of the models in extracorporeal membrane oxygenato (ECMO) from developing country

P Puwadon Thitivaraporn[1]; S Chiramongkol[1]; K Boonthim[1]; W Chiravanich[2]; N Pornpatrtanarak[1]; C Kittayarak[1]; J Namchaisiri[1]; S Singhatanadgige[1]; P Ongcharit[1]; V Benjacholamas[1]
[1]*King Chulalongkorn Memorial Hospital, Cardiovascular thoracic surgery department, Bangkok, Thailand*; [2]*King Chulalongkorn Memorial Hospital, Cardiac Anaesthesiology department, Bangkok, Thailand*

On behalf of: Chula Cardiac Center

Objectives: This study was to describe and evaluate the proper situation, timing and predicted outcomes of extracorporeal membrane oxygenator (ECMO) implantation in developing country and to validate prior proposed models for prediction of mortality.
Methods: Data on ECMO used for cardiopulmonary support and e-CPR in children and adults were extracted from database from January 2012 to August 2016. Demographic data included age, diagnosis, procedure codes, type and aim of ECMO support, pre and post-ECMO mechanical support parameters, postop complications, ECMO cannulation details and technique, and postop patient condition. Data also included time interval from the point that ECMO was indicated to the point that ECMO was initiated. We validated prior proposed 4 models using receiver operative characteristic curve (ROC) and their area under the curve (AUC): 1) Respiratory Extracorporeal Membrane Oxygenator Surviving Prediction (RESP) Score, 2) Extracorporeal membrane oxygenator network (ECMOnet) score for VV-ECMO, 3) Survival After Veno-arterial ECMO (SAVE) score and 4) the Sequential Organ Failure Assessment (SOFA) Score for VA-ECMO. The secondary outcomes were descriptive data of ECMO cost. Associations between each of 4 models and 30-day and one-year survival were determined by hazard ratio (HR) and 95% confidence interval (CI) calculated using Cox proportional hazards regression.
Results: 41 patients received ECMO, of which 23 were male (56.1%) at median age of 29.5 ± 27.4 year. Indication for ECMO were 6/41 for respiratory support, 27/41 for cardiac support and 8/41 in e-CPR group which correspond with VV-ECMO 14.6% and VA-ECMO at 85.4%. ARDS is the most common diagnosis in patients required VV-ECMO while low cardiac output syndrome is the most common diagnosis in VA-ECMO. ECMO was successfully weaned off in 15/41 (36.6%) while the survival to discharge rate was 12/41 (29.3%). VV-ECMO survival rate was 3/6 (50%) and VA-ECMO survival rate was 9/35 (25.7%). Among survivor group, 4/12 patients (33.3 %) needed ventricular assisted device (VAD) implantation (1/4 LVAD and 3/4 BiVADs). AUC of each model were 0.688, 0.664, 0.750 and 0.625 for SOFA, SAVE, ECMOnet and RESP score, respectively. Only ECMOnet score of ≥ 7.5 was associated with increased mortality at 30 days (p = 0.03) and at 1 year (p = 0.03). Median ECMO duration was 125.5 (8-745) hour and median length of stay was 22.00 (2-167) days. The median cost of ECMO was 7,900 USD.
Conclusion: Despite limited resource and ECMO fund, the external validation using data from developing country support prior proposed models compared to data from Extracorporeal Life Support Organization (ELSO). From the 4 models, SOFA, SAVE and RESP were not associated with survival at 30 days and 1 year. However, ECMOnet score of ≥7.5 was associated with increased mortality at 30 days (p = 0.03) and at 1 year (p = 0.03).



ROC curve

P2244

Sex differences in implantable cardioverter defibrillator utilisation and outcomes among patients with heart failure from Asia

Y Yvonne Chia[1]; THK Teng[2]; ESJ Tan[3]; WT Tay[2]; AM Richards[3]; LH Ling[3]; W Shimizu Sw Park[4]; CL Hung T Ngarmukos[5]; HB Liew S Zhang[6]; C Narasimhan B Siswanto[7]; EB Reyes Cm Yu[8]; M Macdonald[9]; J Yap[2]; I Anand[10]; CSP Lam[2]
[1]*Duke-NUS Graduate Medical School Singapore, Singapore, Singapore*; [2]*National Heart Centre Singapore, Singapore, Singapore*; [3]*National University Heart Centre, Singapore, Singapore*; [4]*Nippon Medical School, Tokyo, Japan; Sejong General Hospital, Bucheon, Korea Republic of*; [5]*Mackay Memorial Hospital, Taipei, Taiwan;*

Ramathibodi Hospital, Bangkok, Thailand; [6]*Queen Elizabeth Hospital, Malaysia; Fuwai Hospital, Cardiology, Beijing, China People's Republic of*; [7]*CARE Hospital, Hyderabad, India; National Cardiovascular Center Universitas, Jakarta, Indonesia*; [8]*Manila Doctors Hospital, Manila, Philippines; Prince of Wales Hospital, Hong Kong, Hong Kong SAR People's Republic of China*; [9]*Changi General Hospital, Singapore, Singapore*; [10]*University of Minnesota, Minneapolis, United States of America*

Background: Implantable cardioverter-defibrillators (ICDs) are guideline recommended for heart failure (HF) patients with reduced ejection fraction (HFrEF). Yet, little is known regarding sex differences in ICD utilisation and outcomes in Asian patients with HFrEF.
Purpose: In a large prospective multinational cohort of Asian patients with HFrEF, we aimed to compare ICD utilisation, determinants and outcomes between men and women.
Methods: We studied guideline ICD eligible patients with HF and ejection fraction≤35% and New York Heart Association Class II-III from 11 Asian regions (China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand). ICD recipients had an ICD or cardiac resynchronisation therapy with defibrillator (CRT-D) at baseline. Patients were followed for independently adjudicated events including all-cause mortality and sudden cardiac deaths (SCDs). Multivariable regression models were used to examine the impact of sex on ICD utilisation and mortality outcomes.
Results: Among the 3081 (21% women) eligible patients (mean age 58 ± 13 yr), there were 362 (17% women) ICD recipients. Compared to men, women were more likely to have non-ischemic HF (60% vs 38%) and higher ejection fraction (>30% vs ≤30%, 27% vs 22%) but less likely to smoke (91% vs 47%) or consume alcohol (94% vs 66%) (all $p < 0.01$). Educational status predicted ICD uptake (pre-university and above vs below, OR=2.25, 95% CI 1.80-2.83), with interaction by sex (p-interaction=0.03) such that less educated women were less likely to receive an ICD vs men (OR=0.61, 95% CI 0.38-0.98). Over a median follow-up of 394 days, 406 (13%) patients died (88% CV deaths, 29% SCDs). Women were at lower risk for SCDs (HR=0.47, 95% CI 0.26-0.85) compared to men. ICDs reduced all-cause mortality (HR=0.96, 95% CI 0.44 – 0.04) and SCDs (HR=0.35, 95% CI 0.16-0.79) overall. Sex did not modify the effect of ICD on all-cause mortality (p-interaction=0.80) but significantly modified the effect of ICD on SCD (p-interaction=0.02), such that the protective effect of ICD was found in men (HR=0.23, 95% CI 0.08-0.63) but not women (HR=2.18, 95% CI 0.38-12.44) likely due to smaller numbers of events in women.
Conclusions: Among Asian patients with HFrEF, there is sex disparity in ICD utilisation particularly among the less educated. Despite lower usage of ICDs, women were at lower risk of SCD compared to men.

P2245

Additional value of contrast-enhanced cardiac magnetic resonance imaging for patients with coronary artery disease and ejection fraction over 35% presenting with unexplained syncope

F Outteryck[1]; S Boule[1]; F Pontana[2]; B Longere[2]; A Coisne[1]; S Ninni[1]; E Drumez[3]; F Brigadeau[1]; C Marquie[1]; D Klug[1]; M Remy Jardin[2]; D Lacroix[1]
[1]*Lille University Hospital, Cardiovascular medicine, Lille, France*; [2]*Lille University Hospital, Cardiovascular imaging, Lille, France*; [3]*Lille University Hospital, Biostatistics, Lille, France*

Background: In patients with coronary artery disease (CAD) presenting with unexplained syncope and preserved left ventricular ejection fraction (LVEF), a programmed ventricular stimulation (PVS) is indicated in those with previous myocardial infarction (MI). Providing evidence of infarct scar remains challenging. Purpose – We investigated the value of Cardiac Magnetic Resonance imaging (CMR) to assess the presence of myocardial scar and to predict the inducibility of ventricular tachyarrhythmia during PVS.
Methods: From June 2011 to April 2014, all patients with CAD and LVEF over 35% presenting for unexplained syncope were included. Assessment of infarct scar was compared between conventional diagnostic work-up (medical history, ECG, echocardiography) and CMR. Results – The study population consisted of 66 patients (age 70 ± 10.6; males 81.8%; LVEF 54 ± 8%). Evidence of myocardial scar was provided by medical history (n = 26; 39.4%), ECG (n = 25; 37.9%) and echocardiography (n = 24; 36.4%). Discrepancies between conventional diagnostic work-up and CMR regarding the diagnosis of infarct scar were reported in 20 cases (30.3%). Among them, 6 had a positive PVS. A lower LVEF on echocardiography (48% vs. 55%, p = 0.04) and CMR (43% vs. 53%, p = 0.009), a greater left ventricular end diastolic volume by CMR (87ml/m^2 vs. 69ml/m^2, p = 0.01) and the presence of Q wave (57.1% vs. 28.9%, p = 0.03) were associated with positive PVS.
Conclusion: Among patients with CAD and LVEF over 35% presenting for unexplained syncope, discrepancies were reported in 30.3% of cases regarding the assessment of infarct scar between conventional work-up and CMR. The additional value of CMR to predict the inducibility of ventricular tachyarrhythmias remains unknown.

P2246

Ventricular arrhythmias after surgical correction of post-infarction left ventricular aneurysms II - III type for M. Di Donato - L. Menicanti in patients with an ejection fraction less than 30%.

A Alexander Kozlov[1]; A Gornostaev Alexander[1]; S Durmanov Sergey[1]; V Bazylev Vladlen[1]
[1]*Penza Center for Cardiovascular Surgery, Penza, Russian Federation*

Patients with coronary heart disease with low ejection fraction and left ventricular aneurysm, constitute a high risk of sudden cardiac death. After surgical treatment of aneurysms II - III type classification M. Di Donato - L. Menicanti survival of patients over a three year period is 51-60%. There are no clear recommendations on the timing of ICD implantation after surgical correction of coronary heart disease in this group of patients.
Aims: To determine the type and timing of ventricular cardiac arrhythmias after surgical treatment of post-infarction left ventricular aneurysms II - III type for M. Di Donato - L. Menicanti in patients with an ejection fraction less than 30%.
Methods: 16 patients with ejection fraction < 30% and left ventricular aneurysms II - III type classification M. Di Donato - L. Menicanti ICDs implanted in the early postoperative period after surgical correction of coronary heart disease. Diagnosis of ventricular cardiac arrhythmias was carried out at full-time follow - up, and with the use of remote monitoring system CareLink. The duration of follow-up was 579,3 ± 285,3 days.
Results: In all the time of observation in 43.7% (7 of 16) patients had life-threatening ventricular arrhythmias. In-hospital ventricular tachycardia occurred in 5 patients. In the intensive care department ward VT recorded in 2 patients, 3 patients in the rehabilitation stage, which required the application of ICD - therapy. In-hospital mortality were not observed in this group of patients. In the late period VT occurred in 2 patients. Total observation time 3 patients died, mortality was 18.7%. In the dead of patients according to the follow - up was not observed ventricular arrhythmias, presumably patients died from progression of chronic heart failure.
Conclusions: In our series of observations after surgical correction of left ventricular aneurysms II - III type for M. Di Donato - L. Menicanti in patients with an ejection fraction less than 30% within one year of ventricular tachycardia occurred in 7 patients (43.7%). In 5 patients, these arrhythmias developed in the early postoperative period (up to 10 days). ICD implantation in the early postoperative period is useful for prevention of sudden cardiac death in these patients.

P2247

Systolic dysfunction in the context of acute coronary syndrome: evaluation of events and implantation of ICD

T Tatiana Duarte[1]; S Goncalves[1]; C Sa[1]; M Fonseca[1]; R Marinheiro[1]; R Rodrigues[1]; L Parreira[1]; F Seixo[1]; R Caria[1]
[1]*Hospital Center of Setubal, Cardiology, Setubal, Portugal*

Introduction: Although the advances in the treatment of coronary arterial disease, arrhythmic events are an important cause of death in this population.
Implantation of a cardioverter defibrillator (ICD) as primary prevention reduces mortality in patients (pts) with moderate-severe systolic dysfunction (LVEF < 35%) after an acute myocardial infarction (AMI). The implantation of device should be delayed at least 40 days after the acute event.
Aim: To evaluate, in a population with systolic dysfunction (LVEF < 35%) after an AMI, the presence of arrhythmics events and death, during the first 40 days after the acute event; To determine the prevalence of ICD implantation.
Methods: Were evaluated consecutive pts admitted to a Coronary Intensive Care Unit in the context of AMI with moderate to severe systolic dysfunction, over a period of 3 years. Patients in whom the LVEF were not quantified were excluded.
The population was characterized according to baseline characteristics, type of AMI, degree of systolic dysfunction and therapy. Were evaluated the presence of arrhythmics events and death in the first 40 days after AMI, the prevalence of ICD implantation and the causes for non-implantation.
Results: We studied 52 pts (77% (n = 40) males, mean age 72 years ± 10). Sixty-two percent of pts (n = 32) had a diagnosis of STEMI and 67% (n = 35) were in Killip class I. The LVEF was quantified between 35-30% in 52% of the population (n = 27); 29-20% in 35% (n = 18) and < 20% in 17% (n = 9).
Six pts (16%) at discharge did not have indication to ICD because life expectancy < 1 year, only 46 pts would be candidates for ICD implantation. No arrhythmics events or sudden death were recorded in the first 40 days after AMI.
An ICD was implanted in 54% of pts (n = 28).
Forty days after the acute event, 26 pts did not have ICD due to: improvement of the LVEF in 46% (n = 12); 27% (n = 7) died in the period between the 40th day and 3

months after the acute event by: recurrent MI with evolution in cardiogenic shock in 29% (n = 2), acute pulmonary edema in the context of heart failure in 42 % (N = 3) and unknown cause in 29% (n = 2). Six patients (16%) lost follow-up by the cardiologist, but remain alive.
Conclusion: In our study, the death between the 40th day and 3 months after acute event was associated to heart failure or recurrent MI but not due to an arrhythmic event. The LVEF was recovered in about a quarter of pts. In this population, the ICD implantation between the 40th day and 3 months after acute event would not have been effective in reducing of the mortality.

P2248
Relation of QRS duration to response to cardiac resynchronization therapy in patients with left bundle branch block

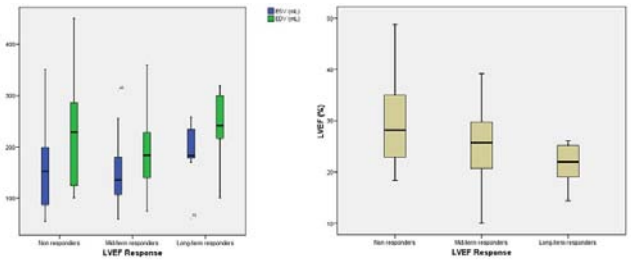
M Matteo Beltrami[1]; B Sassone[2]; M Bertini[3]; L Padeletti[1]
[1]University Hospital Careggi, Dipartimento Cuore e Vasi, Università degli Studi di Firenze, Firenze, Italy; *[2]SS.ma Annunziata Hospital, Azienda Unità Sanitaria Locale Ferrara, Department of Cardiology, Cento (FE), Italy*; *[3]University of Ferrara, S. Anna Hospital, Department of Cardiology, Ferrara, Italy*

Introduction: Cardiac resynchronization therapy (CRT) is an established treatment in patients with drug-refractory heart failure and wide QRS complex as surrogate of left ventricular (LV) mechanical dyssynchrony. However, the relation between the LBBB electrical activation sequence and the consequent mechanical dyssynchrony of the LV is not completely clear, indeed a substantial percentage of patients with LBBB is still not responder to CRT.
Purpose: Our aim was to investigate the relation between QRS duration and LV dyssynchrony in LBBB patients who underwent CRT.
Methods: We retrospectively studied 165 patients with LBBB who underwent CRT implantation according to the current guidelines. A 6-month reduction of LV end-systolic volume ≥15% identified responders to CRT. Baseline LV dyssynchrony was defined as the delay between peak systolic velocities of the septum and lateral wall assessed by color-coded tissue Doppler imaging.
Results: Baseline characteristics of responders (61%) and nonresponders (39%) were comparable except for greater LV dyssynchrony (75 ms [25%–75% IQR 60-90] vs 30.5 ms [25%–75% IQR 14.5-70.5], p = 0.0001) and narrower QRS duration (160 ms [25%–75% IQR 148-171] vs 180 ms [25%–75% IQR 156-190], p = 0.0001) in responders. At multivariate analysis only QRS duration and LV dyssynchrony remained independent predictors of response to CRT. The ROC curve analysis showed that 61 ms was the lower limit of septum-to-lateral wall delay corresponding with the highest accuracy (sensitivity 72%, specificity 70%) to predict response to CRT [area under the curve = 0.705 (95% confidence interval 0.613 to 0.797)]. In patients with nonischemic etiology of cardiomyopathy the linear regression analysis documented a significant inverse relationship between QRS duration and LV dyssynchrony, as dyssynchrony progressively decreased as QRS widening increased (p = 0.006). This was not evident in patients with ischemic etiology.
Conclusion: In LBBB patients with nonischemic etiology and marked QRS widening the absence of LV dyssynchrony may account for a lower response to CRT as compared to patients with intermediate QRS widening.

P2249
Echocardiographic characteristics predictors of delayed response with cardiac resynchronization therapy

J Juan Sanchez Serna[1]; FJ Pastor Perez[1]; M Navarro Penalver[1]; JJ Santos Mateo[1]; E Guerrero Perez[1]; AI Rodriguez Serrano[1]; IP Garrido Bravo[1]; DA Pascual Figal[1]
[1]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiología, Murcia, Spain

Background: Delayed echocardiographic response (>1 year) to cardiac resynchronization therapy (CRT) has been described as a frequent entity with similar prognosis to initial response (< 1 year).
Purpose: The main purpose of this study is to define the echocardiographic characteristics in patients with non-ischemic dilated cardiomyopathy (NIDCM) who present delayed response to CRT.
Methods: We realized a retrospective study of patients with NIDCM who underwent CRT implantation according to current indications. Echocardiographic data were collected at pre-implantation time (Tbase), approximately one year follow-up (Tini) and end follow-up (Tend). Echocardiographic response was defined by left ventricular ejection fraction (LVEF) if it increased ≥ 10% and by reverse remodeling (RR) if the end-systolic volume (ESV) decreased ≥ 15%. Patients were divided into 3 echocardiographic response groups: mid-term responders (MR) who showed a significant echocardiographic improvement at the 1-year follow-up; long-term responders (LR) who showed no improvement at 1 year but who exhibited significant improvement at end follow-up; and nonresponders (NR) who never displayed significant echocardiographic improvement.
Results: From December 2002 to June 2014, 181 patients with NIDCM underwent CRT device implantation in our center. Of these, 96 had complete follow-up. The mean time from implant to echocardiographic assessment in the Tini was 331.4 ± 173.1 days and until Tend was 1654.6 ± 907.1 days. Considering RR, the distribution was 75% MR, 9.4% LR and 15.6% NR, taking into account the response to LVEF, 63.5% were MR, 9.4% were LR and 27.1% were NR. Regarding to RR, no significant differences were found comparing baseline echocardiograms among LR, MR and NR patients. Considering the response to LVEF, those with LR had larger ventricular volumes than MR (end-dyastolic volume (EDV): 245.3 ml vs 191.4 ml, p = 0.03, ESV: 191.3 ml vs 145.2, p = 0.03), and worse LVEF than the NR (23.1% vs 30.3%, p = 0.04) (Figure).
Conclusions: Delayed response in LVEF improvement after CRT exists and is associated with the presence of worse ventricular function and greater degree of adverse remodeling in the baseline study. However, baseline echocardiographic data do not discriminate patients with delayed RR response.



Figure

P2250
The prognostic role of NT-proBNP but not of Global Longitudinal Strain in heart failure patients receiving cardiac resynchronization therapy

NPE Kadoglou[1]; AGW De Lepper[1]; MC De Kleijn[1]; IHF Herold[1]; ARA Bouwman[1]; FALE Bracke[1]; P Houthuizen[1]
[1]Catharina Hospital, Eindhoven, Netherlands

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Background: Cardiac resynchronization therapy (CRT) is highly effective in a specific subpopulation with drug-refractory heart failure (HF). However, its beneficial impact on prognosis is not fully predictable.
Purpose: To investigate the prognostic role of baseline NT-pro-B-type natriuretic peptide (NT-proBNP) and global longitudinal strain (GLS) levels in HF patients receiving CRT-D.
Methods: We enrolled 93 patients, aged 74 ± 10 years, with stable ischemic HF [NYHA class II/III, ejection fraction ≤35%], who underwent CRT-D implantation, fulfilling the current international criteria. At baseline and 3 months after implantation, we assayed NT-proBNP and echocardiographic findings in all patients. Patients with >15% increase of end-systolic volume (ESV) were considered as CRT-responders (n = 67), while the rest as CRT-non-responders (n = 26). During follow-up we recorded deaths (primary end-point) or deaths/HF hospitalizations (secondary endpoint).
Results: At baseline, no significant differences were detected in all parameters between groups (p>0.05). During a median follow-up of 58 months, 23 patients died, while another 17 patients were hospitalized for HF decompensation. A lower percentage of CRT-responders achieved either primary (log rank test p < 0.001), or secondary end-point (log rank test, p < 0.001) compared to non-responders. After adjustment for prognostic factors (age, gender, baseline NYHA class, QRS duration), baseline NT-proBNP levels, were associated with higher occurrence of primary (HR=1.31, 95%CI: 1.18-1.43, p = 0.002) and secondary end-points (HR=1.48, 95%CI: 1.29-1.57, p < 0.001) in the whole cohort. Notably, NT-proBNP remained an independent determinant of mortality (logistic regression analysis: p = 0.032) within CRT-responders group. On the other hand, baseline GLS values were not significantly associated with either response to CRT or prognosis.
Conclusions: In patients with ischemic HF undergoing CRT-D, baseline NT-proBNP levels, but not GLS values, showed an additive prognostic value to routine clinical and electrocardiographic selection criteria. Our findings require further investigation.

P2251

Acute effects of cardiac resynchronization therapy on left atrial size and function as assessed by conventional two-dimensional echocardiography

S Silvia Lupu[1]; I Sus[2]; A Mitre[3]; R Rudzik[4]; I Beke[4]; D Dobreanu[3]
[1]University of Medicine and Pharmacy of Tirgu-Mures, Center for Advanced Medical and Pharmaceutical Research, Tirgu-Mures, Romania; *[2]University of Medicine and Pharmacy of Tirgu-Mures, Tirgu-Mures, Romania*; *[3]University of Medicine and Pharmacy of Tirgu-Mures, Emergency Institute for Cardiac Disease and Transplantation, Tirgu-Mures, Romania*; *[4]Emergency Institute for Cardiac Disease and Transplantation, Tirgu-Mures, Romania*

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Cardiac resynchronization therapy (CRT) has previously been shown to improve left atrial (LA) size and function within months after the procedure, but no data is currently available regarding the immediate impact of CRT. The aim of the current study was to assess acute changes in LA size and function and to provide possible explanations for these variations. We enrolled 25 patients with CRT who were evaluated before and within days after after the procedure. Patients were submitted to an extensive investigation protocol, including echocardiography, which focused mainly on left atrial volumes indexed to body surface were measured at the end of ventricular systole (LAVI max), before atrial systole (LAVI preA), and at the end of ventricular diastole (LAVI min) and further used for calculating the total emptying fraction, active emptying fraction and passive emptying fraction of the LA. LAVI max decreased within days after the implant procedure 45,5 (38,2-56,7) vs. 42,9 (32,1 to 56,2), p <0.05, as did LAVI min – 27,1 (22,9-41,9) vs. 25,9 (17,8-38,1), p <0.05, and LAVI preA – 40,0 (31,3-53,0) vs. 35,5 (25,8-49,1). Mitral regurgitation was also significantly improved (p <0.001). None of the LA function parameters changed significantly within days after CRT. Significant correlations were obvious between LA volumes and the degree of mitral regurgitation before the procedure, but not afterwards. The diastole duration to cardiac cycle ratio was correlated to LAVI max (Spearman's rho= 0,441, p <0,05) and LAVI min (Spearman's rho 0,417, p <0.05) after CRT, but not before. LA indexed volumes regress within days after CRT, most likely as a consequence of immediate mitral regurgitation improvement and atrio-ventricular dyssynchrony reduction, while functional parameters remain unchanged.

P2252

Cardiac resynchronization therapy: what is the prognostic value of ventricular dyssynchrony by echocardiography?

S Sara Guerreiro[1]; M Castro[1]; J Carmo[1]; P Adragao[1]; C Fonseca[2]; N Cardim[3]; F Macedo[4]; D Bonhorst[1]
[1]Hospital de Santa Cruz, Lisbon, Portugal; *[2]Hospital de Sao Francisco Xavier, Lisbon, Portugal*; *[3]Hospital Luz, Lisbon, Portugal*; *[4]Sao Joao Hospital, Porto, Portugal*

Background: Cardiac resynchronization therapy (CRT) is recommended on patients with heart failure, ejection fraction less than 35% and QRS duration greater than 120 ms, independently of echocardiographic evidence of mechanical ventricular dyssynchrony (MVD).
The aim of this study was to evaluate the impact of MVD evaluation by echocardiography before CRT implantation in clinical response of patients.
Methods: Prospective and multicentre national registry in which patients with ejection fraction less than 35% who underwent implantable cardioverter-defibrillator or CRT were included. A sub-population of 82 patients underwent CRT implantation and MVD evaluation by echocardiography (55 men; age 68± 10 years) were analysed. The primary endpoint was the relationship between the degree of improvement of the New York Heart Association (NYHA) functional class during the one-year of follow-up and the echocardiographic parameters of inter- and intraventricular dyssynchrony, determined previous to the device implantation.
Results: In the baseline assessment, 34% of the patients (n = 28) had ischemic cardiopathy of etiology and 44% (n = 36) idiopathic dilated cardiopathy. The mean ejection fraction was 27 ± 6% and the majority of patients were in the class III (62%, n = 51) and in the class II (35%, n = 29) of NYHA. Intraventricular dyssynchrony was present in 67% of patients (n = 55) and interventricular dyssynchrony in 41% (n = 34). The mean duration of the QRS was 150 ± 23ms and 82% of the patients (n = 67) presented left bundle branch block pattern. During a median follow-up of 12 months, there was a significant improvement in functional class in which most patients were classified as class I (20%, n = 16) and II (60%, n = 49) - Figure 1. Intraventricular dyssynchrony was a predictor of NYHA class improvement (HR 6.1; 95% CI, 1.4 - 26.3; p = 0.015), unlike interventricular dyssynchrony.
Conclusion: Intraventricular dyssynchrony evaluated by echocardiography was a predictor of improvement in the symptoms of heart failure after CRT implantation. IT suggests that MVD may be used for a better selection of patients proposed for cardiac resynchronization therapy.

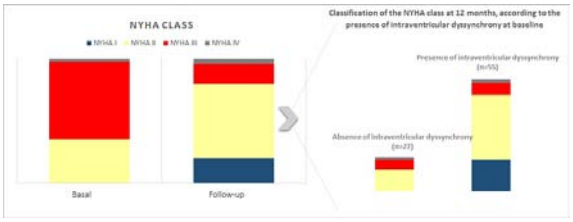


Figure 1

P2253

Clinical and ultrasound correlates of cardiac resynchronization therapy in patients with congestive heart failure

D David Mrikaev[1]; E Golukhova[1]; T Mashina[1]
[1]Bakoulev Center for Cardiovascular Surgery RAMS, Noninvasive Arrhythmology, Moscow, Russian Federation

Background: Cardiac resynchronization therapy (CRT) improved greatly symptoms and survival in heart failure (HF) patients. Randomized clinical trials demonstrated that still a lot of patients with standard clinical selection criteria do not respond to CRT favorably. Accordingly, quantification of left ventricular (LV) dyssynchrony by echocardiography has emerged as an important potential tool to predict patient response. The aim of our study was to evaluate prognostic values of echocardiographic parameters for predicting CRT outcomes in heart failure patients with left bundle branch block.
Methods: 40 patients with HF at the mean age of 61.7 ± 10.4 years were enrolled in our study. They were divided into 2 groups: group 1 (n = 25) included patients with dilatation cardiomyopathy (DCM), group 2 (n = 15) included patients with ischemic cardiomyopathy (ICM). The inclusion criteria were: NYHA functional class II-IV, LVEF < 35%, QRS>130 ms. Ultrasound examination included detailed anatomical scan in 2-D and 3-D mode. We calculated LV systolic dissynchrony indexes (SDI and Tmsv-Dif-16) based on the 16-segmental 3D LV model. Systolic dyssynchrony index-Ts-SD was calculated by Strain Rate Imaging, and intraventricular dyssynchrony was estimated by Speckle Tracking.
Results: We revealed, that SDI and Tmsv-16-Dif had an inverse relationship with LVEF. In patients with DCM LVEF increased from 34% ± 3% to 39% ± 10% after CRT with a decrease in SDI from 11.32 ± 4.9% to 8.85 ± 2.11% (p < 0,05), and the Tmsv 16-Dif - from 42.7 ± 4.7% to 25.11 ± 5.6% (p < 0,05). In patients with ICM LVEF increased from 37.4% ± 3% to 42% ± 12% after CRT, while reducing SDI from 12.6 ± 4.4% to 8.1 ± 5.6% and Tmsv-Dif-16 from 37.5 ± 6.9% to 29.3 ± 4.6% (p < 0,05 for both). The Ts-SD in the 1 group was 45.9 ± 15.1ms, in the 2nd group, 35.8 ± 7.2ms. Thus, after the biventricular pacing the dyssynchrony indexes (SDI, Tmsv 16-Diff) decreased and LVEF increased in both groups (r=-0.83, p < 0.05). Patameters of radial dyssynchrony were more important than longitudinal dyssynchrony concerning CRT outcomes. Radial dyssynchrony was initially greater in those patients who subsequently responded to CRT (in patients with ICM). There was a high correlation between LVEF and radial dyssynchrony (r=0.81, p < 0.05) in both groups.
Conclusions: The intraventricular dyssynchrony indexes (SDI, Tmsv 16-Diff and Ts-SD - TDI) were highly effective in predicting CRT outcomes in both groups. For patients with ICM the best predictor of CRT response is the radial dyssynchrony by Speckle Tracking, which appears to be associated with lower LVEF of this group

P2254

New prospects of cardiac resynchronization therapy in patients with mild heart failure

VA Sujayeva[1]
[1]Republican Scientific and Practical Centre of Cardiology, scientific laboratory of chronic ischemic heart disease, Minsk, Belarus

Objective: to carry out complex assessment of a functional condition of the blood circulatory system according to both echocardiography (EhoCG) and Spiro Bicycle Ergometry Test (spiroBET) at patients with mild chronic heart failure NYHA class II in various terms after cardiac resynchronization therapy (CRT).
Methods: The research included 26 patients (6 (23%) – women, 20 (71%) with mild chronic heart failure NYHA class II. 15 (58%) from 26 pts had ischemic cardiomyopathy, 11 (42%) – dilated cardiomyopathy. The age included in a research made from 39 to 67 years (on average 55.0 ± 8,1 years). All patients received optimal medicament therapy including ACE inhibitors, diuretics, beta-blockers. Tolerance to physical loading (TPL) was estimated in spiroBET which was performed at Schiller AG AT-104 ErgoSpiro using Bruce protocol. We also made transthoracic EhoCG with assessment of the standard structural and morphological parameters and also

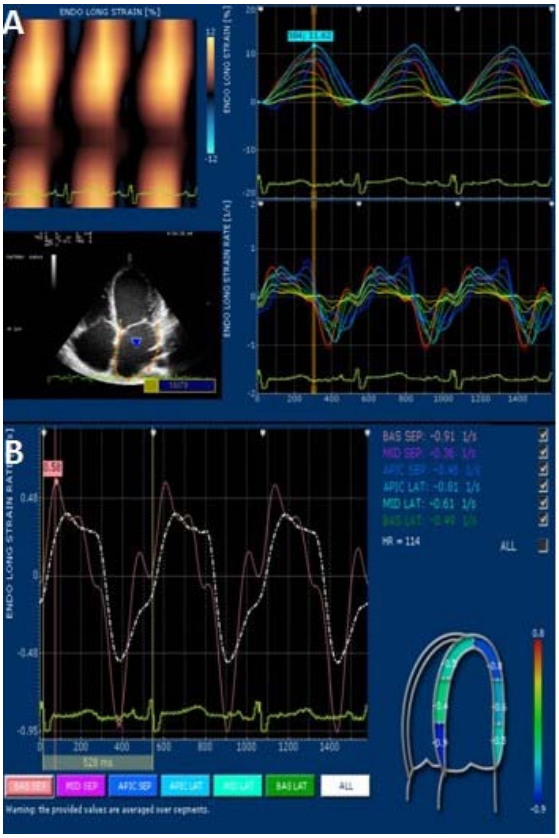
myocardium dyssynchrony was carried out. I test was made before CRT implantation, II test was made at 3 month after, III test – at 6 month and IV test– at 12 month after CRT implantation.
Results: At the I test the Ejection fraction (EF) of Left Ventricle was 29.0 ± 5.9% in averaged on group. TPL according to spiroBET was 61.4 ± 31.4 Wt, the maximal oxygen consumption (VO2max) reached only 8.0 ± 4.2 ml/kg/min. All above demonstrates significant impairment not only myocardial contractility, but also objective TPL and aerobic capacity, despite existence only II NYHA class of heart failure. At the II test 88% of patients had significant improvement in myocardial contractility – EF increased up to 36.7 ± 5.9% ($p < 0.05$). The same tendency was at III and IV test – EF was 34.9 ± 9.7% and 33.6 ± 15.4%, correspondingly ($p < 0.05$). Patients with positive dynamics of contractility were made 'Responders' Group (RG). In others 12% patients significant improvement of structural and morphological parameters we didn't find, they made 'Non-Responders' Group (NRG). At III test the ratio of RG/NRG was 78%/12%, at IV test – 82%/18%, respectively. However, improvement of myocardial contractility didn't bring to either TPL or VO2 max increasing. TPL was 65.6 ± 22.9 Wt at II test, 52.8 ± 26.3 Wt – at III test and 61.4 ± 28.2 – at IV test ($p > 0.05$). VO2 max was 10.3 ± 1.5, 5.8 ± 3.9 and 8.5 ± 3.8 ml/kg/min at II, III and IV test, correspondingly.
Thus, after implantation of CRT, despite significant improvement of myocardial contractility and geometry essential TPL and the aerobic functional capacity didn't increase. It can be bound to a small number of observations. Identification of pathophysiological mechanisms of this phenomenon requires continuation of a research.

HEART FAILURE IMAGING

P2255
Left atrial mechanical function in patients with non-ischemic dilated cardiomyopathy: A speckle tracking echocardiography study

K Wagdy[1]; N Faheem[2]; A Samaan[3]; HM Badran[2]
[1]Aswan Heart Centre, Adult cardiology , Aswan, Egypt; *[2]Faculty of medicine , Cardiology , Menofia, Egypt*; *[3]Cairo University, Cardiovascular, Cairo, Egypt*

Background: Left atrium (LA) plays an integral role in maintaining optimal cardiac performance throughout the cardiac cycle via three major functions; reservoir, conduit and contractile functions. LA volumes and function are well established independent prognostic factors in heart failure patients.
Purpose: Evaluation of mechanical functions of LA in patients with non-ischaemic dilated cardiomyopathy (DCM).
Methods: The study included 73 patients (Median age 36 years, 46 men) with non-ischaemicDCM and another group of 25 age and gender matched healthy volunteers. The study took place in our University. Trans-thoracic echocardiography was used for evaluation of left ventricle dimensions and function, LA antero-posterior diameter, maximal and minimal volumes and LA emptying fraction. Speckle tracking echocardiography was used for assessment of LA global longitudinal strain (S) and strain rate (SR). The left atrium was divided into 6 segments; the global longitudinal strain and strain rate was calculated as the mean value of these 6 segments. LA peak systolic strain (S sys) and systolic SR (SRsys) measured at LV systole were used as a surrogate for LA reservoir function while early diastolic SR (SRe) and late diastole SR (SRa) were used as surrogates for LA conduit and active emptying functions respectively.
Results: In comparison to the control group, DCM patients had significantly larger left ventricular (LV) end diastolic dimension (66.8 ml vs. 45 ml) and lower LV ejection fraction (32% vs. 65%). LA antero-posterior diameter was significantly larger in DCM patients (40.8 cm vs. 27.2 cm) with markedly lower LA emptying fraction (32.29 vs. 62.04). Analysis of LA speckle tracking showed significantly lower LA S sys (12.82% vs 39.6 %)and LA SRsys (0.76 S-1vs. 1.84 S-1), significantly lower SRe (-0.63 S-1 vs. -2.04 S-1) and significantly lower SRa (-0.71 S-1 vs.-1.23 S-1)in DCM patients compared to the control group.
Conclusion: In patients with non-ischaemic DCM, all LA mechanical functions are significantly reduced. Speckle Tracking Echocardiography can be used for assessment of LA mechanical function in these patients for prognostic purposes.



Left atrial strain and strain rate

P2256
Impact of total ischemic time on diastolic function and left atrial volume index in patients with STEMI: late reperfusion is a major determinant of persistent diastolic dysfunction

L Ludovico Lazzari[1]; D Bovelli[1]; G Ambrosio[2]; E Boschetti[3]
[1]Az. Osp. "S. Maria", Cardiology Department, Terni, Italy; *[2]Hospital Santa Maria Della Misericordia, Cardiology and Cardiovascular Pathophysiology Division \ University of Perugia, Perugia, Italy*; *[3]Az. Osp. "Santa Maria" Terni \ University of Perugia, Cardiology Department, Terni, Italy*

Background: Data about the impact of total ischemic time (TIT) on left ventricular diastolic function (LVDF) and on atrial remodelling after a ST-elevation myocardial infarction (STEMI) are lacking.
Purpose: we assessed non-invasive left ventricular filling pressure (LVFP) and left atrial volume index (LAVI) changes over time in patients with a first-ever STEMI, undergoing primary percutaneous coronary intervention (PCI), to determine whether the TIT could be a predictor of persistent left ventricular diastolic dysfunction (LVDD).
Methods: 29 patients (mean age 61 ± 9, 1 female) were enrolled. Exclusion criteria were a TIT > 12 hours, history of coronary artery disease or cardiomyopathy, presence of any moderate or severe valvular disease, age > 75 years old, post-PTCI TIMI flow < 3, a LAVI > 28 ml\m^2 and a left ventricular ejection fraction < 45%. Serial echocardiographic evaluations were performed 48 hours after the onset of symptoms and at a 6 months follow-up (FU). Evaluation of LVDF was based on integrated assessment of trans-mitral Doppler flow pattern, tissue Doppler imaging and PW-Doppler of pulmonary veins. The average E\e' ratio was used as a non-invasive surrogate for LVFP. Patients were divided in two different groups according to the mean TIT (323 ± 154 minutes): early reperfusion group (TIT ≤ 5 hours, 15 patients) and late reperfusion group (TIT > 5 housr, 14 patients). Left atrial enlargement was defined as a LAVI ≥ 28 ml\m^2 at FU.
Results: A normal diastolic function was observed only in the early group at baseline evaluation (26.7% vs 0%, $p = 0.03$). The average E\e' ratio showed no difference at baseline between the two groups (9 ± 2.5 vs 8.6 ± 2.5, p = NS). At FU, the estimated-LVFP (average E\e') remained stable in the early group (-0.4, p = NS), while it showed an elevation in the late group (+1.6, $p = 0.05$), leading to a significant difference (8.6 ± 2.8 vs 10.2 ± 3.2, $p = 0.02$). Likewise, baseline LAVI was similar

in both groups (24.4 ± 2.5 vs. 24.3 ± 2.3 ml\m^2, p = NS) but, while LAVI remained stable at FU in the early group (+ 0.6 ml\m^2, p = NS), a left atrial enlargement was seen in the late group (+ 7,4 ml\m^2, p = 0.04), leading to a significant difference (25 ± 2.3 vs 31.7 ± 1.4 ml\m^2, p = 0.01); suggesting therefore a persistence of LVDD in the late revascularization group. Patients with LAVI ≥ 28 ml/m^2 had longer TIT (386 ± 153 vs 220 ± 86 min, p = 0.003) and higher average E/e' ratio (10.4 ± 3.1 vs. 7.1 ± 1.5, p = 0.004) than those with LAVI < 28 ml/m^2. At FU, the main predictors of a LA enlargement were the TIT (r = 0.532; p = 0.03 – OR = 1.01, 95% CI 1.00 – 1.02, p = 0.01) and the average E/e' ratio (r = 0.520; p = 0.04 – OR = 2.07, 95% CI 1.10 – 3.88, p = 0.02).
Conclusion: TIT affects LVDF and atrial remodelling. An higher TIT lead to a persistent LVDD quantifiable through the progressive increase in estimated-LVFP (average E\e' ratio) and LAVI.

P2257
Is reduced left atrial expansion index the best predictor of increased left ventricular filling pressures ?

I Imen Hamdi[1]; A Belouaer[1]; C Chourabi[1]; K Houissa[1]; H Mahfoudhi[1]; R Dahmani[1]; A Haggui[1]; N Hajlaoui[1]; D Lahidheb[1]; W Fehri[1]; H Haouala[1]
[1]*Cardiology departement, Military Hospital of Tunis, Tunis, Tunisia*

Aim: The aim of the study was to assess the value of the left atrial expansion index (LAEI) for the estimation of left ventricular filling pressures and its relation with N-terminal pro-B- type natriuretic peptide (NT-proBNP) levels in patients with ischemic cardiomyopathy.
Methods: This prospective study enrolled 49 patients (mean age : 62.7 years, range 44-89, 85% male) with ischemic cardiomyopathy (mean Left ventricular ejection fraction : 47.57 %). All patients underwent transthoracic echocardiography and NT-proBNP measurement within 24 hours. The LAEI was calculated as (Vol max –Vol min) x 100% / Vol min, where Vol max was defined as maximal LA volume and Vol min was defined as minimal volume.
Results: Simple regression analysis demonstrated a significant linear correlation between LAEI and Log NT-proBNP (r=0.807, p < 0.0001). Significant but weaker correlations were found between Log NT-proBNP and E/E' (r=0.543, p < 0.0001), indexed LA maximum volume (LAVI max) (r=0.397, p = 0.006), mitral deceleration time (TDE) (r=0.268, p = 0.072), E/A (r=0.347, p = 0.01). Significant correlation was also found between LAEI and E/E' (r=0.517, p < 0.0001).
The area under the receiver-operating characteristic curve showed that LAEI had good diagnostic power for E/E' > 15 at cutoff value of 52%, with a sensitivity of 84% and a specificity of 78%.
In a multiple linear regression model with Log-NT-proBNP as dependent variable and age, E/A, TDE, E/E', LAVI max and LAEI as predictors, LAEI was the only parameter that remaind an independent predictor of elevated NT-proBNP levels (R^2=0.651, p < 0.0001), the relation to LAEI was the strongest (β= -0.807).
Conclusion: Reduced LAEI is an important predictor of elevated left ventricular filling pressures in patients with ischemic cardiomyopathy.

P2258
Is left atrial volume index over late diastolic mitral annulus velocity a useful parameter to predict filling pressures ?

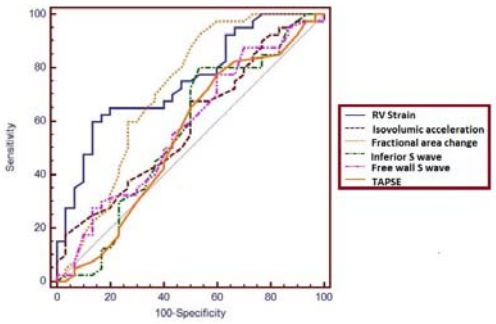
I Imen Hamdi[1]; C Chourabi[1]; A Belouaer[1]; K Houissa[1]; M Ghommidh[1]; N Ben Mansour[1]; A Haggui[1]; N Hajlaoui[1]; D Lahidheb[1]; W Fehri[1]; H Haouala[1]
[1]*Cardiology departement, Military Hospital of Tunis, Tunis, Tunisia*

Aim: Combined interpretation of late diastolic mitral annulus velocity (A') with left atrial volume index (LAVi) may help to predict elevated left ventricular filling pressures. Our aim was to assess the usefulness of the LAVi/A' ratio to identify increased filling pressures.
Methods: This prospective study enrolled 49 patients (mean age : 62.7 years, range 44-89, 85% male) with ischemic cardiomyopathy (mean left ventricular ejection fraction : 47.57 %). All patients underwent transthoracic echocardiography and N-terminal pro-B- type natriuretic peptide (NT-proBNP) measurement within 24 hours.
Results: Significant correlation was found between LAVi/A' and NT-proBNP levels (r=-0.536, p < 0.001). On the receiver operation characteristic curve analysis for the determination of increased NT-proBNP levels, the area under the curve of LAVi/A' was comparable to those of E/E' (0.802 Vs 0.805, p = 0.001).
A LAVi/A' of 3.3 was the best cut-off value to identify NT-proBNP > 450 ng/L, with a sensitivity of 83% and a specificity of 70%.
Conclusion: LAVi/A' may be a useful parameter to identify elevated filling pressures in patients with ischemic cardiomyopathy.

P2259
2D-speckle tracking right ventricular strain to assess right ventricular systolic function in left ventricular systolic dysfunction.

S Mouton[1]; H Ridon[1]; M Fertin[1]; A Duva Pentiah[1]; C Goemine[1]; G Petyt[1]; N Lamblin[1]; A Coisne[1]; C Foucher-Hossein[1]; D Montaigne[1]; P De Groote[1]
[1]*Cardiology Hospital of Lille, Nord, Lille, France*

Background: In patients with left ventricular systolic dysfunction, an accurate estimation of right ventricular (RV) systolic function remains difficult in routine.
Purpose: The aim of the study was to determine the diagnostic accuracy of 2D-speckle tracking RV strain in patients with systolic heart failure.
Methods: Seventy-six patients with dilated cardiopathy and left ventricular ejection fraction ≤ 45% had an analysis of the RV strain. Feasibility, reproducibility and diagnostic accuracy of RV strain were analyzed and compared to other echocardiographic parameters of RV function, taking into account radionuclide RV ejection fraction (± 40%) as gold standard.
Results: RV strain feasibility was 93.9% for the free-wall. RV strain reproducibility was good (intra-observer and inter-observer bias and limits of agreement of 0.16 ± 1.2% [-2.2-2.5] and 0.84 ± 2.4 [-5.5-3.8], respectively). Mean RV strain showed the highest diagnostic accuracy to predict depressed RV ejection fraction (area under the curve (AUC) 0.75) with moderate sensitivity (60.5%) but high specificity (87.5%) using a cutoff value of -16%. It was correlated to radionuclide RV ejection fraction (R = -0.51, p < 0.0001).
Conclusion: RV strain appears as a complementary and more accurate tool than previous RV echocardiographic parameters for the diagnosis of RV systolic dysfunction.



Diagnostic accuraty of RV parameters

P2260
Enlarged left atrium and increased basal heart rate predict exercise capacity in heart failure patients

P Ibrahimi[1]; A Batalli[1]; A Ahmeti[1]; SH Elezi[2]; MY Henein[3]; G Bajraktari[1]
[1]*University Clinical Center of Kosova, Clinic of Cardiology, Prishtina, Kosovo Republic of*; [2]*Faculty of Medicine, University of Prishtina, Clinic of Cardiology, Prishtina, Kosovo Republic of*; [3]*Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden*

Background and aim: Heart failure (HF) is a major and growing health problem characterized by high mortality, frequent hospitalization, reduced quality of life and a complex therapeutic regimen. Six minute walking test (6-MWT) may serve as a reproducible test for assessing exercise capacity in HF patients and can be clinically predicted. The aim of this study was to assess clinical, biochemical and echocardiographical predictors of limited exercise capacity in HF patients.
Methods: The study subjects were 135 consecutive clinically stable HF patients (64 ± 11 years, 66 [47%] female, classified as NYHA I-III). Echocardiography, including tissue Doppler measurements, was performed in all patients. A six minute walk test (6-MWT) distance was performed in all patients, who were divided into two groups based on the 6-MWT distance (Group I: ≤ 300 m and Group II: >300 m).
Results: Patients with limited exercise performance (≤ 300 m) were older (p < 001), more frequent female (p = 0.007) and diabetics (p = 0.003), had lower level of hemoglobin (p = 0.02), larger left atrium (LA, p = 0.003), higher basal heart rate

(p = 0.009), higher E/e' ratio (p = 0.01) and lower septal systolic myocardial velocity (p = 0.03) compared with good performance patients.
Enlarged LA [2.856 (1.439-5.666), p = 0.003], older age [1.110 (1.036-1.188), p = 0.003], increased basal heart rate [1.055 (1.012-1.099), p = 0.012] and the presence of diabetes [3.321 (1.022-10.796), p = 0.046] independently predicted poor 6-MWT performance.
Conclusions: In patients with HF, the limited exercise capacity assessed by 6-MWT, is related mostly to the enlarged left atrium as e reflection of longstanding increased left ventricular filling pressure, increased basal heart rate, in addition to the older age and the presence of diabetes. These findings highlights the need of the optimal medical treatment of HF patients towards the decreasing LV filling pressure and heart rate.

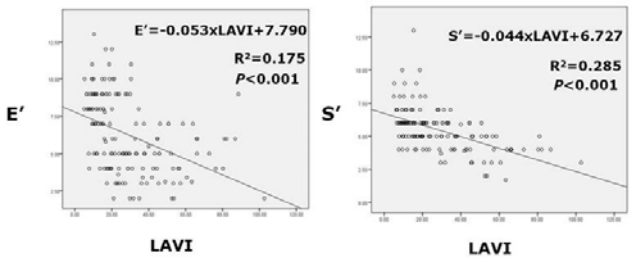
P2261

Left atrial size influences on left ventricular longitudinal tissue velocity

JH Jihyun Yoon[1]; EY Choi[1]; PK Min[1]; BK Lee[1]; HM Kwon[1]; JY Kim[1]; YW Yoon[1]; BK Hong[1]; SJ Rim[1]
[1]Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea Republic of

Purpose: Reduced longitudinal tissue velocity of left ventricle (LV) has been considered early signs of systolic and diastolic dysfunction. However, if Left atrial (LA) superior-inferior dimension increases, longitudinal motion may be restricted within fixed mediastinal space. In this study, we hypothesized that not only myocardial function but also LA size may influence longitudinal tissue Doppler velocity. To verify this hypothesis, we studied patients with Duchenne muscular dystrophy (DMD) who have been known to have dilated cardiomyopathy (DCM), but less heart failure symptoms.
Methods: The study population comprised 100 idiopathic DCM patients (65 men, 57.1 ± 16.6 years) and 101 DMD patients (98 men, 23.8 ± 15.3 years) with left ventricular (LV) ejection fraction (LVEF) < 50 % on echocardiography. Comprehensive echocardiographic measurements of LV chamber and function were performed accompanied with mitral septal annular (S') and early diastolic (e') velocities measurement using tissue Doppler imaging.
Results: Despite no significant difference in LVEF, S' and e' were significantly higher in DMD patients compared to idiopathic DCM patients (6.2 ± 1.4 cm/sec vs. 4.9 ± 1.6 cm/sec, p < 0.001 and 7.9 ± 2.0 cm/sec vs. 4.8 ± 1.9 cm/sec, p < 0.001, respectively). LA volume index (LAVI) was significantly lower in patients with DMD (16.1 ± 11.7 mL/m2 vs. 39.2 ± 20.2 mL/m2, p < 0.001). S' and e' were significantly corelated to LAVI (p < 0.001 for S' and p < 0.001 for e') and its relationship remained significant even after controling for age, gender, LVEF and underlying diseases. (p < 0.001for S' and p = 0.039 for e').
Conclusions: Patients with DCM associated with DMD have relatively preserved myocardial longitudinal function compared to idiopathic DCM as assessed by tissue Doppler. Myocardial longitudinal velocities are influenced by LA size as well as myocardial function.

		Unstandardized Coefficient	Standardized Coefficient	p-value
S'(R= 0.647)	Age	-0.022 ±0.009	-0.302	0.019
Sex	0.447 ± 0.339	0.113	0.189	
LAVI	-0.030 ± 0.008	-0.362	< 0.001	
Hypertension	0.521 ± 0.364	0.135	0.155	
ESRD	0.361 ± 0.726	0.037	0.620	



P2262

Exercise-induced atrial remodeling

S Sondes Smaali[1]
[1]La Rabta University Hospital, Tunis, Tunisia

Funding Acknowledgements: the department of cardilogy

Introduction: Athlete's heart is characterized by a geometrical remodeling of the left atrium (LA).
Purpose: To evaluate atrial functional remodeling due to training.
Methods: 85 men aged 18 to 32 years old were included in this monocentric prospective study. 65 athletes (group trained T) training at least 8 hours per week were compared to 20 healthy sedentary subjects (group S). Transthoracic echocardiogram was performed on competitive period.
Results: Group T presented a higher end-systolic volume (83.56 ± 14.00 Vs 52.46 ± 7.39 ml , p < 0.001) compared to group S.
During exercise there was no difference between groups for global systolic function evaluated by ejection fraction (EF) (50.02 ± 1.7 Vs 50.03 ± 1.38 % ,p = 0.09) and for reservoir phase evaluated by the systolic peak velocity of lateral wall derived from DTI (S') (5.76 ± 0.71 5.34 ± 1.01 cm/ , p = 0.08).
Conclusion: Remodeling of LA in athletes was marked by mild enlargement of LA with a preserved global systolic function and sub normal contribution of the reservoir phase for left ventricle filling at exercise.

Echocardiographic parameters of LA

	ATHLETES (T, n=65)	Sedentary (S , n=20)	p
LAA (cm^2)	26.91±2.73	19.92±1.60	< 0.001
ESV (ml)	83.56±14.00	52.46±7.39	< 0.001
EDV (ml)	42.20±14.31	26.40±6.04	< 0.001
LA EF (%)	50.02 ± 1.7	50.03 ± 1.38	p = 0.009
S'(cm/s)	5.76±0.71	5.34±1.01	p = 0.008

LAA: left atrium area , ESV : end systolic volume , EDV : End diastolic volume , LA EF : Left atrium ejection fraction , S': the systolic peak velocity of atrium lateral wall ranged from DTI.

P2263

The results of applying different algorithms for the estimation of left ventricle diastolic function in the group of patients with chronic heart failure and preserved ejection fraction

O A Olga Petrova[1]; V N Larina[2]; M N Alekhin[1]
[1]Central state medical academy of department of presidential affairs, Moscow, Russian Federation; *[2]The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation*

The article presents a comparison of the evaluation of left ventricular (LV) diastolic function (DF) by echocardiography results in patients with chronic heart failure (CHF) and preserved ejection fraction (EF) of the LV using the algorithm of the 2009 European Association of Echocardiography and American Society of Echocardiography (2009 EAE/ASE) guidelines in comparison with the 2016 algorithm of the American Society of Echocardiography and European Association of Cardiovascular Imaging (2016 ASE/EACVI).
Methods: We included 55 patients with CHF (age of 69.6 ± 9.6 years, of whom 26 males), sinus rhythm and preserved LV EF (59.6 ± 3.1%). 43 patients suffered of coronary heart disease, 53 patients had arterial hypertension, 8 patients had an old myocardial infarction. 10 patients had NYHA functional class I, 38 patients were in NYHA class II and 7 were in class III. LV DF was assessed using algorithms the 2009 ASE/EAE and the 2016 ASE/EACVI. Pulsed-wave tissue Doppler early diastolic velocity (e′ velocity) at lateral and septal basal regions of mitral annular (MA), left atrial maximum volume index (LAVI) were evaluated in accordance with the 2009 ASE/EAE algorithm. In addition to the two above-described criteria, E/e′ ratio and peak velocity of tricuspid regurgitation were analyzed in accordance with the 2016 ASE/EACVI algorithm for judging the presence of LV diastolic dysfunction (DD). Identification of 3 or more of the criteria regarded as having LV DD, in the presence of one characteristic was normal LV DF, detection of 2 listed criteria was considered as an indeterminate result.
Results: The velocity parameters of transmitral flow, e′ velocity of MA and LAVI were measured in all patients. The peak velocity of tricuspid regurgitation was adequately measured in 46 patients out of 55. 26 patients (46%) had DD, 5 patients had a normal DF, 24 patients had an indeterminate result in accordance with the algorithm 2009 EAE/ASE. 12 (21%) patients had DD (p < 0.01 compared with the algorithm 2009 EAE/ASE), 31 patients had a normal DD (p < 0.001 compared to the algorithm

2009 EAE/ASE), and 12 patients had an indeterminate result ($p < 0.01$ compared with the algorithm 2009 EAE/ASE) in accordance with the algorithm 2016 ASE/EACVI. Among the 31 patients with normal LV DF 24 patients had one of the signs of DD: in one case the peak velocity of tricuspid regurgitation was more than 2.8 m/s, in 3 cases LAVI was more than 34 ml/m2 and 20 patients had reduced early diastolic velocity MA in accordance with the algorithm 2016 ASE/EACVI.
Conclusion: The algorithm application proposed by the 2016 ASE/EACVI to LV DF assess in the group of patients with CHF and preserved LVEF leads to a significant decrease in the number of indeterminate results (from 43% to 21%, $p < 0.01$) and the number of patients with LV DD (from 46% to 21%, $p < 0.01$) when compared with the algorithm 2009 EAE/ASE.

P2264

Cardiac sympathetic activity and ventricular dyssynchrony in patients with heart failure referred for cardiac resynchronization therapy

K Zavadovsky[1]; V Viktor Saushkin[1]; I Kostina[1]; Y Lishmanov[2]; D Lebedev[3]; S Popov[3]
[1]Cardiology Research Institute, Tomsk NRMC, Nuclear Medicine Department, Tomsk, Russian Federation; *[2]National Research Tomsk Polytechnic University, Tomsk, Russian Federation*; *[3]Cardiology Research Institute, Tomsk NRMC, Department of surgical treatment of cardiac rhythm disorders and pacing, Tomsk, Russian Federation*

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Background: Cardiac resynchronization therapy (CRT) is currently one of the main treatment modalities for patients with severe heart failure. Unfortunately, about 30% of patients undergoing CRT are non-responders. In our opinion, assessment of cardiac sympathetic activity and ventricular dyssynchrony may help to develop new predictors of CRT outcomes.
Purpose: The aim of the study was to evaluate cardiac sympathetic activity and ventricular dyssynchrony in patients with chronic heart failure before cardiac resynchronization therapy.
Methods: The study comprised 51 patients (mean age of 49 ± 8 years) with severe contractility dysfunction of the left ventricle (LVEF $< 30\%$; NYHA III-IV). All patients underwent a comprehensive clinical and functional examination including gated SPECT myocardial perfusion imaging (gSPECT-MPI), 123I-MIBG imaging and gated blood-pool SPECT (GBPS). Systolic and diastolic functions (EDV, ESV, and EF) as well as mechanical intraventricular dyssynchrony of both ventricles were analyzed. Moreover, we analyzed abnormalities of 123I-MIBG (summed 123I-MIBG score) and 99mTc-MIBI accumulations (normalized SSS and SRS) in the left ventricular (LV) myocardium. All examinations were performed using GE Discovery NM/CT 570C with cadmium-zinc-telluride detectors.
Results: According to stress and rest gSPECT-MPI, all patients had heterogeneous myocardial perfusion pattern. The median values of normalized SSS and SRS were 14% (12-19%) and 5% (2-7%), respectively. Most often, areas of reduced 99mTc-MIBI accumulation were located in the LV apex. In all patients, decreases in contractility and dilatation of both ventricles were detected: median LV EDV was 401 mL (312-511 mL); median right ventricular (RV) EDV was 280 mL (216-388 mL); median LV EF was 26% (17-27%); and median RV EF was 23% (21-44%). Based on GBPS data, severe mechanical dyssynchrony of both ventricles was detected. The median value of LV intraventricular dyssynchrony was 129 ms (103-161 ms); RV intraventricular dyssynchrony was 123 ms (82-152 ms). The value of interventricular dyssynchrony was less than 50 ms. The summed 123I-MIBG score was 25% (21-31%) which was significantly greater than normalized SSS and SRS ($p = 0.03$ and $p = 0.04$, respectively). Areas of reduced 123I-MIBG accumulation matched the myocardial perfusion defects localizations.
Conclusion: Our findings suggest that patients with chronic heart failure had severe ventricular contractility dysfunction and mechanical dyssynchrony of both ventricles. Moreover, sympathetic activity/perfusion disturbances mismatch was detected in these patients. These data will be used in the follow-up study after CRT device implantation in order to develop new predictors of CRT outcomes.

P2265

Role of 123-Iobenguane myocardial scintigraphy in predicting short term left ventricular functional recovery and indication to ICD implantation after coronary revascularization

M Mauro Feola[1]; M Testa[2]; C Ferreri[2]; S Chauvie[3]; A Biggi[3]
[1]Cardiovascular Rehabilitation-Heart Failure Unit, Fossano, Italy; *[2]School of Geriatry University of Turin, Turin, Italy*; *[3]Santa Croce E Carle Hospital, Nuclear Medicine Service, Cuneo, Italy*

123I-Iobenguane myocardial scintigraphy (MIBG), which identifies sympathetic nervous system dysfunction, has been shown to be an effective predictor of sudden cardiac mortality in patient with congestive heart failure (CHF) and could be a useful instrument to early identify adverse clinical events.
Methods: patients with CHF, a New York Heart Association classification (NYHA) of II or III and a left ventricular ejection fraction (LVEF) $\leq 35\%$ were eligible for cardiac defibrillator (ICD) placement under current LVEF-based criteria in the Guidelines. All patients listed for ICD underwent a MIBG before the implantation, in order to assess the prognostic value of an early cardiac MIBG to predict appropriate ICD indication according to recent Guidelines.
Results: 16 patients (100% males; age 65.4 ± 9.6 years) with mean LVEF $29.2 \pm 4.96\%$ entered the study. All patients had a coronary artery disease (CAD) treated by coronary artery bypass graft (CABG) in ten cases (62.5%) , by a percutaneous coronary angioplasty (PTCA) in five and both procedures in one patient. The myocardial perfusion/MIBG scintigraphy has benne performed in the first 15 days after the coronary revascularization. In 15 subjects (93.7%) the heart/mediastinum (H/M) ratio was calculated < 1.6 (mean 1.3 ± 0.17) and the wash-out rate (WR) was $4.91 \pm 4.03\%$. The semiquantitative analysis of the images demonstrated, as previously reported, a larger MIBG uptake defect (summed score $= 26.25 \pm 11.9$) in comparison with Tc99 tetrofosmin uptake defect (summes score$=21.8 \pm 8.9$). The LVEF improved at follow-up from $29.2 \pm 4.96\%$ to $31.3 \pm 7.1\%$ and in 5/16 patients proved to be >35% at 3-month follow-up after CABG or 40-day follow-up after primary PTCA. An ICD was implanted in 10/16 % of patients (one patient refused the implantation). According to the left ventricular functional recovery, the sensitivity, specificity, positive predictive value and negative predictive value of an H/M ratio ≤ 1.25 at MIBG was calculated, respectively, in 87.5%, 83.3%,705, 83.3%.
Conclusion: MIBG myocardial scintigraphy might be a promising method for excluding a short-term left ventricular functional recovery after coronary revascularization, permitting a quick decision about ICD implantation in primary prevention.

P2266

99mTc-HMPAO-labeled leukocyte SPECT/CT infective endocarditis evaluation in patients with heart failure

K Katarzyna Holcman[1]; M Kostkiewicz[1]; W Szot[2]; B Malecka[3]; A Zabek[3]; K Boczar[3]; A Lesniak-Sobelga[1]; M Hlawaty[1]; S Wisniowska-Smialek[1]; P Rubis[1]; P Podolec[1]
[1]John Paul II Hospital, Jagiellonian University Medical College, Department of Cardiac and Vascular Diseases, Kraków, Poland; *[2]Department of Hygiene and Dietetics, Jagiellonian University Medical College, John Paul II Hospital , Kraków, Poland*; *[3]John Paul II Hospital, Jagiellonian University Medical College, Department of Electrocardiology, Kraków, Poland*

Background: Infective endocarditis (IE) is one of the most common life-threatening infection syndromes, with remaining high mortality. Single photon emission tomography and computed tomography with technetium99m-hexamethylpropyleneamine oxime–labeled leukocytes (99mTc-HMPAO-SPECT/CT) has an added diagnostic value in patients with suspected IE.
Purpose: The aim of this study was to evaluate 99mTc-HMPAO-SPECT/CT inflammatory lesions in patients withheart failure (HF).
Methods: We included 40 consecutive patients with suspected IE based on standard medical diagnostic process. All participants had measured N-terminal pro-brainnatriuretic peptide (NT-proBNP) serum level. Patients had transthoracic (TTE) and transesophageal echocardiography (TTE). There were evaluated: left ventricle ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), size of heart chambers, morphology and function of the valves, lesions typical for IE. All patients had 99mTc-HMPAO-SPECT/CT - evaluated for presence and location of increased radioactivity foci, which correspond to accumulation of radiolabeled leukocytes.
Results: 72,5% of patients had diagnosed HF. 40% of 99mTc-HMPAO-SPECT/CTs were classified as positive for IE. Extracardiac foci were observed in 47,5% of patients. They were found in: intestine (26%), vascular system (26%), gallbladder (21%). Extracardiac accumulation of radiolabeled leukocytes was observed statistically significant more often in patients with HF ($p < 0,05$). Occurrence of those foci correlated with LVEF ($p = 0,012$) and both left ventricle end-diastolic diameter (LVED) and end-systolic diameter (LVES) (respectively $p = 0,003$ and $p = 0,005$).
Conclusions: This study highlights the diagnostic value of 99mTc-HMPAO-SPECT/CT in assessing IE suspicion, especially in evaluating the localization of infection. Extracardiac accumulation of radiolabeled leukocytes was observed statistically significant more often patients with HF.

parameter	mean value	one standard deviation
NT-proBNP [pg/mL]	8082	29196
LVEF [%]	44,6	17,8
LVED [mm]	56	12
right ventricle proximal outflow tract diameter (RVOT) [mm]	33	7
TAPSE [mm]	18	6
right atrium area (RAA) [cm2]	22	9
left atrium area LAA [cm2]	25	8

BIOMARKERS

P2267
NT-proBNP correlates with LAVi and LVMMi in patients with beta-thalassemia major

MSD Dimova[1]; BNK Kanazirev[1]; VK Kaleva[1]; SG Gercheva[1]; LG Gercheva[1]; KIP Petrova[1]
[1]*Medical University of Varna, Varna, Bulgaria*

Background: The main cause of death of β-thalassemia major patients is early cardiac complications and especially heart failure that have been attributed to secondary iron overload despite optimal chelation.
Purpose: To discriminate high output state from high output failure in patients with β-thalassemia major by means of heart failure biomarkers –NT-proBNP and echocardiographic parameters.
Methods: In 32 treated adult patients (18-62 years) with β-thalassemia major NT-pro BNP was investigated together with echocardiographic parameters to diagnose presence of heart failure. A control group of 28 healthy individuals was also used to compare with patients with both increased (9 patients) (TM NT-pro-BNP +) and normal NT-pro-BNP (TM NT-pro-BNP-).
Results: Left ventricular mass index (LVMi) and left atrial volume index (LAVi) and relative wall thickness (RWT) of TM patients were bigger compared to controls and, and LAVi was significantly greater in TM NT-proBNP + group. Correlations were as follow: NT-pro-BNP with LAVi- 0,672 and 0,399 with LVMMi. Strain, Systolic myocardial velocity (Sm) and end-diastolic diameter (EDD) were increased significantly compared to controls, but not between TM NT pro-BNP- and TM NT pro-BNP + groups. NT –proBNP correlated poorly with MRI iron loading T2*- 0,199.
Conclusions: Left ventricular hypertrophy, structural remodeling and LA volumes were the most significant differences between healthy controls and TM patients. Strain and systolic myocardial velocity were also diminished. The only significant difference between TM NT-proBNP- and TM NT-proBNP + patients were LA volumes.

P2268
Assessment nt-probnp in patients with chronic systolic heart failure depending of the quality of life

V Ivanov[1]; YU Savitska[1]; V Maslovskyi[1]; O Kovalchuck[1]
[1]*National Pirogov Memorial Medical University, Internal medicine #3, Vinnitsa, Ukraine*

Purpose: To assessment the level of NT-proBNP in patients with LV systolic chronic heart failure, depending from the quality of life by MHFLQ and MOS-SF-36 questionnaire.
Materials and methods: The study is based on the results of complex clinical and laboratory examination 113 patients aged 60,2 ± 0,74 with systolic chronic heart failure (CHF) II-III FC by NYHA of ischemic and hypertensive etiology. The basis of allocation of different clinical groups were taken the quality of life (QoL) indicators: total score by MHFLQ, physical (PH) and mental (MH) health determined by MOS-SF-36 questionnaire. The method of variation statistics were allocated 3 gradation changes following parameters: relatively low (RL), relatively satisfactory (RS) and relatively high (RH). Thus was formed the following clinical groups of patients:
— total score MHFLQ: 1st group (RL QoL) — ≥61 points, 2nd group (RS QoL) — 60 — 41 and 3rd group (RH QoL) — ≤ 40 points;
— largest PH of MOS-SF-36 questionnaire: 1st group (RL PH) — index ≤29, 2nd group (RS PH) — 30 — 35 and 3rd group (RH PHC) — ≥36.
— largest MH of MOS-SF-36 questionnaire: 1st group (RL MH) — index ≤44, 2nd group (RS MH) — 45 — 63 and 3rd group (RH MH) — ≥64. All of research corresponding to the principles of the Declaration of Helsinki of the World Medical Association.
Results: Found that levels of NT-proBNP in the cohort ranged from 904 to 3836 pg/ml (in average — 1977.5 ± 88.8 pg/ml).
Analysis the level of NT-proBNP depending on QoL by MHFLQ testified that in the group of RL QoL the indicator of biomarkers and the number of patients with high level (>2130 pg/ml) NT-proBNP dominated by similar values in groups RS and RH QoL (2552 pg/ml vs. 1880 and 1650 pg/ml, p<0,009 and 51.6% vs. 22.6% and 25.8% respectively, p<0,04).
Determining the level of NT-proBNP in groups PH of MOS-SF-36 questionnaire showed higher levels of the marker and frequency of registration of cases the value of NT-proBNP >2130 pg/ml in patients with RL PH compared with the corresponding values in the group is RH PH (2224 vs. 1692 pg\ml, p = 0.008 and 36.4% vs. 12.5%, p < 0.05, respectively).
The analysis parameters NT-proBNP depending from MH of MOS-SF-36 questionnaire showed that the levels of biomarkers in a group with a RL MH more than a group of RH MH (2221 vs. 1714 pg/ml, respectively, p = 0.02). The distribution of the different levels of NT-proBNP in groups MH of MOS-SF-36 questionnaire showed a significant increase in the frequency of cases registered the high level of NT-proBNP in the group of RL compared to the RH MH group (35.4% vs. 11.8% respectively, p < 0.04).
Conclusions: It was shown that in patients with systolic CHF II-III FC by NYHA of ischemic and hypertensive etiology level of NT-proBNP, to some extent, associated with the levels of the quality of life by MHFLQ, physical and mental health determined by MOS-SF-36 questionnaire.

P2269
Effect of sacubitril/valsartan therapy on risk stratification biomarkers in a real-world heart failure population

M J Barrett[1]; M Hammond[2]; S Zhou[2]; R O Hanlon[3]; P Campbell[1]; K Mcdonald[1]
[1]*St Vincent's University Hospital, Cardiology, Dublin, Ireland*; [2]*Heartbeat Trust, Dublin, Ireland*; [3]*St. Michael's Hospital, Heart Failure Unit, Dublin, Ireland*

Background/Introduction: Sacubitril/valsartan is a novel therapy in treatment of patients with reduced ejection fraction heart failure (HFrEF). This compound appears to have different effects on the two commonly used natriuretic peptide (NP) assays. We have few data on biomarker response in a routine clinical population treated with sacubitril/valsartan.
Purpose: To assess the effect of sacubitril/valsartan on cardiac biomarkers in a community population of patients with HFrEF managed in a disease management programme.
Methods: Patients commencing sacubitril/valsartan therapy and achieving maximum tolerated dose were included (n = 61). Baseline measurements of BNP, NTproBNP and ST2 were performed. Once patients were maximized on therapy, serology was repeated. Median time to achieve maximum dose was 66 days.
Results: Our population represent a typical HFrEF cohort with a mean age of 68 years (older than the PARADIGM population – mean age 63.8), 65% male and with a mean left ventricular ejection fraction of 30%. 39 patients (63.9%) achieved the maximum dose of 97/103mg. A further 8 (13.7%) and 14 patients (22.9%) reached maximum tolerated doses of 49/51mg and 24/26mg, respectively. Follow-up biomarker samples were taken 2-4 weeks after patients were deemed stable at

P2267: Comparison between TM NT-proBNP- vs cont

Patients	Heart Rate	NT-pro BNP	EDD	RWT	LVMi	LAVI	EF%	Strain	Sm	T2*
TMNT-proBNP-	81±11***	60,9±31,8***	51±3***	0,50±0,1*	140±20**	29,2±11,9**	63±7*	31,03±9,42*	10,4±1,3*	24,4±8,8
Controls	70 ± 8	31,6±10,6	45 ± 4	0,40±0,06	85 ± 9	14,6 + 4,7	68 ± 4	37,62±6,44	11,5±2,6	
TM NT-proBNP +	81±10 ns	297,8±131,1***	52±6	0,46±0,08 ns	137 + 38 ns	37,9±17,2 *	62±8 ns	32,37±6,99 ns	10,5±1,3 ns	31,7±6,7

TM NT-proBNP- vs controls and TM NT-proBNP + vs TM NT-proBNP-: *p>0, 05 ** p>, 01 *** p>, 001, ns

their peak tolerated dose. Biomarker profile at commencement and follow-up are detailed in Table 1, below.
Conclusion(s): Although serum BNP levels were not significantly altered at follow-up, it could be theorized that the greater than 50% fall in NTproBNP reflects a reduction in prohormone secretion, but with reduced degradation of the active BNP moiety resulting in an overall 'balancing' effect.
Analysis of this early experience with a new compound demonstrates similar natriuretic peptide response to that seen in PARADIGM, a response that would,support a positive impact on ventricular function. The failure to observe any chnage in ST2 in this population to date may reflect the short period of follow up but also,indicate persistent high risk in this cohort.

Biomarker profile before / after therapy

	Baseline	Follow-up	P value
BNP (pg/mL)	209	256	>0.99
NTproBNP (pg/mL)	1592	655	0.0078
ST2 (ng/mL)	47.3	58.3	0.3396
Potassium (mmol/L)	4.4	4.3	0.23
Creatinine (μmol/L)	99.8	113.3	0.0188
eGFR (mL/kg/1.73m^2)	62.8	55.1	0.1416

P2270
B-type natriuretic peptide and stage B heart failure in the prediction of cardiovascular events and death in hypertension.
J Gallagher[1]; C Watson[1]; S Zhou[1]; S James[1]; C Keane[1]; M Ledwidge[1]; K Mcdonald[1]
[1]*University College Dublin, Dublin, Ireland*

Background: The prevalence and morbidity of hypertension continues to grow globally and improved methods of stratifying risk and identifying organ damage earlier are required. Methods such as echocardiography and population based risk scores are suggested by guidelines as approaches to aid in risk stratification. However, biomarkers such as natriuretic peptides may help provide such an approach also.
Purpose: This aim of this study was to determine the role of BNP and stage B heart failure defined as echocardiographic abnormalities in refining risk prediction in a community based population with hypertension and to determine the use of BNP and the SCORE cardiovascular risk prediction model in the cohort of patients with uncomplicated hypertension.
Methods: We analysed data from the STOP-HF cohort including participants with hypertension with and without a history of a cardiovascular event at baseline. We investigated the ability echocardiography abnormalities at baseline and of B-type natriuretic peptide levels in predicting future major adverse cardiovascular events (MACE) and death. We also investigated the use of the European Society of Cardiology cardiovascular risk score - SCORE - to predict these events in the uncomplicated cohort. 81
Results: In total 572 patients (427 with uncomplicated hypertension) were included. Thirty three patients had a MACE or died during follow up. In a univariate analysis, BNP was predictive of MACE and death in all groups. Echocardiography abnormalities were not predictive of MACE and death in any group. Both BNP and SCORE had predictive value. BNP adds to the predictive value of SCORE as determined by likelihood ratios. The net reclassification improvement for BNP compared to stage B heart failure was 0.20.
Conclusion: This study demonstrates that in patients with hypertension, BNP is better than echocardiography abnormalities alone in the prediction of risk of MACE and death in a community-based cohort of patients with complicated and uncomplicated hypertension.

P2271
Features of correlation between NT-proBNP and circadian blood pressure profile in patients with arterial hypertension and chronic heart failure with preserved ejection fraction of the left ventricle
I Gubareva[1]; N Kryukov[1]; E Gubareva[1]
[1]*Samara State Medical University, Internal Medicine Department, Samara, Russian Federation*

The aim of the study is to examine the characteristics of brain natriuretic plasma level (NT-proBNP) in patients with arterial hypertension (AH) and heart failure (HF) with preserved ejection fraction of the left ventricle (HFpEF).
Research methods: the study included 346 men, whose average age was 46,68 ± 10,44 year. The patients were divided into groups: group 1 - patients with AH and without HF (n = 180); group 2 - patients with AH and HFpEF (n = 86). The control group included representative by age healthy men with normal blood pressure, without HF (n = 80). All patients underwent echocardiography, daily monitoring of arterial pressure (MAP), defined NT-proBNP in plasma by ELISA.
Results: most patients of 1 group, according to MAP remained a two-phase rhythm ("dipper") systolic blood pressure (SBP) and diastolic blood pressure (DBP). In 20% of cases there was a lack of decrease in SBP and DBP ("non-dipper"). In group 2 diurnal profiles of BP were heterogeneous for SBP and DBP. In the daily profile of SBP equally met "dipper" 33% and "non-dipper" - 44%. In 21% of cases there was excessive blood pressure reduction at night – the "over-dipper" in 2% of cases – "night-peaker". Circadian profile of DBP was dominated by patients with "non-dipper" - 51% of cases, the "dipper" - 21%. Equally noted excessive reduction and increase of DBP at night "over-dipper" and "night-peaker" - 14%. The level of natriuretic peptides was the highest in the group "non-dipper", "night-speaker" and differ significantly from patients with a normal circadian profile of blood pressure and profile of the "over-dipper" as for SBP, and the circadian profile of DBP. Correlation analysis of the data revealed an inverse relationship of NT-proBNP and the SBP daily index (p = -0,498; p = 0,035), SBP square index (g=-0,474; p = 0,040), the index of SBP variability (p = -0,606; p = 0.006). The regression model to determine diastolic myocardial stress, within the parameters of MAP and the level of NT-proBNP was developed.
Results: Natriuretic peptides are involved in the formation of diurnal profile of arterial pressure and can be used for stratification of a cardiovascular risk in patients with arterial hypertension.

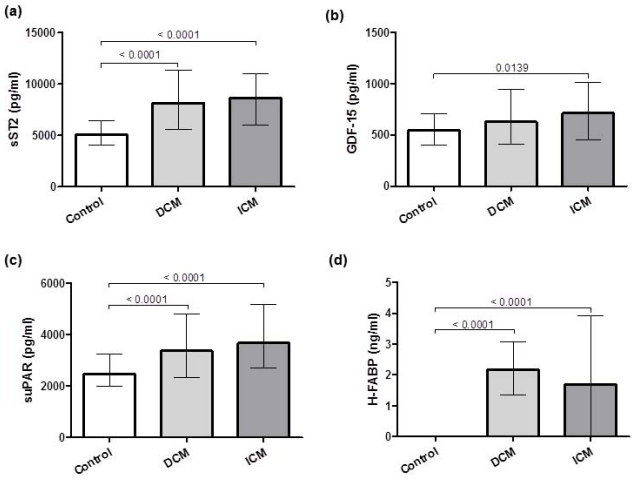
P2272
Brain natriuretic peptide levels and renal function in the diagnosis of heart failure in the elderly
ME Escande[1]; MB Emmanuel Beillard[2]; NE Nathalie Escande Beillard[3]
[1]*Private Hospital Beauregard, HOPITAL PRIVE 13012 MARSEILLE, Marseille, France*; [2]*DUKE-NUS Medical School, singapour, Singapore*; [3]*Institute of Medical Biology ,Biopolis, Singapour, Singapore*

Aim of the study: BNP levels are accurate in the diagnosis of heart failure and useful in clinical practice. Relationship between BNP, heart failure (HF) and renal function are little known in the elderly. Renal function influence the optimal cut point of BNP in patients with a Glomerular Filtration Rate (eGFR) lesser than 60 ml/min/1.73 m 2.
Methodology: A total of 71 patients (mean age = 85 years) were admitted in a Cardiogeriatric Unit. We noted several parameters, age, gender, the presence or the absence of Systolic Heart Failure (clinical history and physical examination), the echographic measure of the left ventricular ejection fraction, the eGFR value calculated by simplified MDRD formula and the BNP value. We divided these patients into six groups according the presence of HF and eGFR value higher than 60ml/min/1.73m 2 ,or between 30 and 60 or between 15 and 30.
Results: Our results show that the BNP value is higher in all the three groups of patients with Heart Failure with or without diminution of the eGFR: for example, 1220 pg/ml in the presence of HF versus 788 pg/ml in the absence of HF in the two groups with the eGFR is calculated between 15 and 30 ml/min/1.73m 2.
Conclusion: BNP is a helpful tool in clinical practice for the diagnosis of Systolic Heart Failure in the presence of renal impairment in the elderly with a higher biomarker cut point.

P2273
Association of the novel cardiovascular biomarkers ST2, GDF-15, suPAR and H-FABP with clinical parameters in heart failure patients
P Jirak[1]; M Lichtenauer[1]; B Wernly[1]; V Paar[1]; I Rohm[2]; C Jung[3]; A Yilmaz[4]; UC Hoppe[1]; PC Schulze[2]; D Kretzschmar[2]; R Pistulli[2]
[1]*Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria*; [2]*University Hospital of Jena, Department of Cardiology, Jena, Germany*; [3]*Medical Faculty, University Duesseldorf, Division of Cardiology, Pulmonology, and Vascular Medicine, Duesseldorf, Germany*; [4]*Elisabeth Klinikum , Clinic of Internal Medicine II, Schmalkalden, Germany*

Background: Heart failure (HF) with reduced ejection fraction still remains a major therapeutic challenge and has an impact on morbidity, hospitalisation rates and health-care costs. Biomarkers represent an indispensable tool in the clinical setting for diagnosis and monitoring of treatment in patients suffering from HF.
Purpose: Aim of this study was to investigate the role of novel cardiovascular biomarkers, namely suppression of tumorigenicity (ST2), growth-differentiation factor-15 (GDF-15), soluble urokinase plasminogen-activator-receptor (suPAR) and heart-type fatty acid binding protein (H-FABP) in patients suffering from ischemic cardiomyopathy (ICM) or dilative cardiomyopathy (DCM).
Methods: A total of 200 patients were enrolled in this current study, 65 that were diagnosed with DCM and 59 patients that suffered from ICM were included. 76

patients without coronary artery disease or signs of heart failure that underwent coronary angiography because of angina pectoris were included as controls. Diagnosis of cardiomyopathy was established after a complete diagnostic work-up including coronary angiography for validation of diagnosis. During outpatient visits, plasma samples of all patients were obtained and analyzed for ST2 (assessing hemodynamics and inflammation), GDF-15 (remodeling and inflammation), suPAR (inflammation) and H-FABP (ischemia) by use of ELISA after informed consent.
Results: Levels of ST2, suPAR and H-FABP were significantly higher in ICM and DCM patients compared to the control group ($p < 0.0001$), while GDF-15 showed a significant increase in ICM patients ($p = 0.0139$) but not in DCM patients ($p = 0.176$). However, there were no significant differences between ICM and DCM in biomarker levels (ST2 $p = 0.6725$, GDF-15 $p = 0.3503$, suPAR $p = 0.3521$, H-FABP $p = 0.1191$). Ejection fraction correlated inversely with cardiac biomarkers (ST2 $p < 0.0001$, GDF-15 $p = 0.0394$, suPAR $p = 0.0029$, H-FABP $p < 0.0001$), while BNP levels showed a positive correlation with biomarker levels (ST2 $p < 0.0001$, GDF-15 $p < 0.0001$, suPAR $p < 0.0001$, H-FABP $p = 0.0004$). Similarly, CRP levels showed a positive correlation with cardiac biomarkers (ST2 $p = 0.0006$, GDF-15 $p = 0.0041$, suPAR $p = 0.0258$, H-FABP $p = 0.0002$). Renal insufficiency (ST2 $p < 0.0001$, GDF-15 $p < 0.0001$, suPAR $p < 0.0001$, H-FABP $p < 0.0001$) and diabetes (ST2 $p = 0.0021$, GDF-15 $p = 0.0055$, suPAR $p = 0.0339$, H-FABP $p = 0.0010$) were significantly associated with a rise in cardiac biomarkers, while hypertension seemed to have no effect on biomarker levels in HF-patients (ST2 $p = 0.4911$, GDF-15 $p = 0.4593$, suPAR $p = 0.2410$, H-FABP $p = 0.3141$).
Conclusion: By integrating the information obtained by measuring levels of several important factors in HF, tested novel biomarkers represent a promising opportunity for a more precise diagnosis incorporating different pathophysiological processes present in HF.

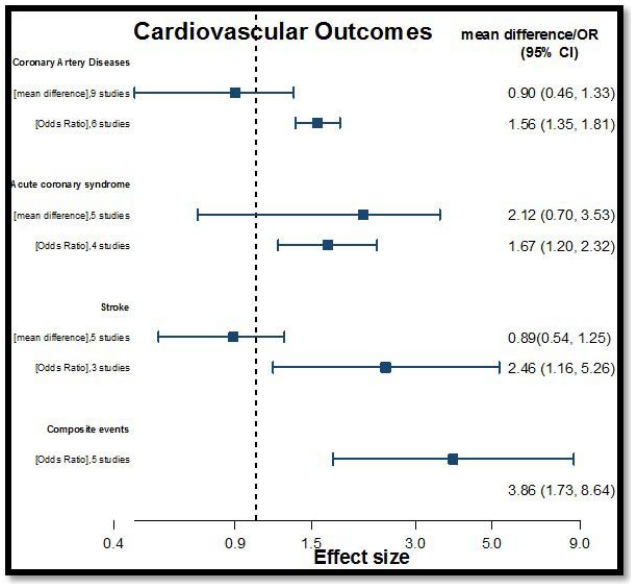


P2274

Neutrophil lymphocyte ratio and risks of cardiovascular diseases: a systematic review and meta-analysi

MS Angkananard[1]; DR Anothaisintawee[2]; DR Thakkinstian[2]
[1]Faculty of Medicine, Srinakharinwirot University, Division of Cardiovascular Medicine, Department of Medicine, , Nakhon Nayok, Thailand; *[2]Ramathibodi Hospital, Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Bangkok, Thailand*

Background: Inflammation is a main process in the pathogenesis of atherosclerosis. Neutrophil lymphocyte ratio (NLR) has recently emerged as an inflammatory biomarker to anticipate the risk of cardiovascular diseases (CVDs). Here we quantify the predictive impact of NLR on risk of CVDs.
Methods: Medline and Scopus databases were searched. We included observational studies of adults in any settings with NLR as studied factor. The outcomes of interest were either composite or individual outcome of at least one of the CVDs including cardiovascular(CV) death, acute coronary syndrome(ACS), coronary artery disease (CAD), chronic stable angina, receiving coronary revascularization and any types of stroke. Mean difference and ORs were pooled across studies using a random effect model. Source of heterogeneity was explored by performing a meta-regression and subgroup analysis.
Results: Twenty-eight studies comprising 49,806 subjects were included in this meta-analysis. Patients with higher NLR had a significantly greater odds of having CAD, ACS, stroke and composite outcomes than patients with lower NLR with a pooled odds ratio of 1.56 (95% CI: 1.35, 1.81), 1.67 (95% CI: 1.20, 2.32), 2.46 (95% CI: 1.16, 5.26), and 3.86 (95% CI: 1.73, 8.64), respectively. The weighted mean difference of NLR in patients with CAD, ACS, and stroke outcomes were 0.90 (95% CI: 0.46, 1.33), 2.12 (95% CI: 0.70, 3.53), and 0.895 (95% CI: 0.54,1.25) respectively.
Conclusion: NLR was linearly associated with subsequent risks of CVDs. Thus, it might be helpful in risk stratification, or improvement of risk prediction if putting it in existing CVD predicting models.



Summarized pooling effect of NLR vs. CVD

P2275

High sensitivity troponin T predicts adverse outcome in non-ischemic hypertensive heart failure

S Susana Ravassa Albeniz[1]; C Gallego[2]; R Querejeta[3]; B Lopez[1]; K Echegaray[3]; A Campbell[4]; A Gonzalez[1]; A Dominiczak[5]; C Delles[5]; J Diez[1]
[1]Centre for Applied Medical Research. University of Navarra, Pamplona, Spain; *[2]Cardiovid Clinic , Division of Cardiology, Medellín, Colombia*; *[3]Donostia University Hospital, San Sebastian, Spain*; *[4]University of Edinburgh, Centre for Genomic and Experimental Medicine, Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom*; *[5]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom*

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Background: No data exists on the associations of the circulating biomarkers of cardiomyocyte injury high-sensitivity troponin T (hs-TnT), annexin A5 (AnxA5), and cardiotrophin-1 (CT-1) with prognosis among patients with chronic heart failure (HF) attributable to hypertensive heart disease.
Purpose: We aimed to determine whether these biomarkers identify patients with non-ischemic hypertensive HF at high risk for adverse outcome.
Methods: The relationship between hs-TnT, AnxA5 and CT-1 and a composite outcome of hospitalization for HF (HHF) or cardiovascular death was examined in 235 patients with hypertensive HF and without obstructive coronary artery disease (CAD) from the Leizaran cohort, with a median follow-up of 5.44 years. The findings were validated in an independent cohort (Generation Scotland) of 60 patients with the same diagnosis.
Results: In the Leizaran cohort, while hs-TnT was associated with the outcome (hazard ratio=1.67, P=0.003) independently of other relevant co-variables, AnxA5 and CT-1 were not. Adding hs-TnT to a basic model, including left ventricular ejection fraction and N-terminal pro-brain natriuretic peptide (NT-proBNP), improved risk discrimination as assessed by Harrell's C-statistics, integrated discrimination and net reclassification improvements ($P \leq 0.04$). Receiver operating characteristic analysis identified hs-TnT$\geq$23.5ng/l as a predictor of outcome in HF patients (HR=2.10,

P=0.006). The prognostic value of hs-TnT was confirmed in the Generation Scotland cohort. In sensitivity analyses, after excluding participants with CAD during follow-up, our findings remained consistent.
Conclusions: Circulating hs-TnT identifies patients with non-ischemic hypertensive HF at high risk of HHF or cardiovascular death for whom more intensive monitoring and management of cardiomyocyte injury may be needed.

P2276
Combined baseline and one-month changes in Big Endothelin-1 and BNP plasma concentrations predict clinical outcomes in patients with left ventricular dysfunction after acute myocardial infarction

A Olivier[1]; N Girerd[1]; JB Michel[2]; JM Ketelslegers[3]; R Fay[1]; JM Vincent[4]; P Bramlage[5]; B Pitt[6]; F Zannad[1]; P Rossignol[1]
[1]INSERM, Centre d'Investigations Cliniques 9501, Université de Lorraine, CHU de Nancy, Institut Lorrain du cœur et des vaisseaux, Nancy, France and INI-CRCT F-CRIN Network, Vandoeuvre-les-Nancy, France; *[2]Inserm, UMRS 1148 University Paris Diderot, Paris, France*; *[3]Universite Catholique de Louvain, Brussels, Belgium*; *[4]Pfizer Inc, New York, United States of America*; *[5]Institute for Cardiovascular Pharmacology & Epidemiology, Mahlow, Germany*; *[6]University of Michigan, School of Medicine, Ann Arbor, United States of America*

Objective: Increased levels of neuro-hormonal biomarkers predict poor prognosis in patients with acute myocardial infarction (AMI) complicated by left ventricular systolic dysfunction (LVSD). The predictive value of repeated (one-month interval) Brain natriuretic peptides (BNP) and Big-endothelin 1 (BigET-1) measurements were investigated in patients with LVSD after AMI.
Methods: In a sub-study of the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS trial), BNP and BigET-1 were measured at baseline and at 1 month in 476 patients.
Results: When included in the same Cox regression model, baseline BNP (p for trend=0.0003; HR for 3rd tertile vs 1st tertile=9.20 (3.03 - 8.0), $p < 0.0001$) and BigET-1 (p for trend=0.026; HR=3.25 (1.36 - 7.73), $p = 0.008$) as well as the relative changes (after 1 month) from baseline in BNP (p for trend=0.049; HR=2.25 (1.13 - 0.47), $p = 0.02$) and BigET-1 (p for trend=0.045; HR=1.84 (0.91 - 3.73), $p = 0.09$) were predictive of the composite of cardiovascular death or hospitalization for worsening heart failure. Adding baseline and changes in BigET-1 to baseline and changes in BNP led to a significant increase in prognostic reclassification as assessed by integrated discrimination improvement index (5.0%, $p = 0.01$ for the primary endpoint).
Conclusions: Both increased baseline and changes after one month in BigET-1 concentrations were shown to be associated with adverse clinical outcomes, independently from BNP baseline levels and one month changes, in patients after recent AMI complicated with LVSD. This novel result may be of clinical interest since such combined biomarker assessment could improve risk stratification and open new avenues for biomarker-guided targeted therapies.

P2277
Biomarker prognostic value in heart failure with mid-range ejection fraction

M De Antonio[1]; J Lupon[1]; J Barallat[1]; M Domingo[1]; J Nunez-Villota[2]; P Moliner[1]; E Zamora[1]; C Rivas[1]; B Gonzalez[1]; V Diaz[1]; M Rodriguez[1]; J Santesmases[2]; C Diez-Quevedo[1]; C Pastor[1]; A Bayes-Genis[2]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; *[2]University Hospital Clinic of Valencia, Valencia, Spain*

Background: Recently the ESC created a new classification of heart failure (HF) according to left ventricular ejection fraction (LVEF): reduced (HFrEF) when LVEF is < 40%, mid-range (HFmrEF) when LVEF is between 40% and 49%, and preserved (HFpEF) when LVEF is >50%. The intermediate group of HFmrEF is incompletely characterized.
Purpose: We sought to explore the prognostic value of a biomarker panel in HFmrEF relative to HFrEF and HFpEF.
Patients and methods: 1069 patients were included in the study (age 66.2 ± 12.8 years, 72% male, 51% of ischemic aetiology). 800 patients were classified as HFrEF, 134 as HFmrEF and 135 as HFpEF. 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) Cystatin-C (N=804), Neprilysin (N=1069), and soluble transferrin receptor (sTfR) (N=794) were measured in consecutive ambulatory HF patients followed during 4.9 ± 2.8 years (6.6 ± 2.3 for alive patients). The composite end-point of cardiovascular death or HF-related hospitalization was assessed.
Results: 534 patients died during follow-up, 284 of them from cardiovascular causes and 231 suffered a HF-related hospitalization. The composite end-point including cardiovascular death and HF-related hospitalization occurred in 356 patients. Hazard ratios for the different biomarkers in the three groups of the ESC classification are shown in the table. In general the power of risk prediction of all biomarkers was higher in HFmrEF patients than in HFrEF and HFpEF patients, except for Neprylisin, that emerged with better prognostic capacity in HFpEF patients. The difference between HFrEF and HFmrEF was especially big related to hs-TnT, in which the hazard ratio was more than doubled.
Conclusions: Biomarkers commonly used for risk prediction in HFrEFcan be even more useful for stratifying the risk of HFmrEF patients.

	HFrEF (N=800)	HFmrEF (N=134)	HFpEF (N=135)
NTproBNP	1.76 (1.55-2.00), $p < 0.001$	2.71 (1.88-3.89), $p < 0.001$	1.28 (0.97-1.68), $p = 0.08$
hs-TnT	1.72 (1.51-1.95), $p < 0.001$	4.58 (2.73-7.66), $p < 0.001$	2.08 (1.50-2.89), $p < 0.001$
ST2	1.38 (1.23-1.56), $p < 0.001$	1.95 (1.41-2.70), $p < 0.001$	1.05 (0.81-1.37), $p = 0.71$
Galectin-3	1.40 (1.24-1.57), $p < 0.001$	1.85 (1.44-2.37), $p < 0.001$	1.78 (1.35-2.35), $p < 0.001$
hs-CRP	1.32 (1.14-1.53), $p = 0.001$	1.64 (1.13-2.39), $p = 0.01$	1.19 (0.89-1.60), $p = 0.24$
Cystatin-C	1.39 (1.25-1.55), $p < 0.001$	1.67 (1.32-2.11), $p < 0.001$	1.46 (1.16-1.84), $p = 0.001$
Neprilysin*	1.11 (0.98-1.25), $p = 0.09$	1.14 (0.86-1.50), $p = 0.36$	1.37 (1.12-1.69), $p = 0.003$
STfR	1.19 (1.05-1.35), $p = 0.008$	1.56 (1.13-2.15), $p = 0.007$	1.21 (0.90-1.62), $p = 0.21$

All log-transformed and per 1 SD. *Age included in the model.

P2278
Multiplex cytokine profiling reveals altered cytokine patterns in patients with peripartum cardiomyopathy: correlation to recovery after 6 months

TP Tobias Jonathan Pfeffer[1]; MR Ricke-Hoch[1]; C Falk[2]; M Kasten[1]; D Berliner[1]; K Sliwa[3]; J Bauersachs[1]; D Hilfiker-Kleiner[1]
[1]Hannover Medical School, Cardiology, Hannover, Germany; *[2]Hannover Medical School, Institute of Transplant Immunology, IFB-Tx, Hannover, Germany*; *[3]University of Cape Town, Cape Town, South Africa*

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Background: Peripartum cardiomyopathy (PPCM) is defined as heart failure with systolic left ventricular (LV) dysfunction emerging towards the end of pregnancy or in the first postpartal months in previously healthy women. The aetiology of the disease is largely unknown but inflammation, especially increased expression of pro-inflammatory cytokines, i.e. IL-6 and TNFa have been reported in African PPCM patients. In order to get new insights into the pathophysiology and to identify PPCM-specific biomarkers, we performed a multiplex cytokine profiling in serum of PPCM patients from a German cohort and healthy postpartum controls.
Methods and Results: Serum levels of 27 different cytokines were measured using a cytokine mutliplex assay (27-Plex, BioRad) in PPCM patients (n = 51) at the time of diagnosis. Healthy pregnancy-matched postpartum (PP) women served as controls (n = 24). Cardiac function was impaired in PPCM patients with an average LV ejection fraction (LVEF) of 24 ± 7% at diagnosis and 49 ± 11% after 6 months.
The cytokines and chemokines that appeared significantly (Shapiro-Wilk normality test, test for significance using unpaired t-test or Mann-Whitney test) elevated in PPCM patients were: IL-1b (p: 0.001); IL-4 (p: 0.0023); IL-5 (p: 0.0025); CXCL8 (p: 0.0045); IL-9 (p: 0.0011); IL-10 (p: 0.0099); IL-12 (p: 0.0057); IL-13 (p: 0.0045); IL-15 (p: 0.0209); IL-17 (p: 0.0017); CCL11 (p:<0.0001); FGFb (p: 0.0002); GM-CSF (p: 0.0006); IFNg (p: 0.0019); CXCL10 (p: 0.0067); CCL2 (p: 0.0104); CCL3 (0.0003); PDGF (p: 0.0021); CCL4 (p: 0.0047); CCL5 (p: 0.0132); VEGF (p: <0.0001). In contrast, to African patients, neither IL-6 nor TNFa were significantly upregulated in this German PPCM patient cohort.
Next we analysed if baseline cytokine levels could predict recovery from PPCM by stratifying patients with a persistently severely reduced systolic left ventricular function (LVEF≤35%) versus patients with partial or full recovery (LVEF>35% after 6 months follow up. Only CCL4 serum levels at diagnosis were significantly higher (p: 0.0255) in patients with persistently reduced LVEF compared to patients with recovered LVEF.
Conclusion: The broad elevation of immune mediators underlines the importance of inflammatory processes in this German PPCM collective. However, the cytokine pattern differs from African PPCM patients suggesting potential differences in the

aetiology of PPCM from different ethnic or geographic background. CCL4 serum levels may serve as a novel prognostic marker for recovery from PPCM.

P2279

MicroRNA-423-5p levels correlate with markers of hypoperfusion and organ injury and are associated with 90-day mortality in cardiogenic shock.

T A J Toni Antti Juhani Jantti[1]; H Segersvard[2]; T Tarvasmaki[1]; J Lassus[1]; Y Devaux[3]; M Vausort[3]; K Immonen[2]; K Pulkki[4]; I Tikkanen[2]; P Lakkisto[2]; V-P Harjola[1]

[1]Helsinki University Central Hospital, Helsinki, Finland; *[2]Minerva Foundation Institute for Medical Research, Helsinki, Finland*; *[3]CRP-Sante, Luxembourg, Luxembourg*; *[4]Eastern Finland Laboratory Centre, Kuopio, Finland*

On behalf of: CardShock study group

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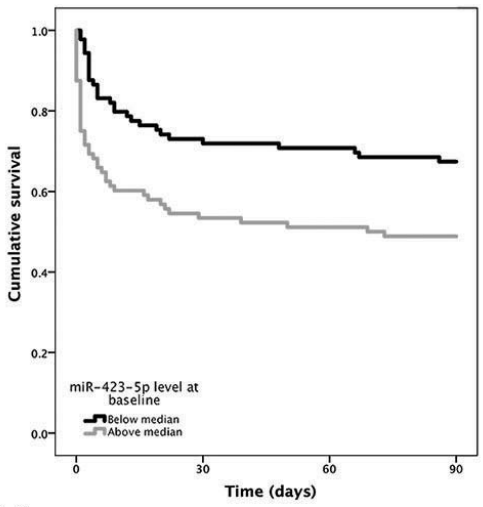
Background: MicroRNAs (miRNAs) are short non-coding RNAs that have a central role in regulating gene expression. MiRNAs can be detected in plasma, body fluids and tissues. Circulating miRNAs are emerging diagnostic and prognostic biomarkers of cardiovascular disease. Past studies have shown an association between circulating levels of miR423-5p with the diagnosis and prognosis of heart failure. However, there have been no studies of miR-423-5p in cardiogenic shock.
Purpose: To examine the levels of miR-423-5p in cardiogenic shock patients and their potential to predict mortality.
Methods: We measured the admission plasma levels of miR-423-5p in 179 patients enrolled in the prospective European multi-center CardShock study. The associations of miRNA levels with established biomarkers (high- sensitivity troponin T [hsTnT], alanine aminotransferase (ALT), lactate and creatinine), clinical data and 90-day all-cause mortality were analysed using SPSS statistical software.
Results: The etiology of cardiogenic shock was mainly acute coronary syndrome, comprising 79% of the patients in the cohort. The 90-day all-cause mortality was 42,0%. Median miR-423-5p level was 0.005 (interquartile range 0.002-0.013).
MiR-423-5p levels at baseline were significantly higher in non-survivors than in survivors (median for non-survivors 0.008 vs. 0.004 for survivors; Mann-Whitney U-test $p = 0.003$). Patients with above median levels of miR-423-5p also had higher levels of lactate (3.7 vs. 2.4 mmol/L, $p = 0.001$) and lower eGFR (56 vs. 70 mL/min/1.73m2, $p = 0.002$) compared to patients with below median levels of miR-423-5p. Levels of miR-423-5p correlated significantly with markers of hypoperfusion and organ damage, namely ALT, lactate and creatinine (Spearman correlation coefficients (r) 0.38, 0.28 and 0.19, respectively, $p < 0.001$ for ALT and lactate and $p = 0.01$ for creatinine). MiR-423-5p also correlated with hsTnT level at 24 hours ($r=0.33$, $p < 0.001$). In Kaplan Meier analysis, above median levels of miR-423-5p were associated with higher all-cause 90-day mortality (Figure 1). In Cox regression analysis, above median levels of miR-423-5p were associated with all-cause 90-day mortality with an unadjusted hazard ratio (HR) of 1.9 (95% confidence interval (CI) 1.2-3.1, $p = 0.006$). After adjusting for the risk factors included in the CardShock risk score, the association between above median levels of miR-423-5p and all-cause 90-day mortality remained significant (HR 2.0, 95% CI 1.2-3.2, $p = 0.007$).
Conclusions: Circulating plasma levels of miR-423 at baseline are associated with mortality and markers of hypoperfusion in cardiogenic shock and may potentially aid in the early risk stratification in cardiogenic shock.



Survival function for miR-423-5p

P2280

Endovascular shedding markers in patients with heart failure with reduced ejection fraction

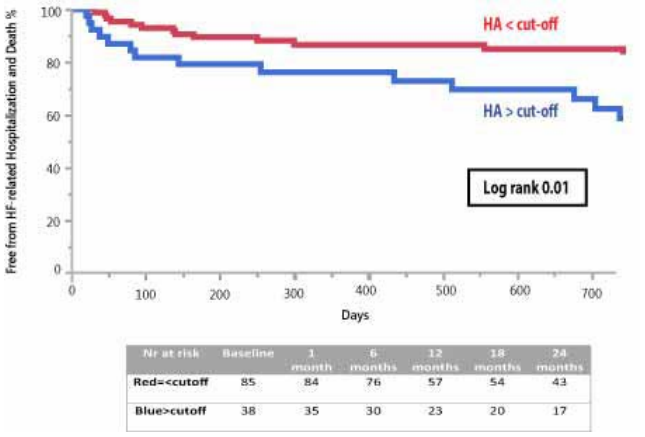
P Petra Nijst[1]; J Cops[2]; P Martens[1]; Q Swennen[2]; M Dupont[1]; W Tang[3]; W Mullens[1]

[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium; *[2]Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt (3500), Belgium*; *[3]Cleveland Clinic Foundation, Cleveland, United States of America*

Background: Increased endothelial glycocalyx degradation has previously been associated with tissue edema formation, endothelial dysfunction, renal impairment and mortality in patients with cardiovascular disease.
Aims: To explore the role of glycocalyx shedding markers; hyaluronic acid (HA) and syndecan-1, in patients with heart failure with reduced ejection fraction (HFREF), and to study their potential association with other HF-related variables and outcome.
Methods: In 123 patients with HFrEF a medical history, clinical investigation and venous blood samples for shedding markers and other HF-related biomarkers were obtained. Cut-off values of normal were derived from a cohort of normal subjects ($n = 30$). The study end point was a composite of all-cause mortality and hospitalization for HF. HFrEF patients were prospectively followed up till 2 years.
Results: The cut-off value of normal for plasma values of HA was 50.2 ng/ml and for Syndecan-1 was 365.4 ng/ml. Median HA levels and syndecan-1 levels in HFrEF patients were respectively 29.4(10.7;61.6) ng/ml and 48.5(33.6;80.8) ng/ml. Overall, HA-levels were significantly higher in HFrEF patients compared to healthy subjects but only 31% of HFrEF patients had HA levels above the cut-off. There was no significant difference among HFrEF patients and healthy subjects regarding syndecan-1 levels. HFrEF patients with elevated HA-levels had worse outcome (log rank=0.01) which remained significant after correction for established risk factors (HR 2.53 (1.13-5.69); $p = 0.024$). Based on multivariate analysis, there was no significant relation between levels of shedding markers and neurohumoral activation (plasma renin activity, serum aldosterone, NT-proBNP), myocardial injury (HS-trop), inflammation (CRP) or other baseline characteristics.
Conclusion: The glycocalyx shedding marker HA is significantly elevated in a subgroup of HFrEF patients and an independent predictor for worse clinical outcome independent of other established risk factors and HF related processes. There was no significant difference between syndecan-1 levels in HFrEF patients and normal subjects.

Adjusted Hazard Ratio

Variable	HR	95% CI	p-value
eGFR < 60 ml/min/1.73m2	4.41	1.68-12.96	0.002
elevated Hyaluronic Acid (>50.2 ng/ml)	2.53	1.13-5.69	0.024
History of myocardial infarction	2.53	0.95-8.78	0.065
NT-proBNP (ng/L)	1.21	0.17-6.47	0.833
Age>75 years	1.09	0.46-2.56	0.836



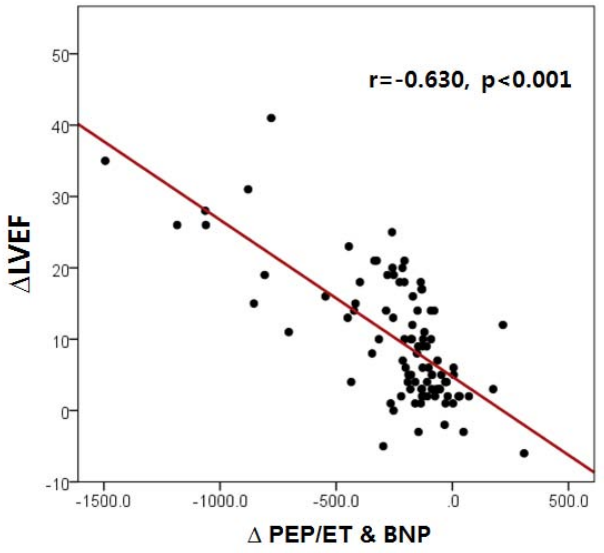
LEFT VENTRICULAR FUNCTION

P2281

Clinical meaning of the ratio of brachial pre-ejection period to brachial ejection time in patients with left ventricular systolic dysfunction: a comparison with BNP

K-H Kyoung-Ha Park[1]; WJ Park[1]; SJ Han[1]; HS Kim[1]; SH Jo[1]; SA Kim[1]
[1]*Hallym University Sacred Heart Hospital, Cardiology, Anyang-Si, Gyeonggi-Do, Korea Republic of*

Background: An increase in the ratio of the brachial pre-ejection period to brachial ejection time (PEP/ET) is correlated with a decrease of left ventricular ejection fraction (LVEF).
Purpose: To investigate whether the change value (Δ) of PEP/ET is a useful predictor of LVEF in patients with LV systolic dysfunction.
Methods: We consecutively enrolled 104 patients with LVEF < 45%. PEP/ET, B-type natriuretic peptide (BNP), and LVEF were evaluated at baseline and at 6-month follow-up.
Results: Compared to the baseline measurements, the 6-month values of ΔLVEF, ΔBNP, and ΔPEP/ET were 9.8 ± 9.0% (from 36.3 ± 9.2% to 46.3 ± 12.5%, p < 0.001), -168.5 ± 255.4 (from 271.4 ± 282.5 to 104.1 ± 129.6, p < 0.001), and -0.060 ± 0.069 (from 0.413 ± 0.097 to 0.358 ± 0.079, p < 0.001), respectively. There were significant correlations between ΔLVEF and ΔPEP/ET (r=-0.515, p < 0.001) and between ΔLVEF and ΔBNP (r=-0.581, p < 0.001). We evaluated about ΔPEP/ET&BNP, which was formulated as ΔBNP added to ΔPEP/ET*1000. The correlation between ΔLVEF and ΔPEP/ET&BNP was significant (r=-0630, p < 0.001). However, ΔPEP/ET&BNP did not have a stronger correlation with ΔLVEF compared to the correlation between ΔLVEF and ΔBNP (r=-0.630, p < 0.001 vs. r=-0.581, p < 0.001; Steiger's Z=0.496, p = 0.620; Figure).
Conclusions: In patients with LV systolic dysfunction, ΔPEP/ET is a useful indicator of changes in LVEF. However, there is no additional benefit to using PEP/ET over BNP.



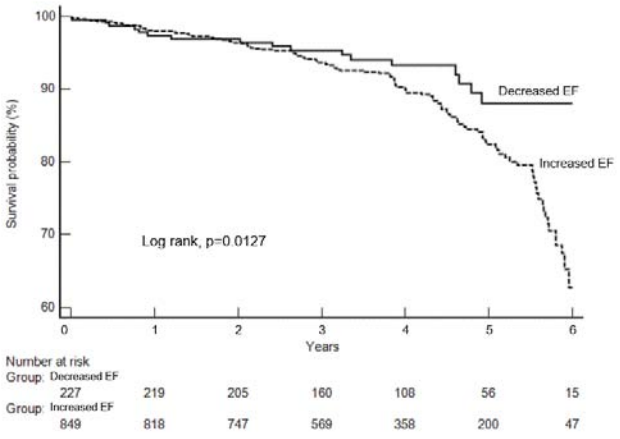
Correlation LVEF_PEP/ET&BNP

P2282

Impact on change of left ventricular function on long-term clinical outcome in patients with preserved ejection fraction after acute myocardial infarction

J J Jin Jin Kim[1]; BH Hwang[1]; SW Jang[1]; J Jang[1]; CJ Kim[1]; YS Koh[1]; PJ Kim[1]; ES Lim[1]; WJ Lee[1]; KB Seung[1]; K Chang[1]
[1]*Catholic University Hospital, Seoul, Korea Republic of*

Background: Left ventricular (LV) dysfunction has been associated with greater mortality after acute myocardial infarction (AMI). However, among patients with preserved ejection fraction (EF) after AMI, few data exist that increased or decreased LV function is altered long-term clinical outcome.
Methods: A total of 5,464 patients with AMI were consecutively enrolled from January 2004 to August 2014. Baseline and follow-up echocardiography were performed when enrollment and 1 year after AMI. After excluded patients with similar LV function, patients with preserved ejection fraction (≥ 50%) were divided according to the difference of baseline and follow-up LV ejection fraction (LVEF). All-cause mortality within a follow-up period of 6 years was examined in groups of patients with increased and decreased more than 5% of LVEF.
Results: Median follow-up duration was 43.1 months (interquartile range 32.4 to 59.1 months). Patients with increased LVEF were more likely to have diabetes, but the two groups did not differ in age, sex, presence of hypertension, and status of smoking. Patients with increased LVEF had greater all-cause mortality (7.5% vs. 13.3%, p = 0.017). Increased LVEF as assessed by echocardiography was an independent predictor of all-cause mortality after adjusting confounding risk factors (hazard ratio: 1.686, confidence interval: 1.010-2.816, p = 0.046).
Conclusion: In patients with preserved EF after AMI, although LVEF is restored, change of LV function increases the risk of all-cause mortality independent of co-existing risk factors.



KM Curve for All-cause Mortality

P2283

The study of drug therapy effectiveness in the correction of morphological and functional myocardium changes in patients with arterial hypertension and bronchial asthma

TEI Tarlovskaya Ekaterina[1]; AAO Odegova Alla[2]
[1]*Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russian Federation*; [2]*Kirov State Medical University, Internal medicine, Kirov, Russian Federation*

Timeliness: The prevalence of bronchial asthma (BA) among patients with arterial hypertension (AH) is about 25-30%. The worsening of bronchial patency in patients with AH associated with BA is accompanied by blood pressure (BP) increase. The frequent using of sympathomimetics leads to heart rate increase and also, as we had seen, to sinus tachycardia, as well as a more rapid onset of remodelling, hypertrophy and diastolic dysfunction of the left ventricle of the heart (LV).
Purpose: To evaluate the effect of therapy by diltiazem-retard and ivabradine on morphological and functional changesof the heart muscle in patients with AH associated with BA. Material and methods. 67 patients with mild and the average degree (1,2 degree) of AH associated with BA were involved in the study. All patients received baseline treatment of BA by inhaled glucocorticosteroids (IGCS) and β2-agonists (β2-AM) short-acting. There was treatment of AH with tablet of indapamide 2.5 mg, and patients observed the recommendations about non- treatment AH therapy.Echocardiography on Acuson 128XP \ 10c equipment (USA) was performed to all subjects. Patients were divided into 2 groups without significant difference by technique of random sampling. Group 1 involved 35 patients with average age is 58.5 + 8.34 years, who received diltiazem-retard. Group 2- 32 patients with average age is 55.2 + 9.21 years, who received ivabradine (Coraxan).The treatment lasted for 24 weeks. Results. There was improvement of morphological parameters of left heart (significant decrease of LVMMI (p=0,01) and IVST (p=0,012)), and alsoimprovement of diastolic function parameters(E/Ap = 0.001, IVRTp = 0.015) during 24-weeks treatment with diltiazem- retard. The changes of systolic function LV was not found in group 1 (p=0,83). As a result of 24 weeks therapy there was decrease of IVST (p=0,021), left ventricle end-diastolic diameter (p=0,034), and also left ventricular posterior wall thickness (p=0,001), LVMMI (p=0,002) in comparison

with baseline measures in group 2. It was noticed the improvement in left ventricular diastolic function as a result of LV hypertrophy regression, such as: increasing the E /A ($p = 0.016$) and decreasing IVRT ($p = 0.011$), as well as decrease of pulmonary artery systolic pressure ($p = 0.015$). The changes of systolic function LV was not found in group 2 (p=0,58).
Conclusions: As a result of 24 weeks treatment with ivabradine in patients with AH associated with BA there was more significant LV hypertrophy regression and improvement of LV diastolic function in comparison with diltiazem therapy.

P2284
Diastolic myocardial dysfunction in patients with chronic heart failure due to arterial hypertension and ischemic heart disease

MA Osadchuk[1]; NP Korzhenkov[1]; IN Vasilyeva[1]; KS Solodenkova[1]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Purpose: To identify the features of left ventricle (LV) diastolic function (DF) disturbances in patients with chronic heart failure (CHF) caused by arterial hypertension (AH) and coronary heart disease (CHD).
Methods: The study involved 65 pts, mean age – 57.6 ± 2.2 years. The study group consisted of 22 pts with AH in combination with IHD with symptoms of CHF FC I-III by NYHA. Assessment of CHF FC showed that 43.4% of pts had I FC, 50.0% – II FC and 6.6% of pts had III FC. The first comparison group consisted of 22 pts with AH, the second group – of 21 pts with CHD without CHF symptoms. All pts in addition to standard clinical and laboratory tests were performed echocardiography by a standard technique. The study was carried out on the Sonos unit (PHILIPS) using apical access and sectoral sensor 3.5-5.0 MHz.
Results: Comparative analysis showed that the LV DF in pts with CHF due to AH and IHD was broken mainly by hypertrophic type. Comparison with those of other groups showed more pronounced disorders: decrease in the transmitral flow peak velocity ratio (VE/VA MV) in comparison with AH pts – 36.7%, and in comparison with IHD pts - 16.5% ($p < 0.05$). In pts with CHF we observed higher values of linear and volumetric parameters of the left atrium in comparison with pts with isolated forms of disease without heart failure ($p < 0.05$). Furthermore, diastolic dysfunction amplified with increasing of blood pressure degree in pts with AH and CHD. This was confirmed by established correlation relationship between the isovolumetric relaxation time (IVRT), values of atrioventricular index and left ventricular myocardium mass ($r = 0.61$ and $r = 0.60$; $p < 0.05$) in pts with CHD and III degree hypertension indicating an increase of myocardial stiffness. Also, in pts with CHF we established correlation between IVRT and stroke volume index ($r = -0,7455$; $p = 0.007$), which confirms the obvious reduction in the functional activity of the myocardium in the absence of reliable evidence of impaired contractility.
Conclusions: Comparative analysis revealed features of diastolic dysfunction in pts with CHF due to the influence of two diseases. On the basis of this data it can be concluded that it is the state of diastole to a large extent determines the functional reserve of the heart and determines the degree of progression of CHF.

BASIC SCIENCE: CANCER AND CYTOKINES

P2286
Inhibition of cardiac lymphangiogenesis in imatinib-induced cardiomyopathy

K Urbanek[1]; D Madeddu[2]; S Cavalli[2]; C Frati[2]; A Falco[2]; CA Lagrasta[2]; B Lorusso[2]; G Mazzaschi[2]; D Donato Cappetta[1]; L Berrino[1]; A De Angelis[1]; F Quaini[2]
[1]Second University of Naples, Department of Experimental Medicine - Section of Pharmacology, Naples, Italy; *[2]University of Parma, Department of Medicine and Surgery, Parma, Italy*

Background: Imatinib mesylate (IM) is the backbone drug for the treatment of chronic myeloid leukemia, gastrointestinal stromal tumors and hypereosinophilic syndrome. It inhibits the Abl-tyrosine kinase and possesses a potent activity against mutated oncogenic forms of the receptor tyrosine kinases platelet-derived growth factor receptor (PDGFR). Tyrosine kinase inhibitors that represent a turning point in modern medicine have been implicated in cardiovascular side effects and patients treated with IM may develop periorbital and peripheral oedema. A defective lymphatic drainage might be responsible for the observed fluid retention, and a similar mechanism may be operative within the myocardium that, as a compact tissue, is highly sensitive to changes in lymph flow. The critical role of tyrosine receptor PDGFR signalling in lymphangiogenesis further supports the possibility that PDGFR-targeting drugs can impair cardiac function by affecting the integrity of myocardial lymphatic vasculature.
Purpose: To test whether IM-induced heart failure involves cardiac lymphatics. Analyses were also conducted on hearts from two patients who died of heart failure while under IM treatment.
Methods: Autoptic myocardial samples of two IM-treated patients who died of heart failure were analyzed. For animal studies, 8 week-old male Wistar rats were subjected to i.p. injections of 100mg/kg IM three times a week for three weeks. Hemodynamic data were collected and the heart was collected for morphometric, immunofluorescence and electron microscopy analysis. Immunofluorescence and immunogold staining were performed on myocardial samples incubated with anti-LYVE1 to detect lymphatic vessels and anti-LC3 for autophagy.
Results: Ultrastructural abnormalities of IM-treated human hearts were characterized by interstitial oedema, mitochondrial damage and several features of autophagy in all myocardial cell compartments. Importantly, Masson's trichrome staining did not reveal increased collagen accumulation, indicating that myocardial fibrosis was not a characteristic finding of IM-induced cardiomyopathy. In animal studies, IM treatment affected animal survival in the absence of severe myelotoxicity. Hemodynamic analysis detected altered left ventricular end-diastolic pressure and positive and negative dP/dT, together with a slight decrease in systolic blood pressure. These changes were accompanied by increased theoretical water content and reduced lymphatic vessel density in the myocardium. Finally, matrigel assay on isolated human and rat lymphatic endothelial cells exposed to IM documented reduced cell proliferation and tube formation.
Conclusions: Our findings show that inhibition of tyrosine kinase by IM is translated at myocardial level in structural and functional alterations of cardiac lymphatics in the absence of myocardial fibrosis. These data indicate that defective lymphangiogenesis may contribute to tyrosine kinase inhibition-induced cardiovascular events.

P2287
New role of EPAC in the Anthracyclines-induced cardiotoxicity

M Maxance Ribeiro[1]; M Mazevet[1]; M Laudette[2]; B Crozatier[1]; F Lezoualc'h[2]; J Chen[3]; J-P Benitah[1]; A-M Gomez[1]; C Lemaire[1]; E Morel[1]
[1]University of Paris-Sud 11, Signaling and cardiac physiopathology U1180, Chatenay-Malabry, France; *[2]Institute of Cardiovascular and Metabolic Diseases, Toulouse, France*; *[3]University of San Diego, La Jolla, United States of America*

Doxorubicin (Dox) is an anthracycline commonly used to treat many types of cancer; unfortunately this chemotherapeutic agent often induces side effects such as cardiotoxicity leading to dilated cardiomyopathy (DCM). The cardiotoxicity of Dox has been related to reactive oxygen species generation, DNA intercalation and topoisomerase II inhibition, resulting in DNA damage and ultimately in cardiomyocyte death. Therefore, there is a need for new treatment options and strategies aiming at reducing Dox side effects in the heart. Among these mechanisms, β-adrenergic signaling and especially Epac (exchange protein directly activated by cAMP) signaling could be worth investigating as Epac activates small G proteins (Rac1 and Rho A) which are known to be involved in Dox-induced cardiotoxicity. Therefore, we have investigated the time/dose-dependent Dox effect on Epac signaling in both in vivo mice model (C57Bl63/ Knock-out Epac1 mice, iv injections, 12mg/kg cumulative dose) and in vitro (primary culture of neonatal rat cardiomyocytes (NRVM, 24h, Dox 1μM). In vivo, Dox-treated mice developed a DCM (a succession of functional and molecular alterations at 2, 6 and 15 weeks post-treatment with a final DCM development) associated with $Ca2+$ homeostasis dysfunction (increase of $Ca2+$ waves and $Ca2+$ leaks). In vitro, as measured by flow cytometry and western blot, Dox (1μM) induced DNA damage and cell death in NRVM after 24h of treatment. This cell death is associated with apoptotic features including mitochondrial membrane permeabilization, caspase activation, cell size reduction and relative plasma membrane integrity. We also observed that Dox led to a reduction of the expression of Epac1 and Epac2 isoforms, while Epac activity and cAMP level were increased. The inhibition of Epac1 (ESI09, CE3F4), but not of Epac2 (ESI05), prevented DNA/TopIIβ complexes, decreased Dox-induced DNA damage, cardiomyocyte death and loss of mitochondrial membrane potential and apoptosis. These results were confirmed in vivo; indeed, Dox-induced cardiotoxicity was prevented in Epac1 knock-out mice as evidenced by unaltered cardiac function (no DCM) and calcium homeostasis at 15 weeks post-treatment. In conclusion, inhibition of Epac1 could be a valuable therapeutic strategy to limit Dox-induced cardiomyopathy during cancer chemotherapy.

P2288
Doxorubicin inhibits protective autophagy through a PI3Kgamma/Akt/Ulk1 pathway downstream of TLR-9

A Ghigo[1]; M Li[1]; V Sala[2]; N Pianca[3]; S Sciarretta[4]; F Morello[5]; M Sandri[3]; T Zaglia[3]; M Mongillo[3]; E Hirsch[1]
[1]University of Torino, Dept. of Molecular Biotechnology and Health Sciences, Torino, Italy; *[2]University of Turin - Molecular Biotechnology Center, Turin, Italy*; *[3]University of Padova, Department of Biomedical Sciences and Venetian Institute of Molecular Medicine, Padova, Italy*; *[4]Sapienza University of Rome, Department of Medical and Surgical Sciences and Biotechnologies, Latina, Italy*; *[5]A.O.U. Città della Salute e della Scienza di Torino, Emergency Department, Torino, Italy*

Purpose: Anthracyclines, like doxorubicin (Dox), are among the most potent anti-tumor drugs, but their clinical use is hampered by severe cardiotoxicity leading to heart failure. We demonstrated previously that genetic inhibition of phosphoinositide 3-kinase γ (PI3Kγ) protects against Dox-induced cardiomyopathy (manuscript in preparation), but the underlying molecular mechanisms are still unexplored. Here, we test the hypothesis that PI3Kγ acts as a sensor of the cardiac damage elicited by anthracyclines and promotes maladaptive remodeling through inhibition of protective autophagy.
Methods: Neonatal cardiomyocytes (NCMs) were isolated from mice expressing a kinase inactive PI3Kγ (PI3Kγ kinase-dead; KD) and wild-type (WT) controls, and treated with Dox (1 mM) or TLR-9 agonist ODN1826 (1 μL/ml) $\pm$ PI3Kγ inhibitor AS605240 (500 nM) or TLR9 antagonist ODN2088 (1 μL/ml), for 1 hour before analyzing Akt/mTOR/Ulk-1 signaling. For in vivo studies, WT and KD mice were treated with 4 mg/kg Dox and hearts harvested for electron microscopy (EM) and signaling studies at 3 days.
Results: We found that in Dox-damaged hearts, PI3Kγ signaling is engaged downstream of toll-like receptors, and in particular TLR-9, which have been previously reported to sense danger signals generated by injured cardiomyocytes, like mitochondrial DNA (mitoDNA)(Oka et al. Nature 2012). In NCMs, Dox significantly increased the phosphorylation of PI3K downstream targets and autophagy inhibitors, Akt, mTOR and Ulk-1. These effects were completely prevented by the TLR9 antagonist ODN2088, the PI3Kγ selective inhibitor AS605240 and genetic PI3Kγ inactivation (KD NCMs). Notably, the TLR9 agonist ODN1826, mimicking mitoDNA, similarly upregulated Akt/mTOR/Ulk-1 signaling in WT but not in KD NCMs. In vivo, enhanced activation of this PI3Kγ-dependent pathway correlated with a significant block of autophagy in Dox-treated hearts. Notably, genetic inhibition of PI3Kγ restored autophagosome formation, as evidenced by enhanced accumulation of LC3II. In addition, EM studies confirmed the presence of autolysosomes containing injured mitochondria in KD but not in WT hearts. This eventually correlated with completely preserved ultrastructure in KD cardiomyocytes in contrast to severe mitochondrial damage and vacuolization in WT controls.
Conclusion: Altogether, these data demonstrate that PI3Kγ prevents autophagic disposal of anthracycline-damaged mitochondria, likely leading to metabolic derangement and, ultimately, to heart failure. We propose PI3Kγ inhibition as a novel strategy to reactivate targeted autophagy and limit cancer therapy-related heart disease. Intriguingly, PI3Kγ inhibitors also have major antitumor properties and might provide the unique opportunity to "kill two birds with one stone" in cancer patients undergoing chemotherapy.

P2289
Galectin-3 inhibition prevents cardiac dysfunction in murine experimental type 3 cardio-renal syndrome

M Mathilde Prud'homme[1]; M Coutrot[1]; M Genest[2]; S Kinugasa[2]; S Placier[2]; E Polidano[1]; R Merval[1]; J-M Launay[1]; CE Chadjichristos[2]; M Legrand[1]
[1]Inserm UMR-S 942, Paris, France; *[2]Inserm UMR-S 1155, Paris, France*

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Introduction: Acute Kidney Injury (AKI) has been strongly associated with both short and long-term mortality in hospitalized patients. The Cardio-renal Syndrome type 3 (CRS-3) is characterized by an initial AKI that leads to an acute cardiac injury and/or dysfunction. Galectin-3 (Gal-3) is a galactoside-binding lectin and known to be involved in inflammation, fibrogenesis, and cardiac remodeling. Gal-3 has a key role in cardiac dysfunction in a mouse model of CRS-3.
Methods: and Results: In C57Bl6 and Gal-3 KO mice we performed nephrectomy of the right kidney and 25 minutes ischemia of the left kidney followed by reperfusion (IR). Two groups of WT mice were treated by MCP (Modified Citrus Pectin, an inhibitor of Gal-3), 3 days before surgery or one day after surgery. Mice were sacrificed at different time points after reperfusion (3, 6, 12, 24, 48, 72h and 28 days). Renal dysfunction was observed at 24h (increased x10 serum creatinine and Blood Urea Nitrogen levels, $p < 0.001$). Functional renal parameters returned to baseline levels at 2-3 days post-IR. Renal IR induced acute heart damage illustrated by the increase in cardiac markers of injury (BNP and QSOX1-mRNAs, $p < 0.01$) and inflammation (CD68, MCP1 and Galectin-3-mRNAs x2) in WT mice, almost prevented in Gal-3 KO and treated mice, but cardiac function remained normal. As in the kidney, all stress markers returned to basal levels within 3 days post-IR but markers of cardiac inflammation (CD68 and TGFβ x2: $p < 0.01$) remained elevated at day 28 post-IR in WT mice. This sustained inflammation in WT mice was accompanied by a cardiac dysfunction (-10% in fraction shortening, $p < 0.001$) and fibrosis (x3, $p < 0.001$) 28 days after renal IR prevented in Gal-3 KO and treated mice.
Conclusion: Altogether, data indicated that in WT mice a renal IR provokes an early cardiac injury and long-term cardiac dysfunction prevented by the inhibition of Gal-3. Gal-3 seems to have a key role in cardiac dysfunction in this murine model of CRS-3.

P2290
Role of Galectin 3 in acute renal disease.

M Magali Genest[1]; M Prud'homme[2]; S Kinugasa[1]; S Placier[1]; J-L Samuel[2]; M Legrand[2]; C-E Chadjichristos[1]
[1]HOPITAL TENON, INSERM UMR-S 1155, PARIS, France; *[2]Inserm UMR-S 942, Paris, France*

Introduction: Acute kidney injury (AKI), being associated with relatively high short-term mortality is a major problem of public health. It is characterized by a sudden decline of renal function. In the intensive care setting, AKI remains an important predictor of clinical outcomes and results in cardiac dysfunction in type 3 cardio-renal syndrome (CRS3). We recently demonstrated that Galectin 3 (Gal-3) is involved in cardiac inflammation and fibrosis. The objective of this study was to determine Gal-3 role in AKI following renal ischemia / reperfusion (IR) and to analyze its implication in the CRS3.
Materials and Methods: 2-month-old C57B1/6J WT and KO Gal-3 mice underwent right nephrectomy followed by 25-minute ischemia and reperfusion of the left kidney at different time points (6, 24 and 48h), or a sham operation. Mice were divided into 4 groups, WT Sham, KO-Sham, WT-IR and KO-IR.
Results: IR induced a peak of histological and functional renal damage in WT mice 24 hours after reperfusion, as well as an increase in the expression of Gal-3 at both mRNA and protein levels. Immunolabeling showed that Gal-3 was localized in the renal tubular cells and in the macrophages of the injured kidneys. Furthermore, KO Gal-3 mice presented more severe renal damage than WT at 48 h, with more pronounced macrophage infiltration.
Conclusion: The expression of Gal-3 is increased after renal IR. This protein could have a protective role in AKI following an IR, given that Gal-3 KO presents improved renal structure and function. In contrast, we observed less cardiac damage in these mice. Thus, Gal-3 could play a dual role in CRS3.

P2291
RAAS genetic polymorphism and glomeruli filtration reduction in patients with chronical heart failure

SU Volkova[1]; KA Tomashevich[2]; EU Efanov[1]
[1]Tyumen State Medical University, Tyumen, Russian Federation; *[2]"Neftyanic" hospital, Tyumen, Russian Federation*

Aim: To estimate RAAS genetic polymorphism association with glomeruli filtration reduction in patients with CHF. Materials and methods. 51 patients with CHF were included into investigation (27 women, mean age - 73,1 $\pm$ 11,3 years old) with clinical features of CHF, 3-4 NYHA class. 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 (homosygot in allel 1, allel 2 or heterosygot) detection for AGTR1 genes and AGT and in detection allel D-deletion or allel I – insertion Alu – consequences in intron ACE gen. Data were statistically processed with standard methods.
Results: We coincided RAAS genotypes frequency with comorbidity in patients with CHF. We analyzed association of genotypes with chronic kidney disease incidence with glomeruli filtration rate less than 60 ml/min (62.7%) as well as 30 ml/min (11.1%). We found no significant association of RAAS genetic polymorphisms with GFR rate reduction less than 60 ml/min. At the same time heavy kidney impairment (GFR < 30 ml/min) was associated with some polymorphisms of A1166S and Met274Thr. GFR < 30 ml/min was associated with allele 1166Cpresence (A1166S genotypes and 1166C homozygote (11,1%) if GFR < 30 ml/min, Versus 0% of homozygote A1166, $\chi 2$=4,11, p= 0, 043, p (F)= 0, 063) and 174Met allele (11,1% if GFR < 30, Versus 0% of genotype Tht174Thr, $\chi 2$=4,11 p= 0, 043, p (F)= 0, 063). At the same time statistical analysis revealed the tendency to higher blood hemoglobin level in patients with 1166C allele (119,4 $\pm$ 20,14 g/l versus 111,12 $\pm$ 13,3 g/l in patients without it in genotype, p=0,091). We can also say that Met235 allele presence was associated with lower creatinine level (114,2 $\pm$ 47,3 mmol/l versus 151,0 $\pm$ 41,2 mmol/l without it, p=0,036).
Conclusion: In our research we found some RAAS genotypes association with GFR reduction. Assuming that literature data show very controversy results about RAAS genetic polymorphism association with reduced GFR in patients with CHF, further study are actual.

P2292
PI3Kgamma inhibition rescues mice from acute cardiac contractile dysfunction and sudden death caused by calcineurin inhibitors

B Bernadin Ndongson Dongmo[1]; LR Moltzau[1]; KW Andressen[1]; M Baretta[2]; MV Cosson[1]; A Ghigo[3]; M Brodhun[4]; E Hirsch[3]; R Bauer[2]; FO Levy[1]
[1]University of Oslo, Pharmacology, Oslo, Norway; *[2]University Hospital of Jena, Institute of Molecular Cell Biology, Jena, Germany*; *[3]University of Turin, Center of Molecular Biotechnology, Turin, Italy*; *[4]Helios-Klinikum, Pathology, Erfurt, Germany*

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Purpose: Calcineurin inhibitors (CNI) as cyclosporin A and tacrolimus are the most commonly used immunosuppressive drugs following solid organ transplantation and in various autoimmune diseases. But, CNI therapies are also associated with severe side effects like arterial hypertension, atherosclerosis, insulin resistance, brain, liver and renal complications, and cardio-toxicity. However, the effects of CNI on cardiac contractile function are poorly studied. In this study, we have investigated the acute effect of CNI on cardiac contractile function and the beneficial effects mediated by PI3Kg inhibition.
Methods: The intact heart left ventricle contractility (Pressure-Volume-Conductance) was evaluated in mice 5h after intra-peritoneal injection of CNI in WT, PI3Kg KO (total deletion of PI3Kg), PI3Kg KD ("kinase dead"; lacking PI3Kg kinase function) and in WT treated with selective inhibitor of PI3Kg. Thereafter, cardiomyocytes were studied using several biochemical approaches to investigate the beta adrenergic signaling pathway including PLB activation, cAMP production and phosphodiesterase (PDE) activity. Finally a long term follow up with histological studies in cardiac tissue as well as ECG using telemetry and survival analysis was performed.
Results: We intriguingly found 5h after CNI injection an important reduction (<50%) of cardiac contractility (End-systolic elastance; Ees) that was confirmed in vitro with a down-regulation of beta-adrenergic signaling upon cardiomyocyte stimulation with CNI (4h). Interestingly, these effects were completely absent after the same treatment in transgenic mice and cardiomyocytes (PIKg KO, PIKg KD), and in mice and cardiomyocytes treated simultaneously with PI3Kg selective inhibitor. Following up these findings, we have also observed in cardiac sections (H&E, TUNEL) 15h after CNI, the presence of necrotic cells as well as myofibre break-up indicating a possible sign of ventricular fibrillation. Whereas the observed side effects of CNI were correlated with higher mortality, the group of mice simultaneously treated with PI3Kg inhibitor interestingly exhibited a better survival rate ($p < 0.05$).
Conclusion: In this study, we observed an acute cardio-depressive effect of CNI associated with sudden death and established the rationale for PI3Kg inhibition as a potential therapeutic approach.

P2293

Role of matrix metalloproteinase-2 isoforms in diabetic heart

H W Lee[1]; SJ Lee[1]; MY Lee[1]; SH Song[1]; JH Ahn[1]; JS Park[1]; JH Oh[1]; JH Choi[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]; MH Park[1]
[1]Pusan National University Hospital, Department of Cardiology, Busan, Korea Republic of

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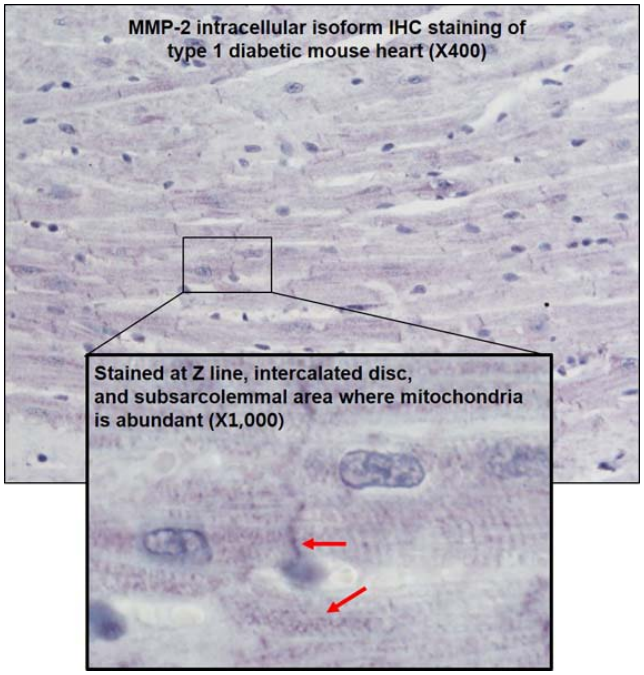
Background: Diabetic cardiomyopathy (DM CMP) is defined as cardiomyocyte damage and ventricular dysfunction in diabetic condition, which is independent of the concomitant coronary artery disease and/or hypertension. Matrix metalloproteinases (MMPs) are reported to account for pathogenesis of DM CMP by increasing myocardial extracellular collagen contents. Recently, intracellular isoforms of MMP-2 were reported. They are usually located at nucleus and mitochondria induced by oxidative stress, and reported to account for cardiac dysfunction through activating innate immunity and apoptosis at intracellular level in ischemic heart model. Purpose: We hypothesized that intracellular isoforms of MMP-2 are also induced by high glucose stimulation, where oxidative stress is also induced. Therefore, we aimed to evaluate the intracellular isoforms of MMP-2 in vivo and in vitro diabetic heart model.
Methods: Rat cardiomyoblast (H9c2 cell) was cultured with 30mM of high glucose concentration for 24 or 48hours. In vivo type 1 diabetic mouse model was made by 40mg/kg of streptozotocin intraperitoneal injection for consequent 5 days. After sacrificing mouse at 12 and 24 weeks, quantitative real-time polymerase chain reaction (qRT-PCR) of isoforms of MMP-2 and innate immunity/apoptotic markers were done as well as pathological analysis including immunohistochemical (IHC) staining. Results: Quantitative RT-PCR and immunofluorescence staining showed that there was expression of intracellular isoforms of MMP-2 in H9c2 cell compared to negative expression in control group. There was no definite histologic change of diabetic cardiomyopathy. For the IHC staining and qRT-PCR, however, there was distinct expression of intracellular isoforms of MMP-2 in diabetic mouse heart. Conclusion: Intracellular isoforms of MMP-2 were induced by high glucose stimulation in in vitro and in vivo diabetic heart model. Further evaluation of its role in diabetic cardiomyopathy should be followed.



MMP-2 intracellular isoform in tissue

P2294

The role of BNP on adipose tissue adaptations promoted by left ventricular chronic pressure overload

NG Nadia Goncalves[1]; C Moura[1]; AF Silva[1]; PG Rodrigues[1]; G Conceicao[1]; MF Santos[1]; R Roncon-Albuquerque[1]; AF Leite-Moreira[1]; I Falcao-Pires[1]
[1]University of Porto, Faculty of Medicine, Department of Physiology and Cardiothoracic Surgery, Porto, Portugal

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Introduction and aims: The progression of chronic pressure overload (CPO) is associated to cardiac cachexia as a consequence of insufficient energy supply. Additionally, some studies demonstrate that the heart secretes cardiokines able to modulate the adipose tissue (AT) structure and function promoting adiposopathy. In this study we investigate the effects of CPO in AT during the early stages of the disease.
Methods: Wistar rats were submitted to ascending aortic banding (Ba group; 0.6mm diameter) or sham procedure (Sham group). After 8 weeks, left ventricular (LV) function and structure (echocardiography and invasive hemodynamics) was evaluated and samples (LV and AT) collected for histological and molecular evaluations. Plasma was obtained for quantification of circulating B-type natriuretic peptide (BNP). Finally, visceral AT from normal rats was incubated with the BNP plasma concentrations detected in the Sham and Ba group (0.27 and 0.47ng/ml respectively) for 24h and then collected for molecular studies.
Results: Eight-weeks of banding increased LV systolic pressure and triggered cardiac remodeling with fibrosis and cardiomyocytes' hypertrophy when compared to Sham animals. The same group was at a compensated stage of the disease with higher ejection fraction, however a stiffer myocardium was observed with increased end diastolic pressure-volume relation and passive force of isolated cardiomyocytes. Despite similar adiposity between the 2 groups, aortic constriction triggered adipocyte atrophy as well as AT increased fibrosis and dysfunction, as observed by overexpression of pro-inflammatory adipokines. The incubation of AT from normal rats with BNP confirmed that the elevated circulatory levels of this cardiokine were able to induced increased expression of pro-inflammatory adipokines by the AT.
Conclusions: We demonstrated that higher circulatory levels of BNP promoted by LV CPO are able to induce adiposopathy characterized by remodeling of the AT and overexpression of pro-inflammatory adipokines.

	Sham	Ba
LV systolic pressure (mmHg)	110 ± 3.6	153 ± 10.5 *
Heart/tibial length (g/cm)	2.3 ± 0.05	3.3 ± 0.30 *
LV cardiomyocyte cross-sectional area (μm²)	382 ± 23.6	484 ± 33.6 *
LV fibrosis (%)	4.2 ± 0.52	6.3 ± 0.94 *
LV ejection fraction (%)	78 ± 0.9	89 ± 1.9 *
LV end diastolic pressure volume relationship	0.04 ± 0.006	0.11 ± 0.031*
LV passive force at 2.2μm (mN/mm²)	3.3 ± 0.29	4.4 ± 0.57
Plasma BNP (ng/ml)	0.27 ± 0.048	0.47 ± 0.080 *
AT/tibial length (g/cm)	7.9 ± 0.88	7.5 ± 0.25
AT fibrosis (%)	7.2±0.31	8.7±0.61 *
Adipocyte CSA (μm²)	1659±103.8	1287±85.1 *
AT TNFα (AU)	0.03±0.013	0.06± 0.018 *
AT IL-1β (AU)	0.04 ± 0.01	0.28 ± 0.15 *
TNFα (AU) after incubation with BNP	26380 ± 1428	31125 ± 1455 *
IL-1β (AU) after incubation with BNP	9038 ± 678	12221 ± 1086 *

Data presented as mean± SEM. * p<0.05 vs Sham.

Table

P2295

Effects of ranolazine in a model of doxorubicin-induced left ventricle diastolic dysfunction

D Cappetta[1]; K Urbanek[1]; G Esposito[1]; R Coppini[2]; E Piegari[1]; LP Ciuffreda[1]; L Santini[2]; F Rossi[1]; L Berrino[1]; A De Angelis[1]
[1]Second University of Naples, Department of Experimental Medicine - Section of Pharmacology, Naples, Italy; *[2]University of Florence, Department of Neuroscience, Drug Research and Child's Health (NeuroFarBa) - Division of Pharmacology, Florence, Italy*

Background: Doxorubicin (DOXO) is a highly effective anticancer drug but its clinical application is impeded by cardiotoxicity. Asymptomatic diastolic dysfunction can be the earliest manifestation of DOXO cardiotoxicity. Therefore, a search for therapeutic intervention that can interfere with early manifestations and possibly prevent late cardiotoxicity is warranted. Increased DOXO-dependent reactive oxygen species may explain, in part, Ca2 + and Na + accumulation that contributes to diastolic dysfunction and development of heart failure.
Purpose: We tested whether the administration of ranolazine (RAN), an anti-anginal drug, immediately after completing DOXO therapy, can affect diastolic dysfunction and interfere with the progression of functional decline.
Methods: Fischer 344 rats received a DOXO cumulative dose of 15 mg/kg over a period of 2 weeks. After the assessment of diastolic dysfunction, the animals were administered with RAN (80 mg/kg/die) for the following 4 weeks.
Results: While diastolic and systolic function progressively deteriorated in DOXO-treated animals, treatment with RAN relieved diastolic dysfunction and prevented worsening of systolic function decreasing mortality. RAN lowered myocardial NADPH oxidase 2 expression and 3-nitrotyrosine content. A reduced NCX and Nav 1.5 expression and an increment of SERCA2 were also detected. In addition, RAN lowered DOXO-induced increased phosphorylation and oxidation of Ca2 + /calmodulin-dependent protein kinase II and decreased fibrosis.
Conclusions: RAN, by modulating cardiac Ca2 + and Na + handling proteins and oxidative stress, was effective in attenuating DOXO-induced diastolic dysfunction and prevented the progression of cardiomyopathy.

P2296

Allogeneic amniotic membrane-derived mesenchymal stem cell therapy is cardioprotective, restores myocardial function, and improves survival in a model of anthracycline-induced cardiomyopathy

A Giraldo[1]; J Talavera[2]; MJ Fernandez-Del-Palacio[2]; C Mico Valls[2]; E Garcia-Navarro[2]; N Marin[3]; JM Moraleda[3]; G Brooks[1]
[1]University of Reading, Institute for Cardiovascular and Metabolic Research, Reading, United Kingdom; *[2]University of Murcia, Department of Small Animal Medicine and Surgery, Veterinary School, Murcia, Spain*; *[3]Hospital Clínico Univeristario Virgen de la Arrixaca, Haematology Department, IMIB, Murcia, Spain*

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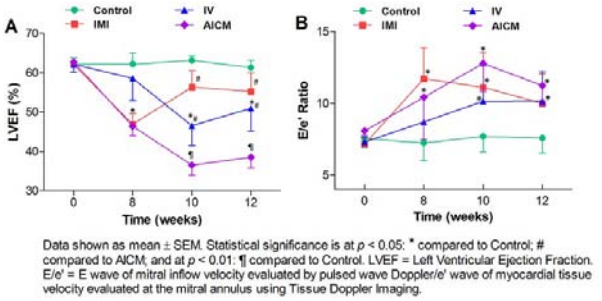
Introduction: Recent data suggests that anthracycline induced cardiomyopathy (AICM) is a stem cell disease affecting the local (myocardial) and systemic stem cell niches, which limits autologous stem cell therapy in this condition. We hypothesized that an allogeneic stem cell transplant approach using amniotic membrane-derived mesenchymal stem cells (AM-MSC) could be an effective therapy for this condition. Using a model of AICM, we evaluated the effects on ventricular systolic and diastolic function as well as survival, of AM-MSC therapy administered via intravenous route (IV), compared to administration via percutaneous contrast echocardiography-guided intramyocardial injection (IMI).
Methods: Cardiomyopathy was induced in New Zealand rabbits with IV daunorubicin (4 mg/kg, weekly for 6 weeks). One group received IV therapy with 5 million/kg AM-MSC (IV Group, n=8), 24 hours after each weekly cycle of daunorubicin. A second group received one dose of 5 million AM-MSC, 8 weeks after the first dose of anthracycline, via contrast echocardiography-guided percutaneous IMI (IMI Group, n=8). A third group received no cell therapy (AICM Group, n=8). A final group neither received daunorubicin nor cell therapy, thus constituting an age-matched Control Group (n = 8). A complete echocardiographic exam was performed at baseline and repeated every two weeks.
Results: In all groups, ventricular systolic and diastolic function was normal at baseline (Figure 1A-B). The IV group did not exhibit significant alterations of myocardial function at 8 weeks, consistent with a cardioprotective effect (Figure 1A-B). In contrast, significant alterations of both systolic and diastolic function by daunorubicin were observed in IMI and AICM groups at 8 weeks, consistent with the development AICM. Whilst ventricular systolic function significantly improved at 10 and 12 week time points in IMI group, it continued to deteriorate in AICM group. Of note, significant alterations in myocardial function were apparent in IV group after 10 weeks, but significantly less conspicuous than in AICM group, suggesting delayed-onset cardiotoxicity. Survival in rabbits from IMI and IV groups was improved (77% and 75%, respectively) compared to AICM group (22%) ($p < 0.04$).
Conclusions: The observation of early cardioprotection from AICM in IV group at 8 weeks, with later decline of LVEF from 10 weeks suggests that anthracyclines induced delayed-onset cardiotoxicity, which affected, at least in part, endogenous as well as exogenous stem cells, thus hindering long term cardioprotection. The significant recovery of LVEF at 10 and 12 weeks in the IMI group, suggest that this is an effective therapy once cardiomyopathy ensues. Further studies with an extended time course of IV administration of allogeneic AM-MSC are required to evaluate whether this therapy may confer prolonged cardioprotection from AICM, as well as to elucidate the mechanisms of delayed-onset cardiotoxicity observed in IV group.



Data shown as mean ± SEM. Statistical significance is at $p < 0.05$: * compared to Control; # compared to AICM; and at $p < 0.01$: ¶ compared to Control. LVEF = Left Ventricular Ejection Fraction. E/e' = E wave of mitral inflow velocity evaluated by pulsed wave Doppler/e' wave of myocardial tissue velocity evaluated at the mitral annulus using Tissue Doppler Imaging.

Figure 1

P2297

MicroRNA-155 promotes LPS-induced myocardial NO overproduction and amplifies cGMP-PKG signaling pathway by targeting CD47

F Francisco Vasques-Novoa[1]; R Cerqueira[1]; C Quina-Rodrigues[1]; S Ribeiro[1]; R Soares-Dos-Reis[1]; F Goncalves[1]; TL Laundos[2]; DS Nascimento[2]; AF Leite-Moreira[1]; R Roncon-Albuquerque Jr[1]
[1]University of Porto, Faculty of Medicine, Porto, Portugal; *[2]University of Porto, i3s - Instituto de Investigação e Inovação em Saúde, Porto, Portugal*

Purpose: Sepsis-associated cardiovascular dysfunction (SACVD) remains a leading cause of death in critically ill patients. Among several pathophysiological mechanisms, excessive NO production and signaling have been shown to negatively affect cardiac contractility and vascular reactivity. CD47, a transmembrane receptor for TSP1, mediates a potent inhibitory effect on NO-cGMP-PKG signaling pathway and its role in SACVD remains unknown.
Methods: Protocol 1: Experimental sepsis was induced using LPS injection (40mg/Kg, ip) in C57BL/6J (WT; n=40) and miR-155-/- (KO; n=40) male mice. Cardiac function was evaluated through echocardiography. Myocardial water content and microvascular permeability (Evans blue method) were assessed. Myocardial NO, cGMP levels and PKG activity were evaluated. Quantification of miR-155, CD47, NOS2, NOS3 and phospho-VASP (Ser239) were assessed by immunoblotting (this

analysis was repeated in protocol 2 and 3). Protocol 2: Human cardiac microvascular endothelial cells (HMVEC-C) were incubated with LPS (20mg/mL) or vehicle and NO production was assessed under inhibition of miR-155 (LNA), CD47 activation with TSP1 and knockdown of CD47 (siRNA), with appropriate controls. Protocol 3: Vascular response to TSP-1 was analyzed in mouse aortas and human internal mammary arteries after LPS/vehicle exposition. Dose-response curves to Ach were performed for each group under control or physiological TSP-1 stimulation (2.2nM) conditions.
Results: LPS upregulated miR-155 expression in mouse and human samples. In experimental sepsis, this was accompanied by impaired cardiac contractility and increased myocardial microvascular permeability. MiR-155 KO animals presented with attenuated LPS-induced cardiac dysfunction and edema, compared with WT. CD47 was validated as miR-155 target by a luciferase assay. Experimental sepsis in WT was associated with CD47 downregulation and iNOS upregulation, increased myocardial NOx content, cGMP levels, VASP phosphorylation and PKG activity, all of which were attenuated in KO mice. In HMVEC-C, LPS incubation induced miR-155 upregulation, NO overproduction and CD47 downregulation. MiR-155 inhibition attenuated NO production and iNOS overexpression. TSP-1 incubation decreased NO production in Ctrl cells; this effect was lost with LPS incubation, but regained with miR-155 inhibition. MiR-155-mediated recovery TSP-1 inhibitory effect on NO production was CD47-dependent. In control arterial rings, TSP1 incubation significantly decreased the NO-mediated relaxation – this effect was lost in WT LPS, but preserved in miR-155 KO LPS.
Conclusions: MiR-155 is uprerulated in septic myocardial and vascular tissue. Mice lacking miR-155 present an attenuation of myocardial NO overproduction, edema, contractile dysfunction and mortality. CD47, a previously unappreciated target of miR-155, is downregulated during sepsis, potentiating the depressor effect of cGMP-PKG signaling on myocardium and vascular function.

P2298

Altered expression of thyroid hormone biosynthesis machinery in the ischemic heart. Potential role of epigenomics

E Esther Rosello-Lleti[1]; C Gil-Cayuela[1]; E Tarazon[1]; A Ortega[1]; F Lago[2]; JR Gonzalez-Juanatey[2]; L Martinez-Dolz[1]; M Rivera[1]; M Portoles[1]
[1]Hospital Universitario y Politécnico La Fe, Cardiocirculatory Unit , Valencia, Spain; *[2]Instituto de Investigación Sanitaria de Santiago, Cellular and Molecular Cardiology Research Unit, Santiago de Compostela, Spain*

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Background: Abnormal thyroid hormone (TH) metabolism is significantly associated with impaired left ventricular (LV) function and death. Although TH was traditionally thought to be produced exclusively by the thyroid gland, an increasing number of studies report TH production in other tissues.
Purpose: We aimed to determine whether the genes required for TH biosynthesis are expressed in the human heart, and to investigate whether their expression is altered in patients with ischemic cardiomyopathy (ICM) and is related to variations on epigenetic patterns.
Methods: Twenty-three LV tissue samples were obtained from ICM patients undergoing heart transplantation and control donors for RNA sequencing analysis. We increased the LV samples to 27 for the ELISA determination of total T4 and T3 tissue levels. For epigenomic studies, 850K Infinium MethylationEPIC BeadChip platform was performed.
Results: Using RNA-sequencing, we identified the expression levels of all components required for TH biosynthesis in human heart tissue. We observed significantly altered expression of genes encoding thyroperoxidase (TPO; $P < 0.05$) and dual oxidase 2 ($P < 0.05$), the main enzymatic system of TH production, and significant relationships between their altered expression and LV remodeling parameters. In addition, epigenetic analysis revealed a differential methylation pattern in TPO, and triiodothyronine tissue levels were significantly decreased ($P < 0.01$).
Conclusions: These results showed that the human heart expresses the TH biosynthesis machinery, being altered its main enzymatic system in patients with ICM. Given the relevance of TH in cardiac pathology, our results may provide the basis for new therapeutic approaches based on TPO for treating ICM.

P2299

Effects of streptozotocin-induced type I diabetes mellitus on the pacemaker of the heart

Y Yu Zhang[1]; YW Wang[1]; Y Joseph[1]; AQ Mohammed[2]; X Cai[1]; N Gardiner[3]; FC Howarth[2]; H Dobrzynski[1]
[1]University of Manchester, Institute of Cardiovascular Sciences, Manchester, United Kingdom; *[2]Medicine and Health Sciences, Department of Physiology, Al-Ain, United Arab Emirates*; *[3]Faculty of Life Science, manchester, United Kingdom*

Purpose: Cardiovascular complications are common in type I diabetes mellitus and, for example, there is an increased risk of bradyarrhythmias as a result of dysfunction of the cardiac conduction system (1). The sinoatrial node (SAN) is the pacemaker of the heart and one component of the cardiac conduction system. We have shown that in vivo there is a decrease in heart rate in the streptozotocin-induced diabetic rat (266 ± 13 versus 316 ± 11 beats/min; $P < 0.05$). The aim of this study was to investigate the cellular basis of the bradycardia in the rat model.
Methods: We generated streptozotocin-induced diabetic rats as previously described (2). We investigated function using the Langendorff-perfused heart, isolated SAN and isolated SAN cell (patch clamp). Protein expression was investigated using immunohistochemistry. We labelled HCN4 (responsible for the funny current, If), Kir3.1 (responsible for the ACh-activated K+ current, IK,ACh) and RyR2 (sarcoplasmic reticulum Ca2+-release channel). The research was conducted in accordance with legislation in UAE and UK.
Results: Compared to control rats, diabetic rats showed a 428% increase in blood glucose and 16% increase in heart to body weight ratio ($n = 16$ control and n=16 diabetic rats; $P < 0.05$). The heart rate measured in the Langedorff heart was decreased by 17.4% in diabetes from 298 to 246 beats/min ($n = 5$ control and n=4 diabetic rats; $P < 0.05$). The beating rate of the isolated SAN preparation was decreased by 17.3% from 305 to 252 beats/min ($n = 4$ control and n=3 diabetic rats; $P < 0.05$). Application of 2 μM ryanodine to the SAN preparation to incapacitate RyR2 caused arrhythmia in the diabetic preparations, but not in control preparations ($n = 4$ control and n=3 diabetic rats). If was measured in nodal cells isolated from 4 control rats ($n = 29$ cells) and 3 diabetic rats ($n = 33$ cells). The If density was 21.0 ± 2.8 versus 14.3 ± 1.2 pA/pF, and the cell capacitance was 20.2 ± 1.0 versus 14.7 ± 0.9 pF in control and diabetic rats, respectively. Immunolabelling of SAN tissue sections showed that HCN4 channel expression was significantly increased by 73%, whereas Kir3.1 and RyR2 expression was significantly decreased by 9% and 34% in diabetes ($n = 4$ control and n=4 diabetic rats). Downregulation of If density and RyR2 could explain the lower heart rate of the diabetic rats.
Conclusions: We conclude that there are complex functionl changes in the SAN in diabetes. Such remodelling may increase the risk of bradyarrhythmia in type 1 diabetes.

P2300

Maternal overnutrition programs cardiac dysfunction independently of post-natal diet in mice

E Elena Loche[1]; HL Blackmore[1]; AAM Carpenter[1]; DS Fernandez-Twinn[1]; J Beeson[1]; TJ Ashmore[1]; A Pinnock[1]; SE Ozanne[1]
[1]University of Cambridge, Wellcome Trust-MRC Institute of Metabolic Science, Cambridge, United Kingdom

Purpose: Gestational exposure to maternal obesity increases the risk of cardiovascular disease in the offspring. Exposure to overnutrition during fetal life is likely to be followed by continued exposure to the same calorie-rich environment post-natally. The aim of this project was to characterize the consequences of combined exposure to a maternal and post-natal obesogenic diet on offspring cardiac structure and function.
Methods: A well-established mouse model of maternal diet-induced obesity where C57bl/6 dams are fed a high fat/high simple carbohydrate diet during pre-gestation, gestation and lactation was used. Male offspring from control (C-) and obese (O-) were assigned at weaning to either a control (-C) or obesogenic diet (-O), generating 4 experimental groups (CC, CO, OC and OO). Metabolic profile, cardiac structure and function, gene expression, and blood pressure were assessed in male offspring at 8 weeks of age.
Results: Dams fed the obesogenic diet were significantly heavier on the day of mating ($p < 0.0001$), and remained heavier throughout pregnancy and at weaning compared to controls. Young adult (8 weeks) offspring exposed to maternal overnutrition had heavier hearts (17%) than control mice (effect of maternal diet $p = 0.005$). A post-weaning obesogenic diet also increased heart weight (effect of offspring diet $p = 0.019$). Circulating levels of insulin and leptin were increased by feeding the obesogenic diet, and further elevated by the maternal exposure. Mice born to overnourished mothers developed pathological ventricular remodelling associated with re-expression of cardiac fetal genes (Nppa, Myh7, Myh7:Myh6 ratio), interventricular septum thickening ($p = 0.0004$), increased left ventricular area ($p = 0.02$), cardiac systolic dysfunction with reduced ejection fraction and fractional shortening. Most importantly, up-regulation of genes involved in cardiac contraction was observed in fetuses from obese dams as early as in utero.
Conclusions: Maternal overnutrition programs adverse cardiac remodelling and dysfunction in adult male offspring. These findings suggest that a maternal calorie-rich uterine environment is a critical determinant of cardiovascular disease risk in the next generation.

BASIC SCIENCE – ANIMAL EXPERIMENTATION

P2301

Cobalamin and folate protect mitochondrial oxidative capacity and contractile function in myocardial dysfunction

J Piquereau[1]; M Moulin[2]; M Moulin[1]; G Zurlo[1]; G Zurlo[2]; P Mateo[2]; P Mateo[1]; M Gressette[1]; M Gressette[2]; J-L Paul[2]; J-L Paul[3]; C Lemaire[1]; C Lemaire[2]; R Ventura-Clapier[2]; R Ventura-Clapier[1]; V Veksler[1]; V Veksler[2]; A Garnier[2]; A Garnier[1]
[1]University of Paris-Sud 11, UMR-S 1180, Inserm, Chatenay-Malabry, France; *[2]University of Paris-Sud 11, Chatenay-Malabry, France*; *[3]European Hospital Georges Pompidou, Paris, France*

Background: As a key regulator of energy metabolism, the transcriptional co-activator PGC-1α appears as a relevant therapeutic target to rectify the chronic energy deficit observed in heart failure (HF). Based on results obtained from a cellular screening assay showing a positive effect of cobalamin (Cb, vitamin B12) on PGC-1α signaling pathway, the present study aimed at investigating the potential protective role of Cb in pressure overload-induced HF.
Methods: and results: Mice were pre-treated with Cb and folate supplemented diet (SD) for 3 weeks before transverse aortic constriction (TAC). Four weeks after TAC, cardiac parameters were measured by echocardiography and animals were sacrificed. TAC-induced left ventricle (LV) hypertrophy and drop of ejection fraction (EF) were significantly lower in mice treated with SD than in mice fed with normal diet. Alterations in mitochondrial oxidative capacity and mitochondrial biogenesis induced by pressure overload were markedly improved by SD. In SD-TAC mice, exploration of the signaling pathways involved in the post-translational regulation of PGC-1α showed a higher activation in AMPK, a lower expression level of the acetyltransferase GCN5 and a higher expression level of PRMT1. This was associated with a lower protein acetylation and a higher protein methylation levels in SD-TAC mice that were accompanied by a sustained expression of genes involved in mitochondrial biogenesis (Tfam, Nrf2, Cox1 and Cox4), suggesting a preserved activation of PGC-1α after TAC in mice fed with SD. Inasmuch as oxidative stress and homocysteinemia were unchanged by SD, it seems that the beneficits procured by SD in this model would not be related to the antioxidant properties and the effect on homocysteinemia of these vitamins.
Conclusion: These results showed that Cb and folate could protect the failing heart by preserving energy status through maintenance of mitochondrial biogenesis.

P2302

Cardiac compliance is acutely modulated through cGMP-PKG signalling

A M Andre Mendes Leite Moreira[1]; J Almeida-Coelho[1]; JS Neves[1]; N Hamdani[2]; WA Linke[2]; I Falcao-Pires[1]; AP Lourenco[1]; AF Leite-Moreira[1]
[1]Faculty of Medicine University of Porto, Physiology and Cardiothoracic Surgery, Porto, Portugal; *[2]Ruhr University Bochum (RUB), Cardiovascular Physiology, Bochum, Germany*

On behalf of: ESC Working Group on Myocardial Function

Purpose: Increased diastolic stiffness due to titin hypophosphorylation and low protein kinase G (PKG) activity is a hallmark of heart failure with preserved ejection fraction (HFpEF). Acute load sensitivity is a well-known factor of decompensation in HFpEF which has been mainly ascribed to vascular and systolic stiffening but other factors such as a diastolic stiffness response to volume overload (VO) may be at play. We aimed to investigate whether there is a diastolic response to acute VO, cardiac stretch-induced compliance (SIC), and to ascertain the potential involvement of cGMP-PKG-signalling in this response in several animal models and the human heart.
Methods: Left ventricle (LV) of rat intact hearts, LV and right atrial muscle strips of cardiac surgery patients and rabbit right ventricular papillary muscles were acutely stretched for 15 minutes. Passive tension (PT) was measured in skinned cardiomyocytes extracted from non-stretched and stretched LV before and after incubation with PKG or protein phosphatases (PP). Different groups of rabbit muscles were incubated with a natriuretic peptide receptor-A antagonist (NPRA), an inhibitor of NOS, a NO scavenger, the latter 3 simultaneously or an inhibitor of PKG (PKGi). Titin phosphorylation was assessed in non-stretched and stretched muscles incubated with PKGi. Myocardial cGMP levels and vasodilator-stimulated phosphoprotein (VASP) phosphorylation were quantified in stretched and non stretched samples. Hemodynamic pressure-volume response to VO was assessed in sham and transverse-aortic-constriction (TAC) rats and was also assessed by echocardiography in healthy volunteers and in cardiac surgery patients before and after Trendelenburg positioning and VO, respectively.
Results: After the initial increase in response to stretch/VO, diastolic pressure and PT decreased sustainedly over 15 minutes in all species and experimental preparations. Skinned cardiomyocytes from stretched hearts showed decreased PT which was abrogated by PP incubation while those from non stretched LV decreased PT after PKG incubation. Stretched samples showed increased cGMP levels and hyperphosphorylation of VASP. Titin phosphorylation was higher in stretched samples and lesser by PKGi. SIC was significantly blunted by PKG inhibition or by joint NPRA + NOS inhibition + NO scavenging and was also absent in TAC animals. TAC hearts showed titin hypophosphorylation and no increase upon VO. In humans, healthy volunteers and cardiac surgery patients showed E/E' and end-diastolic pressure decrease after VO, respectively. In patients with severe LV hypertrophy the effect was blunted.
Conclusions: We describe a novel adaptive mechanism of increased myocardial compliance in response to acute VO that is mediated by titin phosphorylation through cGMP-PKG signalling. The mechanism was translated to human physiology and may be abolished in the hypertrophic heart suggesting a potential role in the pathophysiology of HFpEF.

P2303

Endothelium-derived C-type natriuretic peptide regulates blood pressure through the maintenance of endothelial function

K Kuwahara[1]; K Nakao[2]; T Nishikimi[2]; Y Nakagawa[2]; H Kinoshita[2]; T Tokudome[3]; N Minamino[4]; T Kimura[2]; K Kangawa[3]; K Nakao[5]
[1]Shinshu University, Department of Cardiovascular Medicine, Matsumoto, Japan; *[2]Kyoto University Graduate School of Medicine, Cardiovascular Medicine, Kyoto, Japan*; *[3]National Cerebral and Cardiovascular Center, Department of Biochemistry, Osaka, Japan*; *[4]National Cerebral and Cardiovascular Center, Department of Molecular Pharmacology, Osaka, Japan*; *[5]Kyoto University Graduate School of Medicine, Medical Innovation Center, Kyoto, Japan*

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Background: Previously we reported the secretion of C-type natriuretic peptide (CNP) from vascular endothelial cells and proposed the existence of a vascular natriuretic peptide system composed of endothelial CNP and smooth muscle guanylyl cyclase-B (GC-B), the CNP receptor, and involved in the regulation of vascular tone, remodeling and regeneration.
Purpose: In this study, we assessed the functional significance of endothelium-derived CNP in the regulation of blood pressure in vivo.
Methods: We generated and analyzed vascular endothelial cell-specific CNP knockout (CNP ecKO) and vascular smooth muscle cell-specific GC-B knockout (GC-B smcKO) mice.
Results: Both CNP ecKO and GC-B smcKO mice showed neither the skeletal abnormality nor the early mortality observed in systemic CNP or GC-B knockout mice. CNP ecKO mice exhibited significantly increased blood pressures and an enhanced acute hypertensive response to nitric oxide synthetase inhibition. Acetylcholine (ACh)-induced, endothelium-dependent vasorelaxation was impaired in rings of mesenteric artery isolated from CNP ecKO mice. Furthermore, the impairment of ACh-induced vasorelaxation was enhanced in CNP ecKO arteries pretreated with the NOS inhibitor L-NAME and the cyclooxygenase (COX) inhibitor indomethacin, suggesting that the impairment of endothelium-dependent vasorelaxation in CNP ecKO mice involves NO- and prostaglandin-independent pathways, possibly an endothelium-derived hyperpolarization factor (EDHF) system. In addition, endothelin-1 (ET-1) gene expression was enhanced in pulmonary vascular endothelial cells from CNP ecKO mice, which also showed significantly higher plasma ET-1 concentrations and a greater reduction in blood pressure in response to an endothelin receptor antagonist than their control littermates. By contrast, GC-B smcKO mice exhibited blood pressures similar to control mice, and acetylcholine-induced vasorelaxation was preserved in their isolated mesenteric arteries. Nonetheless, CNP-induced acute vasorelaxation was nearly completely abolished in mesenteric arteries from GC-B smcKO mice. Consistent with this finding, acute hypotensive effects induced by intravenous administration of CNP were markedly attenuated in GC-B smcKO mice.
Conclusions: These results demonstrate that endothelium-derived CNP contributes to the chronic regulation of vascular tone and systemic blood pressure by maintaining endothelial function independently of vascular smooth muscle GC-B.

P2304

Pharmacological inhibition of microRNA-132 effectively reverses myocardial infarction-induced heart failure in small and large animal models

AE Foinquinos Marin[1]; J Fiedler[1]; J Remke[1]; K Zimmer[1]; A Just[1]; M Gyongyosi[2]; S Batkai[1]; T Thum[1]
[1]Hannover Medical School, Institute for Molecular and Translational Therapeutic Strategies, Hannover, Germany; *[2]Medical University of Vienna, Vienna, Austria*

Purpose: Adverse remodelling after myocardial infarction (MI) is an essential pathological characteristic in heart failure (HF), and microRNAs (miRs, miRNAs) are known to play a key role in this condition. Previously, our group identified miR-132 as

one of the main regulators of cardiomyocyte hypertrophy and highly elevated in cardiac samples from HF patients. Moreover, mice overexpressing miR-132 developed hypertrophy and fibrosis and died from HF at an early stage. Hypertrophy and fibrosis in the remote myocardium are also mechanisms involved in adverse remodelling in patients post-MI often leading to heart failure. Therefore, we wanted to validate whether miR-132 intervention would be beneficial in this process.
Methods: and Results: Pharmacological inhibition of miR-132 by LNA-based oligonucleotides (antisense or scrambled) was done at day 7 and 14 post-MI in a mouse model of experimental MI. Hemodynamic parameters, measured by echocardiography and left ventricular (LV) pressure volume catheter, were assessed at the study end point 4 weeks post-MI. These results show that post-MI antimiR-132 treatment ameliorated cardiac function: both left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) were reduced after miR-132 silencing in post-MI mice. We then observed by Longitudinal Strain Rate (LSR) analysis that antimiR-132 treatment led to a recovery of the function in the remote areas after MI. At the molecular and histological level, repression of key genes involved in adverse remodeling highlighted the protective cardiac effects of antimiR-132 treatment. After confirming the efficacy of the treatment in a mouse model, we tested this concept in a clinically relevant large animal model. Domestic pigs had a balloon-mediated occlusion of the left anterior descending artery (LAD) for 90 min followed by reperfusion. AntimiR-132 or placebo treatment were delivered by anterograde slow infusion into the coronary artery by a catheter at day 3 and intravenously 4 weeks post-MI. Based on magnetic resonance imaging (MRI) data, 8 weeks post-MI, the volumes and cardiac mass were well preserved and the expression of hypertrophic genes was decreased after antimiR-132 delivery. In addition, we specifically investigated regional function of the post-MI myocardium using segmental contraction analysis. Segmental velocity was improved in most of the remote area segments. The regional improvements could also be observed by NOGA catheter measurements, giving a functional assessment based on electrophysiological properties.
Conclusions: The presented data show that antimiR-132 treatment is beneficial post-MI and attenuates adverse cardiac remodeling by improving global cardiac performance and reducing hypertrophy. These data provide further evidence of this miRNA's translational and clinical relevance and encourages the future therapeutic testing of miR-132 inhibitors on the road of clinical application in HF patients.

P2305
Regulation of beta adrenoceptor evoked inotropic responses by inhibitory g protein, adenylyl cyclase isoforms 5 and 6 and phosphodiesterases

MV Marie Victoire Cosson[1]; HG Hiis[1]; FO Levy[1]; KA Krobert[1]
[1]*Oslo University Hospital, pharmacology, Oslo, Norway*

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Purpose: Our data indicate that inhibitory G protein (Gi) inhibits adenylyl cyclase (AC) independently of the receptor. The two major subtypes of AC in the heart are AC5 and AC6. Compartmentalization of β1-adrenoceptor- (β1AR) versus β2AR differs depending on the subcellular localization of the AC subtypes. Deletion of AC6 impairs left ventricular responsiveness to βAR ligands and it is unknown if AC5 or 6 differentially regulate β1AR- versus β2AR-mediated inotropic responses. Determine if intrinsic Gi inhibition is AC subtype selective and whether there is a differential role of AC5 and AC6 to mediate β1AR- and β2AR-evoked inotropic responses. In addition, determine if there is an interplay between Gi and phosphodiesterases 3,4 (PDE3,4).
Methods: We measured β1AR- and β2AR-mediated changes in contractility in left ventricular muscle strips from wild type (WT), AC5 and AC6 knockout (KO) mice. First, with or without pertussis toxin (PTX) to inactivate Gi and/or after inhibition of PDE3 or PDE4.
Results: AC6KO mice revealed increased noradrenaline potency (EC50) at the β1AR compared to WT and AC5KO. Furthermore, AC6KO mice revealed an adrenaline-evoked β2AR-inotropic response only after PDE3 or PDE4 inhibition whereas both were required in WT and AC5KO. A β2AR-mediated inotropic response was also observed after PTX treatment alone in all groups
Conclusion: Gi tonically inhibits AC since PTX enhances both β1AR- and β2AR-mediated inotropic responses despite Gi not coupling to β1AR. PDE4 seems to be the primary PDE regulating the β1AR response in all groups. Inhibiting Gi and PDE3 or PDE4 appears to synergistically enhance adrenaline-evoked β2AR-inotropic response in WT. We therefore propose that inhibiting Gi and PDEs allows cAMP to leak from the β2AR to the β1AR contractile compartment.

P2306
Angiotensin 1-7 blunts in vitro induced acute heart failure.

V Cobet[1]; L Tacu[1]; E Cobet[2]; V Rotaru[1]; L Ciobanu[3]; A Rotaru[4]
[1]*State University of Medicine and Pharmacy, Chisinau, Moldova Republic of*; [2]*State University of Moldova , Biopharmaceutical chemistry , Chisinau, Moldova Republic of*; [3]*Institute of cardiology , Chisinau, Moldova Republic of*; [4]*Harvard Medical School, Cambridge, United States of America*

Background: Angiotensin 1-7 (Ang 1-7) comprises consistent evidences regarding cardiovascular regulatory benefits due to Ang II receptor AT1 modulation via mass receptor.
Aim: Evaluation of the Ang 1-7 cardiac effects in the in vitro induced acute heart failure.
Material and methods: Acute heart failure (AHF) was induced using the model of isolated rat pumping heart perfused by Krebs solution without glucose during 20 min according to Neely-Rovetto model (glucose is a single energetic substrate in this model) – control series. In another series heart has been perfused without glucose, but Ang 1-7 was added till final concentration of 10-7 M – medicated series. Left ventricle (LV) functional parameters were assayed during inotropic stimulation by norepinephrine (NE) and endothelin 1 (ET-1) in concentration of 10-6 M, or ischemia-reperfusion impact (15 min of total ischemia followed by 20 min of reperfusion) reproduced in Langendorff isovolumic isolated heart.
Results: Cardiac output (CO) significantly decreased after 20 min perfusion of isolate heart without glucose by 25,9% ($29,4 \pm 1,3$ vs $39,7 \pm 2,1$ ml/min). Action of Ang 1-7 led to a less decline of CO compared to control ($34,8 \pm 1,6$ vs $29,4 \pm 1,3$ ml/min, $p < 0,05$). NE stimulation induced an increase of control CO by 10,7% associated by LV end-diastolic pressure (LVEDP) elevation of 30,3% while in medicated series response was better: CO increased by 14,4% and LVEDP boosted only by 17,6% (($19,3 \pm 1,6$ (Ang 1-7) vs $27,4 \pm 1,7$ (control) mm Hg, $p < 0,05$). Stimulated by ET-1 control isolated heart responded by a negative inotropic effect, and both systolic LV pressure and CO fallen respectively by 13,2% and 9,6%. Ang 1-7 insured a positive inotropic response during ET-1 action leading to CO and LV systolic pressure increase respectively by 10,5% and 11,7%. Ang 1-7 also improved the dynamics of LVEDP during ischemia-reperfusion. Thus, LVEDP was in medicated series significantly less than control index at finish of both ischemia ($41,3 \pm 3,2$ vs $55,4 \pm 4,4$ mm Hg) and reperfusion ($17,2 \pm 1,4$ vs $28,7 \pm 2,2$ mm Hg) periods.
Conclusion: Angiotensin 1-7 is a component of renin-angiotensin-aldosterone system which has a benefic action on acutely developing heart failure due to energy privation, manifested by improvement of inotropic response of NE and reinstated positive inotropic of ET-1 action as well as significant diminution of LVEDP during ischemia-reperfusion syndrome.

P2307
Bioenergetic properties of inotropic drugs

A Dietl[1]; M Michael Kohlhaas[1]; D Puetz[1]; AG Nickel[1]; C Maack[1]
[1]*Saarland University Hospital, Department of Internal Medicine III, Homburg, Germany*

Background: Cardiogenic shock is an unmet clinical need since catecholamines increase mortality in patients with acute heart failure. Newer inotropes target sarcomeres to increase contraction. Levosimendan sensitizes troponin C to calcium (Ca), while EMD 57033 (a "classical" Ca2+ sensitizer) and the novel inotrope omecamtiv mecarbil (OM) act downstream of troponin C at the level of actin-myosin interaction. Since the mitochondrial redox state is under the control of ADP (oxidizing NADH for ATP production) and Ca (stimulating the Krebs cycle to regenerate NADH), and Ca-sensitization may increase work (=ADP) at any given Ca, we evaluated the bioenergetic properties of these inotropes.
Methods and results: Cardiac myocytes were isolated from guinea pig and mouse hearts and field-stimulated at 1-5 Hz and 37°C. EMD 57033 shortened diastolic and systolic sarcomere lengths without affecting cytosolic Ca (measured by indo-1). The redox states of NAD(P)H and FAD (autofluorescence) were oxidized by EMD. This elevated mitochondrial ROS emission (determined by DCF) during β-adrenergic stimulation with isoproterenol (Iso). Levo alone increased sarcomere shortening only modestly at 1 and 10 μM, but its potency and efficacy were substantially increased by pre-incubation with low β-adrenergic stimulation (Iso; 1 nM). Under these conditions, the increase in sarcomere shortening was explained by increases in cytosolic Ca, while the redox states of NAD(P)H and FAD remained stably reduced. At concentrations that cover therapeutic plasma concentrations in clinical trials, OM (0.1-3 μM) prolonged the time and amplitude of sarcomere shortening, but also the time of relaxation, and increased baseline diastolic tension. These effects on sarcomere function were associated with slight (though significant) oxidation of NAD(P)H/FAD, while the mitochondrial membrane potential (measured by TMRM) remained unchanged. Low (1 nM) or intermediate (30 nM) Iso concentrations prevented OM-induced oxidation. However, 30 nM Iso aggravated diastolic dysfunction and provoked arrhythmias in >50% of cases in OM-treated myocytes. In isolated cardiac mitochondria, OM (3 μM) did neither affect respiration, ROS production nor redox state. Conclusions: Pure Ca sensitization with EMD 57033 increases systolic function, but at the same time impairs diastolic function, oxidizes the mitochondrial redox state and elevates ROS emission. Levosimendan requires a PDE-inhibitory effect to increase Ca and sarcomere shortening, but this Ca elevation matches energy supply to demand and prevents mitochondrial oxidation. At concentrations that improve systolic function, OM impairs diastolic function and slightly oxidizes mitochondrial redox state, which may predispose to arrhythmias during substantial (but not low) concomitant β-adrenergic stimulation.

P2308

Potential role of the Nav1.5 sodium channel in cardiopulmonary remodeling in a context of heart failure following myocardial infarction in mice.

A Fonteneau[1]; E Amosse[1]; B Jagu[1]; A Carcouet[1]; A Hivonnais[1]; T Le Tourneau[1]; F Charpentier[1]; G Gilles Toumaniantz[1]
[1]*Research unit of l'Institut du thorax, Nantes, France*

The sodium channel Nav1.5, encoded by the Scn5a gene, is responsible for the initiation and propagation of the cardiac action potential. In heart failure following myocardial infarction, which remains the major cause of morbidity and mortality in cardiovascular field, modifications of ionic channels are described and associated with lethal arrhythmias.
Objectives: – Mutations carried by genes encoding for channels with acquired forms of arrhythmias and post-MI remodeling, are not well characterized. In this context, we have investigated the role of Nav1.5 genetic alterations in the occurrence of ventricular arrhythmias, structural remodeling and cardiac contraction abnormalities during the acute phase of MI.
Methods: The Nav1.5 contribution was evaluated after permanent occlusion of coronary artery performed on mouse model invalidated at the heterozygous state for Scn5a (Scn5a+/- mice; 12 weeks old). After validation of the infarction by echocardiography, these animals were studied in vivo by echocardiography and ECG and in vitro using molecular and biochemical investigations during the first 48 hours post-MI.
Results: Animals placed in this context, revealed that Scn5a+/- animals have a higher mortality due to arrhythmic events. In addition, the ECG recorded by telemetry during 48 hours post-MI revealed that Scn5a+/- mice present an increased incidence of premature ventricular beats (5.6 ± 2.7 & 33.1 ± 11 PVB/hour respectively for WT-MI and Scn5a+/- MI mice) without any difference in structural and functional remodelling compared to WT-MI. However, mRNA expression revealed that Scn5a+/- MI mice present an up-regulation of pro-inflammatory factors IL-6 (3.7 ± 0.9 & 17.4 ± 9.3 Relative Expression respectively) and IL-1β mRNA ($1,8 \pm 0.3$ & 4.6 ± 0.8 RE respectively) and downregulation of Cx43 mRNA (0.61 ± 0.08 & 0.39 ± 0.03 RE respectively) without interstitial fibrosis induction. During our investigations, the Scn5a dominantly expression in heart was confirmed but a significant expression was recorded in lungs, suggesting possible Nav1.5 inter-organ functional implications. Pulmonary function tests on transgenic mice have shown respiratory hypo responsiveness under metacholin (Penh/base=$5,9 \pm 0,8$mN & $3,1 \pm 0,6$mN respectively). The intrinsic pulmonary remodelling was investigated. Modest fibrosis and muscular remodelling are suggested by qPCR and histology and do not appear to be concomitant to inflammatory response.
Conclusions: These observations, 48 hours post-MI, suggest that Scn5a+/- mice present factors for the establishment of a more severe post-ischemic heart failure. In addition, preliminary results obtained on small series of animals revealed that Scn5a+/- mice seem to have a more pronounced LV remodelling at 4 weeks post-MI. Moreover, it would be possible to study in case of loos of Nav1.5 expression and/or function the pulmonary impacts in post-ischemic heart failure via inter-organ implications.

P2309

Expression of angiomotin in myocardial infraction: relationship with ki-67 expression and the vascular endothelial growth factor.

A Angelos Tsipis[1]; AM Athanassiadou[1]; E Petrou[1]; D Miliopoulos[2]; A Gkouziouta[2]; P Athanassiadou[1]
[1]*University of Athens, Department of Pathology, Athens, Greece*; [2]*Onassis Cardiac Surgery Center, Division of Cardiology, Athens, Greece*

Introduction: Angiomotin (Amot) is an angiostatin binding protein that promote endothelial cell migration and angiogenesis and has been found to be involved in tumorogenesis. Ki-67 is a nuclear antigen, strictly correlates with cell proliferation and is expressed in all phases of the cell cycle except G0. The aim of this study was to investigate the expression of angiomotin, Ki-67 and VEGF in myocytes after myocardial infarction.
Material and methods: We studied myocardial samples of hearts with histologic findings of acute myocardial infarction (group A, n=50), old myocardial infraction (group B, n=50) and myocardial samples of normal heart (control group, n=20). An immunohistochemical method was performed with the use of Angiomotin, Ki-67, VEGF and Bcl-2 antibodies
Results: Amot expression was observed in the nucleus and cytoplasm of tissue cells.
High concordance of Angiomotin and VEGF expression was detected in 82% of samples with old myocardial infarction ($p = 0.020$). Bcl-2 positive expression was intense at the risk areas in 75% of samples with acute myocardial infarction. In old myocardial infraction the bcl-2 positive samples demonstrated weak staining as in the control group. The expression level of Amot was increased in cases from positive samples with a high level of ki67 ($p < 0,001$).
Conclusions: The increased expression of angiomotin, Ki-67 and VEGF in infracted myocardium, suggest the presence of myocyte proliferation and this may be a compensatory mechanism that could be replace damaged myocardium.

P2310

NTU-B alleviates fibroblasts activation during cardiac remodeling

H-C Hui-Chun Ku[1]
[1]*National Taiwan University, Taipei, Taiwan ROC*

Fibroblast is the most common cell type of the connective tissues and the principal source of the extensive extracellular matrix. Differentiation of fibroblast into myofibroblast is a critical event in the progression of diseases that leads to tissue remodeling and dysfunction. Polyphenol has been demonstrated to exhibit free radical scavenging activity; however, the low bioavailability limits the use in clinic. So we modified the chemical structure with side chain to improve stability. In the present study, we examined the effect of the novel compound, NTU-B, on fibroblasts activation. Cardiac fibroblasts were isolated from adult mice hearts, and were incubated with angiotensin II (Ang II), a peptide hormone that cause cardiac remodeling, in the presence or absence of NTU-B. Ang II exposure induced the differentiation of cardiac fibroblasts into myofibroblasts, as indicated by the increased expression of α-smooth muscle actin (αSMA), and this effect of Ang II was inhibited by the pretreatment of NTU-B. NTU-B also decreased Ang II induced NADPH oxidase 4 (NOX4) expression and superoxide generation in cardiac fibroblasts. Furthermore, NTU-B decreased Ang II induced fibroblast proliferation, while using NADPH oxidase inhibitor also found the similar results, indicating that inhibition of superoxide production by NTU-B may contribute to the alleviation of fibroblast activation. Our results provide new insights regarding the cardioprotective effects of NTU-B and provide an efficient therapeutic strategy to attenuate cardiac fibrosis and remodeling.

P2311

RDX7675 reduces intestinal potassium absorption to a greater extent than patiromer or sodium polystyrene sulfonate in mice

J P Davidson[1]; C Dowd[1]; A J King[1]; P Kumaraswamy[1]; J S Caldwell[1]; R C Blanks[1]; J W Jacobs[1]
[1]*Ardelyx, Inc., Fremont, United States of America*

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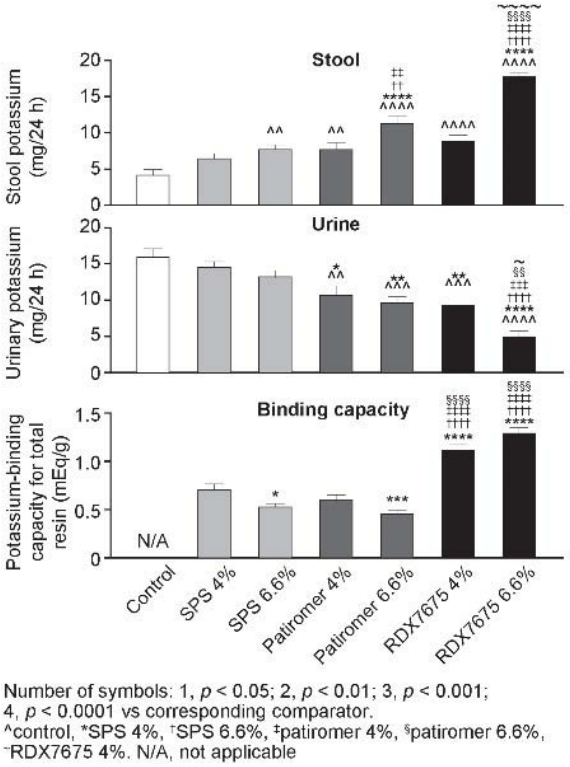
Background: Patients with heart failure or chronic kidney disease, especially those taking RAAS inhibitors, are at risk of developing hyperkalaemia, which can lead to cardiac arrhythmias and even death. Available therapies for hyperkalaemia include the potassium-binding resins sodium polystyrene sulfonate (SPS), and the calcium salt patiromer (in the US). RDX7675, the calcium salt of a novel polystyrene sulfonate-based resin, is a potassium binder being investigated as a potential treatment for hyperkalaemia.
Purpose: To evaluate the effects of RDX7675 on absorption of potassium and other electrolytes in mice and compare them with SPS and patiromer. We hypothesised that the magnitude of the effects of RDX7675 on potassium absorption would be similar to, or greater than, those of the other treatments.
Methods: Seven groups of eight male mice (CD-1, 8 weeks old) were given either standard chow (control) or chow containing 4% or 6.6% by weight RDX7675, patiromer or SPS for 72 h. To account for the different salt and chemical structures of the ion exchange resins, the weight of the negatively charged resin (active moiety) was used to calculate the dosage. Following a 48-h acclimation period, excreta were collected over 24 h for electrolyte analyses. The potassium-binding capacity was calculated as stool potassium excreted (mEq) per gram of resin administered (calculated as both active moiety, and total resin including counter ion). Statistical analyses were performed using one-way analysis of variance followed by Tukey's test (post hoc).
Results: Compared with control, 24-h stool potassium was higher in all treated groups except SPS 4%, with the highest levels seen in the RDX7675 6.6% group ($p < 0.0001$; Figure). Urinary potassium was lower in mice treated with RDX7675 or patiromer vs control; the lowest level was seen in the RDX7675 6.6% group ($p < 0.0001$; Figure). The potassium-binding capacity of RDX7675 was similar at both doses, and was greater than both patiromer and SPS ($p < 0.0001$; Figure). The SPS groups had a large increase in sodium load, where mean 24-h stool and urinary sodium levels were significantly greater than all other groups ($p < 0.0001$). The RDX7675 and patiromer groups had higher 24-h stool sodium excretion compared with control ($p < 0.05$), and significantly lower urinary sodium levels than control ($p < 0.001$). The effects on potassium and sodium were similar when normalised for wet/dry stool mass and food intake.
Conclusions: RDX7675 reduced potassium absorption to a greater extent, and had higher potassium-binding capacity, than either patiromer or SPS in mice.

Compared with control, calcium-based agents RDX7675 and patiromer reduced intestinal sodium absorption; in contrast sodium-based SPS increased sodium absorption. Studies in humans are required to confirm the potential of RDX7675 as a treatment option for patients with hyperkalaemia.



Number of symbols: 1, $p < 0.05$; 2, $p < 0.01$; 3, $p < 0.001$; 4, $p < 0.0001$ vs corresponding comparator.
^control, *SPS 4%, ᵀSPS 6.6%, ‡patiromer 4%, §patiromer 6.6%, ¯RDX7675 4%. N/A, not applicable

Potassium pharmacodynamics

P2312

The efficiency of growth hormone in pts with heart failure due to dilated cardiomyopathy

I A Igor Tsoy[1]; TA Abdullaev[1]; YR Akhmatov[1]
[1]*Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan*

The aim. To study the clinical efficacy of growth hormone in pts with idiopathic dilated cardiomyopathy (DCM) on a background of optimal therapy.
Materials and methods: 13 pts (Wed age 41,1± 6,4 y.o.) with DCM of both sexes (7/6 as m/f) who were on optimal medical therapy of CHF in the state of compensation over the past year. All pts were on optimally selected basic treatment (the maximum recommended dose reached 92% of pts). We added 12 units of Human Growth Hormone per week as subcutaneous injections. Duration of treatment / follow-up was 1 month. In addition to assessing the clinical condition at the end of a six-minute walking test (6MWT) and the scale of assessment of the clinical status by Mareev, echocardiography assessment of the data was carried out. At baseline and after 1 month of observation the concentration of growth hormone (GH) (originally, 4,2± 2,2 mIU/l) and insulin-like growth factor (IFR1) (originally, 126,4± 12,4mkg / ml) were determined
Results: Tolerability of treatment assessed as satisfactory, in one case there is a violation of elapsed independently after the course. After 1 month IFR1 reliable growth was recorded at 25.1% (up to 168,4± 7,8mkg / ml) and growth hormone - by 37.3% (up to 6,7± 2,05mIU / l, are both p < 0 , 05). At the same time, there was a subjective improvement in well-being pt, reflected in a reduction of weakness, increase of physical activity. Objectively score for Mareev scale decreased insignificantly by 12% (p> 0.05), meanwhile, there is an increase in 6MWT initially 271,3± 22,1 meters, the dynamics of 312.8± 38,2m (p <0,05). The parameters of intracardiac hemodynamics underwent the following changes: the average ejection fraction (EF) of LV rose slightly constituting 33,9± 1,7% and 33,4± 3,1%; p = 0.12, which was accompanied by inaccurate differences in linear dimensions of the heart; EDD 7,12± 0,1 and 7,05± 2,3 cm (p> 0.05). It was noted a marked change from the right heart, where the RV decreased from 3.86± 4,6sm to 3,42± 5,78 cm (p> 0.05), in parallel with the decrease in PASP misleading from 49.6± 12.6 mm Hg to 46,5± 8,6 mm Hg
Conclusions: 1 month course of injections of growth hormone in the treatment of pts with DCM well tolerated, improves both clinical and functional parameters.

BASIC SCIENCE – BIOMARKERS

P2313

ProBNP glycosylation at T71 directly inhibits plasma furin activity and modulates plasma levels of furin targets in heart failure

H Nougue[1]; JM Launay[1]; N Vodovar[1]
[1]*Inserm UMR-S 942, Paris, France*

Background: proBNP glycosylation at threonine 71 (T71) prevents the processing of proBNP into NT-proBNP and BNP by furin through steric hindering of the cleavage site. Our previous work showed that in acute heart failure (AHF), the increased production of proBNP is accompanied by a decrease in proBNP T71 glycosylation and an increase in plasma furin activity, albeit no change in concentration. These results suggested a potential direct inhibitory effect of proBNP T71 glycosylation on plasma furin activity.
Methods: Human furin and proBNP were purified from Human embryonic kidney (HEK293) overexpressing cells. In this system, 54% of proBNP molecules were glycosylated at T71. proBNP was gradually deglycosylated by limited digestion with O-glycosidase (Sigma). ProBNP with various degree of proBNP T71 glycosylation was mixed in vitro with purified furin; furin activity was measured by a fluorescence assay. Furin incubated beforehand with glycosylated proBNP was incubated with the plasma of 6 AHF patients and MR-proAdrenomedullin (ADM), proBNP levels were measured by sandwich immunoassay.
Results: There was a very strong linear negative correlation between furin activity and the degree of proBNP T71 glycosylation ($\rho = -1$, P = 0.016, Figure1A): the higher the T71 glycosylation, the lower the activity. Accordingly, the addition of furin pre-incubated with glycosylated proBNP showed a strong negative correlation between the variations in plasma levels of MR-proADM and proBNP levels, and furin activity ($\rho = -1$, P = 0.016 for both): the higher the glycosylation, the lower the furin activity, and the lower the processing of MR-proADM and proBNP.
Conclusion: Altogether, these data demonstrated that glycosylation of proBNP at T71 not only prevents the processing of proBNP by sterically hindering the cleavage site, but also acts as a direct furin inhibitor. These results strongly suggest that glycosylated proBNP-mediated furin inhibition modulates the plasma levels of furin targets. Since furin targets include biomarkers, this study warrants the development of a compensatory algorithm to estimate the fraction of biomarkers degraded by furin, hence better evaluating the production of these biomarkers. Finally, together with BNP-mediated neprilysin inhibition, these data reinforce "B-type natriuretic peptides" as a regulator of the response to AHF.

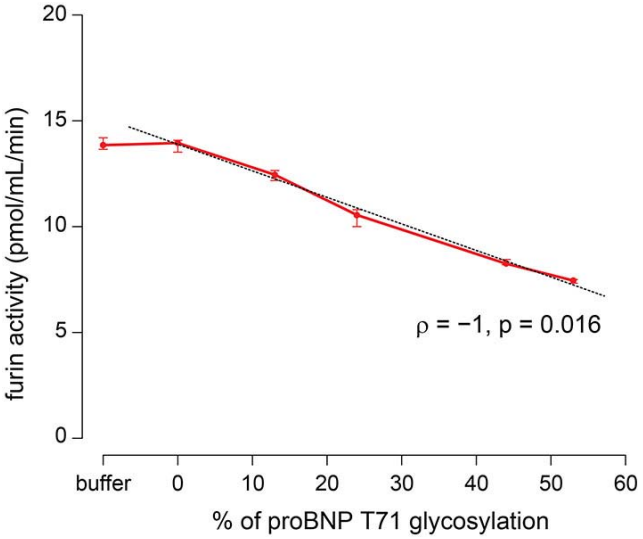


Figure 1

P2314

Transcriptomic profile of c-type natriuretic peptide in an in vitro model cell line after exposure to tuscany sangiovese grapevine juice

B Svezia[1]; M Cabiati[2]; E Bertolini[1]; V Lionetti[1]; ME Pe'[1]; S Del Ry[2]
[1]*Sant'Anna School of Advanced Studies, Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy*; [2]*Institute of Clinical Physiology of CNR, Pisa, Italy*

Background: Grape juice has vascular protective effect by stimulating endothelial eNOS expression, but the mediator is still unknown. Recent evidence showed that C-type natriuretic peptide (CNP), secreted by the endothelium, is a paracrine mediator of cardioprotection against ischemic injury through activation of endothelial nitric oxide synthetase (eNOS) after binding its specific guanylyl ciclase receptor B (NPR-B).
Purpose: The aim of this study was to evaluate whether Tuscany Sangiovese grapevine juice (SGJ) protects stressed coronary endothelial cells in a CNP-dependent manner.
Methods: Murine coronary endothelial cells (MCEC-1) were long-term (24h) treated with sterile SGJ at increasing concentrations (group A: 10% vol/vol juice; group B: 25% vol/vol juice). Untreated cells were used as control (group C). In additional experiments, MCEC-1 were exposed to hydrogen peroxide (200 μM/24h) in the absence (group D) or presence of SGJ 10% (group E) or 25% vol/vol (group F). MTT assay was performed to evaluate viable cell metabolism. CNP, NPR-B and eNOS mRNA profile was assessed by Real-Time PCR analysis, where each value was normalized with the expression of three mostly stabled genes (Rpl13a, Ppia, Tbp). We also evaluated VEGF transcriptomic profile in order to confirm the oxidative stress condition induces by hydrogen peroxide.
Results: Metabolic cell viability was significantly increased in SGJ-treated cells compared to respective controls (group C and D). CNP and eNOS mRNA levels in group B were higher than in group C: (CNP: 0.527 ± 0.093; eNOS: 2.56 ± 0.822) vs. (CNP: 0.083 ± 0.017; eNOS: 0.287 ± 0.043) with $p = 0.0065$ and $p < 0.0001$ respectively. Similarly, NPR-B gene expression resulted significantly increased by higher dose of SGJ: group B (1.157 ± 0.159) vs. group C (0.383 ± 0.172). In stressed cells, we have observed similar transcriptomic changes: group F (CNP: 0.626 ± 0.161; eNOS: 1.33 ± 0.391 a.u.) vs. group D (CNP: 0.226 ± 0.083; eNOS: 0.56 ± 0.131) with $p = 0.047$ and $p = 0.017$ respectively. NPR-B gene expression in MCEC-1 was stimulated by H2O2 per se (+170%, $p = 0.013$), but treatment with SGJ 10% or 25% vol/vol further increased its expression compared to untreated cells by 168% ($p = 0.008$) and 188% ($p = 0.011$). Significant correlations were observed between CNP and NPR-B in normal and stress conditions ($r=0.948$, $p = 0.014$ and $r=0.791$, $p = 0.011$ respectively).
Moreover, VEGF mRNA expression increased in stressed cells (group C vs. group D, $p = 0.029$). Conclusion: We have demonstrated, for the first time, that grapevine juice from of Tuscany Sangiovese berries enhances CNP and eNOS mRNA levels in coronary endothelial cells at rest and under oxidative stress. Accordingly, the treatment with SGJ stimulates the gene expression of NPR-B and preserves the decay of cell viability following exposure to H2O2. Our data open a new avenue in the development of nutraceutical approach of cardioprotection.

P2315

Amyloid light chain increases brain natriuretic peptide (BNP) expression and induces oxidative stress response in cardiomyocytes

S J Stephen Tam[1]; L Li[1]; M Renz[1]; PJ Dolan[1]; T Nijjar[1]; E Goldbach[1]; GG Kinney[1]; W Zago[1]
[1]*Prothena Biosciences Inc, South San Francisco, United States of America*

Background: AL amyloidosis, the most common form of systemic amyloidosis, is characterised by the accumulation of aggregated, misfolded immunoglobulin light chain (LC) protein (amyloid) in one or more organs. Amyloid deposition in the heart (observed in ~70% of patients) and other organs leads to organ dysfunction and may result in death, associated mainly with cardiac involvement. No therapies are approved for AL amyloidosis, and current approaches do not directly target the misfolded LC protein, which is the underlying cause of organ dysfunction. NT-proBNP measures are used clinically to assess patient prognosis and potential response to treatment and have been recommended by the Amyloidosis Research Consortium for use as a surrogate endpoint predictive of survival in clinical trials. In AL amyloidosis the elevation in NT-proBNP levels is believed to occur in response to a direct cytotoxic effect of light chain species to cardiomyocytes via the p38 MAPK signalling pathway. This response contrasts with congestive heart failure, where NT-proBNP is regulated by mechanical strain and neurohormones.
Purpose: Investigate the potential direct effects of amyloid LC on cardiomyocyte homeostasis by assessing transcriptional regulation of BNP precursor gene and elevation of an oxidative stress response marker.
Methods: Primary rat cardiomyocytes were incubated with a mixture of soluble and insoluble LC aggregates derived from a number of LC sequences described in patients with AL amyloidosis. Both BNP and the oxidative stress marker HO1 transcription were assessed by quantitative real-time PCR.
Results: LC treatment of rat primary cardiomyocytes was associated with significantly increased transcription of prepro-BNP. The effect was dependent on LC sequence, dose and incubation time. LC aggregates also induced a rapid and significant elevation of HO-1, indicative of cellular insult driven by oxidative stress.
Conclusions: We showed that a heterogeneous mixture of aggregated and non-aggregated LC, which recapitulates the presumed extracellular milieu in patients with AL amyloidosis, promoted BNP and HO-1 transcriptional activation. These results support previous findings that NT-proBNP levels are modulated directly by LC-induced cardiotoxicity and may explain the robust correlation between NT-proBNP levels and survival in patients with AL amyloidosis.

P2316

Natriuretic peptide receptor c - could it be the next therapeutic target in heart failure?

K Katarzyna Kodziszewska[1]; P Leszek[1]; B Sochanowicz[2]
[1]*Institute of Cardiology, Warsaw, Poland*; [2]*Institute of Nuclear Chemistry and Technology, Centre for Radiobiology and Biological Dosimetry, Warsaw, Poland*

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Background: Even though natriuretic peptide receptor C (NPR-C) is responsible for removal of natriuretic peptides (NPs) from the circulation to the same extent as neutral endopeptidase, it is not solely a clearance receptor. The effects of NPR-C include regulation of vascular tone and blood flow. It appears that some of the antiproliferative actions of ANP and electrophysiological effects (i.e. regulation of calcium currents) of CNP are regulated by the NPR-C via modulation of c-AMP-dependent pathways. Aim: We sought to determine whether modulatory effects of NPR-C on adenylyl cyclase (AC) could be observed in cardiac tissue and whether NPR-C function changes in the heart as well as other tissues under pathological conditions of heart failure.
Methods: NPR-C activity was measured by assessing cAMP levels before and after stimulation of the receptor with an NPR-C-specific ligand: cANF4-23. Receptor activity was evaluated in 11 failing hearts (left ventricle) from patients undergoing heart transplantation (HTx) and 11 hearts (left ventricle) of healthy donors not allocated to HTx. For comparison, NPR-C activity was assessed in aortic tissues obtained from 17 heart failure patients and 8 control aortas obtained from heart donors. Results: In heart tissues, no change in cAMP levels was observed in failing or non-failing hearts following NPR-C stimulation compared to baseline (respectively: $p = 0.1153$ and $p = 0.7283$). In aortic tissues, there was no change in cAMP levels from baseline following NPR-C stimulation in specimen obtained from heart failure patients ($p = 0.1519$), while in the aortic tissues of healthy subjects the change was significant ($p = 0.0383$). Conclusions: Our studies suggest that in the heart NPR-C plays predominantly a role of a clearance receptor, while its anti-proliferative actions may be significantly diminished as implicated by lack of response to stimulation. Contrarily, in the vasculature the modulatory action of NPR-C on cAMP levels is retained, but only under physiological conditions. In heart failure the effect is abolished - possibly due to overstimulation by high levels of circulating NPs or receptor regulation by other humoral factors. Therefore, blocking of NPR-C in heart failure is likely to significantly increase NP levels without causing adverse effects on cardiac remodeling or regulation of vascular tone. The in vivo effects of NPR-C blockage are yet to be examined, but the receptor itself seems to be a graceful therapeutic target in treatment of heart failure.

P2317

Cardiac expression of Gal-3, GDF-15 and TIMP1, but not their plasma levels, are related to cardiac function; a heart failure biomarker lesson from mice

H H W Herman Sillje[1]; W Du[1]; RA De Boer[1]
[1]*University medical center Groningen, Groningen, Netherlands*

Background: With the promise of added diagnostic, prognostic and guided therapy potential, heart failure (HF) biomarkers have reached center stage in clinical research. Comprehensive animal studies that allow more in depth investigations, are, however, scarce. We investigated atrial natriuretic peptide (ANP), Galectin-3 (Gal-3), Growth Differentiation Factor-15 (GDF-15) and Tissue Inhibitor of Matrix Metalloproteinases-1 (TIMP-1) at multiple levels and within different tissues in mice post myocardial infarction (MI) and after transverse aortic constriction (TAC).
Methods: For MIs, the left ascending coronary artery was either ligated temporally (small infarcts) or permanent (large infarcts). Mice were analyzed at multiple time points up to 8 weeks. For cardiac pressure overload a constriction was generated at the aortic arch and these TAC mice were investigated at 4 and 8 weeks. Sham operated animals were used as controls. Magnetic resonance imaging, hemodynamic pressure measurements and histochemistry was performed to investigate cardiac function and structure. ANP, Gal-3, GDF-15 and TIMP-1 gene expression and protein levels were determined in multiple tissues, including blood plasma.

Results: ANP, Gal-3, GDF-15 and TIMP-1 cardiac gene expression and protein levels were all increased after TAC and MI and showed significant inverse relations with ejection fraction (EF). Moreover, cardiac protein levels of Gal-3, GDF-15 and TIMP1 correlated with cardiac fibrosis. In plasma, NT-proANP levels correlated with ejection fraction, but plasma levels of Gal-3, GDF-15 and TIMP-1 were not elevated 8 weeks post-MI, despite low EF. Increased plasma Gal-3 and TIMP-1 levels were only observed shortly (within one week) after MI, concomitant with a strong transient increase in cardiac expression. This suggests that cardiac contribution to plasma levels is limited and that other organs, in which these biomarkers were highly expressed, co-determine plasma levels. Importantly, after TAC, plasma levels of TIMP-1 and GDF-15 increased, and this paralleled increased expression of these genes and proteins in the lung.
Conclusions: Only plasma NT-proANP levels were strongly correlated with LV function in mice. Increased Gal-3, GDF-15 and TIMP1 cardiac expression is related to myocardial fibrosis, but cardiac expression does not substantially influence plasma levels. Their increased plasma levels in heart failure most likely reflect stress in other tissues, or only becomes apparent in severely diseased hearts