European Journal of Heart Failure Supplements (2012) **11**, S185–S236
doi:10.1093/eurjhf/hss015

POSTER SESSION 4

Monday 21 May 2012, 14:00–18:00

Location: Poster Area

ACUTE HEART FAILURE

60154
Acute heart failure as first manifestation of adrenal tumor

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Aim: To describe the interesting case of a patient who presented to the emergency department due to acute dyspnea.
Material: A 48 year old man, presented to the ER of our hospital complaining of severe nocturnal dyspnea in the past 4 days. The patient was a tourist from Czech Republic. His medical history was free and he was not on medication of any kind.
On physical examination the patient appeared severely ill ,with clinical findings consistent with acute pulmonary edema onset. The heart auscultation revealed a gallop rhythm . Blood pressure 270/160 mm Hg. ECG: LVH, left atrium enlargement.
The patient was admitted to the cardiological department where he was treated for pulmonary edema .Additional to the standard treatment with furosemide ,nitrates etc the patient was treated with levosimendan iv.
The initial heart ultrasound revealed an EF 30%, left ventricular dilatation and hypertrophy ,mitral valve insufficiency 2/4. In the following days the EF improved to 45%.
At his admission the patient had normal renal function values ,but the next days, despite the controlled falling of the blood pressure , acute renal failure occurred (creatinine levels up to 6,5),probably due to renal hypoperfusion. Renal function improved when blood pressure was stabilized to levels no lower than 160 mmHg.
Computed tomography of the abdomen revealed the presence of a tumor of the left adrenal gland, probably pheochromocytoma.
Conclusion: The interesting in this patient's case lies in the fact that despite the presence of malignant hypertension involving at least two target organs (heart-kidneys),the patient had no symptoms before the acute heart failure onset.

60589
Quality of life in patients with heart failure

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Summary: Heart failure is a common disease that requires frequent and long hospitalizations, the active participation of health workers and family members in the care of such patients, and it leads to reduction of physical activity and lifestyle changes with the patient, which significantly affects the quality of life of patients with heart failure. Objective of this study was to determine quality of life of patients with heart failure using SF-36 questionnaire, as well as to determine the value of Framingham criteria application as predictors of SF-36 score value.
Respondents and methodology: Using a prospective study, analysis of life quality was performed for 120 patients suffering from heart failure, divided into 4 groups according to NYHA classification of heart failure. The control group consisted of 30 subjects who do not suffer from heart failure. Framingham criteria were used to confirm heart failure diagnosis. Assessment of quality of life was performed using the SF-36 questionnaire.
Results: Study group consisted of 150 participants where 76 (51%) of male, and 74 (49%) females, divided into 4 groups according to NYHA, where every group had 30 subjects (20%), and one control group of 30 subjects (20%). There were no statistically significant differences in gender representation (X2=1.70; df=4; p=0.79) between analyzed groups. Also, there was no statistically significant difference in age between the groups (ANOVA; F=0.74; p=0.57). The values of SF-36 score expressed as the median in the control and 4 NYHA groups were: 98,6; 90,76; 70,14; 36,45; 25,41(Ht= 116,84; p<0,0001). Statistically significant negative correlation was determined in number of large and small Framingham criteria, and SF-36 score (r=-0.790, r=-0.660; p<0,0001). Multivariate analysis was used to confirm significant predictive potential in number of large (B=-15,23; %95CI=-19,55 do -10,90; p=0,01) and small criteria (B=-4,67; %95CI=-8,18 do -1,16; p<0,001) on value of SF-36 score.
Conclusion: Quality of life in patients with heart failure is deteriorated and related with severity of the clinical features. Framingham criteria can be used as life quality predictors in such patients.

60719
Outcome of patients presenting with STEMI and cardiogenic shock- contemporary single center's experience

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Objectives: Acute ST-elevation myocardial infarction (STEMI) presenting with cardiogenic shock is associated with dismal prognosis. In the recent decade significant advances have been made in reperfusion techniques and pharmacological treatment. We, therefore, aimed to assess the outcome of these patients during the past decade and identify major factors that impact their prognosis.
Methods: We identified 161 patients who presented with STEMI, cardiogenic shock and underwent primary percutaneous coronary intervention (PCI) between 2001 and 2010. Patients were allocated into 2 groups based on period of presentation: 2001-2005 (n=70), 2005-2010 (n=61). Clinical outcomes up to 6 months were evaluated.
Results: Patients in the latter period were younger, had lower rates of renal failure and higher rates of stent use. Despite these differences, mortality did not differ and remained high in both periods (52-59% at 6 months). Time frames, from onset of symptoms to arrival to the emergency department and to performance of coronary intervention were similar in both periods. Intra-aortic balloon pump use was similar in both periods. In multivariate analysis, factors associated with one month mortality were: diabetes (OR=3.2, 1.3-7.8, P=0.01), LVEF<40% (OR=1.8, 1.2-2.8, P=0.009), GFR<60 ml/min/m^2 (OR=1.8, 1.2-2.4, P<0.0001) and glycoprotein IIb/IIIa inhibitors use (OR=0.4, 0.1-1.05, P=0.07). The combination of diabetes and renal failure was associated with particularly high mortality (Table 1).
Conclusions: Prognosis of patients presenting with STEMI, cardiogenic shock and treated with primary PCI during the past decade, remains poor. Better risk-stratification may help improve their grave outcome.

30 day mortality rate

Renal Failure		
-	+	Diabetes Mellitus
50%	84%	+
21%	69%	-

60223

Congestive heart failure secondary to intraventricular asynchrony: a curious mechanism

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We report the case of a 58-year-old man, former smoker, with history of hypertension, inferior myocardial infarction in 1995 and stent implantation in the right coronary artery, left bundle branch block, with multiple unexplained admissions for congestive heart failure. Medications included acetylsalicylic acid, enalapril, carvedilol, and simvastatin. He refers progressive dyspnea and orthopnea. Physical examination highlights mitral systolic murmur II/VI and bilateral crepitation. Blood analysis including hemogram, coagulation, hepatic and renal function panel and cardiac enzyme were completely normal. An electrocardiogram showed sinus rythm at 95 beats per minute, inferior necrosis and intermittent frequency-dependent left bundle-branch. A transthoracic echocardiogram was also obtained, which showed mildly dilated left ventricle, inferior akinesia and intraventricular asynchrony. The estimated left ventricular ejection fraction (LVEF) was 42% and there was severe mitral regurgitation secondary to tenting of both leaflets without organic involvement. As we suspected acute heart failure in a patient with moderate left systolic dysfunction and severe mitral regurgitation due to intraventricular asynchrony caused by frequency-dependent left bundle-branch block, beta-blocker therapy was initiated resulting in a slower heart rate and disappearance of left bundle branch block. The subsequent echocardiogram revealed a non-dilated left ventricle, inferior akinesia, absence of intraventricular asynchrony, LVEF of 50 % and only mild mitral regurgitation.
In conclusion, slowing heart rate with beta-blockers results in disappearance of left bundle branch block which leads to resolve intraventricular asynchrony and severe mitral regurgitation with patient improvement.

60211

Trends in publications on stress-induced cardiomyopathy

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Purpose: Stress-induced cardiomyopathy (SIC), also known as Takotsubo cardiomyopathy, was originally described in Japan and thought to mainly affect Asian women but the syndrome is now being increasingly reported from countries all over the developed parts of the world. The prevalence is unknown but SIC has been reported to be present in approximately 2% of patients presenting for emergency PCI. However, there have as yet been no large cohort studies attempting to address the prognosis, etiology or epidemiology of SIC.
Methods: A PubMed literature search of the terms takotsubo, tako-tsubo, "stress-induced cardiomyopathy", "stress cardiomyopathy" and "apical ballooning"was conducted between 20110804 and 20110816.
Results: After reviewing 1042 peer-reviewed articles, we found reports of 7621 SIC patients. 748 of these publications were case reports. The reviewed material includes data published from 42 different countries. An increasing amount of SIC-patients are reported each year ($p<0.05$). The most SIC cases have been reported from the United States. Germany and Italy also report more cases of SIC than does Japan. Sweden reports the most SIC cases per capita and is followed by three other European countries (Figure 1). 5855 female and 703 male patients were described.
Conclusion: SIC is reported from all parts of the developed world. Sweden has reported the greatest number SIC patients per capita. The results of this review indicate that SIC may be at least as common in the European and US populations as it is in the Asian.

60267

Clinical and epidemiological characteristics of patients with acute heart failure: gender - dependent survey

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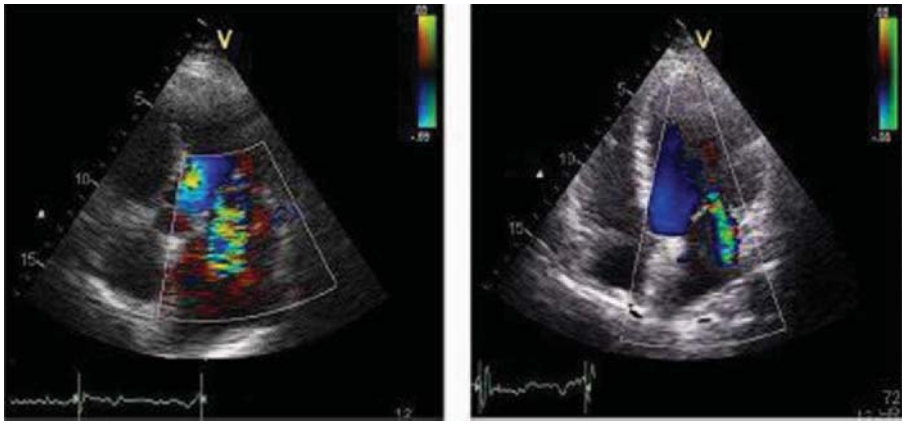
Aim: Heart failure (HF) is one of the leading causes of death worldwide. The aim of present study was to investigate clinical and epidemiological characteristics of the Emergency Department (ED) patients (pts) presenting with acute HF (AHF).
Methods: In the hospital there were 22,713 ED pts in year 2010, 1,526 (6.7%) with diagnosis of AHF. Prospective, observational study included 726 AHF patients treated during six months period. Symptoms, comorbidities, physical findings, clinical presentation of AHF, APACHE II and SAPS II were recorded.
Results: Out of 726 pts there were 317 (43.6%) males and 409 (56.3 %) females, who presented with dyspnea (85.5%), fatigue (61.1%), orthopnea (53.1%), and chest pain (24.9%), without significant difference in hospital outcome. There were statistically significant differences in comorbidities and clinical presentation between males and females. Females had higher blood pressure (32.8:20.7; $p<0.001$) and atrial fibrillation



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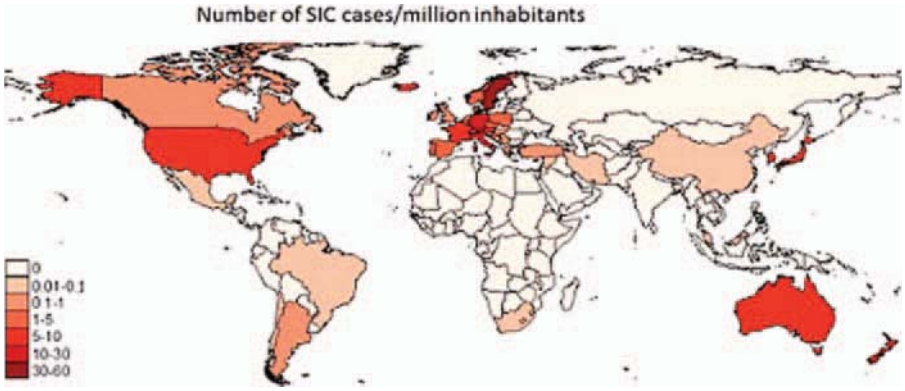

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(AF) incidence (53:44.4%; p=0.028) on admission, were treated with digoxin more frequently (38.3:28.2%; p=0.011); presented with hypertensive AHF (26.7:19.7%; p=0.046), with higher SAPS II score (28.5:26.6 points; p<0.001). Frequency of dilatative cardiomyopathy (15.5:5.9%; p<0.001), lower ejection fraction (39.1:45.4%; p=0.003), dilatation of all four heart chambers (18.3:6.3%; p=0.022), and clinical presentation of AHF following acute coronary syndrome (ACS) (5.7:2.2%; p=0.046) were higher in males. Males also presented more frequently with right-sided pleural effusion (PE) (16.8:14.7; p=0.002), bilateral PE (19.0:14.0%; p=0.019), and hepatomegaly (36.9:16.0%; p=0.002). There were more cigarette smokers (27.1:11.5%; p<0.001) and COPD pts (32.0:21.2%; p<0.001) among males.

Conclusion: Early identification and treatment of gender dependent comorbidities and clinical presentation of AHF could improve life quality of AHF pts and help to treat them more efficiently. Early identification and tenacious treatment of hypertension and AF in females, and ACS and COPD in males might improve outcome of AHF pts.

60023

Characterization of acute heart failure hospitalizations in a portuguese cardiology department

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Purpose: We describe the clinical characteristics, hospital management and outcomes of patients (pts) hospitalized with Acute Heart Failure (AHF) in a Portuguese CardiologyDepartment. We sought to identify factors associated with increased length ofstay (LOS), long-term re-hospitalization due to HF or death.

Methods: In this retrospective cohort study we reviewed the medical records of all pts admitted to our Cardiology Department during 2010. We selected those with either a primary diagnosis of AHF or with AHF secondary to another acute cardiac event. The occurrence of death and readmission due to HF were followed through 2011 (mean follow-up time of 18 months).

Results: From the total of 924 pts admitted during one year, 201 (22%) presented AHF. Mean age of AHF pts was 69 $\pm$ 13 and 61% were male. The main precipitating factor was ACS (63%), followed by arrhythmia (14%). De novo AHF was more common (53%), than decompensation of Chronic HF (47%). Fifteen percent had an AHF hospitalization in the previous year. The most common clinical presentations were HF in the context of ACS (63%) followed by decompensate CHF (47%) and acute pulmonary edema (21%). Hypertension (66%) and dyslipidemia (51%) were the most frequent comorbidities. On admission 73% of pts had Left Ventricular Ejection Fraction (LVEF)<0.50. Target doses of renin-angiotensin-aldosterone system blockers and of β-blockers were achieved only in a minority of pts. Median LOS was 11 [P25 — P75: 7 — 16] days and in-hospital mortality rate was 5.5%.Re-hospitalization rate due HF was 21% at six months and 24% at 12 months. Most re-hospitalizations (52%) occurred during the first six weeks after discharge. All-cause mortality was 16% at 12 months. The independent variables associated with an increased LOS were HF hospitalization during the previous year (p=0.040), BNP > 500 pg/ml (p<0.001) and Intensive Care Unit admission (p=0.002). In a predictive multivariate Cox regression model for the composite outcome of re-hospitalization or death, the most important variables were HF hospitalization during the previous year (HR 3.177 [95% CI 1.405 —7.185]), serum sodium < 135 mEq/L on admission (HR 1.995 [95% CI 1.032 —3.856]), atrial fibrillation (HR 1.791 [95% CI 1.021 — 3.142]) and depressed LVEF (HR 0.518 [95% CI 0.268 — 0.998]).

Conclusions: Pts admitted to our Cardiology Department typically presented new-onset AHF, due to an ACS, causing depressed LVEF. Several predictive factors of death or re-hospitalization emerged from our analysis that can help identifying high-risk pts to be followed in a HF management program after discharge.

61137

Balloon aortic valvuloplasty in severe aortic stenosis and its impact on pulmonary hypertension, mitral regurgitation and left ventricular systolic function

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Purpose of the study: Balloon aortic valvuloplasty (BAV) is a palliative treatment for patients with severe aortic stenosis (AS) and high risk for surgical valve replacement. We assessed the impact of BAV on pulmonary hypertension, mitral regurgitation and systolic left ventricular function in patients who were not suitable candidates for surgery.

Patients and methods: We retrospectively analyzed 51 patients (male 10, female 41; mean age 82 years; mean logistic EuroSCORE 22,7) with severe AS who underwent BAV in our institution between May 2009 and January 2011. Inclusion criteria for BAV were severe, symptomatic AS and any of the following: increased perioperative risk, bridge to surgical aortic valve replacement or transarterial aortic valve implantation (TAVI), before urgent major non-cardiac surgery, patients who refused surgery. Description of the procedure: BAV was preformed via transfemoral approach. Balloon inflation (balloon Optimed, 16 to 22 mm x 40 mm) was repeated from 2 to 4 times with a goal to reduce peak to peak transaortic pressure gradient by at least 50%. Echocardiographic examination was performed before and after BAV and during the follow-up at three months.

Results: After a successful BAV we observed a significant increase in AVA (from 0,61 to 0,72 cm2, p<0,001) accompanied by a fall in peak and mean transvalvular gradients (mean transvalvular gradient: from 47 to 38 mmHg, p<0,001) with no significant influence on LVEF (from 55% to 56%, p=0,75). Patients were divided into two groups based on pulmonary artery systolic pressure (PASP): group I (N=23; 51,1%) with PASP >50 mm Hg and group II (N=22; 48,9%) with PASP < 50 mm Hg. There were no differences in LEVF between the groups. In group I we observed a significant decrease in PASP (from 67 mmHg to 60 mmHg, p=0,039) and a significant reduction in mitral regurgitation (from 2,8/4 to 2,1/4; p=0,029), in group II the reduction of PASP and MR was not statistically significant (from 41 to 40 mmHg, p=0,840 and 1,9/4 to 1,7/4, p=0,66 respectively). The reduction in PASP persisted at 3 months follow up.

Conclusion: The reduction in PASP may be associated with unloading of the left ventricle and the reduction of mitral regurgitation that can occur after BAV. Thus BAV might be used both as palliative procedure as well as a diagnostic procedure in evaluation of degree spontaneous down-grading of mitral regurgitation in patients considered for dabble valve surgery. However, BAV has no impact on left ventricular systolic function.

60042

Uric acid, allopurinol therapy and mortality in patients with acute heart failure

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Background: Uric acid (UA) is the final product of the purine metabolism and its levels are often elevated in the patients with chronic heart failure (CHF). The prognostic role of serum UA in the patients with acute heart failure syndromes (AHF) is less evident.

Study objective: To explore the prognostic role of serum UA measurment in the hospital and long-term mortality assessment in the AHF subjects from the Acute- HEart FAilure Database registry (AHEAD). The AHEAD registry comprised 4153 patients hospitalized at the AHEAD participating centres with AHF sydromes.

Patients and Methods: The study included 1255 patients who were admitted to the AHEAD participating centres with acute decompensated CHF, de novo HF or cardiogenic shock between September 2006 and October 2009, and who had information of serum uric acid concentration on hospital admission available. The hospital and long term mortality was followed using the centralised database of the Ministry of Health, Czech Republic.

Mean age of the cohort was 73.4 years, female population represented 43%, median hospital stay was 8 days, the mean hospital mortality was 7,6%.

Results: Median UA concentration of the AHF patients was 432 μmol/l (7.26 mg/dl), median eGFR was 49.0 ml/min, NT-proBNP level was 5 510 pg/ml. Among other laboratory variables UA concentration > 515 μmol/l (8.67 mg/dl) was associated with increased hospital mortality (p < 0.001), as well as eGFR < 30 ml/min (p < 0.001), Na $\leq$ 135 mmol/l and positive troponin. UA concentration > 500 μmol/l (8.41 mg/dl) were associated with increased long term mortality (p < 0.001), followed by eGFR < 30 ml/min (p < 0.001), Na $\leq$ 135 mmol/l and haemoglobin < 130 g/l (p < 0.001). One year survival of the patients discharged from the hospital (n = 1159) was 75.6% and two years survival was 66.8 %. Survival of the patients treated with allopurinol for hyperuricaemia was significantly lower compared to untreated subjects (70.1 vs 77.2 for one year survival and 60.3 vs 68.5 for two year survival).

Conclusion: Increased UA levels as well documented allopurinol therapy for hyperuricaemia were in the AHF patients associated with increased hospital and long-term mortality. Allopurinol therapy is not a cause but the identifier of the subjects at risk.

61009

Aortic stenosis in shock: how far can we go?

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Introduction: Acute heart failure (AHF) in patients with severe aortic stenosis (AS) and left ventricular (LV) systolic dysfunction is well known for its dire prognosis. Balloon aortic valvulotomy (BAV) has been suggested as a bridge to surgery in haemodynamically unstable patients in spite of suboptimal results and very high procedural risks.

Case report description: A 67 years-old man was admitted with non-ST elevation myocardial infarction, Killip-Kimball I. Previous medical history consisted of high blood pressure, diabetes mellitus and obstructive sleep apnea. Cardiac catheterization showed: two-vessel disease (left anterior descending and right coronary arteries) and severe AS (aortic valve gradient of 97mmHg) with good LV systolic function. Aortic valve replacement (AVR) plus bypass grafting was planned. During hospitalization, the patient suffered an acute myocardial infarction evolving to cardiogenic shock, which required mechanical ventilation, norepinephrine and dobutamine infusions. Faced with a potentially fatal outcome, we proceeded to percutaneous coronary revascularization and BAV on the same setting. The patient had progressive clinical improvement allowing for withdrawal of aminergic support in 3 days, spontaneous ventilation in 4 days and hospital discharge 15 days later on dual anti-platelet therapy (DAPT). Transthoracic echocardiography (TTE) showed LV with severe systolic dysfunction (ejection fraction 30%) and mean aortic gradient of 36mmHg. AVR surgery was planned for within 30 days after completing DAPT. However, before the planned AVR surgery, the

patient was readmitted for acute pulmonary edema followed by cardiac arrest. He was successfully resuscitated and transferred to the cardiac care unit on mechanical ventilation and noradrenaline infusion. Although it was easy to withdraw vasopressor support, regardless of similar TTE parameters every attempt to wean him off the ventilator was unsuccessful due to heart failure. As a last resource, levosimendan infusion was started. After 24 hours we were able to suspend mechanical ventilation. Control TTE showed LV systolic function improvement (ejection fraction 43%) and mean aortic gradient increase to 47mmHg. The patient underwent successful AVR and is currently in class NYHA II.

Conclusions: This clinical case is a good example of how a patient with severe AS and coronary artery disease can suddenly evolve to cardiogenic shock and how the therapeutic strategy has to adjust. Percutaneous BAV and levosimendan were safe and effective in the treatment of acute heart failure acting as a bridge to surgery.

61080

Stratification of intensive care patients after open heart surgery

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The EuroSCORE model is a risk-stratification system with good predictive value for early mortality, postoperative complications, prolonged length of stay, and long-term mortality. But there is necessary a valuable tool for classification patients in Cardiac Surgery intensive care unit according severity of their acute heart failure (AHF) status.
Objective: To assess factors related to severity of AHF status of patients in Cardiac Surgery intensive care unit.
Methods: One hundred twenty two patients (43 women and 79 men), middle age 60,5(53;66) years undergoing coronary artery bypass graft and heart valve surgery at the Belarusian Centre "Cardiology" were divided on 4 groups according severity of AHF in the postoperative period. First group consisted of 43 patients without complications. Second group included 27 patients with less than 12-hour dobutamine infusion due to AHF. Third group patients (n=32) were received inotropic support more than 12-hour after operation. Fourth group consisted of 20 patients with long term mechanical and inotropic support in postoperative period. The relationship between postoperative AHF severity and SvO2, systolic arterial pressure (SAP) after correction of shivering and hypovolemia, echocardiographic left ventricular (LV) or right ventricular (RV) ejection fraction (EF), metabolic disorders (lactate, urea, creatinine, bilirubine levels and acid-base balance), electrocardiographic signs/biochemical markers of myocardial damage (MD), pulmonary edema (PE) were studied by multivariate linear logistic regression with ordinal multinominal response.
Results: Most accurate stratification of patients according their postoperative AHF severity was achieved by independent variables of electrocardiographic signs/biochemical markers of MD (b=2.49, $p<0.001$), left ventricular ejection fraction less than 35% (b=1.53, $p<0.001$), lactate more than 2.2 mM/l (b=1.25, $p<0.01$) and PE (b=0.75, $p<0.01$). So obligatory attribute of 4 gr. pts were electrocardiographic signs/biochemical markers of MD. Presence of three other independent variables were also associated with severe AHF. Presence of two any factors of three (except electrocardiographic signs/biochemical markers of MD) were associated with moderate AHF. Presence of one of three factors was associated with mild AHF.
Conclusion: Severity of patients in cardiac surgery intensive care unit is determined by electrocardiac signs/biochemical markers of myocardial damage, pulmonary edema, left ventricular ejection fraction (less than 35%) and lactate level (more than 2.2 mM/l) with reasonable accuracy.

60549

Short and long-term outcome of impedance-guided preemptive therapy provided to prevent pulmonary congestion-edema in the course of acute myocardial infarction

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Background: Patients sustaining an acute myocardial infarction (AMI) frequently develop pulmonary congestion-edema (PEd) during their hospitalization. Currently, treatment is initiated after the appearance signs of lung fluid overload. Ongoing monitoring of the status of lung fluid content (LFC) in AMI patients may enable the prediction of impending PEd and preemptive therapy, thus precluding PEd and improving outcomes.
Aims: We sought to find out whether non-invasive lung impedance (LI) guided preemptive diuretic treatment of AMI patients developing PEd improves clinical outcomes.
Methods: LI was determined by using a new noninvasive method to measure the electrical resistance of the lungs. Any increase in LFC results in LI decrease. Previously we have found that a decrease of 12-14% from normal LI value reflects the beginning transition from interstitial to alveolar edema. In the present study we prospectively randomized 222 patients (2:1 ratio) admitted for their first AMI without known chronic heart failure (CHF) and signs of PEd at admission and who expressed a >12% LI decrease to conventional therapy or LI-guided preemptive diuretic treatment.
Results: 148 patients were treated conventionally (Gr1) and 74 preemptively according LI (Gr2). Groups were well matched with regard to clinical, instrumental and laboratory parameters.
In Gr1 all patients developed different stages of PEd. Treatment was begun only at symptom onset. In Gr2 LI-guided preemptive treatment was started immediately after randomization at asymptomatic stage of evolving PEd and halted its development in 89% of patients. Unadjusted analysis shown that hospital stay, 1-year re-hospitalization rate after discharge, 6-years development new CHF and survival rate was better in Gr2 patients ($p<0.001$).
Adjustment for such parameters as age, LVEF, maximal CK, diabetes, hypertension, hyperlipidemia, smoking, level of creatinine and hemoglobin at admission shown that LI-guided preemptive treatment improved clinical outcome. Length of hospital stay reduced (OR=5.35, CI: 3.2-8.1, $p<0.0001$), 1-year re-hospitalization rate reduced (OR=3.7, CI:2.2-6.1, $p<0.001$), 6-years occurrence of new CHF reduced (OR=3.5, CI:1.3-7.5, p=0.002) and 6-years survival rate was better (OR=3.2, CI:1.2-9.1, p=0.027). Off different clinical and laboratory parameters the major influence on clinical outcome had age, diabetes mellitus, LVEF <30% and maximal CK (>2220 mg/dl), ($p<0.001$).
Conclusions: LI-guided preemptive therapy halts progression to PEd in 89% of patients, and significantly reduces hospital stay, recurrent admissions, evolution of CHF and mortality.

60587

Left ventricular dysfunction in acute myocardial infarction: are there "good" inotropes?

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Purpose: The clinical heterogeneity of acute heart failure and the low number of controlled trials are the main causes of uncertainty on the most appropriate management. Levosimendan (Lv) improves myocardial contractility without increasing oxygen requirements and induces peripheral and coronary vasodilatation. The purpose of this study was to compare patients (P) with acute myocardial infarction (AMI) and left ventricular dysfunction according to the use or not of Lv.
Methods: Retrospective study of 168 P (60.7% male; age 73.2 ± 11.8 years), admitted for AMI, along 24 months, with Killip-Kimball (KK) ≥ 3 and/or left ventricular ejection fraction (LVEF) $< 35\%$. P were separated in 2 groups according to the use of Lv. A follow-up (FU) (10.7 ± 7.4 months) regarding LVEF and MACCE was done.
Results: Lv was used in 17.9% (n=30) of P. Lv P were younger (67.3 ± 10.7 vs 74.5 ± 11.7; $p<0.001$); more often presented with ST elevation AMI (83.3% vs 42.8%; $p<0.001$) and cardiogenic shock (40.0% vs 21.7%; p=0.032); they had higher maximum troponin I (316.4 ± 357.1 vs 56.9 ± 104.9; $p<0.001$) and more frequently had LVEF < 30% at admission (66.7% vs 30.9%; p=0.001). Lv P had lower incidence of previous coronary artery disease (CAD) (13.3% vs 30.4%; p=0.057) and chronic heart failure (6.7% vs 34.8%; p=0.002). Regarding therapeutic strategy, Lv P more often were treated with Gp IIb/IIIa inhibitors (53.3% vs 16.7%; $p<0.001$), vasopressors (50% vs 23.9%; p=0.004) and intra-aortic balloon pump (20.0% vs 2.9%; $p<0.001$). There were no differences in the performance of coronary angiography; however Lv P more often were revascularized (83.3% vs 66.1%; p=0.068). No differences were found regarding the severity of CAD, the incidence of cardio-renal syndrome or in-hospital mortality (30.0% vs 22.5%; p=0.380). At discharge, therapeutic strategy was similar in both groups, except for a greater prescription of spironolactone in Lv P (42.9% vs 21.1%; p=0.034). During FU there was a similar increase in LVEF (6.2 ± 14.8 vs $3.4 \pm 8.2\%$; p=0.690) and in MACCE incidence (40.9% vs 43.4%; p=0.829).
Conclusions: In this study levosimendan was a therapeutic option in patients with more acute and more severe left ventricular dysfunction. The similar incidence of adverse events both in-hospital and during follow-up suggests a potential anti-stunning and anti-ischemic effect of levosimendan in this setting.

60315

No effect of Intravenous immunoglobulin (IVIg) on left ventricular remodeling after acute myocardial infarction

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Background: Left ventricular (LV) remodeling take place after acute myocardial infarction (MI), and 25-30% of patients subsequently develop heart failure (HF).Enhanced inflammation, a requirement for adequate wound healing, occurs after MI, but too strong inflammation may contribute to LV remodeling. Our hypothesis was that modulation of the inflammatory response after MI would be beneficial by reducing myocardial damage and remodeling, and improve myocardial function.
Methods: 62 patients with acute ST elevation myocardial infarction (STEMI) treated by percutaneous coronary intervention (PCI), with LV ejection fraction (LVEF) <40% or <45% and 3 adjacent dysfunctional segments as assessed by echocardiography, were randomized in a double-blinded fashion. They were given intravenous immunoglobulin (IVIg), initially as induction therapy (one daily infusion [0.4 mg/kg] for 5 days), and thereafter as monthly infusions (0.4 mg/kg) or placebo for 26 weeks. The primary end point was change in LVEF from baseline to 6 months as assessed by MRI.
Results: Our main findings were: (i) LVEF increased significantly from 38 ± 10 (mean $\pm$ SD) to $45 \pm 13\%$ after IVIg and from 42 ± 9 to $49 \pm 12\%$ after placebo with no difference between the groups. LV volumes were unchanged in both groups. (ii) The scar area decreased significantly by 3% and 5% in the IVIg and placebo group, respectively, with no difference between the groups. (iii) During the induction therapy

from baseline to day 5, there was a significant increase of TNFα, sTNFR, TNF/sTNFR1 ratio, IL-10 and MCP-1, and a decrease in the number of lymphocytes and neutrophils during IVIg, with no significant changes during placebo, resulting in significant differences in changes between the groups. (iv) There was no interaction with time to treatment, infarct size, and ventricular function as assessed by NT-proBNP or LVEF, or inflammatory reaction as assessed by CRP.
Conclusions: IVIg therapy in the subacute phase after STEMI, has no effect on LV remodeling or function . Challenges by balancing adaptive and maladaptive inflammatory responses during the acute phase and a spontaneous improvement of LV function in the placebo group may possibly explain the lack of effect.

60414
Validation of a new questionnaire to measure physical well-being in patients with chronic heart failure (CIBIS-ELD Study)

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Purpose: Chronic heart failure (CHF) patients suffer from progresing impairment in quality of life (QoL). Physical well-being is an essential component of the quality of life concept. No simple validate tool exists to measure the physical well-being in CHF patients. We used data from the CIBIS-ELD Study to validate a questionnaire on physical well-being with respect to data quality, scale assumptions, construct validity and reliability.
Methods: The Physical Well-Being Questionnaire (FEW-16) is a short 16 item questionnaire using a six-point Likert-scale with answer options of "fully applies" to "does not apply at all". The questionnaire covers 4 scales: resilience, ability to enjoy, vitality, and inner peace. Each scale consists of 4 Items. In 234 patients with documented CHF (mean age 73+/-6, men 55%, NYHA II 70%, LVEF 47%) we applied questionnaires for physical well-being FEW-16 as well as QoL (SF-36) and patient health questionnaire on depression (PHQ-D). Data were collected at baseline. The scores of each scale were correlated with the quality of life data as well as the clinical parameters.
Results: Cronbach's α was 0.84 for resilience, 0.80 for ability to enjoy, 0.88 for vitality, 0.87 for inner peace and 0.95 for whole FEW-16 score. Pearson's Correlations of FEW-16 with SF-36 and PHQ-D are displayed in table 1. The FEW-16 scale scores correlated weakly with clinical parameters. The Intra-class correlation coefficient is 0.87 (95% CI 0.84—0.89, ICC 1,k).
Conclusion: The FEW-16 shows reliability, internal consistency and intraclass correlation and correlates with the validated SF-36 questionnaire. Surprisingly, physical well-being scores correlate more strongly with psychological well-being of SF-36 and PHQ-D than with clinical parameters of vitality such as 6MWT and LVEF. This may indicate that physical well-being is strongly associated with mental factors rather than purely dependant on physical vitality. We suggest the FEW-16 is an adequate measure of well-being in patients with CHF.

Table 1. Pearson's CCC of FEW-16 with S

	Resilience	Ability to enjoy	vitality	inner peace	FEW-16 score
SF-36 vitality	0.670**	0.669**	0.714**	0.656**	0.783**
SF-36 psych. well-being	0.579**	0.631**	0.602**	0.779**	0.745**
SF-36 psych	0.528**	0.565**	0.588**	0.677**	0.680**
PHQ-D	-0.568**	-0.634**	-0.665**	-0.681**	-0.736**

** indicates significance of p < 0,01 (both ways).

60622
Constrictive pericarditis: a major diagnostic challenge

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Introduction: Constrictive pericarditis is a rare entity, representing a major diagnostic challenge.
Clinical case: We describe a case of a 56 year-old man with a history of myocardial infarction (1999), having evolved with severe dilation of the left ventricle (LV), apical aneurysm, severe LV systolic dysfunction (LVSD) and mitral regurgitation (MR) due to posterior mitral leaflet prolapse. In 2004, he was submitted to a conservative mitral valve surgery, having evolved with LV slight dilation, moderate LVSD and slight MR. Three years after surgery (2007), started progressive heart failure aggravation, showing signs of peripheral congestion, without pulmonary congestion. The electrocardiogram showed atrial fibrillation and left bundle branch block. The echocardiogram reevaluation showed severe LV dilatation with severe LVSD; mitral annulus normally inserted, with mild MR, and revealed a restrictive transmitral flow pattern. There was also moderate tricuspid insufficiency, with gradually worsening, signs of pulmonary hypertension and slight compromise of right ventricular function. The chest radiograph revealed signs of apical pericardial calcification. Although treatment optimization, there was progressive worsening of clinical status. So, the patient was admitted to the Cardiology Department for clinical stabilization. Given the lack of therapy response, the patient was proposed for heart transplantation. For complementary evaluation, the patient performed cardiac catheterization that showed moderate coronary artery disease, pericardial calcification in the anterolateral and apical segments and equalization of end-diastolic pressures of cardiac chambers, showing the typical "dip and plateau" pattern at the both ventricles pressure curves. Given these data, the diagnosis of constrictive pericarditis was made, and its etiology was attributed to postpericardiotomy pericarditis, following surgery made four years ago. Pericardiectomy was considered a high risk intervention to this patient, so pre-heart transplant evaluation has been advanced. In November 2008, the patient got his heart transplant, without complications. The pre-discharge ETT showed preserved biventricular systolic function, and since then, the patient evolved favorably and is currently asymptomatic.
Conclusion: This case shows the importance of high clinical suspicion for the diagnosis of constrictive pericarditis, an entity potentially treatable when recognized in time.

60541
A new radiological score for the verification of evolving pulmonary congestion-edema in the course of acute myocardial infarction

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Background: Twenty five percent of patients sustaining acute myocardial infarction (AMI) develop pulmonary congestion-edema (PEd) as a result of increased lung fluid content (LFC). There is no method to monitor a changes in LFC. Lung impedance (LI) that decreases with increasing LFC may be indicator of LFC, but needs verification. Periodic chest radiographs are the most commonly used means, of assessing LFC. Disadvantages of this modality are relatively high inter- and intra-observer variability. The latter is possibly due to the fact that currently x-rays are analyzed qualitatively and there is no simple and reproducible radiological score (RS) to be used. We designed radiological score (RS) based on numerical summation lung edema signs. LI reflects LFC and was measured by new 50 times more sensitive surfaces device based on transverse distribution of electromagnetic energy through the chest.
Aim: To evaluate, in AMI patients developing PEd, the dynamics of a proposed RS with the status of LFC as assessed by changes in the clinical score (CS) and in LI measurements.
Results: Study population included patients admitted for AMI, with no radiological and clinical signs of PEd at admission.
RS of 0-2 characterized patients with no lung edema, 3-4 with interstitial edema, a 5-6 mild alveolar lung edema, and 7-8 and 9-10 signified moderate and severe alveolar edema. Patients were undergone to 96 hrs of monitoring. 2237 x-rays were done.
480 of 636 patients did not develop PEd (CS0).Their RS was 0.3 ± 0.5 at the beginning. Maximal decrease of LI from initial during monitoring in this group was 6.3 ± 6.1 % ($p<0.001$). At this time RS was 1.3 ± 1.2 ($p<0.01$).
156 patients developed PEd. At CS1 (rales at lung bases) RS was 5.2 ± 0.9 ($p<0.001$) and LI decreased by 21.9 ± 5.2% ($p<0.001$). At CS2 (rales at low half lung) and 3(rales over all lung), RS were 6.9 ± 1.1 and 9.8 ± 0.5 ($p<0.001$). LI decreased by 30.1 ± 8.3% and 39.3 ± 7.3%, respectively ($p<0.001$). PEd CS correlated with RS ($r=0.6$, $p<0.001$) and with LI ($r=-0.6$, $p<0.001$). RS correlated with LI ($r=-0.9$, $p<0.001$). Changes in RS and LI strikingly preceded the detection of lung rales.
Conclusions: RS was shown to be a simple and reliable method to assess changes in LFC in patients developing AHF and well correlated with the degree of lung congestion.

60326
Renal dysfunction and acute heart failure. Preliminary experiments on the use of NGAL as a marker of early renal tubular damage

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Worsening renal function (WRF) occurs frequently in pts with acute heart failure (AHF) and is related to adverse outcome. The kidney injury is usually recognized late by measurements of plasma creatinine (Cr) and estimated glomerular filtration rate (eGFR). A new lipocalin associated with neutrophil gelatinase (NGAL) has been proposed as an early marker of tubular damage. Important methodological issues are still unsolved, such as timing of measurements and pathological threshold.
The aim of the study was to evaluate in pts admitted for AHF, serum NGAL (Alere system), Cr and eGFR (MDRD) at entry and for 3 consecutive days if NGAL was always normal and for 5 days if at least one measurements was above normal range. We performed 108 measures of NGAL in 30 pts. The average value of NGAL was 141.3 ± 100.9 ng/mL (range <60-625). NGAL at entry was significantly related to kidney function (creatinine $r=0.51$, $p<0.001$ and eGFR $r=-0.49$, $p<0.001$), while among the other clinical data it resulted weekly correlated only with hemoglobin ($p<0.001$) and PCR ($p=0.01$). At baseline 13 pts had moderate renal dysfunction and 4 severe. WRF during hospitalization was observed in 7/13 pts with moderate dysfunction, and 1/13 with normal renal function. In the 4 subjects with severe dysfunction at entry no further deterioration occurred. Baseline NGAL was only slightly higher in pts who developed WRF (151 ± 90 vs 119 ± 75 ng/ml, ns).

Nineteen pts completed the protocol of repeated NGAL measurements. The 8 pts with WRF, showed a rise in Cr and eGFR: at day 1 (n=1), at day 2 (n=3), at day 3 (n=3) and at day 4 (n=1), in all cases NGAL increased significantly in the previous 24h (average 78%, range 25-200%). In 4 subjects with a high NGAL at entry (mean 155.5 ng/ml), reduction of congestion by diuretic was accompanied by a significant decrease of both NGAL and Cr. In the 5 pts with normal NGAL at the first 3 measurements, no changes in Cr and eGFR were observed. Only in 2 cases we could not demonstrate a direct relationship between changes in NGAL and Cr or eGFR but these pts had already a severe renal dysfunction at entry.

In conclusion a correct timing of NGAL measurement seems crucial to accurately predict those patients with AHF, who will develop WRF. The NGAL at entry is related with baseline Cr and eGFR, but does not seem to predict kidney damage during subsequent hospitalization and in some cases it can even decreases when congestion improves. Probably at this stage of knowledge, a serial measurement of NGAL in the first days of recovery may be more informative than the classical indicators of WRF.

HEART FAILURE DIAGNOSIS

60462

Prognostic significance of myocardial stress markers in left ventricular remodeling in patients with kidney transplants

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Aim of the study — to evaluate the prognostic significance of brain natriuretic peptide level variation in left ventricular remodeling in recipients after kidney transplantation in long-term post-operative period.

The participants of the study were 54 patients 38-52 years old. The first group consisted of 34 patients who underwent kidney transplantation more than 6 months before assessment. Control group consisted of 20 patients with arterial hypertension comparable in age, gender and traditional cardiovascular risk factors distribution to the recipients from the study group. In comparative analysis of echocardiography findings the proportion of patients with normal geometry model of left ventricle was significantly lower in the study group of patients 6 months after kidney transplantation comparing to the control group (31,28 $\pm$ 4,36, 54,12 $\pm$ 7,09 for 100 patients examined, $p<0,05$). In kidney recipients eccentric hypertrophy of left ventricle myocardium dominated in the structure of remodeling (61,24 $\pm$ 5,17, 34,52 $\pm$ 3,19 for 100 patients examined, $p<0,01$), disturbance of diastolic function was found (E/Amv 0,91 $\pm$ 0,04 m/s, 1,08 $\pm$ 0,03 m/s, $p<0,05$). In long term post-operative period in patients who underwent kidney transplantation thickening of anterior aortic wall was found (2,46 $\pm$ 0,15 mm, 1,03 $\pm$ 0,01 mm, $p<0,05$), more frequently the extension of aortic root was found (34,72 $\pm$ 4,29, 5,43 $\pm$ 1,54 for 100 patients examined, $p<0,001$). Serum level of NT-proBNP was increased in both groups, no significance between differences was found (703,7 $\pm$ 90,1 pg/ml, 665,9 $\pm$ 20,3 pg/ml, $p>0,05$).

Preliminary results show the increase of the number of patients with structural and functional changes in myocardium among kidney recipients, that is probably determined not only by the duration of chronic kidney failure on the stage of waiting list, but also by the administration of immunosuppressive therapy in post-operative period. No significant difference in brain natriuretic peptide level increase was found between groups. In long-term post-operative period in the subgroup of kidney transplant recipients with normal left ventricle contractility function, there was no connection between NT-proBNP level and markers of left ventricle remodeling.

61023

Pedictors of ischemic cardiomyopathy in coronary angiography for heart failure with reduced ejection fraction

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Background: Coronary angiography (CA) in heart failure (HF) with no definite etiology is often justified for diagnostic evaluation of ischemic cardiomyophaty (IC). However the patients who benefit from this strategy are not yet defined.

Objective: To evaluate the prevalence of IC by angiographic criteria, as well as their predictors, in patients with heart failure and left ventricular ejection fraction (LVEF) reduced with unknown etiology.

Methods: Consecutive outpatients with HF and systolic dysfunction (LVEF $<$ 45%) with undefined etiology after the initial noninvasive evaluation, who underwent CA for the diagnosis of IC. The angiographic criteria used for IC were based on previously published definitions. Were excluded from analysis patients with previous know coronary artery disease (CAD), positive serology for Chagas disease, congenital heart disease, severe valve disfunction and heart transplantation patients. We collected demographic data, NYHA functional class, LVEF and presence of segmental wall motion abnormalities on echocardiography, as well as risk factors for (CAD) and history of angina.

Results: 152 patients were included for analysis. Among these, 105 (69%) were male with mean age of 53 ($+$ -10.3) years and LVEF: 27.7% ($+$ -7.7). The prevalence of IC by angiographic criteria was 14 patients (9.2%). The predictors for IC are summarized in Table 1. In the univariate analysis only the presence of angina was predictive of IC ($p = 0.006$). Four (2.6%) patients had procedure-related complications.

Conclusion: The performance of CA in patients with HF and systolic dysfunction with unknown etiology, had a low diagnostic yield for IC. Only a history of angina was a predictor of coronary obstructions consistent with IC.

Table 1

	Ischemic cardiomyopathy	Non-ischemic cardiomyopathy	p
Age, yrs	50 +- 10	54 +- 10	0.220
Male, no	12 (85.7%)	93 (67.4%)	0.228
Angina	7 (50%)	22 (15.9%)	0.006
NYHA 3-4	8 (57.1%)	47 (34.1%)	0.142
$\geq$ 3 CAD Risk Factors	9 (64.3%)	71 (51.4%)	0.41
LVEF, %	27.07	27.8	0.738
Segmental wall motion abnormalities	35 (35.7%)	23 (16.9%)	0.14

NYHA (New York Heart Association Funcional Classification); CAD (coronary artery disease); LVEF (left ventricular ejection fraction).

60458

An evaluation of NT-proBNP testing in the diagnosis of heart failure

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Purpose: Increasing prevalence of heart failure has increased demand on Echocardiography services, affecting waiting times and expenditure. Low levels of NTproBNP make heart failure unlikely, high levels indicate a poor prognosis. The aim of this study was to evaluate use of NTpro-BNP in decision-making in diagnosis and management of heart failure, impact on Echocardiography services, and cost-effectiveness.

Methods: Data was collected on patients with NTpro-BNP measured in May 2009. Data included age, sex, symptoms, co-morbidities, ECG, reason for request, NTpro-BNP result. Medical notes were examined for clinical impact of result and details of echo request.

Results: 676 requests were received. Of these, medical records of 156 patients were examined. 87 patients were male, 69 were female, mean age 69.7years. The majority presented with dyspnoea. Normal NTpro-BNP excluded heart failure as cause of symptoms in 44 patients, abnormal values enabled clinicians to initiate heart failure therapy. Raised NTproBNP in heart failure patients led to up-titration of therapy. In 44 patients with normal NTpro-BNP, 25 had no Echo and were appropriately screened. However, 17 patients had Echo despite normal NTpro-BNP and were inappropriately screened. NTpro-BNP analysis costs £12, Echo costs £75. Total cost - 156 tests (£12 per test) = £1872. Cost saving for 25 patients appropriately screened and not referred for Echo - 25x £75= £1875. 17 patients were screened inappropriately costing (17x £75) + (17x12) = £1479. If these patients were appropriately screened £1275 would have been saved and waiting lists reduced.

Conclusions: This audit shows NTpro-BNP testing is a useful test when requested appropriately. NTproBNP expedites the patient journey ensuring correct clinical referral and avoidance of inappropriate investigations.

60923

Contribution of tissue Doppler in the detection of preclinical diastolic left ventricular dysfunction in moderate aortic stenosis

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Aim: Left ventricular (LV) diastolic dysfunction is common in severe aortic stenosis. The purpose of this study is to evaluate left ventricular (LV) diastolic function in asymptomatic patients with moderate aortic stenosis. Moderate aortic stenosis (AS) is defined by a valve area between 1 and 1.5 cm^2.

Materials and methods: The study population consisted of 30 asymptomatic patients with isolated moderate aortic valve stenosis (mean aortic valve area= 1.26 $\pm$ 0.2 cm^2) and 33 age- and sex-matched control subjects. All included subjects had no evidence of hypertension, diabetes mellitus, ischemic heart diseases or chronic pulmonary diseases. Conventional echocardiography and tissue Doppler imaging (TDI) analysis were performed in all patients and healthy controls.

Results: LV ejection fraction, the Tei index and the mitral annulus systolic velocities measured by TDI were similar in both groups. However, mitral annulus early diastolic velocities (Em) measured by TDI were markedly reduced in patients with moderate AS (7.2 $\pm$ 1.1 cm/s vs. 12.7 $\pm$ 1.8 cm/s, $p<0.01$) with higher ratio of early diastolic transmitral pulsed Doppler E to Em (E/Em) velocities (14.5 $\pm$ 1.7 vs. 8.6 $\pm$ 1.5, $p<0.01$) suggesting impaired diastolic function.

Conclusion: In the presence of normal systolic function, diastolic LV function may deteriorate in asymptomatic patients with isolated moderate aortic stenosis. Tissue Doppler imaging may provide a useful tool to detect early subclinical LV diastolic dysfunction.

60150
The nonlinear parameter short time Poincare plot is marker of systolic dysfunction of left ventricle in patients with myocardial infarction

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Introduction: There are not to much data and evidences related to connection of Poincare plot form and systolic dysfunction of left ventricle.The analysis of Poincaré plots form based on short-term recordings offers a a new relative simple diagnostic method based on pattern shapes.
Aim: of the study was to determine value of Poincare plot as a marker of systolic dysfunction of left ventricle,measured during 10 minutes recording first day,seventh day and two week after onset of myocardial infarction.
Method: We analysed prognostic significance of Poincare plot pattern shape as a point using only visual judgement of different forms.We included 1250 patients in the study and in follow up (survival time 71,range I-80 months).End-point of the study was cardiovascular and total motality.All patients were tested in Neurocardiological unit during third week after myocardial infarction. using next diagnostic methods:ECG with commercial software Schiller AT-10(short time spectral analysis of RR variability with analysis of Poincare plot as a nonlinear parameter and late potentials);24-hour ambulatory ECG monitoring(meanRR interval,long term heart rate variability analysis included SDNN parameter);echocardiography examinations(systolic disorder defined as EF$<$30%).We analysed Poincare plot first day in Coronary care unit by all patients and by some patients 7th day.
Results: Poincare plot in shape as a point measured 1st and 7th day was more present in patients with systolic dysfunction($p=0.001$,$p=0.003$).There was not statistical significance in measurements after three weeks.Short time mean RR interval(ECG)had lower value in group with systolic disorder($p=0.004$).The time domain parameters SDNN and RMSSD as a indexes of general autonomic and vagal function,and spectral parameter TP(Total Power)(Holter ECG) had lower values in patients without systolic dysfunction of left ventricle($p=0.013$,$p=0.003$,$p=0.001$).
Conclusion: The short time Poincare plot in the visual form as a point is a marker of severe autonomic dysfunction and systolic disorder of left ventricle in patients with myocardial infarction.

60086
A validated score for the assessment of heart failure severity in adults late after Mustard or Senning palliation of transposition of the great arteries

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Introduction: Congenital heart disease (CHD) is a heart failure (HF) state. Many measures of HF severity have been characterised in CHD including neurohormonal activation, ventricular function and exercise capacity. There has however been no description of a validated symptom score or quality of life measure, which allows clinical assessment of HF severity in this population. In a prospective HF study in adults late after atrial switch surgery for transposition of the great arteries (TGA) we examined the relationship between various objective measures of HF severity and the Minnesota Living With Heart Failure Questionnaire (MLWHFQ) score.
Methods: 92 consecutive adults with Senning or Mustard surgery for TGA between January 2010 and July 2011 had assessment of NYHA functional class, measurement of NT-proBNP levels, and surface electrocardiogram (ECG). Patients were invited to complete a MLWHFQ; a further 41 underwent CMR and CPEX testing.
Results: Mean age at clinic attendance was 31 ± 6.5 yrs, median age at repair 8 (0.1-96) months. 51% (n=47) underwent Mustard palliation; 60% (n=55) were male. Median score for MLWHFQ 6(2-19), correlating with age at clinic attendance ($p=0.002$, $r=0.31$) and age at original repair ($p=0.0007$, $r=0.35$). Those with Mustard palliation had significantly higher score than those with Senning repair (8(3-28) vs 4(0-12) $p=0.03$), as did those in NYHA II compared to class I (23(7-45) vs (4(1-12) $p<0.0001$). Median NT-proBNP was 24(16-43)pmol/L and was significantly correlated to MLWHFQ ($p=0.001$, $r=0.34$). Mean QRS duration 96 ± 20ms and showed a significant relationship to MLWHFQ ($p<0.0001$, $r=0.41$). MLWHFQ showed a significant relationship with chronotropic index ($p=0.01$; $r=0.34$), VE/VCO2 slope ($p=0.0028$; $r=0.48$) and peak VO2 ($p=0.001$; $r=0.49$) but had no relationship to any CMR derived parameter of systemic RV size or function.
Discussion: We find that symptom scores relate to other reliable indicators of HF status in adults late after atrial redirection surgery of TGA, over and above the qualitative information provided by CMR assessment of systemic RV function. The MLWHFQ is a simple, practical and readily reproducible self assessment tool easily applied in the outpatient setting that could help identify patients at high risk of adverse outcome.

ARRHYTHMIAS AND TREATMENT

60008
A rare case of recurrent tachycardia induced cardiomyopathy due to atrial flutter

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Introduction: Tachycardia induced cardiomyopathy (TIC) is defined as atrial or ventricular dysfunction as a result of prolonged elevated heart rate that is reversible upon control of the arrhythmia. Here we describe a first reported case of recurrent TIC due to atrial flutter.
Case report: Patient is a 61 years old Caucasian male with hypertension and hyperlipidemia admitted with 3 days history of progressively worsening palpitation and dyspnea. There is no history of paroxysmal nocturnal dyspnea or orthopnea or chest pain or syncope. He is currently on Asprin, Metoprolol succinate, Lisinopril, Amlodipine and Atorvastatin. He has history of atrial flutter in 2007 with 2:1 hear block. Transesophageal echocardiogram (TEE) revealed moderately decreased left ventricular (LV) systolic function with EF 35% and global hypokinesia. There was no left atrial thrombus hence he received direct current cardioversion (DCCV) to revert back to sinus rhythm. The follow-up echocardiogram in 2 months later revealed normal LV size and systolic function.
He had seconde episode of atrial flutter in 2008, at that time TEE revealed decreased LV systolic function with EF of 35% and no thrombus in left atrium or left atrial appendage. Subsequently he received DCCV to revert back to sinus rhythm. The follow-up echocardiogram in 3 months later revealed normal LV size and function. He is been regularly followed up in cardiology office until this episode in 2010. Physical examination was unremarkable except for tachycardia. Baseline lab data including cardiac enzymes and thyroid function test was normal. Chest X ray was normal. Baseline EKG on admission revealed atrial flutter with 2:1 AV block. Due to recurrence of atrial flutter with DCCV, catheter ablation was proposed. Pre-ablation TEE revealed normal LV size with moderately reduced function and no evidence of clot in LA or LAA. Subsequent electrophysiology study with 3D cardiac mapping revealed a flutter circuit and this was ablated successfully. Patient was discharged on beta-blockers, ACE inhibitors and Dabigatran. The follow-up 2D echocardiogram in 2 months revealed normal LV size and function.
Conclusion: TIC is a reversible condition characterized by ventricular dysfunction resulting from increased atrial or ventricular rates. Treatment for TIC is to correct the underlying tachycardia. Recurrence of the TIC is a series problem , hence definite therapy focusing abolishment of tachyarrythmia is recommended.

60854
Time course of improvement of left ventricular function after treatment of incessant tachyarrhythmia

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Background: Some patients with chronic hear failure manifested as dilated cardiomyopathy(D-CMP) restored LV systolic function after termination or controlling of tachycardia. We observed time course of improvement of LV dysfunction and clinical outcome in patients with reversible LV systolic dysfunction after treatment of tachycardia and clinical factors affecting improvement of LV dysfunction.
Methods: Serial heart rate and echocardiographic parameters; LV diastolic and systolic dimension, fractional shortening, ejection fraction were determined in 23 patients (17 men, Age 60.1 ± 11.5 yrs) initially diagnosed as D-CMP and fully recovered from LV dysfunction after termination or controlling of tachycardia. Non-parametric analysis methods were used to compare difference between groups.
Result: Mean duration of follow-up was 23.4 ± 14.8 (ranged 3-60) months. Underlying disease were hypertension in 7(30.4%), hyperthyroidism in 3(13.0%), chronic obstructive pulmonary disease in 3(13.0%), chronic alcoholism and severe burn in each 2(8.6%) cases of our subjects. Six cases (26.1%) had no accompanying disease and showed only atrial fibrillation (lone atrial fibrillation). Most frequent type of tachyarrhythmia was atrial fibrillation with rapid ventricular response as 19 subjects (86.1%). Recovery of LV function was achieved within 1 months in 12 (52.2), between 1 month and 6 months in 4 (17.4%) and over 6 months in 7 (30.0%) cases after termination or controlling of tachycardia. Subjects improved within 1 month (group A) were older than that of over 1 month (group B) (65.7 ± 6.5 vs 54.0 ± 12.8 yr, $p<0.001$) and had longer duration of symptom of heart failure (1.4 ± 1.0 vs 3.9 ± 2.1 months, $p<0.01$). Heart rate at admission, fractional shortening and ejection fraction were not different between two groups, but LV diastolic (55.3 ± 4.8 vs 63.0 ± 6.0 mm, $p<0.01$) and systolic (46.8 ± 4.4 vs 55.9 ± 7.5mm, $p<0.01$) dimensions were significantly smaller in group A than that of group B. There was no case of reexacervated LV dysfunction, but recurrent arrhythmia occurred in 4 cases who had decreased dosage of amiodarone (below 200mg/day) and had no medication. Two cases died of intracranial hemorrhage and lung cancer each other.
Conclusion: These findings suggested that in patients with T-CMP, the time for recovery of LV dyfunction depend on duration of symptom after the onset of heart failure and

degree of structural impairment of LV. Once the LV function was recovered, it is well preserved and showed preferable outcome.

60269

Hypoxic adaptation and arrhythmia prevention in patients with ischemic cardiomyopathy and chronic heart failure

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The purpose of this research was to study the efficiency of using a course of normobaric intermittent hypoxia adaptation (NIHA) before coronary bypass surgery (CABG) in the ischemic cardiomyopathy patients (ICMP) with chronic heart failure (CHF) and its influence on the character of reperfusion complications and life- threatening arrhythmias development.
Materials and methods: Cohort of 70 patients with ICMP (n=35 in the main and control groups) were included into the research. All patients had depressed left ventricle systolic function (LVEF) less than 35% and NYHA functional HF class II-IV. All male patients underwent a course of NIHA before CABG. The indications for CABG were the presence of myocardium more than 50% with accumulation radiopharmaceutical over 50% during SPECT with 99mTc-MIBI in the rest against the presence of a well developed distal channel and the absence of right HF. Functional state of LV was assessed by means of myocardial scintigraphy, echocardiography and daily monitoring of the electrocardiogram.
Results: The initial CHF severity of the patients in both groups was determined by depressed LVEF against maladaptive LV remodeling. We also marked the prevalence of sympathetic activity nervous system (NS) and the number of the potentially life-threatening ventricular arrhythmias (VA). After a course of NIHA we revealed a significant reduction in the average heart rate (HR), the total number of supraventricular (SV) and ventricular extrasystoles and life-threatening VA. It happened due to the microcirculatory processes improvement in the myocardium and in the autonomic balance shift towards the prevalence of parasympathetic NS. We noted the decrease in the total number of myocardium segments with slight and moderate perfusion defects from 7,13 $\pm$0,56 to 5,35 $\pm$0,51 (p = 0,02).The main group were characterized with a more favorable recovery during the intra-and early postoperative period after CABG. We revealed significantly less frequent of perioperative myocardial infarction and ventricular fibrillation, the episodes of ventricular tachycardia during cardiac resuscitation after artificial circulation. In the main group we marked less frequent of inotropic and nitrates support, reduction of SVA, VA and high grade VA in the perioperative period.
Conclusion: For the patients with ICMP and CHF the use of NIHA in the preoperative period can increase the volume of the viable myocardium and thus allowed to assume a more adequate protection from perioperative myocardial ischemia and reperfusion injury during CABG and provides a more favorable recovery during the perioperative period.

60721

Angiotensin II-induced Ca2+ -dependent depolarisations in mouse and human cardiac myocytes

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Angiotensin II (ATII) is a potent vasoconstrictor associated with cardiac remodeling, progression of heart failure and arrhythmia. ATII signals primarily via the Gq-coupled ATII receptor type 1 (AT1) and activates phospholipase C (PLC) signaling pathway including IP3-mediated Ca2+ release and diacylglycerol (DAG) activation of protein kinase C. Recent data suggest that DAG can directly regulate members of transient receptor potential cation (TRPC) channels family. TRPC3 was shown to form a functional complex with NCX, and its activation may lead to alterations in subcellular Na+ and Ca2+ homeostasis. Although dysbalance in Na+ and Ca2+ concentration can lead to arrythmogenic events, no direct evidence is provided whether ATII may induce triggered cellular depolarisations and increase diastolic Ca2+ leak through the SR. Therefore, we investigated the acute effect of ATII on Ca2+ homeostasis in cardiac myocytes (CMs) isolated from mouse and human ventricular tissue.
Methods: Cytosolic [Ca2+] (Fluo4-AM, confocally) was measured in electrically stimulated CMs from mouse (n=20-30 cells per group) and human (n=4 cells per group) hearts not suitable for transplantation. Amplitude of [Ca2+] transients (CaTs) was calculated as F/F0 and diastolic SR Ca2+ leak as frequency of sparks (SparkF, in s-1*pL-1) Arrhythmic depolarisations were identified by synchronized SR Ca2+ release (syncCR, in number*s-1) during diastole. Cells were kept in elevated [Ca2+]o (mouse: 3mM, human: 5mM) and ATII (100nM) was applied for 15 min. To confirm that Na+ influx is essential for depolarisations to occur, we increased intracellular [Ca2+] by application of Na+/K+ ATPase inhibitor ouabain (100μM) in combination with Na+-free external solution.
Results: In mouse cells, ATII increased the electrically stimulated CaTs amplitude from 2.7$\pm$0.2 to 4.1$\pm$0.3 ($p<0.05$), while SparkF increased from 46$\pm$21 to 269$\pm$29 ($p<0.05$). Preliminary results from human CMs support this finding (SparkF: ATII vs. CTRL, 292$\pm$89 vs. 37$\pm$21; $p<0.05$). In mouse cells the incidence of syncCR increased by ATII application (0.81$\pm$0.14) as compared to CTRL (0.10$\pm$0.03 $p<0.05$). Ouabain in combination with Na+-free external solution also lead to increased diastolic leak (SparkF: 154$\pm$31; $p<0.05$), but not syncCR during diastole (syncCR: 0.06$\pm$0.02; n.s. vs. CTRL).
Conclusion: Acute application of ATII increases systolic CaTs, diastolic SR Ca2+. Synchronized diastolic Ca2+ release depends on Na+ influx, suggesting that ATII-induced SR Ca2+ leak is sufficient to trigger spontaneous action potentials in ventricular myocytes.

ATRIAL FIBRILLATION

60857

Cardiopulmonary exercise testing in patients with heart failure and atrial fibrillation under beta-blocker therapy

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Background: Cardiopulmonary exercise testing (CPX) is an objective assessment of physical capacity in patients (pts) with heart failure (HF). Atrial fibrillation (AF) is associated with impaired exercise capacity and have worse outcome in patients with HF. Beta-blockers, is standard therapy in HF patients that is associated of the improvement in functional capacity. However, in those HF patients with AF were not improved as much as those in sinus rhythm.
Aim: to assess the influence of persistent AF on CPX parameters in patients with HF under beta-blocker therapy.
Methods: Forty-three consecutive patients with optimized treatment, 23 with persistent AF (sex, male; age, 54 $\pm$ 8 years; NYHAclass, I — III; LVEF, 27 $\pm$ 6% and etiology: 8 ischemic and 15 non-ischemic) and 20 with sinus rhythm (sex, 5 female; age, 50 $\pm$ 8 years; NYHAclass, I — III; LVEF 31 $\pm$ 6%and etiology: 6 ischemic and 14 non-ischemic). All patients were submitted a treadmill CPX.
Results: We found no significant differences in age, etiology, LVEF, NYHA class, HR (bpm) at the rest and peak;SBP and DBP (mmHg) at rest and peak; O2 pulse (mlO2/beat); VE (l/min); exercise time (min) and slope VE/VCO2 between persistent AF and sinus rhythm. Significant differences in peak VO2 (16.9 $\pm$ 3.5 vs 20.6 $\pm$ 4.6 ml/kg/min,p=0.04) and delta HR (57 $\pm$ 9 vs 43 $\pm$ 6, p=0.04) were noted when compared patients in persistent AF vs with sinus rhythm, respectively.
Conclusion: Persistent atrial fibrillation in patients with HF is associated with lower peak VO2 and higher delta HR as compared to patients with sinus rhythm. Higher delta in patients with HF and persistent AF indicates the sympathetic system's overactivation, despite these patients being under beta-blocker therapy.

60827

Atrial fibrillation, heart failure and sleep apnea:inside the complex relationship

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Aim: Sleep apnea (SA) is a frequent finding in patients (pts) with atrial fibrillation (AF). SA could influence the natural history of AF through the alteration in sympatho-vagal balance due to hypoxemia and arousals. The aim of the study is to assess the impact of SA in AF pts, with or without heart failure (HF).
Methods: 41consecutive pts with non parosysmal AF were investigated at baseline with clinical and echocardiographic evaluation, polysomnography, 24h-ECG-recording with HRV analysis. At 3 and 12 months follow-up visit, clinical and echocardiographic assessment was repeated. Among all pts, 27 of them had AF with HF whereas 14 had only AF.
Results: Patients with AF and HF had higher BNP levels,worse EF% and higher PAPs. Pts with AF and HF had a cardiac frequencies (CF) at baseline ECG and at 24h Holter recording and the difference persists substantially unchanged in day-time only and night-time only reconrdings ($p<.001$). Pts with AF and HF had a decreased variability over the 24 hours, both in time domain and in frequency domain, especially pronounced at night. On polysomnography, similar prevalences of normal exam and OSAS were found between AF pts with or without HF. However, pts with CSA had an increased risk of having HF when compared to pts without CSA (29% vs 5%; OR=5.9; p=.028). Patients with CSA had increased CF at ECG, in the whole 24h as well in day-only or night-only readings (all $p<.05$). At 3-months follow-up there was a significant decrease of CF, an increase of mean EF, and a lower PAPs compared to basal visit in the general population. However, none of these improvements seem present in pts without HF whereas pts with AF and HF experienced a significant reduction of CF between 0 and 3-months (-46.0 bpm) which in turn led to an improvement in EF (+9.9 %), in diastolic and systolic left ventricular diameters and in PAPs (all $p<.05$). In a similar manner, pts with CSA showed a significant improvement in CF, in EF and in PAPs values. At 12-months follow-up, no further improvements were present in patients who have already completed the study (n=20).
Conclusions: Patients with AF and HF have a worse clinical and instrumental profile characterized by higher BNP, lower EF%, higher CFs, reduced HRV and an higher prevalence of central sleep apnea than patients with only AF. CSA is known to be associated with AF and also with HF and contribute to the maintenance of the complex relationship between them. Nonetheless, thanks to effective rate or rhythm control,

patients with AF and HF show a significant improvement after 3 months that persists unchanged at 12-months follow-up visit.

60309

Cheyne-Stokes respiration and incident atrial fibrillation in patients with chronic heart failure

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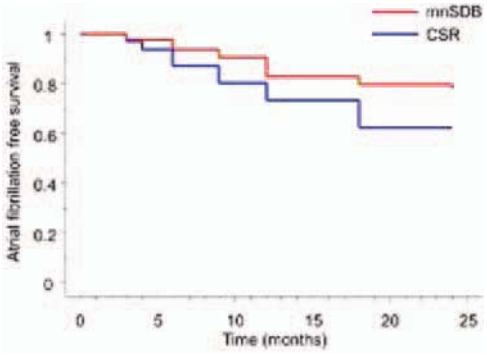
Background: Previous studies confirmed obstructive sleep apnoea (OSA) as independent risk factor for the new onset of atrial fibrillation. The aim of this study was to investigate the impact of Cheyne-Stokes respiration on incident atrial fibrillation (afib) in patients with chronic heart failure (CHF).
Methods: A cohort of 132 patients with CHF (LVEF $\leq$ 45%, NYHA-class $\geq$ 2) who had cardiac resynchronization therapy (CRT) and presented with stable sinus rhythm (SR) were studied. The patients underwent overnight polygraphy with 80 having mild or no CSR (Apnea Hypopnea Index (AHI) $<$ 15/h), 32 having moderate to severe CSR (AHI $>$ 15/h), and 21 having moderate to severe OSA (AHI $>$ 15/h; excluded). During follow-up (24 months) mode-switch episodes of the CRT-device caused by afib were documented.
Results: Kaplan-Meyer-Plot on afib-free survival (Fig. 1) is shown below. Adjusted for sex, age, body mass index, left ventricular ejection fraction, left atrial (LAD)- and ventricular end-diastolic diameter, creatinine, and CRP-level, cox proportional hazard regression analysis (backward selection with AIC) revealed LAD (HR 1.053, 95%CI 1.006 to 1.101; p=0.03) the only independent risk factor for the new onset of atrial fibrillation in our CHF cohort.
Conclusion: In patients with CHF and CRT the presence of untreated CSR is not inevitably associated with an increased risk for the new onset of atrial fibrillation. Larger trials are necessary to clearly elucidate this question.



Abstract 60309 Figure

60630

Predictive factors for new-onset atrial fibrillation in patients hospitalized for acute heart failure syndromes: an analysis of the RO-AHFS registry

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Background: Limited data exist on the incidence and prognosis of new-onset atrial fibrillation (NOAF) in patients hospitalized for acute heart failure syndromes (AHFS).
Objective: To identify predictive factors for NOAF during index hospitalization for AHFS.
Methods: Over a 12 month period, the Romanian Acute Heart Failure Syndromes (RO-AHFS) registry enrolled 3224 consecutive patients at 13 medical centers admitted with a primary diagnosis of AHFS. This is post-hoc analysis of the patients in normal sinus rhythm (NSR) on baseline electrocardiogram (EKG) at presentation. Included patients were divided into two groups based on the presence (+NOAF) or absence (-NOAF) of NOAF. Patient demographics, clinical characteristics, and outcomes were compared between the two groups using using Fisher exact test or the $\chi 2$ test, as appropriate, for categorical variables and a 1-way analysis of variance for continuous variables. Independent predictors of NOAF were identified using a multivariate logistic regression model.
Results: A total of 1842 patients were found to be in NSR on baseline EKG. NOAF was documented in 579 (29.4%) of patients during hospitalization. +NOAF patients tended to be older (72+9 vs. 69.4+8 years, p-value $<$0.001) and male (59% vs. 52%, p-value = 0.01) and had similar LVEF and laboratory values at baseline. In-hospital mortality was comparable between the two groups (+NOAF 7.5% vs. −NOAF 7.1%, p-value = 0.30) but the mean length of stay was significantly longer in +NOAF patients (8.7 with interquartile range 4-11 days vs. 7.3 with interquartile range 3-10 days, p-value=0.03). After multivariate adjustment, independent predictors for NOAF included a prior history of AF (odds ratio [OR] 1.93, 95% confidence interval [CI] 1.71-2.41), age (OR 1.14, 95% CI 1.24-1.58), and left ventricle end-systolic diameter (OR 1.03, 95% CI 1.002-1.034).
Conclusions: NOAF is prevalent during index hospitalization for AHFS and is strongly associated with a prior history of AF and to a lesser extent age.

CANCER / CARDIOTOXICITY

60927

Imatinib mesylate (IM) induced cardiomyopathy involves resident cardiac progenitor cells

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Cardiac side effects have been reported also for new classes of drugs,like Tyrosine-Kinase-Inhibitors(TKIs).Cardiovascular events have been described in patients treated with Imatinib Mesylate(IM)although the mechanism of cardiac dysfunction has not been yet elucidated. We performed in vivo study,treating young rats by 3--weekly-i.p.-injection of 50,100 and 200 mg/Kg IM(IM50,IM100 and IM200)for 3 weeks. All rats died with IM200. Diastolic dysfunction was present even at IM50 and a dose-dependent impairment in Left-Ventricular-End-Diastolic-Pressure(LVEDP)and +dP/dT was observed. Anatomical parameters indicated that only doses above IM100 resulted in concentric type of LV remodelling associated with minimal fibrotic myocardial damage. Body Weight significantly decreased in treated groups, whereas LV weight slightly increased. The ratio wet/dry weight was reduced in a dose dependent manner,-documenting an increased theoretical water content. Cardiomyocytes(CM)were isolated from control and IM treated rat heart showed a dose dependent decrease in cell volume. Immunohistochemical analysis was performed to evaluate genotoxic damage,by detection of DNA double strand breaks(DNAdSB),apoptotic death, by TUNEL assay,and mitotic index,by the nuclear expression of phospho-Hystone3(phH3). At IM50 an increased density of DNAdSB,apoptosis and phH3+ CM was observed,indicating an elevated cell turnover. At IM100 the genotoxic damage and index of apoptotic cell death resulted similar to control, instead the density of phH3+ cells was significantly decreased, suggesting a proliferation arrest. Arteriolar, capillary and lymphatic density in IM treated hearts decreased in a dose dependent manner indicating a negative effect also on vascular compartments. Finally,c-kit+ Cardiac Stem Cells and PDGF-R+ Vascular Progenitor cells showed a dose dependent decrease suggesting that the TK inhibition on kit and PDGFR pathways by IM affects the number of resident progenitors. This toxic effect was also documented by Electron Microscopy. In CM myofibrillar depletion,swollen mitochondria(sm)and gap junction disarray were observed. Sm were also observed in endothelial cells and pericytes Interestingly,an increased incidence of Weibel Palade bodies was present both in blood and lymphatic vessels. In arteriolar smooth muscle cells intracytoplasmatic lakes,nuclear pseudoinclusions,ring shaped mitochondria and disarrangement of emidesmosomes were observed. IM-induced cardiomyopathy involves alteration of cell turnover of all myocardial cell compartments, including resident progenitors. Understanding the mechanisms may open innovative protective strategies.

60244

Ranolazine blunts anthracyclines-cardiotoxicity in experimental models in vitro and in vivo

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Purpose: Anthracyclines are first line drugs against cancer, but produce a well-known cardiomyopathy through multiple mechanisms, which also include, among many, Ca2+ overload due to reduced SERCA2a activity and inappropriate opening of the RyR2, and impaired myocardial energetics. Anthracyclines generate Reactive Oxigen and Nitrogen Species (ROS and RNS), posing the heart at increased demand for oxygen, thus setting the stage for a metabolic ischemia that also activates late INa, the target of ranolazine (RAN). Here, we aim at assessing whether RAN, diminishing intracellular Ca2+ through its inhibition of late INa, and enhancing myocardial glucose utilization (and/or reverting impairment of glucose utilization caused by chemotherapy) blunts anthracyclines cardiotoxicity.
Methods: To assess for toxicity in vitro, rat H9C2 cardiomyoblasts were pretreated with RAN (0.1-1μM) for 72 hours and then treated with doxorubicin (DOX, 0.1 μM) for additional 24 hours. Cells counts were assessed by Trypan exclusion test. To evaluate cardiac function in vivo, fractional shortening (FS) and ejection fraction (EF) were measured by echocardiography in C57BL6 mice, 2-4 mo old, pretreated with RAN (370mg/kg/day, a dose comparable to the one used in humans) per os for 3 days. RAN was then administered for additional 7 days, together with DOX (2.17mg/kg/day ip), according to our well established protocol.

Table 1. LV deformation assessed by STE.

Anthracicline	Dose	LVEF	RotA	RotB	LVtw	LVutwr	LVrad	LVϵ
	mg/m^2	%	°	°	°	°/s	%	%
Baseline	0	61 ± 5.6	8.1 ± 1.4	-5.7 ± 1.5	13.8 ± 1.7	-83.9 ± 23.6	47.8 ± 5.3	-21.2 ± 2.5
6 weeks	118 ± 43†	60.3 ± 6	6.8 ± 1.3†	-5.6 ± 1.6	12.3 ± 1.7†	-77.1 ± 21.9	41.1 ± 5.4†	-19.0 ± 2.4†
12 weeks	178 ± 58†§	58 ± 5.9	5.1 ± 1.2†§	-5.4 ± 1.6	10.6 ± 1.6†§	-74.1 ± 22.1	38.6 ± 5.2†§	-17.2 ± 2.8†§
P-value by ANOVA	<0.001	0.94	<0.001	0.79	<0.001	0.18	<0.001	<0.001

† P < 0.05 vs. baseline; § P < 0.05 vs. 6 weeks by ANOVA followed by Scheffe's test.

Results: After DOX, only 68% of the cells were viable. RAN alone did not affect cell survival, but blunted DOX toxicity, rescuing % cell survival to 87% (p=.01 vs DOX alone). In our in vivo studies, after 7 days with DOX, FS decreased to 50 ± 2%, p=.002 vs 60 ± 1% (sham), and EF to 81 ± 2%, p=0.0001 vs 91 ± 1% (sham). RAN alone did not change FS (59 ± 2%) nor EF (89 ± 1%). Interestingly, in mice treated with RAN and DOX, the reduction in cardiac function was milder: FS was 57 ± 1%, EF was 89 ± 1%, p=0.01 and 0.0009 respectively, vs DOX alone. Conclusions. RAN blunts DOX cardiotoxic effects in 2 different models, in vitro and in vivo. We plan to test RAN as a cardioprotective agent with other antineoplastic cardiotoxic drugs in our experimental models, and to better characterize the cardioprotective mechanisms of RAN in all these settings.

60432
Speckle tracking echocardiography in the early detection of anthracycline-induced cardiotoxicity

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Aim: Anthracyclines are important anticancer drugs, but their use is limited by cardiotoxicity. Current approaches to surveillance, including left ventricular ejection fraction (LVEF), are often inadequate to detect myocardial disease. Speckle tracking echocardiography (STE) was successfully used for the measurement of myocardial deformation and rotation. Therefore, we tested whether myocardial deformation analysis using STE might detecte earlier anthracycline-mediated LV dysfunction.
Methods: We analysed 74 patients (51 ± 11 years) in sinus rhythm, without known cardiac disease and LVEF>50%, referred for echocardiography before therapy with anthracyclines. Echocardiography was performed before and after 6 and 12 weeks of chemotherapy. STE was used to to measure LV peak apical rotation (RotA), peak basal rotation (RotB), LV twist (LVtw), LV global longitudinal strain (LVϵ), LV radial strain (LVrad) and LV untwisting rate (LVutwr).
Results: Averaged cumulative anthracycline doses were 118 ± 43 mg/m^2 at 6 weeks and 178 ± 58 mg/m^2 at 12 weeks. LVϵ, LVrad, RotA, LVtw deteriorated during the follow-up (all p <0.05 by ANOVA), before any LVEF decrease (Table 1). LVutwr and RotB did not show significant changes. Simple linear regression showed that deterioration at 6 weeks of LVϵ (r =0.58, p <0.001), LVtw (r= -0.31, p=0.03) and LVrad (r= -0.29, p =0.04) exhibited significant correlations with the anthracycline dose administreted in the first 6 weeks.
Conclusions: Assessment of myocardial rotation and deformation by STE can detect subclinical anthracycline-induced LV dysfunction, before any LVEF decrease. The early deterioration of STE parameters is correlated with the cumulative anthracycline dose.

HYPERTROPHIC CARDIOMYOPATHY

60631
Eosinophilic myocarditis in a patient with hypertrophic cardiomyopathy

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We report the case of a 60-year-old woman with history of hypertension, family history of hypertrophic cardiomyopathy (HCM) and hyperpigmented skin lesions of unknown etiology. She had clinical heart failure (HF) since 8 years ago, with progressive worsening. A transthoracic echocardiogram showed concentric left ventricular hypertrophy with septal predominance. Electrical instability has been documented (atrial fibrillation with rapid ventricular response and runs of nonsustained ventricular tachycardia). Cardiac magnetic resonance imaging revealed asymmetric septal hypertrophy and multiple foci of delayed enhancement suggestive of myocardial fibrosis. The HCM genetic test was negative. For further clarification, endomyocardial biopsy (EMB) was done, which showed histiocytes and eosinophils infiltration, suggestive of eosinophilic myocarditis. There have not been identified drugs capable of inducing a hypersensitivity reaction. In November 2010, the patient was hospitalized for decompensated heart failure. Analytically, it was found the presence of peripheral eosinophilia and, attending the findings of the EMB, complementary investigation was performed, which included: bone marrow examination and biopsy (no evidence of neoplastic process), thoraco-abdominal-pelvic computerized axial tomography (no significant changes) and parasitic infection test (negative). A skin lesion biopsy revealed inflammatory infiltrate, rich in eosinophils and neutrophils. Given the progressive clinical deterioration, the presence of eosinophilic myocarditis and probable multi-organ systemic involvement, steroid therapy was started, leading to rapid resolution of peripheral eosinophilia.
This case illustrates the occurrence of eosinophilic myocarditis in a patient with suggestive findings of HCM. Eosinophilic cardiomyopathy may result in rapid clinical deterioration in the absence of specific therapy, emphasizing the role of the EMB for the diagnosis.

60813
Pharmacological treatment for patients with hypertrophic cardiomyopathy: little evidence, large gaps in knowledge

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Background: Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, with an estimated prevalence of = 2 million patients (pts) in Europe. Despite recent improvements in diagnosis and clinical evaluation of HCM, pharmacological treatment still relies on empirical use of old drugs or extrapolation of data from pts with other cardiac diseases. A comprehensive evaluation of available evidence for pharmacological treatment in HCM is necessary in order to identify gaps in knowledge and guide focused research initiatives.
Methods: Medline search for original articles, reviews and editorials published in english over the last sixty years (1950-2010) were tracked, addressing the use of any drug in HCM cohorts. Sample size, study design and level of evidence were assessed.
Results: A total of 46 studies on pharmacological treatment of HCM were published, with a very modest increase in the last two decades (22 studies between 1990 and 2010; 1 per annum). A total of 2139 pts were enrolled insixty years (35 per annum). Of these 46 studies, 40 were prospective,randomized trials, enrolling a total of 1493 pts (of which only 7 studies assessed acute effects of a drug), and 6 were retrospective, non-randomized observations, enrolling 646 pts in total. The maximum number of pts in a single prospective study was 118. Overall, ten types of drugs have been evaluated in the 46 studies: 41 were single-drug studies, and 5 assessed multiple different agents, including 3 studies with direct comparison of two agents, and 2 with retrospective multiple drug evaluation. With regard to the specific drug employed, 16 studies focused on non-dihydropiridinic calcium channel blockers, 12 on beta-blockers, 8 on dihydropiridinic calcium channel blockers, 5 on amiodarone, 4 on disopyramide, 4 on angiotensin receptor blockers, and 1 each on angiotensin converting enzyme inhibitors, perhexilline and atorvastatin. With regard to the indication, 17 studies addressed efficacy of treatment on outflow tract obstruction, 8 sudden death prevention and ventricular arrhythmias, 10 diastolic dysfunction, 4 microvascular function, 2 myocardial metabolic profile changes and 5 myocardial fibrosis. No prospective outcome study is available.
Conclusions: There is extraordinarily little evidence supporting commonly used pharmacological treatment options in HCM, as compared, for example to implantable devices and surgery. These data call for urgent implementation of adequately designed pharmacological trials based on the large HCM cohorts that are now followed at many international centers worldwide.

60736
Tissue Doppler imaging to predict clinical course in hypertrophic cardiomyopathy. Prognostic role and comparison with other clinical and instrumental variables

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Purpose: Clinical usefulness of echo-Doppler parameters of left ventricular (LV) diastolic dysfunction in hypertrophic cardiomyopathy (HCM) is presently debated. The aim of the study was to assess the value of tissue Doppler imaging (TDI), and in particular of E/E′ ratio, in predicting the clinical course of patients with HCM.
Methods: Eighty HCM patients consecutively observed in our Department from 2000 to 2010 (60% males, mean age 43 ± 19 years) and studied with echo-Doppler and TDI were prospectively included in the study and followed-up for a combined clinical endpoint (cardiovascular death, heart transplantation or septal myectomy). E/E′ ratio was evaluated by ratio of peak E wave velocity at pulsed Doppler transmitral curve and of E′

wave at basal septal TDI. The patients were divided into 2 groups: - group 1: E/E′ >15 (35 patients/44%); - group 2: E/E′ ≤15 (45 patients/66%).
Results: In comparison with group 2, patients of group 1 were significantly older (51 ± 18 vs 37 ± 19, p=0.001), showed more frequently atrial fibrillation (18% vs 2%, p=0.014), a more severe LV hypertrophy (interventricular septum 22 ± 7 mm vs 18 ± 5 mm, p=0.003; posterior wall 14 ± 4 mm vs 12 ± 3 mm, p=0.012), a larger left atrium area (29 ± 9 cm2 vs 22 ± 8 cm2, p=0.001) and more frequently an intraventricular (IV) gradient > 30 mmHg (28% vs 7%, p=0.03). During a mean follow-up of 46 ± 95 months, 9 patients (11%) reached the combined clinical end-point; event-free survival rates were 80% vs 96% in group 1 vs group 2, respectively (p=0.03). At the univariate analysis E/E′ >15 emerged as a risk factor for the combined clinical end-point (HR 11.34, CI 95% 1.41-91.40, p=0.023), together with IV gradient > 30 mmHg (HR 5.52, CI 95% 1.47-20.68, p=0.011), presence of LV dysfunction (HR 9.55, CI 95% 2.55-35.78, p=0.001) and left atrium area for incremental values (HR 1.06, CI 95% 1.01-1.13, p=0.028).
Conclusions: Evaluation of E/E′ ratio at diagnosis is an important tool in identifying patients with a particularly poor prognosis. Elevated values of E/E′ (>15) are probably related to a more advanced stage of the disease.

61012
Coronary flow reserve on left anterior descending coronary artery in hypertrophic cardiomyopathy: impact of extravascular compressive forces

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Background: Microvascular dysfunction reflected by the decreased coronary flow reserve (CFR) is a common finding in hypertrophic cardiomyopathy (HCM). Decreased CFR is recognized as a major mechanism for ischemia which is related with unfavorable long term outcome. Patophysiology of HCM is diverse, including intravascular changes; reduced capillar density, fibrosis, myocyte disarray and structural abnormalities of small coronary vessels. Extravascular compressive forces due to elevated LV filling pressure, wall stress (as a result of diastolic dysfunction) and left ventricle outflow tract (LVOT) obstruction might additionally contribute impairment of CFR. Plasma levels of NT-pro-BNP in HCM correlates positively with cardiac filling pressures and is excellent marker for the abnormal LV wall stress. In addition, the ratio of early transmitral flow velocity to early diastolic lateral mitral annulus velocity (E/e′) has been shown to be accurate noninvasive predictor of elevated LV filling pressure.
Aims: 1.To examine relations between CFR, assessed in left anterior descending coronary artery (LAD) in HCM patients using transthoracic Doppler echocardiography (TTE) with LV mass and LVOT obstruction gradient. 2.To explore relation between microvascular function, plasma levels of NT-pro-BNP and the ratio of E/e′.
Methods: In 61 pts (mean age 48.7 ± 16 years;27 male) with asymmetric HCM, 20 pts with LVOT obstruction and 41 pts without LVOT obstruction, TTE examination with measurement of CFR in LAD was done. CFR was defined as the ratio between maximal velocity of diastolic coronary blood flow during maximal hyperemia (induced by i.v infusion of adenosine 140mcg/kg/min) and at baseline. To estimate LV filling pressures the ratio of early transmitral flow velocity to early diastolic lateral mitral annulus velocity (E/e′) was done.
Results: When HCM pts with LVOT obstruction were compared to HCM pts without LVOT obstruction, first group had lower value of CFR LAD (1.93 ± 0.42 vs 2.22 ± 0.55,p=0.047). In the whole study group CFR LAD was significantly inversely correlated with LVOT obstruction gradient (r=-0.443, p=0.01). CFR-LAD was also inversely correlated with LVmass (r=-0.351,p=0.006) and with E/e′ (r=-0.44,p=0.001). Levels of ln (NT-pro-BNP) were significantly inversely correlated with CFRLAD in the whole study group (r=-0.573,p<0.001).
Conclusion: In patients with asymmetric HCM, coronary microvascular function determined as CFR is significantly inversely related to LV mass. In addition to microvascular dysfunction in HCM patients, extravascular compressive forces additionally aggravate microvascular function.

DILATED CARDIOMYOPATHY

60666
Unusual course of dilated cardiomyopathy

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A 46 year old male, smoker and hypertensive, was diagnosed with occipital ischemic stroke on CT scan. One week before admission he had an episode of impaired visual acuity. On admission, patient was in NYHA class II heart failure. On examination, he had cardiac enlargement, sinus rhythm 90 bpm with few premature beats, BP 120/80 mmHg, 3/6 mitral systolic murmur; he had no pulmonary rales and no peripheral congestion. ECG showed signs of left ventricular hypertrophy, QRS interval of 128 msec, secondary repolarization changes. Echocardiography visualized enlarged left ventricle (LV) with severely impaired systolic function, severe secondary mitral regurgitation, ventricular spontaneous echo contrast, impaired systolic myocardial deformation (figure). Blood tests showed no inflammatory syndrome, normal white blood cell count, no anemia, mild hepatic cytolysis, without hepatic viral B, C, or HIV infection, no thyroid dysfunction. Therefore, stroke was considered embolic in a patient with dilated cardiomiopathy and arterial hypertension. Treatment with beta-blocker, angiotensin receptor blocker, antialdosteron receptor blocker, diuretic, and oral anticoagulation was initiated. Documented unsustained ventricular tahicardia indicated initiation of cronic amiodarone. Surprisingly, after 3 months patient was free of symptoms, with essentially normal echocardiographam. MRI done after 18 months showed normal LV size and systolic LV function, with normal deformation imaging, also confirmed by a repeated echo scan. In conclusion, this is a case of dilated cardiomyopathy, probably postmyocarditic, complicated with systemic embolism (in sinus rhythm). Follow-up of these patients is important since etiology is sometimes a retrospective diagnosis.

60683
Features of baroreflex functions at patients with dilated cardiomyopathy

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The aim: To study the baroreflex regulation (BRR) at the patients with dilated cardiomyopathy (DC) of III-IV NYHA class.
Methods: 17 pts with DC (11 men and 6 women) have been included in research. A complex of inspections: ECG in rest, EchoCG, Holter- monitoring. Baroreflex regulation was estimated by tilt-test application, with the analysis of HRV parametres.
Results: In reply to orthostatic stress the increment of HR at pts with III NYHA class has made 11,4 %, decrease of the systolic BP on 5,6 %; increase of dyastolic BP on 5,3 %. We determinated an increment of HR at pts with IV NYHA class on 2,7% decrease of the systolic BP on 11.2 %; increase of dyastolic BP on 7,3 %. Orthostatic stress authentical reduction of a spectrum of HF-fluctuations is noted at pts with III NYHA class (-39 ± 6,3 vs - 21 ± 4,8, accordingly in groups, p=0,000).
Conclusion: Orthostatic influence at DC pts with IV NYHA class in comparison with III NYHA class affected to a lesser degree on HR, but at the same time considerably reduced the SBP. Authentic decrease in capacity of a high-frequency spectrum of the heart rhythm, expressed at patients with III NYHA class was marked.

60626
Dilated cardiomyopathy of toxic etiology: a potentially reversible entity

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Introduction: Dilated cardiomyopathy is a prevalent entity with different causes, which include the toxic etiology, secondary to drugs, such as cocaine and heroin.
Case report: We describe the case of a 46 year-old woman, active heroin and cocaine addict since her 23 years, hepatitis C virus carrier and with a history of hepatitis B (cured) and pulmonary tuberculosis (7 years ago). Admitted in the emergency room with congestive heart failure, with 4 months of evolution, and progressive worsening. At the objective examination, she was hemodynamically stable, afebrile, with decreased breath sounds at the lung bases, hepatomegaly. She didn't show significant alterations of cardiac auscultation. Analytically, it's worth to accentuate the elevated levels of BNP (3600 pg/mL) and transaminases. A chest computed tomography angiography was performed and showed signs of pulmonary congestion with right pleural effusion, with no signs of pulmonary thromboembolism. No significant changes were observed in abdominal ultrasound. Electrocardiogram showed sinus tachycardia and left bundle branch block. For further evaluation, echocardiography was done and showed a dilated cardiomyopathy with severe left ventricle systolic dysfunction (LVSD), with ejection fraction (EF) of 11%, mild right ventricular dysfunction and 2 small apical thrombi have been identified. Given these findings, a diagnosis of congestive heart failure was made in a patient with dilated cardiomyopathy and ventricular dysfunction of toxic etiology. Anticoagulant therapy was initiated and diuretic therapy was optimized, with favorable evolution. She was discharged on the 5th day of hospitalization, oriented to Internal Medicine and Infectiology consultations and to the Center for Assistance to Drug Users. After six months of total drugs abstinence, she was asymptomatic and with BNP levels <10 pg/mL. The echocardiography revaluation showed normal cardiac chamber size and recovery of biventricular systolic function (EF of 62%).
Conclusion: This case shows the importance of recognizing the toxic etiology associated with dilated cardiomyopathy, since, when properly treated, it is potentially reversible and may have an excellent prognosis.

60149
Heart failure in patient with Becker muscular dystrophy

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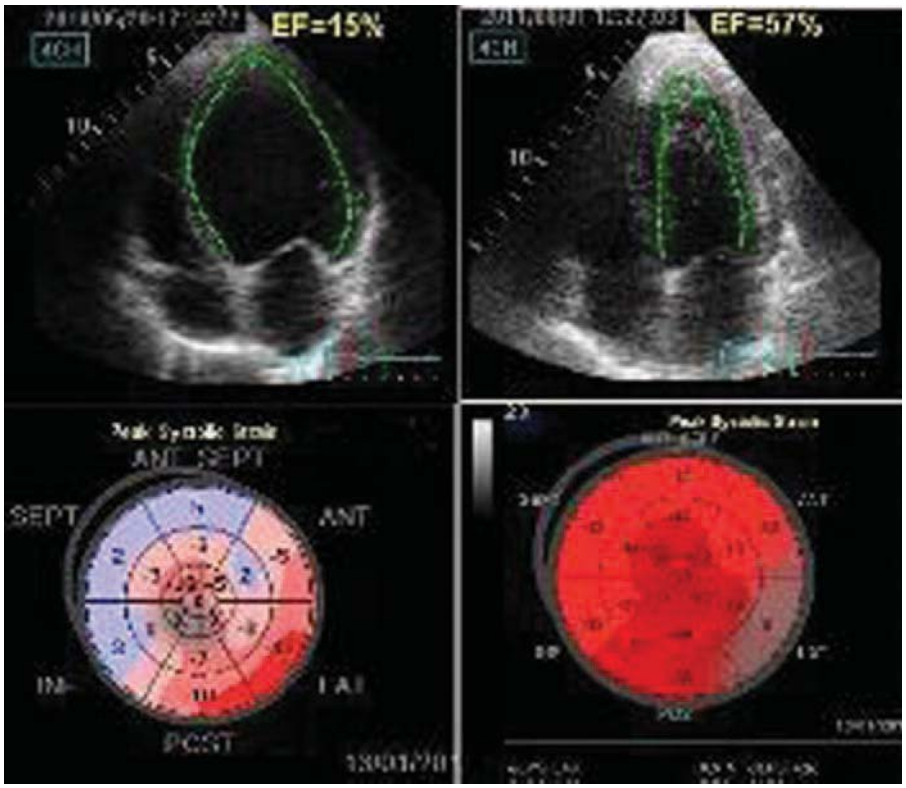
Purpose: This form of X-linked recessive muscular dystrophy results from allelic defects of the same gene responsible for Duchenne dystrophy, with an incidence of about 3 per 100,000 live-born males. Most patients with Becker dystrophy feel first symptoms in the age between 5 and 15, although onset in the third or fourth decade



LV ejection fraction and global strain (Abstract 60666 Figure).

or even later can occur. Cardiac involvement occurs in Becker dystrophy and may result in heart failure.

Case report: A 43-years old male was admitted to our clinic with dyspnea, legs edema, fatigue and weakness. His muscle weakness started when he was 17. Diagnosis of Becker muscle dystrophy was made by muscle biopsy. There was no family hystory of cardiomyopathy or muscle diseases. On admission, his proximal muscles of the limbs seemed to be mildly atrophic, with pseudohypertrophy of calf muscles. The manual muscle test revealed only minimal muscle weakness. The patient was dyspnoic, with pale and distention of jugular veins. Pulmonary rales, apical systolic murmur 3/6°, hepatomegaly and legs edema were noticed. ECG showed nodal rhytm, ventricular heart rate of 64 bpm, ventricular premature beats and negative T waves in I, aVL, V4-V6 leads. The chest radiography revealed generalized cardiomegaly and pulmonary vascular redistribution. Echocardiogaphy discovered enlarged all cardiac chambers with generalized hypocontractility of the left ventricle and ejection fraction of 35%. Doppler echocardiography showed mitral regurgitation 3/4°, tricuspid regurgitation 2-3/4° and pulmonary hypertension of 40 mmHg. Creatine kinase and its MB fraction were in normal range. After management of heart failure he is discharged from our clinic after ten days and he was feeling well three years after hospitalization.

Conclusions: Becker dystrophy is later in onset and slower in progression than Duchenne dystrophy. Most patients remain ambulant into adulthood. Management consists of physical procedures and treatment of heart failure.

60930

Effect of levosimendan on coronary artery flow reserve in patients with idiopathic dilated cardiomyopathy and advanced heart failure

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Levosimendan (L) improves myocardial contractility and also has been shown to increase coronary flow by improving endothelial function. The aim of this study was to assess the effects of L on coronary flow reserve (CFR), as assessed non-invasively by transthoracic Doppler echocardiography, in patients (pts) with advanced heart failure (HF) exclusively due to idiopathic dilated cardiomyopathy (IDCM).

Methods: Twenty-five pts with IDCM, 20 men and 5 women of mean age 61 $\pm$ 12y.o. and normal coronary arteries on catheterization, underwent full transthoracic echocardiographic study and assessment of CFR from the left anterior descending coronary artery (LAD), using a 7MHz transducer. The echo study and the CFR assessment was performed before and within 24 hours after continuous infusion of L, which lasted for 24 hours.

Results: Coronary flow from the LAD was successfully recorded in 24 out of 25 pts. Mean heart rate of the pts before and after L infusion was 78 $\pm$ 10bpm and 82 $\pm$ 11bpm respectively (p=NS). Main echo indices of cardiac performance and CFR before and after infusion of L are seen in Table 1:

Conclusion: Treatment with Levosimendan improves coronary flow reserve, as well as systolic cardiac performance in patients with advanced HF due to IDCM.

Table 1

	BEFORE L	AFTER L	p
EF (%)	22.7 $\pm$ 6.2	26 $\pm$ 7	$<$ 0.05
S (TDI) (cm)	5 $\pm$ 1	6.3 $\pm$ 1.2	$<$ 0.01
CFR	1.7 $\pm$ 0,4	2.3 $\pm$ 0.5	$<$ 0.0001

60287

Quetiapine induced peri-partum cardiomyopathy: a case report and review of the literature

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Introduction: Peri-Partum Cardiomyopathy (PPCM) is a rare and life threateningcomplication of pregnancy.

Case Report: A 43-year-old female, presented to labour ward at 24+6 week'sgestation, complaining of abdominal pain. She had a long history of schizoaffectiveillness and had been on many psychotropic drugs, but was tolerating Quetiapinefor the last year. She had nohistory of ischaemic heart disease and her previous pregnancies showed noevidence of cardiomyopathy.

Both echocardiogram and later a cardiac MRI confirmed a diagnosis of dilatedcardiomyopathy. At 32 weeks gestation the patient unexpectedly had a pulse lesselectrical activity cardiac arrest on the coronary care unit. A peri — mortemcaesarean section was performed. Maternal and neonatal resuscitation wassuccessful.

Conclusion: Quetiapine induced cardiomyopathy is poorly defined with very few cases to report in theliterature. The role of cardiac MRI in the diagnosis of PPCM has bettercharacterised this disease. Cardiac MRI is the gold standard for diagnosing left ventriculardysfunction and provides excellent anatomical information on cardiac morphologynon-invasively. Currently,there is no exact evidence on the risk of PPCM on future pregnancies. As aresult patients need to be counselled when considering another pregnancy and bemanaged with a multidisciplinary team. Further research is required so as to better manage such complex patients effectively.

60436

Registry of dilated cardiomyopathy in the Russian Federation. The first results

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Purpose: To assess the prevalence of dilated cardiomyopathy (DCM) among chronic heart failure (CHF) patients.
Methods: Special questionnaires were sent to the hospitals of 21 regions of Russia, which had agreed to participate in the registry. Questionnaires investigated the number of patients with CHF and DCM. 544 patients with dilated cardiomyopathy were included in the study.
Results: Prevalence of dilated cardiomyopathy among CHF patients was 6.5%. Prevalence of idiopathic dilated cardiomyopathy was 3%. Male had 4 times as much dilated cardiomyopathy as female. The maximum rate of dilated cardiomyopathy (60 %) was in 40-60 years-, 20 % - in 30-40 years- and 10 % on 20-30 years- and 60-70 years —old patients. 4,8% of patients with DCM were in NYHA functional class I, 31,7%, - in NYHA class II, 53,4%- in NYHA class III, and 10%.- in NYHA IV class. Infectious diseases preceded dilated cardiomyopathy in 25.3% of cases. 42.7% of those diseases were viral, 9.2% - had a bacterial nature, etiology was unknown in 48.1% of cases.
Conclusions: 1. Prevalence of dilated cardiomyopathy among CHF patients was 6.5%. 2. Prevalence of idiopathic dilated cardiomyopathy was 3%. 3. Infectious diseases preceded dilated cardiomyopathy in 25.3% of cases (42.7% - viral, 9.2% - bacterial nature).

61087

Stretch induced inflammation in dialted cardiomyopathy. Role of fibroblasts

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Background: The transdifferentiation of fibroblasts to pathological myofibroblasts is known to contribute to cardiac extracellular matrix remodelling favouring increased LV stiffness. This transdifferentiation is triggered by inflammatory cells, which transmigrated into the cardiac tissue. Nevertheless, why these inflammatory cells invade into the tissue is still unkown. Here, we investigate the chemotactic properties of myofibroblasts as a stimulator for cardiac inflammation.
Methods: Endomyocardial biopsies were obtained in regard to inflammation and changes in matrix regulation and the number of myofibroblasts in patients with heart failure. Moreover, a human cardiac fibroblast cell culture system using cells from these heart failure patients was used to investigate the response of the fibroblasts to different stress stimuli like increased stretch (in regard to dilatation) and TGF-beta as inductors of transdifferentiation and the expression of chemokines, migratory activity and induction of inflammatory cell activation were analyzed.
Results: We show here that heart failure patients have increased numbers of myofibroblasts in their endomyocardial biopsies. The amount of myofibroblasts correlated to the total cardiac collagen content. These myofibroblasts express increased amount of extracellular proteins in in vitro studies. Moreover, chemokines were produced by myofibroblasts (CCL2, CCL7 and CCL12). Using supernatant from myofibroblasts in migration assays against inflammatory cells, we could document that the chemotactic properties of myofibroblasts were increased significantly by 200% . Moreover, increased gene expression of adhesion molecules (VCAM-1, +250%) could be documented when endothelial cells were treated with supernatant of myofibroblasts. Furthermore, we show an increased adhesion of inflammatory cells on myofibroblasts (+150%). These inflammatory cells were also activated by the supernatant of myofibroblasts and showed an increase in degradatory activity (increased MMP-2 and MMP-9 expression), allowing for easier transendothelial migration through the basal membrane.
Conclusions: Tissue inflammation modulates matrix remodeling by inducing transdifferentiation of fibroblasts to myofibroblasts, leading to collagen accumulation. Myofibroblasts, known as the main contributor for extracellular matrix proteins were also highly chemotactic active and increased the number of inflammatory cells in patients with heart failure. This makes the myofibroblasts as an inflammatory supporter cell and may be one explanation for cardiac inflammation in heart failure in general.

CARDIOMYOPATHY (OTHER)

60978

A rare cause of dyspnea: an unusual clinical presentation of left ventricular noncompaction

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Female 48 years old, born in Morocco living in Spain for 18 years. As background include grade II obesity and hypertension. The patient was admitted to the emergency room for progressive dyspnea of 10 days duration. Heart rate 115 beats per minute. Jugular venous pressure increased to 45 °. Tachycardia, muffled heart sounds, systolic murmur II / VI mitral, presence of third tone. On auscultation lungs revealed decreased breath sounds.
Electrocardiogram: sinus tachycardia at 115 bpm. Chest radiography: global cardiomegaly. Small bilateral pleural effusion and bilateral interstitial infiltrates.
Transthoracic echocardiography, dilated left ventricle with severe diffuse hypokinesia and severe systolic dysfunction (EF 20%). Picture of possible non-compaction cardiomyopathy. Severe diastolic dysfunction with restrictive pattern. Signs of low cardiac output. Normal right ventricular function, non-assessable. Normal valves with mitral regurgitation and mild tricuspid regurgitation. Moderately dilated left atrium. Normal right atrium.
Cardiac magnetic resonance imaging: dilated left ventricle with generalized hypokinesia and severely depressed systolic function with ejection fraction of 23%. Since the middle segments and to the apex is displayed clearly identified a marked trabeculation and compact myocardium noncompaction myocardium. Their relationship is up to 4.5 cm. The right ventricle is not dilated but has global hypokinesia with depressed systolic function and ejection fraction of 35%. In the sequence of delayed enhancement after gadolinium administration observed no areas suggestive of contrast enhancement. Coronary CT angiography: coronary tree without apparent injury.Increased left ventricular trabeculation mid-level compatible with apical left ventricular noncompaction. Diagnostic: non-compaction cardiomyopathy with impaired left ventricular systolic function severely depressed.
Discussion: Noncompaction cardiomyopathy is a rare disorder caused by disruption of the embryonic process of compaction of the myocardium, between the fifth and eighth week of gestation. This process develops from epicardium to endocardium, from base to apex and from the septum to the lateral wall, this being so frequent locations of compacted myocardium.
The prevalence is 0.014% of the all ETTcompleted, and it is a genetic disorder .Most frequent clinical manifestations include heart failure, atrial and ventricular arrhythmias and thromboembolic phenomena.
The diagnosis is usually established by echocardiography although the gold standard is cardiac magnetic resonance.

60791

Cardiac resynchronization therapy in a patient with amyloid cardiomyopathy

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Background: Cardiac involvement in systemic light chain amyloidosis carries poor prognosis. Amyloid deposition in the myocardium can alter regional contraction and cause mechanical dyssynchrony.
Case report: A 70-year-old male with known systemic light-chain amyloidosis, treated with oral chemotherapy (melphalan and dexamethasone), was admitted to our hospital with progressive dyspnoea and peripheral edema. Symptomatic hypotension prevented the patient to reach target doses for heart failure therapy. Echocardiography revealed dilated left ventricle (LV), thickening of the ventricular walls (14mm) and reduced ejection fraction (EF) with restrictive filling pattern. In addition, intraventricular dyssynchrony was detected using M-mode in a parasternal short-axis view. With the presence of prolonged QRS duration (124 ms) and intraventricular dyssynchrony, cardiac resynchronization therapy (CRT) was considered. After 12 months of CRT increased LVEF and reduction of LV volumes were observed. Intraventricular dyssynchrony was no longer present and paced QRS duration narrowed (120 ms). Furthermore, levels of NT-proBNP lowered and patient's physical condition improved (Table 1).
Conclusion: In patients with amyloid cardiomyopathy, prolonged QRS duration and intraventricular dyssynchrony, improvement of LV function could additionally be achieved by CRT.

Table 1

	Baseline	After CRT
LVESV (ml)	213	173
LVEDV (ml)	274	262
LVEF (%)	22	34
SPWMD (ms)	152	53
NYHA	3	2
NT-proBNP (ng/L)	9890	3094
6-MWT	255	412

CRT:cardiac resynchronization therapy, LVESV: left ventricular end-systolic volume, LVEDV: left ventricular end-diastolic volume, LVEF:left ventricular ejection fraction, SPWMD: septal-to-posterior wall motion delay, NT-proBNP:N-Terminal pro brain natriuretic peptide, 6-MWT: 6 minute walk test.

60887

Impact of obesity on survival and New York Heart Association functional class in patients with systolic heart failure

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Background: Several studies have shown that in patients with heart failure (HF), obesity is not associated with increased mortality, but rather is associated with improved survival. This has been referred to as the "obesity paradox".
Objective: To examine the impact of body mass index (BMI) on survival and New York Heart Association (NYHA) functional class in a Saudi outpatient population with chronic systolic HF.

Method: This retrospective, descriptive study, analyzed data from patients with chronic systolic HF and ejection fraction less than or equal 40% attending a Cardiovascular Disease Management program (CVDMP) over a mean follow-up of 48 months.
Patients were classified according to their baseline BMI. Continuous variables were presented as mean and frequencies while categorical variable presented as percentages.
Risks associated with BMI groups were evaluated using multinomial logistic regression model.
Results: Mortality in the total population (n=903) was 3.3% where 47% were above age of 60 and 77% were male. Significant co-morbidities included; 67% diabetes mellitus, 67% hypertension, 12% Bronchial Asthma, 11% thyroid problems, 6% renal failure and 36% of patients had an EF less than 25%.
BMI showed significant increase in the last follow-up compared to baseline ($p < 0.000$). Obesity, measured by BMI, showed statistical impact on reducing mortality for male group ($p < 0.04$), significant impact on worsening NYHA functional class ($p < 0.023$).

Sample description

Age	mean age 59 ± 12 SD
Gender	77% Male
Diabetic	67%
Hypertension	67%
Renal failure	6%
Thyroid problems	11%
ACE/ARBs	97%
B.Blockers	95%
Aldactone	35%
Ischemic cardiomyopathy	68%

60203

Correlation of echocardiographic parameters changes with changes in endomyocardial biopsies of the patients with inflammatory cardiomyopathy

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Background: Endomyocardial biopsy (EMB) is currently considered to be the gold standard of in vivo diagnostics of inflammatory cardiomyopathy (ICM). In a certain part of the patients with ICM is seen spontaneous improvement in echocardiographic parameters. We expect inflammatory changes retreat in the myocardium in such cases. Exact answer whether this is indeed the case can give only control EMB.
Aim: Evaluation of changes in echocardiographic parameters and their correlation with changes in the number of infiltrating cells between the initial and follow-up endomyocardial biopsies.
Patients and Methods: There were evaluated 28 patients with recently incurred left ventricle dysfunction with biopsy-proven myocarditis. After initial diagnostic EMB was performed in 6-month interval control EMB, at the same time points were performed echocardiographic examinations. There were used paired T-test to compare changes in individual parameters and Spearman coefficient for correlations.
Results: There were observed left ventricle (LV) ejection fraction (EF) improvement from 26 ± 9% to 37 ± 11% ($p < 0.001$), reduction in LV systolic dimension (SD) from 57 ± 11 mm to 51 ± 12 mm ($p < 0.001$) and LV diastolic dimension (DD) from 65 ± 10 mm to 61 ± 11 mm ($p < 0.01$), respectively. In the EMBs was found decrease of infiltrating leukocytes (LCA+ cells) number from 20 ± 9 to 14 ± 7 cells/mm2 ($p < 0.01$) and decrease of infiltrating T-lymphocytes (CD3+ cells) number from 6 ± 4 to 3 ± 2 cells/mm2 ($p < 0.001$). Decrease in the number of infiltrating LCA+ cells significantly correlated with the change of LV EF ($R = - 0.41$; $p < 0.05$) and with the change of LV DD ($R = 0.37$; $p < 0.05$); decrease in the number of CD3+ cells correlated with the change of LV DD ($R = 0.47$; $p < 0.05$) and with the change of LV SD ($R = 0.43$; $p < 0.05$).
Conclusion: In a 6-month follow-up there was found significant decrease in the number of infiltrating inflammatory cells in EMB (both LCA+ and CD3+ cells) and also improvement of LV function and size. Change in the number of infiltrating cells was associated with the change of LV EF and LV dimensions.

60641

The clinical course of patients with tachycardia induced cardiomyopathy is better compared to patients with idiopathic dilated cardiomyopathy

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Background-Purpose: Tachycardia induced cardiomyopathy is a separate clinical entity leading to heart failure. At the present study, the clinical course of patients with tachycardia induced cardiomyopathy is compared to the respective of patients with idiopathic dilated cardiomyopathy of recent onset.

Methods: Eleven patients, age 41 ± 8 years, with tachycardia induced heart failure (heart rate >100bpm on EKG or >80bpm average on Holter EKG) were studied retrospectively. Twelve patients, age 49 ± 12 years, with idiopathic dilated cardiomyopathy, similar NYHA functional classification and Ejection Fraction (EF) comprised the control group. All patients were under optimal medical treatment with a target heart rate of <70bpm and blood pressure <110/70mmHg.
Results: At presentation tachycardia induced cardiomyopathy patients had a significant higher heart rate compared to patients with idiopathic dilated cardiomyopathy (100 ± 17 bpm vs 69 ± 7 bpm, p<0,001). No significant differences in functional classification (NYHA 2 ± 0.6 vs 2 ± 0,5),LV end-diastolic diameter (67 ± 8mm vs 67 ± 5mm), end-systolic diameter (58 ± 10,0mm vs 56 ± 8mm) and ejection fraction (28 ± 7% vs 28 ± 8%) were observed between the control group and the tachycardia induced heart failure group.
At 4-month follow-up, patients with tachycardia induced heart failure presented a greater improvement in functional classification (NYHA 1.3 ± 0.5 vs 1.8 ± 0.5, p<0.03), and ejection fraction (56 ± 37% improvement vs 17 ± 30%, p<0.02).
At 12 month follow-up, NYHA functional classification remained better in patients with tachycardia induced cardiomyopathy (1.3 ± 0.5 vs 1.5 ± 0.5, p=0.62) as well as Ejection Fraction (improvement of 76 ± 40% vs 63 ± 65%, p=0.652), although differences were not statistically important due to small sample size. Patients with tachycardia induced heart failure had borderline normal left ventricular dimensions as well as ejection fraction at 12 month follow-up (60 ± 10/41 ± 12mm and 51 ± 11%, respectively).
Conclusions: Tachycardia induced heart failure is characterized by rapid improvement within months from onset of optimal treatment, amelioration of heart failure symptoms and return to near normal echocardiographic findings within one year. Compared to patients with idiopathic dilated cardiomyopathy of recent onset, a greater and more rapid clinical improvement is observed even though both groups improve significantly under optimal treatment.

60526

Left ventricular changes in patients with acromegaly: echocardiographic study

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Growth hormone (GH) and its tissue effector, IGF-I, exert profound effects on the cardiovascular system, causing structural and functional alterations of myocardium - a condition referred to as acromegalic cardiomyopathy.The aim of this study was the echocardiographic assessement of morfological and functional left ventricular (LV) changes in patients with acromegaly. Material and methods: acromegalic group (AG) consisted 36 acromegalic patients (15male, 21 female), with clinicaly prooved acromegaly, 47.62 ± 11.06 myo. Control group (CG) cosisted 32 healthy patients (12male, 20 female), 43.4 ± 10.42myo. All pts were underwent standard color doppler echocardiography examination. Left ventricular dimensions (EDD, ESD), volumens (EDV, ESV), stroke-index (SI), cardic output (CO), LV-mass index and parameters of LV systolic (EF) and diastolic (E/A) function were assessed during examination.Results: in pts with acromegaly there were statistical significantly increasing LV dimensions, volumens, and mass, decreasing E/A ratio, without changes in EFLV, in relation to control group. The results are showed in Table 1. Conclusion: In patiens with acromegaly there were morfological and functional left ventricular abnormalities, with impaired left ventricular diastolic function.

Table 1

	Acromegaly G	Control G	p <
EDD	5.55 ± 0.80	4.86 ± 0.14	0.004
ESD	3.59 ± 0.81	3.07 ± 0.42	0.001
EDV	155 ± 54.56	112.34 ± 24.01	0.001
ESV	58.89 ± 32.86	38.37 ± 13.24	0.001
SI	48.85 ± 13.05	42.25 ± 10.84	0.05
CO	7.09 ± 2.35	5.52 ± 1.27	0.01
LVmassi	129.73 ± 33.7	89.53 ± 16.02	0.001
E/A	0.90 ± 0.38	1.13 ± 0.36	0.01
EFLV	63.54 ± 10.02	64.12 ± 5.32	ns

Legend in text

60877

Theory of chaos in detecting risk for SCD in ARVD cardiomyopathy

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Purpose: New Task Force criteria in detection of ARVD/C published in 2010 by Marcus et al gave narrower and striker noninvasive parameters that raised sensitivity in establishing diagnosis of this rare condition. We wanted to exolore whether HRV raise sensitivity, specificity and positive predictive value in estimating risk for SCD.

Methods: Out of the total number of 80 positively diagnosed patients, 31 were enrolled based on following study criteria: normal ECG Holter recordings and no medical treatment according to severity of ARVD/C (Group 1, n=14 and Group 2, n=7) and regarding presence (subgroup A) or absence (subgroup B) of late potentials (noise interval between 0,1-0,3 μV). Group 3 (control) consisted of 31 randomly assigned normal subjects. The differences between the 3 groups were assessed by ANOVA followed by Bonferroni's post hoc multiple-range tests.
Results: Standard HRV analysis, showed statistical difference between ARVD/C patients and the control group ($p<0.05$), while groups 1 and 2 did not differ, as well as subgroups A and B ($p>0.05$). Newly applied methods of NLD (SDNN index) showed prevalence of parasympathetic activity (as opposed to sportsmen), which was even more obvious through interpolation of data as % of deviation of Mean NN interval in function % frequency ($p<0.005$).
Conclusion: Complex rhythm fluctuations in ARVD/C patients have repetitive day by day pattern. Furthermore, in combination with late potentials they improve sensitivity, specificity and positive predictive value to detect risk for sudden cardiac death.

61002

Parvovirus B19 genome presence in the myocardium and serological findings in patients with new onset dilated cardiomyopathy

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Background: Parvovirus B19 (PVB19) is the most prevalent cardiotropic virus in the myocardium of patients with dilated cardiomyopathy (DCM). The importance of PVB19 presence in the myocardium is currently often discussed.
Aims: To evaluate PVB19 genome presence in the myocardium of patients presenting with new onset idiopathic non-inflammatory DCM and inflammatory cardiomyopathy (iDCM). To determine whether PVB19 genome presence in the myocardium correlates with serological findings of these patients. To compare PVB19 genome presence in the myocardium in groups of patients with myocarditis and without myocarditis.
Study population and methods: 37 patients (7 women) presenting with new onset DCM, mean age 47.2 ± 9.7 years, left ventricular ejection fraction 25.8 ± 8.3%, mean time of heart failure symptoms duration 3.6 ± 2.9 months were evaluated. Myocardial samples were obtained in all patients using endomyocardial biopsy (EMB). Myocardial samples were histologically and immunohistologically evaluated. Positive immunohistolgical findings were defined by the presence of more than 7 T-lymphocytes/mm^2 and/or more than 14 leucocytes/mm^2. Polymerase chain reaction (PCR) was for PVB19 DNA detection used. PVB19 specific IgM and IgG antibodies in the sera were detected by ELISA method.
Results: PVB19 specific IgG were detected in the sera of 30 patients (81%), positive PCR had 21 patients (56.7%) from the whole study population. Myocarditis was diagnosed in 16 patients (43.2%), noninflammatory DCM was detected in 21 patients (56.8%). Both groups of patients did not differ significantly by PVB19 genome presence in the myocardium. Positive PCR were detected in 10 patients with myocarditis and 11 patients with DCM (p=n.s.). PVB19 specific IgG were detected in 12 patients with myocarditis (75%) and 18 patients with DCM (85.7%) (p=n.s.). No patients had positive PVB19 specific IgM. The sensitivity of serological testing for PVB19 DNA in the myocardium was 95.2%, specificity was 37.5%. Negative predictive value was 85.7% and positive predictive value was 66.5%.
Conclusions: Our findings demonstrate high PVB19 seroprevalence which corresponds with PVB19 DNA presence in the myocardium. PVB19 genome was detected in the myocardium regardless of DCM etiology. This suggests PVB19 persistence in the myocardium rather than its direct relationship with myocardial inflammation.

CARDIO-RENAL SYNDROME

60873

Impaired renal function and ventricular arrhythmia risk in post-infarction heart failure patients

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Purpose: To assess the relation between renal function and ventricular arrhythmia risk in post-infarction heart failure patients.
Methods: A total of 24 post-infarction heart failure patients underwent: 12-lead ECG and signal averaged ECG. The maximal duration of the QT interval in the 12 ECG leads (QTmax), the heart rate corrected QT interval (QTc), the Tpeak-Tend interval (Tpe), late ventricular potentials (LVP) and renal function (glomerular filtration rate: GFR and serum creatinine) were assessed.
Results: QTmax was: 460 ± 53 ms, QTc: 550 ± 78 ms, Tpe: 150 ± 20 ms, serum creatinine: 1.55 ± 0.56 mg/dl, GFR: 79.5 ± 34 ml/min and late ventricular potentials were recorded in 15 (63%) patients. Significant correlations were found between the mentioned ECG parameters and GFR and serum creatinine; the best correlation was between QTc and GFR ($r = -0.696$, $p<0.01$). Linear regression analysis revealed significant associations between renal function and ECG parameters. High prevalence for late ventricular potentials (74%), prolonged QTmax (63%) and QTc (89%) was found in patients with a decreased GFR. Multiple regression analysis revealed a significant association between an impaired GFR and prolonged QTc and LVP (multiple R=0.93, R square=0.87, adjusted R=0.82). Elevated serum creatinine and impaired GFR were predictors of prolonged QT intervals and LVP. The most sensitive predictor of prolonged QTmax, QTc and LVP was GFR<90ml/min (sensitivity=0.85, 95%CI: 0.56-0.97; 0.94, 95% CI=0.71-0.99 and 0.93, 95% CI=0.66-0.99, respectively). The most specific predictor of prolonged QT intervals and LVP were GFR<60 ml/min and elevated serum creatinine, respectively.
Conclusions: Ventricular arrhythmia risk is increased in post-infarction heart failure patients with impaired renal function.

60104

Levosimendan treatment compared with standard therapy improves acute cardio-renal syndrome in acute decompensated heart failure

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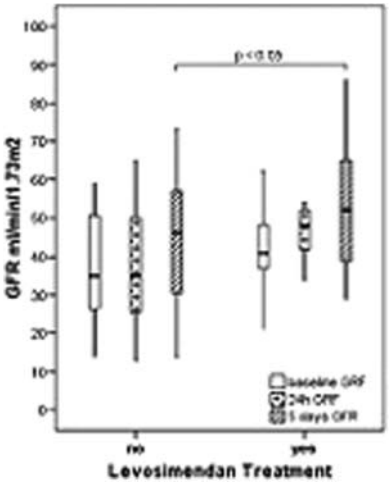
Purpose: Patients with acute worsening of heart function leading to kidney injury and/or dysfunction —acute cardio-renal syndrome (ACRS) - experience higher mortality, morbidity and increased length of hospitalization. There are not agreeing guidelines for managing patients with ACRS. The administration of levosimendan in comparison with standard therapy in acute decompensated heart failure (ADHF) patients with ACRS was analyzed.
Methods: Consecutive patients admitted for ADHF (NYHA class III-IV) were treated with levosimendan infusion (0,1 μg/kg/min) for 24 hours or with standard therapy (digitalis, intravenous furosemide, betablockers, ARAII/ACE inhibitors, spironolactone and intravenous amines and vasodilators when needed). All subjects underwent renal function values determinations (serum creatinine, blood urea nitrogen, 24-h urinary output levels and estimated glomerular filtration rate (GRF) calculated according to the MDRD equation) at baseline, at the end of therapy (24 hours) and five days after therapy.
Results: 21 patients were treated with levosimendan and compared with 19 patients treated with standard therapy. Both groups were similar in age, sex, left ventricular ejection fraction, NT-proBNP, baseline creatinine, GFR levels and cardiovascular risk factors distribution. Renal function indexes (expresed as GFR) at five days after therapy increased (from 43.52 $\pm$ 17.26 to 55.38 $\pm$ 21.15 ml/min/1.73m2; p=0.029) (figure 1) and the length of stay decreased (from 7.7 ± 4.3 to 5.2 ± 1.5 days; p=0.02) significantly in the group of patients treated with levosimendan.
Conclusions: Treatment with levosimendan in ADHF patients seems to provide additional beneficial effects to standar therapy on ACRS. This treatment was associated with a lower length of hospitalization of the patients.



Abstract 60104 Figure

60918

Survival and heart failure therapy in chronic dialysis patients with heart failure with reduced left ventricular ejection fraction

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Background: As the incidence of the cardiorenal syndrome increases, so will the number of patients suffering from heart failure with reduced left ventricular ejection fraction (HFREF) and end-stage renal disease requiring chronic intermittent dialysis. Little is known about the current prevalence, the prognosis and the treatment of these patients.

Methods: In this single-center retrospective study we included 250 patients who started dialysis between 2005 and 2009. This cohort was divided into 2 groups according to left ventricular ejection fraction (LVEF). Patients in group A had a moderately or severely reduced LVEF ($\leq$ 45%). Patients in group B had a preserved LVEF $>$ 45%. Heart failure therapy, all-cause mortality and cardiovascular mortality during chronic dialysis were recorded.
Results: The mean follow-up time was 32,6 months. The prevalence of moderate or severe systolic LV dysfunction was 18% (group A: n=45, group B: n=205). The patients in group A had a significantly worse survival after 12 and 24 months (respectively 68,9% and 55,5% versus 87,3% and 73,0% in group B, p=0,0001). After multivariable analysis, hazard ratio for all-cause mortality was 2,70 (CI 95% 1,6-4,56, p=0,0002). In the subgroup of patients with a LVEF $<$ 30% the hazard ratio increased to 3,45 (95% C.I. 1.71 $-$ 6,94, p=0.0005). Infections were the main cause of death in both groups. The cumulative incidence of cardiovascular death was significantly higher in group A (hazard ratio: 4,78 (95% C.I. 1.99-11,50, p=0.0005), especially in the subgroup with a LVEF $<$ 30% and during the first year of dialysis , due to significant more deaths caused by arrhythmias or heart failure.
In group A 71,1%, 31,1% and 8,9% of the patients received respectively a beta-blocker, ACE-inhibitor and angiotensin-receptor blocker. Only 26,7% of these patients were treated with the combination of a beta-blocker and a RAAS-inhibitor, while 17,8% did not receive any heart-failure therapy. Most heart failure patients only received a low dose of neurohormonal blockers ($\leq$ 25% of the recommended daily dose). The use of these heart failure medications was not significantly different between group A and B.
Conclusions: Almost one in five chronic dialysis patients has heart failure with reduced left ventricular ejection fraction. These patients have a bad prognosis, mainly due to infectious and cardiovascular mortality. Only a minority of these patients receive adequate specific heart failure treatment, in contrast to the current KDOQI-guidelines.

CO-MORBIDITIES (INC COPD, ANAEMIA, CACHEXIA)

60951
Aortic stenosis, heart failure and gastrointestinal bleeding: a clinical case

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Intestinal angiodysplasia and aortic stenosis are chronic degenerative diseases that are often asymptomatic, with a higher prevalence in the population than is clinically apparent. The incidence of both conditions increases with age, and both are associated with traditional cardiovascular risk factors.
A 71-year-old woman, with severe aortic stenosis and hypertension, presented with severe anemia due to recurrent gastrointestinal bleeding of unknown origin and needed repeated transfusion. She presented with chronic heart failure NYHA class II caused by aortic stenosis and anemia. The echocardiography revealed severe aortic stenosis, with a peak aortic pressure gradient of 110 mm Hg, ejection fraction 35%. The endoscopy result was normal. The angiography showed angiodysplasia in the territory irrigated by the first 2 jejunal branches, which were selectively embolized with Gelitaspon. The patient received blood transfusions and intravenous iron. Aortic valve replacement was performed without gastrointestinal bleeding.
Iron deficiency anemia and aortic stenosis are common in elderly, but their association with angiodysplasia and bleeding is not generally recognized. Heyde syndrome, which presents with aortic stenosis and recurrent gastrointestinal bleeding from angiodysplasia, is rare but sometimes life-threatening. Early diagnosis and appropriate treatment of Heyde syndrome is very important and require closer cooperation between specialities.

60147
Cachexia associated with chronic obstructive pulmonary disease, and myocardial repercussions

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Introduction: Chronic obstructive pulmonary disease (COPD) induces cachexia in its final stages, which considerably increases morbidity and mortality. In the present study, the possible effects of cachexia on the myocardium were considered.
Methods: 34 patients (group A, male 21, female 13, age 68 $\pm$ 12 years) with COPD and cachexia were studied using echocardiography. Cachexia was defined as an involuntary loss of body weight by $\geq$ 5% in a period $\leq$ 12 months, and/or a body mass index $<$ 20Kg/m2. Left ventricular mass, ejection fraction, E/Ea ratio and pulmonary artery systolic pressure (PASP) were calculated. 25 patients with COPD and similar demographic characteristics, but without cachexia, constituted control group B. Echocardiographic measurements were compared by the Student's t-test. Known heart disease or other causes of cachexia, apart from COPD, were reasons for exclusion.
Results: Groups A and B had similar PASP values (46 $\pm$ 10mmHg vs 52 $\pm$ 13mmHg). Group A had reduced left ventricular mass (420 $\pm$ 175g vs 530 $\pm$ 188g, p$<$0.01), lower ejection fraction (48 $\pm$ 11% vs 61 $\pm$ 8%, p$<$0.001) and higher E/Ea ratio (16 $\pm$ 4 vs 10 $\pm$ 3, p$<$0.001).
Conclusion: Myocardial involvement in patients with cachexia, due to COPD, is manifested with reduced left ventricular mass, and abnormal indices of systolic and diastolic function.

60144
Anemia management in heart failure patients:data from the obsrvational registry CARMES 1

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Purpose: Anemia and iron deficiency (ID) are frequent, independent comorbidities as well as negative prognostic factors for heart failure (HF) patients (pts).The aim of this study was to observe the prevalence of anemia and ID in hospitalized HF pts, how these comorbidities are treated and which are the results obtained from different therapies.
Methods: We performed a Retrospective Observational Cohort Study of pts with congestive HF admitted to our Dep.of Cardiology and 2 related centers from 1st march 2010 to 30th September 2011.Baseline and follow-up data were obtained from hospital records and telephone contacts. Median follow-up was 6 months. Anemia was defined as hemoglobin $<$12 g/dl in both sexs;ID defined as Iron $<$ 7 mcmol/l and Ferritin $<$100 mcg/l. The primary endpoints were the prevalence of anemia and ID in HF patients at admission and discharge; percentage of patients who reached the target of Hb$>$12 g/dl and/or change in haemoglobin and serum iron levels at 4 weeks after discharge, on the basis of the therapy undergone. The secondary endpoints were mortality and rehospitalization rate at 6 months after discharge.
Results: 418 pts were included in our registry and clinical features are shown in table 1.
Conclusions: It's clear the poor attention paid to identify the cause of anemia, its monitoring over time and its treatment in HF pts. Current therapies, which in any case have an impact on health care costs, are poorly managed and are not sufficiently effective. In fact, only an absolutely insignificant proportion of pts (11%) reach the therapeutic target, and in any case the increase in Hb values does not improve prognosis, especially in terms of re-hospitalization reduction. There is therefore clearly an unmet need, which could be corrected by innovative therapeutic strategies.

Table 1

	Hb admission	Hb discharge	Hb 4 weeks
Anemic pts	10,51 $\pm$ 1,2 (n150/ 418=35,9%)	10,50 $\pm$ 1.02 (n202/ 418=48,3%)	10,51 $\pm$ 0,95 (n118/202=58,4%*)
			*=data not available for all 202 pts
Adverse events	Anemic pts	Non anemic pts	p value
			Rehospitalization at 6 months
24/ 118=20,3%	12/216=5,5%	0,0001	
	Anemic pts on iron therapy	Anemic pts without iron therapy	
			Rehospitalization at 6 months
8/60= 13,3%	16/58=27,6%	0,054	
Mortality at 6 month	7/60=11,7%	30/58=51,7%	0,0001

n=number of patients.
Hb=hemoglobin (g/dl).

60224
Depression in diastolic heart failure

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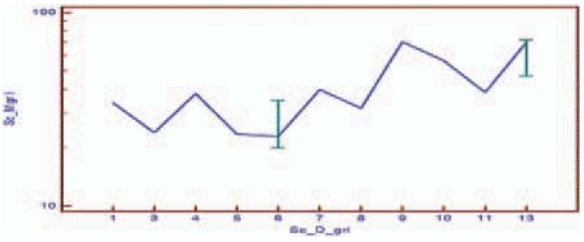
Background: Depression is a prevalent condition in patients with heart failure. To date, there are few studies concerning the depression in patients with diastolic heart failure and preserved ejection fraction.
Purpose: We aimed to evaluate the presence of depression in patients diagnosed with diastolic heart failure.
Material and Method: This case-control survey involved 90 patients hospitalized with heart failure with preserved ejection fraction. Group I consisted of 42 patients diagnosed with depression, while group II consisted of 48 patients without diagnosed depression. The study included 40% men and 60% women. Diastolic heart failure was diagnosed based on echocardiographic criteria. Depression was assessed by scale "Depression " in the questionnaire by F. Fahrenberg. Exercise capacity was measured by distance walked in 6 minutes.Quality of life was assessed by questionnaire Minnesota. Data were analyzed using MedCalc statistical software for Windows.
Results: In univariate statistical analysis, patients with depression showed a significant poorer quality of life and significant higher values for NT-pro BNP and D dimers values,

in comoarison with group II patients. In multivariate analysis, the life quality was independently associated only with the depression score in group I, while in group II- no independent variable was found.
Discussion: Depressive symptoms correlate with poorer quality of life in patients with heart failure. Evidence on whether therapy for depression also improves cardiac outcomes in heart failure patients is inconclusive, and further research on this question is needed.



Independent variables in diastolic HF (Abstract 60224 Figure)

60688
Is anaemia a factor of bad prognosis in acute heart failure?

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Purpose: Anemia has been recognized as a co-morbidity, common and severe, in acute heart failure (AHF), depending on the diagnostic definition, disease severity and clinical characteristics of each patient. In multiple studies have observed an association between anemia and worse prognosis.
Aims: To evaluate the relationship of anemia with the demographic and clinical characteristics in a population with heart failure and determine its prognostic impact by a primary endpoint, defined by death or readmission for AHF and a secondary endpoint defined by mortality, at 6 and 12 months of follow-up.
Methods: A retrospective analysis of 600 patients (51.5% women) admitted to a cardiology service for acute HF. Subdivision into two groups according to the value of hemoglobin (Hb) (GA): anaemic (n = 266) and (GB): not anemic (n = 334), and anemia defined in women with Hb $<$12 g / dl and men with Hb $<$13 g / dl. Conducted follow-up at 6 and 12 months. Statistical analysis using SPSS. Statistical significance at $p \leq 0.05$.
Results: GA has significantly higher age, 78.5 years vs. 76.0 years (p = 0.002). There are no statistically significant differences in relation to gender. GA records higher frequency of blood pressure mean $<$95 mmHg on admission (94.8 mmHg vs. 104.8 mmHg, p $<$0.001), higher BNP levels (945.72 pg / ml vs 679.41 pg / ml p = 0.001) lower natremia values (137.9 mmol /L vs. 140.0 mmol / L, p= 0.002) and higher CRP levels (2.61 mg / dl vs. 2.05 mg / dl, p = 0.021). GA, also, presents lower estimated glomerular filtration rate (MDRD) (49.37 ml /min/1.73 m^2 vs 60.19 mL /min/1.73 m^2, p $<$0.001). Overall, GA presents more complications during hospitalization (p = 0.001) including worsening renal function (25.3% vs 16.5% p = 0.008, HR= 1.717 with 95% CI [1.15 - 2, 57] and longer duration of hospitalization (9.8 days vs. 7.9 days, p = 0.001). GA records the highest rate of mortality at 6 months (10.3% vs 5.2%, p = 0.04, HR = 2.07, CI 95% [1.0-4.3], without reaching differences in primary endpoint (p = 0.09). At 12 months of follow-up, there was a higher mortality rate in GA, but meaningless statistically (p = 0.24).
Conclusion: In the population studied anaemia is associated with higher mortality rate in the short term, however, at 12 months of follow-up, doesn't seem to be a bad prognostic factor.

60922
Burden of impaired pulmonary function and their clinical associates in men with systolic heart failure

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Background: Impaired pulmonary function is often seen in systolic heart failure (HF), however there is little data about its incidence and clinical determinants.
Methods: Spirometry and cardiopulmonary exercise test (CPX) were performed in 204 men with stable systolic HF (age: 57 $\pm$ 11 years, LVEF: 30 $\pm$ 8%, ischaemic aetiology: 49%, NYHA class I/II/III: 56/113/31), none of them had previously diagnosed lung disease and related therapy. Almost all men were taking b-blockers (99%) and ACE inhibitors or ARB (100%). Forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were assessed according to American Thoracic Society/European Respiratory Society Guidelines, and expressed in litre (L) and % of predicted values.
Results: Normal spirometry results (FEV1/FVC$>$70%, FVC$>$80% pred.) was found in 112 (55%) men with HF, only obstructive pattern of breathing (FEV1/FVC$<$70%, FVC$>$80% pred.) in 16 (8%) men with HF, only restrictive pattern of breathing (FEV1/FVC$>$70%, FVC$<$80% pred.) in 49 (24%) men with HF and combination of these two abnormalities (FEV1/FVC$<$70%, FVC$<$80% pred.) in 27 (13%) men with HF. Clinical characteristics of these groups are presented in table.
Conclusions: Impaired pulmonary function is common in men with systolic HF. The presence of restrictive (but not obstructive) pattern of impaired pulmonary function is related to impaired exercise tolerance. Further studies are needed to explain this finding.

Variables	Normal	Obstructive	Restrictive	Obstructive and restrictive
Age, years	56 $\pm$ 12	63 $\pm$ 7	56 $\pm$ 12	60 $\pm$ 9
Ischaemic aetiology of HF, n(%)	50 (45)	10 (63)	23 (47)	16 (59)
LVEF, %	32 $\pm$ 9	32 $\pm$ 6	29 $\pm$ 7*	26 $\pm$ 7**
NTproBNP, pg/mL	516 (176-1219)	700 (276-1632)	1188 (522-2194)***	1701 (735-2728)***
PeakVO2, ml/min/kg	20.8 $\pm$ 5.7	19.7 $\pm$ 5.2	16.4 $\pm$ 4.8***	14.1 $\pm$ 4.0***
Resting heart rate, bpm	78 $\pm$ 13	74 $\pm$ 13	73 $\pm$ 11	77 $\pm$ 16
Peak heart rate, bpm	139 $\pm$ 26	120 $\pm$ 20**	123 $\pm$ 22***	127 $\pm$ 27***
Haemoglobine, g/dL	14.6 $\pm$ 1.1	14.1 $\pm$ 1.0	14.0 $\pm$ 1.3**	14.1 $\pm$ 1.3
hsCRP, mg/L	1.8 (0.7-4.7)	1.4 (0.2-4.4)	4.3 (2.6-8.7)***	1.2 (0.6-4.0)
eGFR, ml/min/1.73	89 $\pm$ 20	77 $\pm$ 22*	88 $\pm$ 26	80 $\pm$ 22
NYHA I/II/III, n	43/57/8	3/11/2	7/28/14	3/17/7

* p$<$0.05, ** p$<$0.01, *** p$<$0.001 (vs. men with normal spirometry results).

60034
Are there any differences between diabetics and non diabetics in chronic heart failure?

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Introduction: The prevalence of heart failure and diabetes are both increasing : 25 to 30 % of patients with heart failure suffer from diabetes, and latter aggravates heart failure. The presence of macro- or micro-angiopathy, cardiac neuropathy or renal failure worsens the clinical pattern and disturbs treatment strategies.
The objectives of our study are to show prevalence of diabetics in heart failure population and to compare epidemiological profiles of diabetics and non diabetics.
Material and methods: We included 1351 patients, diabetics and non diabetics, admitted in united of heart failure in our center of Cardiology from May 2006 to October 2010. All patients were evaluated clinically with monitoring of blood pressure (BP), 6 min walk test and electrocardiogram. Two-dimensional echocardiography and laboratory tests were performed in all patients. Coronarography was realised at 126 patients.
The data are presented as numbers , percentages, and medians with interquartile range.the distribution of variables was compared between diabetics and non diabetics by chi-square test with confidence intervals.
Results: 1351 patients were studied , the median age was 63 years (42- 94 years) and 65 % were men. 367 (27 %) had diabetes. Diabetics patients were younger than non diabetics (56 years and 66 years). Stroke (23% and 18%) and myocardial infarction (37 and 27 %) were more frequent and renal function was more affected in diabetics group. Atrial fibrillation was lower in diabetics group (7 % and 17 %). Ejection fraction of left ventricle was higher (48,5 % and 35 %) in diabetics group , but 51 % of them had diastolic dysfunction with higher filling pressures. There weren't differences in coronarography. Concerning treatment, 34 % of diabetics arrive at maximal beta-blockers treatment (more than non diabetics 16 %). Frequence of decompensation was more important in diabetics group.
Conclusions: So, frequence of diabetes in Moroccan heart failure population is higher. Significant differences exists in comorbidities, ventricular function, maximal beta-blockers treatment and frequence of decompessation between diabetics and non diabetics with chronic heart failure. These findings emphasize the importance of individualised management and need for more comprehensive recruitment of diabetics in clinical trials.

60530
Functional and absolute iron deficiency: are both detrimental on prognosis of heart failure patients?

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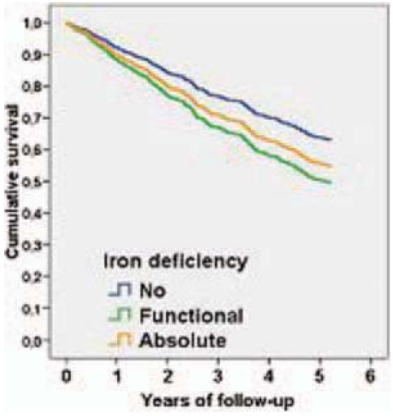
Introduction: Iron deficiency (ID) has shown to worsen prognosis in patients with heart failure (HF). ID can be absolute or functional.
Objective: To assess the prognostic significance of ID (both absolute [defined as ferritin $<$30 μg/L] and functional [defined as ferritin $\geq$ 30 μg/L and transferrin saturation $<$20%]) in a real-life HF outpatient population.
Patients: 878 patients (72% men, median age 70.3 years [IQR 60.5-77.2]) were studied. Aetiology of HF was mainly ischemic heart disease (52.2%). Median LVEF was 34% [IQR 26-43%]. Most patients were in NYHA class II (65.6%) or III (26.3%). Median follow-up was 3.4 years [IQR 1.84-5.04].

Results: ID was present in 452 patients (51.1%), being absolute in 81 (9.2%) and functional in 371 (42.3%). Only 238 patients with ID were anaemic (52.7%). During follow-up 313 deaths were recorded. ID was associated with higher mortality risk (HR 1.48 [IQR 1.18-1.86], p=0.001), specifically in non-anemic population (HR 1.66 [IQR 1.18-2.34, p=0.004]. In the multivariable analysis (backward step), that also included age, sex, LVEF, NYHA functional class, ischemic aetiology, eGFR, and NTproBNP, ID remained in the model. When anaemia was included in the model, ID only remained an independent predictor in non-anemic patients. When absolute and functional ID were analyzed, the latter tended to have worse prognosis (figure) with statistical significance (HR 1.31 [IQR 0.89-1.92], p=0.177 vs HR 1.52 [IQR 1.20-1.93], p<0.001).
Conclusion: ID, mainly functional deficiency, was very frequent in a HF outpatient population of different aetiologies and carried a higher risk of death, specifically in the non-anaemic population.



Cox regression analysis of ID groups (Abstract 60530 Figure)

CYTOKINES AND INFLAMMATION

60392
Different inflammatory response in STEMI patients treated with PCI according the infarction related artery and the role of acute mitral regurgitation

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Background: It is unknown is there any differences between the inflammatory response in STEMI patients according to various infarct-related arteries (IRA) involved.
Methods: Maximal level of CRP measured in acute phase of STEMI patients treated with PCI inside the 12 hours of pain onset were compared between three major IRA territories. Because of the non-normal distribution, CRP levels transformed by the logarithmic transformation (lnCRP). Echocardiographic assessment of left ventrile and mitral function particulary was performed 5 days after admission.
Results: Twohundred and sixty-five consecutive STEMI patients treated with PCI were enrolled in this study [120 (45.28%), 49 (18.49%) and 96 (36.23%) with LAD, RCX and RCA as IRA)]. Mean lnCRP levels in patients with RCX artery were significantly higher than lnCRP of LAD and RCA patients (4.09 ± 0.94 vs 3.58 ± 1.04 vs 3.37 ± 1.10, p<0.001, respectevely). Moderate or severe mitral regurgitation (MR) presented more often in patients with RCX-IRA (42.86% vs 20.83% vs 25.0% for RCX, LAD and RCA, respectively) and significantly contribute to the lnCRP increase in this cohort of patients compare to other two arteries [4.8(4.3-5.3) vs 3.9(2.9-4.9), p=0.024; 3.6(3.0-4.2) vs 4.0(3.3-4.7), p=0.197; and 3.1(2.4-3.8) vs 3.8(2.6-5.0), p=0.382; for the presence of MR in RCX, LAD and RCA, respectively].
Conclusion: Patients with STEMI who have RCX as an IRA have the most pronaunced increase of CRP after succeful mechanical repefusion. The higher incidence of MR in patients with RCX as an IRA, can contribute to this higher inflammatory response.

60218
Peculiarities of chronic heart failure course and prognosis in patients after acute coronary syndrome depending on c-reactive protein level

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Aim: to estimate the value of C-reactive protein (CRP) in course of HF and prognosis of patients after ACS.
Materials and methods: 74 patients with ACS and HF were examined. CRP level of all the patients was measured with the use of high sensitive method. The first stage included single-step clinical examination within the first 3 days from the beginning of ACS course. It included lipid spectrum examination including apolipoproteins, genotypical analysis (genes of protein C, fibrinogen, and apolipoprotein B (ApoB100)), heart systolic function defining with echocardiography and NT-proBNP, assessment of myocardial collagen matrix of LV state with the help of tissue inhibitor of matrix metalloproteinases (TIMP-I) level measuring. The second stage included 2-year examination with endpoints fixation - cardio-vascular death, recurring ACS, CH decompensation.
Results: patients were divided into 2 groups depending on CRP level. The first group included 55 patients (74.3%) with CRP1.1 mg/dL. The average CRP level in the first group made up 0.5+0.3 mg/dL, in the second group - 3.7+2.3 mg/dL (p<0.001). Feedback interconnection of average degree of dependence with CRP level and left ventricle ejection fraction (LV EF) was marked (r= -0.530; p=0.017). Considerably more lower LV EF level of patients with higher CRP level was revealed: 50.2+6.3% vs 54.9+9.3% in the group with normal CRP level (p=0,016). Direct interconnection of average degree of dependence between CRP and NT-proBNP was found: (r= 0.427; p=0.021). Significantly higher NT-proBNP level was marked in the group with higher CRP level: 964.1+464.4 pg/ml vs. 701.4+487.1 pg/ml (p=0.042). Considerably lower ApoA level was marked in the group with high CRP level: 112.1+17.4 mg/dL vs 121.9+18.6 mg/dL (p=0.048). Other lipid spectrum levels didn't have any significant differences depending on CRP. No differences between the groups in the number of patients, who had unfavorable alleles of genes of protein C, fibrinogen and ApoB100 and their combinations in genotype were found. The number of patients with endpoints in the second group was considerably higher than in the first one: 15 (27.2%) vs 11 (57.9%) (p=0.041).
Conclusion: higher CRP level of patients with HF after ACS is associated with more evidently apparent systolic dysfunction and CH (HF severity) according to NT-proBNP, low level of ApoA and bad prognosis. The presence of unfavorable alleles of genes of protein C, fibrinogen, and ApoB100 in genotype is not connected with CRP increase in the ACS onset of CHF patients.

60895
TNF-alpha/TNF- receptor changes in brains of mice with myocardial infarction indicate persistent neuroinflammation

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Background: Acute myocardial infarction evokes production of circulating pro-inflammatory cytokines, including Tumor Necrosis Factor alpha (TNF-alpha). Elevated circulating TNF-alpha levels may enter the brain and induce persisting neuroinflammation. We investigated TNF-alpha and its receptors in brain tissue of mice 2 weeks after myocardial infarction (MI).
Methods: Male 14 weeks old C57 Bl/6 mice were anesthetized and subjected to coronary artery ligation to induce MI or sham surgery. Two weeks later, infarct was verified by ECHO-cardiography, and mice were sacrificed. Heart and lungs were dissected and weighted. Brain was dissected, homogenated, centrifuged to separate membrane from cytosol fraction and processed for Western blot on TNF-alpha, and TNF-receptors (TNF-R1, TNF-R2) with appropriate antibodies.
Results: Coronary artery ligation induced MI of 26 ± 7 % of left ventricular weight, and heart failure was confirmed by increased lung dry weight (35.2 ± 2.2 vs 30.1 ± 0.7 mg), and reduced fractional shortening (19 ± 3 vs 46 ± 1%). TNF-alpha precursor expression was significantly increased in MI versus sham (9.79 ± 0.60 vs 6.99 ± 0.64 AU) and was associated with higher TNF-R1 (5.92 ± 2.39 vs 1.88 ± 0.36 AU) and lower TNF-R2 expression (0.71 ± 0.61 vs 3.01 ± 0.95 AU). Brain tissue stained for microglia showed increased numbers in paraventricular hypothalamus (22 ± 2 vs 13 ± 1 per high power field), but not in cingulate cortex or thalamus.
Conclusion: Peripheral MI and heart failure in mice induces increased TNF-alpha expression at higher TNF-R1 and lower TNF-R2 expression in the brain. This altered TNF-alpha/ TNF-receptor expression may indicate a persistent pro-inflammatory state. Spatially altered number of microglia may suggest localization of this inflammation.

60350
Mitochondrial DNA is a putative activator of cardiac fibroblast toll-like receptor 9 during myocardial infarction

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Background: Bacterial DNA containing CpG-motifs is recognized by Toll-like receptor 9 (TLR9). Mitochondrial DNA (mtDNA) shares common features with bacterial DNA, and is an endogenous ligand for TLR9. In such, we hypothesize that extracellular mtDNA is increased in myocardial infarction (MI) and thus can activate cardiac TLR9. Therefore we investigated the expression and function of myocardial TLR9.
Methods and results: Plasma levels of mtDNA displayed a rapid, transient elevation during human MI and PCI. In comparison, no mtDNA increase could be detected in PCI treated patients with stable angina pectoris. Furthermore, TLR9 mRNA expression in viable cardiac tissue at 3, 7 and 28 days after induction of murine MI displayed peak levels at day 7 post-MI. Murine cardiac myocytes, fibroblasts and endothelial cells were

also isolated and analyzed for the presence of TLR9. TLR9 mRNA was present in all cell fractions, though robustly higher in fibroblasts. Accordingly, all in vitro studies were performed in adult murine cardiac fibroblasts stimulated with different mtDNA mimicking molecules (i.e. CpG ODN) and assayed for the activation of two classical signaling pathways (NFkB and IRF/IFNβ by detection of TNFα and IL-8, and IFNβ, respectively). First, CpG A, B and C displayed different potencies on cardiac fibroblast signaling, with the most potent being CpG B. Using CpG B the dose-response relationship and temporal profile were assessed. Peak mRNA and protein expression levels (IL-8, TNFα and IFNβ) were seen at 5 hours. Furthermore, a robust dose-response relationship was demonstrated with calculated EC50 values being equal for TNFα, IL-8 and IFNβ. We also demonstrated that CpG B-stimulated increases of TNFα and IL-8 depends on endosomal acidification (a requirement for canonical TLR9 activation) as chloroquine effectively attenuated these responses. Finally, we demonstrated that CpG B exclusively signals through cardiac fibroblast TLR9 as a specific TLR9 antagonist (ODN 2088) completely inhibited activation within a narrow dose-inhibition window.
Conclusion: TLR9 is expressed and functional in the myocardium, and the data suggests cardiac fibroblasts as the most important cellular source. This suggests that mtDNA released upon MI can function as a ligand mediating activation of cardiac TLR9.

CARDIAC RESYNCHRONISATION THERAPY / ICD

60697
Long term survival of patients with congestive heart failure receiving ICD/CRT-D devices in a district general hospital

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Background: There is a shortage of outcome data for patients with congestive heart failure (CHF) receiving implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy—defibrillator (CRT-D) devices treated outside of clinical trials. We report the survival status of 180 CHF patients implanted with ICD and CRT-D devices in a district general hospital between January 2001 and December 2011.
Methods and results: In the study period 108 ICDs and 72 CRT-Ds were implanted. The mean follow-up time was 31 $\pm$ 24 months. Females were 11.4%. Median age was 71 years (range 32-86 years). In 66.2% of patients there was an ischemic substrate. A primary prevention indication was present in 53.8%. Risk factors consisted of: hypertension 50.6%; active cigarette smoking 7.2%; hypercholesterolemia 61%; diabetes 28.9%. Past cardiovascular history included previous PCI 31.3%; previous CABG 21.7%, previous stroke 7.8%. Mean EF was 27 $\pm$ 5.8 %. NYHA class III was present in 44.4% of cases and 5% of patients were in class IV. Medical therapy consisted of beta-blockers 86.1%; RAAS Inhibitors 85.5%; Vitamin K antagonists 30.7%. Hb was 12.8 $\pm$ 1.5 mg/dl; Sodium 137.5 $\pm$ 4.2 mEq/l; Potassium 4 $\pm$ 0.4 mEq/l; Creatinine 1.4 $\pm$ 0.83 mg/dl. Mean QRS duration was 139.5 $\pm$ 33.9 msec. AF was present in 25.9% of patients. The 10-year survival rate was 31.4 %. No difference in mortality was observed between primary and secondary prevention groups. The 10-year appropriate therapy rate was 32.2%. Freedom from hospitalization was 90.1% at one year, 69.5% at 5 years and 38.6% at ten years. Freedom from death or HF hospitalization was 14.1 % at 10 years.
Conclusions: Congestive heart failure treated by optimal medical therapy and ICD/CRT-D devices retains a poor long-term prognosis in the all-comers population treated outside of clinical trials.

60404
Worsening of tricuspid regurgitation after pacemaker upgrade to CRT-D as an additional factor accelerating the heart failure progress and the need of cardiac transplantation - case presentation

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CRT is a recommended method of pacing in patients with advanced heart failure. However, ventricular electrode may jeopardize the tricuspid valve function.
We present a case of 53 years old women with heart failure due to hypertrophic cardiomyopathy, after surgical myectomy at 18 years of age. As we admitted the patient to our department for the first time, she had already had the history of the dual-chamber pacemaker implantation (3 years ago) due to the third degree AV block. 7 months before hospitalization the ventricular electrode was removed because of its injury and upgrade to CRT-D was performed. The postprocedural echocardiography examination showed severe tricuspid regurgitation caused by blockage of the posterior leaflet by defibrillating electrode. Although, the patient had already had the tricuspid regurgitation and some episodes of right heart failure before, both valve insufficiency and symptoms worsened significantly after procedure. Moreover, the patient developed permanent atrial fibrillation. We considered the possibility of epicardial pacing with tricuspid valve repair after ventricular electrode removal or tricuspid valve replacement with surgical electrode fixing behind the biological prosthesis ring. Both procedures seemed to have greater risk than potential benefits. Taking into consideration the increasing number of decompensation and coexisting symptomatic left heart failure we referred the patient to heart transplantation which was successfully performed 3 months later.
As the patient described was pacing dependent and at high risk for sudden cardiac death, there was no doubt she needed CRT-D. Recalling the fact that tricuspid valve injury during device implantation is rare but possible, the decision about referring patient to CRT-D/ICD should be done carefully especially in patients with borderline indications and preexisting morphological or functional tricuspid valve impairment.

60397
Echocardiographic reverse remodeling and normalization of left ventricular systolic function after cardiac resynchronisation therapy in patients with advanced heart failure

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Purpose: Cardiac resynchronisation therapy (CRT) improves cardiac function and structure, heart failure symptoms, quality of life, exercise capacity, and reduces morbidity and mortality in patients with dilated cardiomyopathy and advanced heart failure. The aim of this study was to evaluate the echocardiographic improvement after CRT and its mid-term clinical outcome.
Methods and Results: This study included 57 patients (80% men) with idiopathic dilated cardiomyopathy and standard inclusion criteria (NYHA class III or IV heart failure, left ventricular ejection fraction 35%, QRS 120 ms, and optimal medical therapy). Clinical status and echocardiographic parameters (conventional and tissue Doppler imaging) were evaluated before and 12 months after the CRT. Clinical outcome included all-cause mortality and change in NYHA class. Of the 57 patients included (average age was 59. 9 years), 31 (54%) showed echocardiographic left ventricular reverse remodeling (end-systolic volume decreased more than 15 %) and were responders to CRT. Those patients showed significant ($p<0.01$) improvement in left ventricular (LV) systolic function with statistically significant improvement in left ventricular ejection fraction (LVEF), LV fractional shortening, LV rate of pressure (dP/dt), isovolumetric contraction time, and myocardial performance index. Also, LV end-systolic dimension and end-diastolic dimension significantly decreased ($p<0.05$). Two years after resynchronisation therapy dyssynchrony markers (interventricular mechanical delay, septal-to-lateral wall delay, and diastolic filling time in relation to cardiac cycle length) statistically significantly improved ($p<0.05$) as well. In addition, patients that had good response to CRT had higher survival rate than group of non responders and they statistically improved NYHA class. Normalization of left ventricular systolic function was considered when ejection fraction was >54% at echocardiographic follow-up, and was identified in two responders. This result was probably due to severely impaired LV function of our patients prior to CRT.
Conclusion: Left ventricular reverse remodeling, improvement in heart failure symptoms (change in NYHA class) and higher survival rate of our responders to cardiac resynchronisation therapy are indisputable. Reverse remodeling after CRT is related to improved clinical prognosis. Normalization of the LV function at mid-term follow up is determined by its preserved function prior to CRT. Long-term normalization of the LV function is still to be evaluated, as well as its good predictors.

60790
Effectiveness of cardiac resynchronization therapy in elderly patients: the same benefits for an increasing population?

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Background: Heart failure (HF) affects five million patients each year with both prevalence and incidence increasing with age. Cardiac resynchronization therapy (CRT) has been shown to improve HF symptoms and decrease mortality. Whether age negatively affects response to CRT is currently unknown; this is an important issue, because most patients with heart failure are of greater age.
Purpose: The purpose of the study was to asses the effectiveness of CRT in all whole population and to compare the effects of CRT in elderly patients ($\geq$75 years) with younger patients (<75 years)
Methods: This is a prospective observational study of 65 consecutive scheduled for CRT who underwent clinical and instrumental evaluation before and 12 months after device implantation. All patients were investigated with:
- Clinical evaluation
- Minnesota Living with Heart Failure Questionnaire (MLHFQ) score
- Six minutes walking test (6MWT)
- Plasma BNP measurment
- Electrocardiogram
- Echocardiography
- Device interrogation

CRT was performed in 35 elderly patients (53.8%) and 30 (46.2%) younger patients
An increase of left ventricular ejection fraction (LVEF) $\geq$15% defined echo responder and a reduction at least of one New York Heart Association (NYHA) class defined clinical responder.
Results: Main characteristics of enrolled population were : male 52 (80%), mean age 71.5 $\pm$ 9, III NYHA class 49 (75.4%), ischemic heart disease 34 (52.3%), spontaneous QRS duration 151 $\pm$ 23ms and mean LVEF 264.4 $\pm$ 4.8 %
At 12 months follow-up main significant benefits were:
- Reduction of MLHFQ score (from 40.4 $\pm$ 19.2 to 22 $\pm$ 11.4 $p<.001$)
- Improvement of distance walked during 6MWT ($p<.001$) and NYHA functional class ($p<.001$)
- Spontaneous QRS width shortening (-19.9 ms from baseline. $p<.001$)
- Decrease of plasma BNP levels (-214 pg/ml from baseline. $p=.044$)
- Reduction of diastolic ($p<.001$) and systolic diameters ($p=.004$)
- Improvement of mean LVEF (from 26,6% to 34,6% $p<.001$)

In the elderly group the mean age was 78.5 $\pm$ 2.6 compared with 66.7 $\pm$ 15 years in young group. Clinical baseline characteristics between the 2 groups were comparable.

During follow-up, there was a comparable and sustained improvement according to NYHA class, plasma BNP level, spontaneous QRS width, LVEF and reverse remodelling between elderly and younger patients.
The number of clinical and remodelling responders was comparable and we found no significant differences in unplanned cardiac hospitalizations at 12 months between groups.
Conclusions: This work suggests that the full age range of patients with appropriate indications for implantation can benefits from CRT

60322
Finger plethysmography guided optimisation of cardiac resynchronisation therapy devices in clinical practice

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Purpose: Cardiac resynchronisation therapy (CRT) is an established treatment for chronic heart failure patients who remain symptomatic despite optimal medical therapy. Unfortunately there continues to be up to a 30% non-responder rate. This may be reduced by optimising both atrio-ventricular and inter-ventricular (VV) pacemaker settings. The benefit of the former is better established.
Conventional optimisation is performed with echocardiography to determine cardiac performance at different settings. It is time consuming, requires trained staff and equipment, and there is no universally accepted, standardised methodology. A finometer uses finger plethysmography to reliably and quickly obtain haemodynamic data which may be of value in CRT optimisation. We sought to characterise the additive haemodynamic benefit of VV optimisation using a finometer and to assess whether these changes were mirrored by conventional clinical indices of heart failure management and sustained over time.
Methods: 12 consecutive patients (mean age 67) receiving CRT for heart failure under current UK guidelines were included. Ejection fraction, New York Heart Association (NYHA) functional class, Short Form (SF) 36 survey and n-terminal pro-brain natriuretic peptide (NTpro-BNP) level were documented before CRT implantation, at 6 weeks and 3 months. Finometer haemodynamic assessment was made during echocardiographic VV optimisation, using maximal averaged aortic velocity time integral of 3 cardiac cycles.
Results: At 6 weeks 5 patients (42%) reported a decrease by 1 NYHA class (mean pre-implant class = 3) and 6 patients (50%) had improved SF36 scores which were maintained at 3 months. There was no significant change in NTpro-BNP. Ejection fraction increased by an average of 7% (range -6 to + 35).
Following VV optimisation at 6 weeks, 4 (33%) patients had an additional additive increase in stroke volume of 4-5 mls and 7 (58%) patients had an increase in systolic blood pressure of >3mmHg. Every patient with improved haemodynamic indices following VV optimisation had also experienced an improvement in functional class and / or SF36 score. Every patient had baseline CRT settings changed at the first optimisation appointment, but none were changed subsequently at 3 month follow up.
Conclusions: Our patients' clinical response was comparable to published rates. There were demonstrable improvements in optimisation haemodynamics assessed by finger plethysmography which were associated with functional benefit. This technique is particularly useful when echocardiographic windows are poor. The benefit of additional 3 month optimisation is uncertain.

60653
Mitral insufficiency reduction in advanced heart failure patients: impact of cardiac resynchronization therapy

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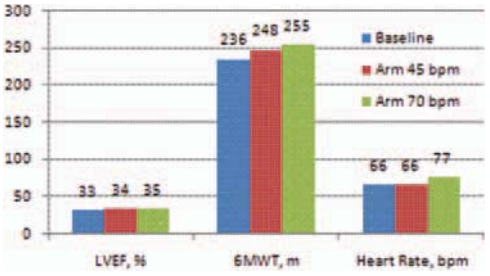
Purpose: Resynchronization of the ventricles leads to reduction of functional mitral regurgitation and to a better clinical profile. We performed this trial to assess positive effects of resynchronization therapy on reduction of mitral insufficiency in our responders' group, as it is shown to be associated with dyssynchrony improvement and left ventricular reverse remodeling after resynchronization at mid-term follow-up.
Methods and results: The trial included 57 patients (80% men) with idiopathic dilated cardiomyopathy and standard inclusion criteria (New York Heart Association class-NYHA class III or IV heart failure, left ventricular ejection fraction $\leq$ 35%, QRS $\geq$120 ms, and optimal medical therapy). Clinical status and echocardiographic parameters (conventional and tissue Doppler imaging) were evaluated before and 12 months after the CRT. Clinical outcome included all-cause mortality and change in NYHA class. Of the 57 patients included (average age was 59. 9 years), 54% showed echocardiographic left ventricular reverse remodeling (end-systolic volume decreased more than 15 %) and were responders to CRT. At twelve month follow-up in responders' group, statistically significant decrease in PISA radius (from 0.64 $\pm$0.15cm to 0.4 $\pm$ 0.25cm, p=0.011) was observed as well as mitral regurgitation velocity-time integral (from 1.3 $\pm$0.4cm to 1.0 $\pm$ 0.5cm, p<0.05), with decrease in PISA (from 2.4 $\pm$ 0.9 cm^2 to 1.8 $\pm$ 1.6cm^2) and the peak velocity of mitral regurgitation (from 4.4 $\pm$ 0.7m/s to 3.9 $\pm$ 0.9m/s). Also, the degree of mitral regurgitation assessed by color Doppler decreased (p<0.01). Improvement of mitral regurgitation was associated with shortening of interventricular mechanical delay (from 60.7 $\pm$ 25ms to 32.5 $\pm$ 28ms, p<0.001) and septal-to-lateral wall delay (from 105 $\pm$ 52ms to 36 $\pm$ 47ms, p<0.001), as was reverse remodeling of left atrium and decrease in left atrium diameters, p<0.05. In addition, all of responders statistically changed NYHA class and improved their clinical status. Survival rate was higher in responders.
Conclusion: Reduction in mitral regurgitation after the resynchronization therapy is associated with left ventricular reverse remodeling and dyssynchrony improvement at mid-term follow up. It is shown to contribute to better clinical status of responders.



Secondary outcomes across study phases (Abstract 60530 Figure)

60281
Prediction of decompensation of heart failure through conjugation of physiological parameters monitored by electronic implantable cardiac devices

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Introduction: Several implantable electronic devices [cardiac resynchronization therapy (CRT) and implantable cardioverter defibrillators (ICD)] monitor physiological parameters that vary previously to the decompensation of heart failure (HF). Therefore, their combination in discriminating algorithms may allow the detection of decompensationprior to the onset of symptoms, allowing timely adjustment of therapy and possibly the improvent of prognosis and the reduction in hospital admissions.
Aim: To identify the combination of physiological parameters with better accuracy in the prediction of HF decompensation.
Methods: Prospective observational study of 47 patients with HF and implanted CRT and ICD. The physiological parameters monitored by the device [(dayly heart rate (DHR) and night (NHR), heart rate variability (HRV), duration of daily activity (DA) and intra-thoracic electrical impedance (TI)] were compared according to the occurrence of symptomatic worsening or hospitalization for HF decompensation. The prognostic impact of physiological parameters in the risk of decompensation was determined by Cox regression analysis and survival analysis Kaplan-Meier method. Considering the thresholds with the best sensitivity-specificity in predicting decompensation, a score predictor of events was determinate.
Results: 47patients were included (81% male, 65 $\pm$ 11 years old, 63% with NYHA functional class I-II, ejection fraction 28 $\pm$ 10%). During the period under monitorization(3177 days) 12 episodes of clinical deterioration and one hospitalization occurred.The DHR and NHR increased in the periods preceding decompensation, while HRV time of DA and TI, gradually decreased. HRV showed the best accuracy in the prediction of decompensation within 30 days (AUC: 0.83), followed by DHR (AUC:0.59), DA (AUC: 0.58) and IT (AUC: 0.42). In a daily analysis, the risk of decompensation was higher in the presence of $\geq$76bpm DHR [Hazard Ratio (HR):2.27] HRV$\leq$40ms (HR: 4.75) and IT $\Omega \leq$60 (HR: 6.53). The risk of decompensation increased with the number of identified criteria (score 1 HR: 3.32, 95%CI 2.388-4.604; p$\leq$0.001), HR = score $\geq$2: 13.49, 95%CI9.524-19.103; p$\leq$0.001) and the predictive accuracy of the prognostic stratification score was high (AUC= 0.75, 95%CI 0.72to 0.77, p$\leq$0.001).
Conclusion: The physiological parameters monitored by the TRC and / or CDI are useful for the monitorization. The combination of DHR, HRV and IT is a powerful predictor of the risk of decompensation and allow the detection of clinical events in the 30 dayspreceding the onset of symptoms.

60490
Effect of programmed heart rate on cardiac function in patients with a cardiac resynchronisation device

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Purpose: Whether it is better to reprogram cardiac resynchronization therapy (CRT) devices to permit or prevent bradycardia in patients with heart failure is uncertain.
Methods: We investigated the effects of reprogramming heart rate of CRT devices either to prevent heart rate dropping below 70 beats per minute (bpm) or below 45 bpm in a double-blind cross-over study with 3 months treatment periods.
Results: Of 63 patients enrolled, the mean age was 64 years and 52 were men (83%). At enrolment, nearly half of patients (n = 31) were in NYHA FC II heart failure (HF), one third (n= 20) were in class III HF and 12 patients (19%) were in class I. Fifty seven patients (91%) completed the$\geq$45 bpm arm, and 54 patients (86%) completed the$\geq$70 bpm arm, 9 patients dropped out before cross-over and 52 patients completed both arms (83%). The mean heart rate was 66 bpm at baseline, 66 bpm and 77 bpm in the low and high rate groups respectively. Symptoms were unchanged during

follow-up. The average 6 minute distance walked at the start of the study was 236 ± 100.6 meters which increased slightly and similarly to 248 ± 101 meters and 255 ± 118 meters in the low and high rate groups respectively. Baseline LVEF was 33.4 ± 9% and increased slightly and similarly to 34.4 ± 9.5% and 34.9 ± 8.8 % respectively.
Conclusions: this study suggests that substantial differences in programmed heart rate do not have a profound overall effect on symptoms, functional capacity or ventricular function in this population. Subtle differences may have been missed due to the modest size of the study and duration of intervention.

60764
Results of a dedicated cardiac resynchronisation therapy optimisation clinic

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Introduction: Cardiac resynchronisation therapy (CRT) is an established therapy for heart failure and dyssynchrony, improving quality of life and prognosis. The challenge lies not only in the implantation of the devices but also in comprehensive follow-up as part of the lifelong management of the patient. Pre-procedural patient factors, device implantation technique and anatomical limitations have an impact on outcome. However, post-implantation programming and optimisation of medical therapies may also have a very significant effect on determining response to CRT.
Method: We report a prospective study of 249 patients (77% male, mean age 71 ± 9 years, 78% ischaemic) undergoing CRT at a single centre. One hundred and forty patients were reviewed in a cardiac physiologist-led optimisation clinic to optimise medications, device programming, percentage biventricular pacing and assess arrhythmias. Each patient was allocated a 30 minute assessment to allow education, titration of medications and optimal device programming. Echocardiographic optimisation, medical assessment, and referral for AV node ablation were available if required. The mean follow-up time was 16 ± 8 months.
Results: CRT-D was implanted in 54% and CRT-P in 46% of subjects. Prior to the cardiac physiologist-led clinic, 69% of patients reported subjective improvement at follow-up whilst 58% had improved by at least one NYHA functional class. Mean ejection fraction improved from 29 ± 8% to 34 ± 11% (p=0.02). At follow-up, 72% of patients had >92% biventricular pacing. One hundred and eight patients had changes made at the optimisation clinic; VV offset was reprogrammed in 42%, AV delay reprogrammed in 4%, base rate or upper tracking rate altered in 3%, and echo optimisation performed in an additional 3%. Thirty percent of patients required same-clinic review by the heart failure specialist nurses or cardiology team, with additional prescription of medications for 26% of patients. Three patients were referred for AV node ablation and one patient was found to have a late lead displacement. The optimisation clinic resulted in 199 patients (79%) reporting improvement (14% NYHA I, 50% NYHA II, 31% NYHA III) and a mean improvement in percentage biventricular pacing of 9%, resulting in 87% of patients with >92% biventricular pacing.
Conclusion: A cardiac physiologist-led CRT clinic allows optimisation of device programming and medical therapy, improving response to CRT from 69% to 79%. These results suggest that all patients should be reviewed in a dedicated CRT-optimisation clinic after device implantation to improve responder rates.

DEVICES

60409
Arterial stiffness at active and standard conducting in patients with chronic heart failure (three year follow-up)

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Purpose: to define the influence of active and standard conducting patients with chronic heart failure (CHF) on rigidity of the arterial wall, clinical condition and the prognosis.
Methods: 211 CHF subjects and 40 healthy subjects were included in the study. Including criteria to the study: CHF symptoms developed after Q myocardial infarction and informed consent of the patients. On admission to the in-patient department the patients were randomized in to 2 groups. The 1st group (106 patients) was managed actively and the 2nd group (105 patients) was managed standart after discharge from the hospital. Monitoring of clinical status and therapy in patients active management group was monitored through telephone contacts with a frequency of 1 time per month, the patients of the standard group was not monitoring. The rigidity of the arterial wall was defined using the arteriograph "TensioClinic, Hungary" with "Tensiomed" program. Statistical processing of the data obtained was performed using software package STATISTICA 8.0. Results were considered statistically significant at p<0,05.
Results: Over three year follow-up actively managed patients demonstrated significant (p<0,05) decrease in systolic and diastolic blood pressure, heart rate, blood serum levels of total cholesterol, a N-terminal prohormone of brain natriuretic peptide, augmentation of 6-minute walk-test distance, left ventricle ejection fraction reduction and number decompensation of CHF as compared to those who were conventionally managed. In the study of arterial stiffness in three years found that patients in group I there is no significant deterioration of the studied parameters. In patients of group II with the first year of reduced time to return the pulse wave (100,3 ± 27,1 to 110,4 ± 30,0, p<0,05) compared with baseline data, the second year of increased systolic blood pressure in the aorta (128,4 ± 22,2 mm Hg and 116,8 ± 10,2 mm Hg, p<0,05) and shortens the time of the expulsion of blood from the left ventricle (290,0 ± 27,0 sec and with 302,8 ± 25,0 sec, p<0,05) compared to the control group. In patients with a standard run with the first year of pulse wave velocity in the aorta (12,1 ± 3,1 m/s and 10,5 ± 2,9 m/s; p <0,05), and augmentation index brachial artery in three years (7,5 ± 20,9% and -3,6 ± 25,2%; p<0,05) higher compared to patients with active management.
Conclusion: One of factors deterioration systolic functions of the left ventricle and the prognosis at patients CHF of group of standard conducting was progressing of infringements of rigidity of the arterial wall.

60671
Predictors of aortic regurgitation after transcatheter aortic valve implantation

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Background: After transcatheter aortic valve implantation (TAVI), aortic regurgitation (AR) is common, usually of mild degree. Little is known about the predictors of this complication.
Purpose: To determine the predictors of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI).
Methods: Sixty four patients (pts) with severe aortic stenosis who underwent TAVI were analyzed. The occurrence of AR was angiographically evaluated after device deployment, and severity determined by Sellers method. Significant AR was defined as AR ≥ 2/4. Several factors were considered as potential predictors of AR after TAVI: clinical and demographic data; aortic annulus diameter assessed by two-dimentional transesophageal echocardiography (TEE) and by multislice computed tomography (MSCT) [maximum diameter — minimum diameter/2]; aortic valve calcium volume assessed by the volumetric method by MSCT; Cover Index (aortic prosthesis diameter - aortic annulus diameter by TEE /aortic prosthesis diameter); and depth of the device in relation to non-coronary and left coronary cusps. Logistic regression analysis was used to identify independent predictors of AR after TAVI.
Results: Post-procedural AR was present in 54 pts (84.4%): grade 1/4 (28 pts; 51.9%); grade 2/4 (14 pts; 25.9%); grade 3/4 (11 pts; 20.4%); grade 4/4 (1 pt; 4%).The incidence of significant AR was 48.1%. The development of significant AR occurred more frequently in male gender (p=0.001), higher previous left ventricle end-diastolic diameter (p=0.042), and higher aortic annulus diameter assessed by MSCT (p=0.01). There was a statistically significant difference regarding the implanted prosthesis diameter: from pts receiving a 29 mm prosthesis (20 pts), most (13 pts) developed significant AR. Using multivariate analysis, only male gender was an independent predictor of AR after TAVI (OR 0.174, 95%IC 0.054-0.574, p=0.004). Lower prosthesis implantation and aortic valve calcium volume were higher in pts with significant AR, although the difference was not statistically significant.
Conclusion: After TAVI, significant AR has a high incidence. Male gender was the only independent predictor of this complication after multivariate analysis. Although the relation between the prosthesis and aortic annulus diameter (Cover Index) didn't achieved statistic relevance in this population, it is crucial to have the exact aortic annulus dimensions in order to choose the right prosthesis size and minimize the occurrence of significant AR.

60846
Percutaneous mitral valve repair in high risk heart failure patients with functional mitral regurgitation: single centre experience

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Purpose: MitraClip implantation is terapeutic option for inoperable or high-risk surgical candidates with functional mitral regurgitation (FMR). We report our single center experience.
Methods: Since October 2008, 63 patients with FMR have been submitted to MitraClip implantation in our centre (51 males, mean age was 68 ± 9.4 years). Functional FMR was ischemic in 46 pts (73%) and idiopathic in 17 pts (27%). All patients underwent standardized assessmet of mitral valve anatomy and functional status; 76.6% pts were in NYHA class III or IV. Preoperative MLHFQ was 39.7 ± 14.6; walked distance at 6-MWT was 186.2 ± 113.2 m. Average LogES was 21.5 ± 14.6%, with 32 pts (50.8%) with a LogES > 20%. Comorbidities included: AF in 35.5%, pulmonary chronic disease in 21%, diabetes in 25.8%, cerebrovascular disease in 9.7%, chronic renal failure in 46.9%.25 pts (39.7%) had a CRT/ICD implanted prior to MitraClip procedure. Average EF was 27.3 ± 9.9%, with 32 pts (50.8%) with an EF< 25%. Left ventricular diastolic andsystolic diameters at baseline were 70 ± 7.5 mm and 54.8 ± 8.8 mm; systolicpulmonary pressure (sPAP) was 46.9 ± 15.5 mmHg. Mitral valve anatomy was assessed by transesofageal echocardiography. Average CD and CL were 1.6 ± 1.5 cm and 3.4 ± 1.2 cm; EVEREST criteria were totally fulfilled in 79.7%.
Results: MitraClip was successfully implanted in all patients; 1 case was converted to open heart surgery because posterior leaflet rupture after implantation. Procedural time (from transseptal puncture to clip delivery system removal) was 104.8 ± 50 min. One

clip was implanted in 18 pts, 2 clips in 41 patients, and 3 clips in4 pts. Overall 30 days mortality was 0%; adverse events included: major vascular complications in 7.1%, blood transfusion in 10.7%, renal replacementtherapy in 5.4%, IABP support in 14.3%, major infections in 3.6%. No cerebrovascular events and AMI occurred. Median length of stay was 4.7 days (1 day median length of stay in the ICU). At discharge 92.2% patients had MR $\leq$ 2+. Freedomfrom MR>2+ at 6 months was 89.1 $\pm$ 4.2%. At 6 months left ventricular EF was 36.6 $\pm$ 11% (p=0.01 compared to preop). Freedom from all cause mortality at 12 months was of 87.7 $\pm$ 5.2%. At latest follow-up 85.3% of FMR NYHA I-II and the MLHFQ was 23 $\pm$ 16.

Conclusions: MitraClip therapy is a valuable alternative to surgery in selected patients with FMR. Although patients treated in current practice are high risk, the procedure remains safe. Longer follow-up is required to confirm these initial statements.

60652

Intermediate results of the reitan catheter pump heart failure efficacy study

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Purpose: The Reitan Catheter Pump (RCP) is an expandable 14F percutaneous circulatory support device. It reduces afterload and increases cardiac index (CI) after implantation in the thoracic part of the descending aorta via the femoral percutaneous access. We report first results of the European study in acutely decompensated chronic heart failure (ADCHF).

Methods: 13 ADCHF patients (65 $\pm$ 9.8 years, 2 female) with need for inotropic and/or mechanical circulatory support were included in the prospective non-randomised multi-centre study. Patients were intensively monitored within first 24h after pump insertion. The device was removed after 24h. Inclusion criteria were left ventricular ejection fraction $<$ 30%, CI $<$ 2.2 l/min/m^2. Study endpoints were CI, pulmonary capillary wedge pressure (PCWP), urine output / serum creatinine, vascular/device related complications and 30-day mortality.

Results: The average CI increased from 1.9 $\pm$ 0.23 l/min/m^2 (before RCP) to 2.3 $\pm$ 0.63 l/min/m^2 after 24 h of RCP support. During RCP treatment there was a significant reduction of PCWP at 4 hours of 21% (27 to 21 mmHg p=0.03). Urine output increased from 63 $\pm$ 56.7 ml/h (baseline) to a maximum of 217 $\pm$ 154.1 ml/h after 12 h of RCP support and was associated with a significant improvement in renal function, reflected by a 21% reduction in serum creatinine at 12 hours (191 to 151 umol/L p=0.003). Two patients being previously rejected from cardiac transplantation underwent successful stabilisation by RCP support. They were reassessed and successfully transplanted within the next months. There were no vascular or device related complications. Two deaths occurred within 30 days (15.4% mortality), one from multi-organ failure and sepsis, and one from intractable heart failure - neither was device related.

Conclusion: In ADCHF patients suffering from acutely decompensated heart failure RCP support was associated with improved hemodynamic and renal function. The RCP may play a role in providing percutaneous cardiovascular and renal support in the ADCHF patients, suggesting renal reversibility in potential cardiac transplant patients. Further data will be reported after completion of the study when 20 patients were included.

SURGERY (CABG, VALVULAR, ARTIFICIAL HEART, OTHER)

60668

Cardiac surgery in patients under chronic hemodialysis

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Background: Open-heart surgery carries a high risk for hemodialysis patients. This study focuses on the short and long-term outcomes of hemodialysis patients undergoing heart surgery.

Material: A total of 56 chronic renal failure patients on hemodialysis therapy underwent some kind of cardiovascular surgery between May 2008 and December 2011. One had a valve abnormality, and the remaining nine had coronary artery disease. All of them were hemodialyzed the day before surgery and 24—48 h after the operation, with Prismaflex CVVHD.

Results: 52 recovered well after surgery, four died of septic shock: one was in terminal congestive heart failure. All operative deaths occurred in the patients who underwent non-elective surgery or were preoperatively in New Heart Association (NYHA) class IV. The factors having an impact on morbidity and mortality seem to be more related to the previous clinical situation and to the urgency of the operation than to the status of chronic renal failure.

Conclusion: An early and adequate assessment of the candidates, when possible avoiding emergency surgery and acute left ventricular dysfunction, as well as careful management during cardiopulmonary bypass procedures (CPB) and the immediate post-surgical period will certainly improve the result of cardiac surgery in these patients, making it similar to those who are not in chronic renal failure.

60518

Is Euroscore II more suitable in patients with low ejection fraction to assess operative mortality risk? Results in a cohort of 3507 patients who underwent Biological Aortic Valve Replacement (BAVR)

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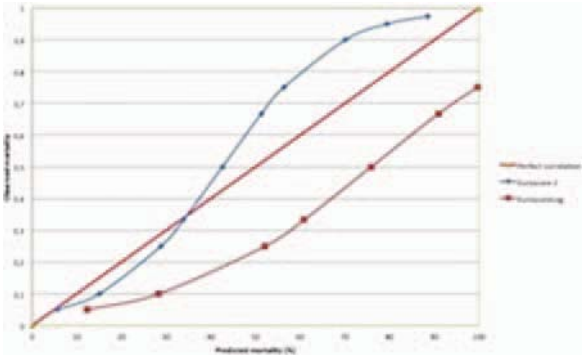
Background: Impaired left ventricular ejection fraction (LVEF) is a well known operative risk factor for aortic valve replacement. Our objectives were to determine the actual operative mortality during BAVR in patients with low ejection fraction in the current era, to evaluate the risk of mortality using the new mortality score Euroscore II and to compare it with the former log Euroscore.

Materiel and Methods: During 2002 and 2010, 3507 consecutive patients (mean age 74.7 $\pm$ 7.6 years; 63.3% of males) underwent BAVR in the same center. Indication for BAVR was aortic stenosis in 83.4% of the cases. A preoperative LVEF$<$50% was found in 12.7% (n=444) of the patients with 9.1%(n=319) of moderate LV dysfunction and 3.6%(n=125) poor LVEF. CABG wasassociated in 43% (n=194) of the patients with LVEF$<$50%. Both log Euroscore and Euroscore II were calculated for each patient.

Results: Mean predicted mortality with log Euroscore and Euroscore II were 14.2 $\pm$ 12% vs 6.3 $\pm$ 8% for patients with LVEF $<$50% and 7.3 $\pm$ 6.3% vs 2.4 $\pm$ 3.1% for patients with normal LVEF respectively.Observed mortalities were 6.5% for patients with LVEF $<$50% versus 2.6%for patients with normal LVEF (p$<$10-4). Graphic relation (fig. 1) between observed and predicted mortalities seems to show a better estimation of the observed mortality in patients with impaired LVEF, despite an underestimation in high scores upper to 30%. By multivariate analysis, risk factors for mortality in the group of patients with impaired LVEF were renal insufisancy (OR=3,35 [1.3-8.7]), non-elective case (OR=3.1 [1,4-6.9]) and cross clamptime (OR=1,01[1,002-1,03]).

Conclusion: Predicting mortality risk in patients with LVEF$<$50% undergoing BAVR by using euroscore II is closer to the observed mortality than the logistic euroscore except in high scores.



Abstract 60518 Figure

60748

The comparison of efficacy and safety of two different antithrombotic regimens in patients with mechanical hearth valve prostheses

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Purpose: Since patients (pts) with mechanical heart valve prostheses are at high risk for thrombosis and systemic embolism, life long oral anticoagulation therapy is recommended in order to prevent these complications. However, this treatment caries the risk of bleeding which can be severe or even fatal. The purpose of the study was to compare the incidence of haemorrhagic and thromboembolic (TE) complications in pts with mechanical heart valve prostheses treated with vitamin K antagonists (VKA) only and combination of VKA and aspirin (ASA).

Materials and methods: Total of 205 pts with mechanical heart valve prostheses have been included (124 at aortic, 63 at mitral position and 18 pts with both valve prostheses), age range 18-86 years, mean age 63.7. They have been followed up for the period of 1697 patients years (pts/yr) - between 4 months to 32 years 9 months. VKA only group consisted of 163 pts and 42 pts received combined treatment - VKA +ASA 100 mg daily. Target INR for aortic valve was 2.0-3.0, for mitral and both valve prostheses was 2.5-3.5. Prothrombin time - INR was determined from capillary blood. INR controls have been performed at outpatient anticoagulant clinic on regular basis and presence of treatment complications was documented.

Results: During the follow up 87 (0.05%/yr) hemorrhagic complications occurred, 53 (0.06%/yr), 24 (0.04%/yr) and 10 (0.05%/yr) in aortic, mitral and both valve groups respectively. No statistically significant difference in the incidence of haemorrhagic complications between VKA only and VKA+ASA group (0.03%/yr vs 0.02%/yr, ns) was found. Thromboembolic complications occurred in 20 (0.01%/yr) cases, 8 (0.009%/yr) in aortic group, 10 (0.02%/yr) in mitral and 2 (0.01%/yr) in both valve group; 14 (0.008%/yr) and 6 events (0.004%/yr) in the VKA only and VKA + ASA group,

respectively. Thromboembolic complications occurred more frequently in VKA only group comparing to VKA + ASA group, but the difference was not statistically significant.
Conclusions: The incidence rates of hemorrhagic complications were found to be similar with both treatment regimens. The combined antithrombotic treatment was slightly but not significantly more efficient in terms of preventing thromboembolic events.

60650
Direct circular repair for left ventricle aneurysm

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Background: Most patients with large left ventricular aneurysm undergo either linear resection of the dyskinetic area or endoventricular patch repair. Both techniques have numerous beneficial effects, but also several adverse ones. In order to avoid these imperfections, direct circular repair (DCR) was created.
Methods: After median sternotomy total revascularization was performed. With inspection the aneurysm localization was marked and the incision was started at the apex of the aneurysm, forwarded toward the border zone with a vital myocardium. For geometric reconstruction, a prolene purse string suture was placed within fibrous sewing ring and pulled to reduce the new created orifice to 1cm. Next, a prolene suture was used over two pericardial stripes to bring the circular cuff together. In case of aneurysmal septal involvement, incision is extended toward the posterior wall, followed by a profound circular suture; so dyskinetic septum is completely excluded. The final continuous over-and-over suture was applied over pericardial strips for definite hemostasis. Including criteria for our prospective study were: severe CAD, large LV aneurysm diagnosed by transthoracic and transoesophageal ultrasound.
Results: From 03/00-12/11, 354 pts with anterior or aneteroapical aneurysm have been operated. Evident haemodynamic improvements were noted: decrease of EDV from 316.5 on 182 ml, ESV from 250 on 102 ml, increase of EF from 20.5% on 37.2%, and CI from 1.8 on 3.2. Valvular reconstructions were performed when indicated. 264pts had been operated under total warm cardioplegia. Mean intubation time was 9 ± 2.3h, mean dosage of cathecholamines was 0.03μcg/kg/min, average inhospital stay $10 \pm 4,6$ days. Early mortality rate was 6.7% (23pts).
Comclusions: Direct circular repair ensures geometric reconstruction of the LV, without use of foreign body after maximal resection and exclusion of the non-viable myocardium. In combination with total myocardial revascularization and valvular reconstruction improves patient's condition with a good clinical benefit.

HEART TRANSPLANTATION

60897
The level of N - gal as a cardiovascular risk marker in heart transplanted patients

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Introduction: Lipocalin-2 (N - gal) is a small stress protein that is foundin the renal tubules and its formation is significantly increased in ischemic kidney lesions. NGAL levels in urine rise in 2 hours of the very first renal injury. NGAL is therefore considered a sensitive and non-invasive indicator of acute renal injury.
The aim of the study was to describe the relationship between levels of NGAL in the urine and cardiovascular risk factors (arterial hypertension, age, obesity, diabetes mellitus, renal disease) in patients after heart transplantation and determining the levels of N - gal in control healthy subjects.
Methodology: A prospective cohort study. Urinary NGAL levels were measured by ELISA - Bio Porto. Data on comorbidities, we obtain the documentation. For cardiovascular risk factors, we consider arterial hypertension (AH), diabetes mellitus (DM), obesity, age and sex. For the purposes of the statistical analysis for each risk factor one point was assigned. For the initial analysis of the suitability of collected data we used descriptive statistics to quantify the interrelationships between variables, we used a correlation analysis. There is a strong statistical significance level $\alpha = 0.05$.
We investigated 52 patients after orthotopic heart transplantation (HTx). The mean age of patients was 53 ± 10, in the control group of healthy subjects 32 ± 6th Mean values and standard deviations of basic indicators are measured in Table 1. The average value of N - gal in healthy subjects was 36 ± 32 ug / l.
Results: Between the values of N - gal and other indicators examined, there is strong statistical dependence.
Conclusion: Values of N - gal in patients after orthotopic heart transplantation are on average four times as compared with healthy subjects. There is no association between N - gal a 'classic' cardiovascular risk. Values of N - gal correlate with the incidence of diabetes and levels of NT Pro BNP.

60443
Heart rate and long term prognosis in heart transplanted patients

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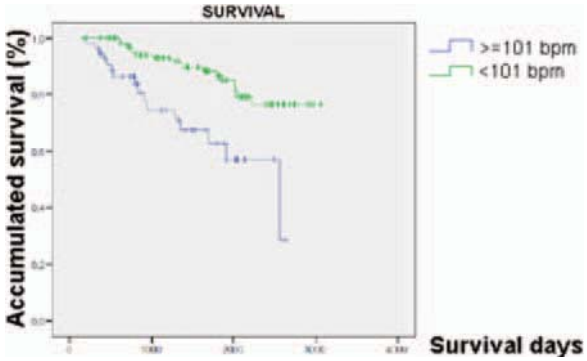
In heart failure, patients with elevated heart rates (HR) have worse long prognosis. Our purpose was to investigate if elevated HR is also harmful in heart transplanted (HT) patients.
Methods: From 2003 until 2010 we recruited 225 HT performed in our center and with a minimum survival of one year. Patients who required pacemaker, cardiopulmonary, pediatrics and re-transplants were excluded. The finally number included in the analysis was 191.
We used the HR obtained by EKG at the year of HT and the survival to make a ROC-curve. The best point under the curve was achieved with 101 bpm. According to this HR (101 bpm) we performed a Kaplan-Meier curve.
Results: 136 patients had at the year of HT $<$101 bpm, and 55 $>=$ 101 bpm. There were no basal differences in boths groups except for primary graft failure, which was more frequent in the $>=$ 101 bpm group (30.9 vs. 17%, p=0.033). Patients with $<=$ 101 bpm had a better long prognosis
Conclusions: Our study shows that HR must be considered as a prognosis factor in HT patients, and further studies must confirm if lowering the HR could be favourable.



Survival rate (Abstract 60443 Figure)

60439
Has the development of metabolic syndrome influence upon the prognosis in heart transplantation patients?

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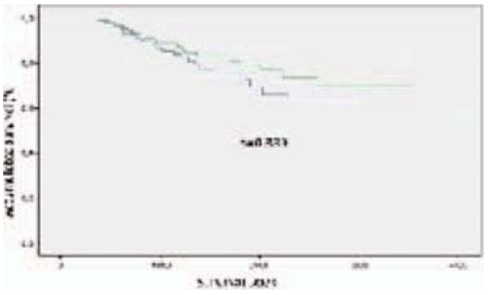
Objective: To study the impact of metabolic syndrome (MS) onset in early stages after heart transplant (HT) over long-term survival.
Materials and methods: 196 patients were studied since 1999 to 2009 with a minimum survival of one year. Three months after HT, MS was diagnosed if the patient met at least three of the following criteria: triglyceride levels 150 mg/mL or treatment for hypertriglyceridemia; cHDL $<$40 mg/dL in men and $<$50 mg/dL in women or pharmacologic treatment to increase levels of cHDL; diabetes mellitus under treatment or fasting basal glycemia levels 100 mg/dL; blood pressure 130/85 mmHg or arterial hypertension under treatment, and a body mass index (BMI) 30. Kaplan Meier (log rank) method was used to calculate long-term survival. T Student and Chi Square method were used for quantitative and qualitative comparisons, respectively.
Results: Among the 196 patients, 96 developed MS and 100 did not. There were no differences in regards to the recipients' gender, pre-HT diabetes, and immunosuppression. Differences were found in age (SM no: 5012 vs. SM yes: 539 years, p=0.001);



Survival rate (Abstract 60439 Figure)

pre-HT creatinine (SM no: 1.020.4 vs. SM yes: 1.210.3 mg/dL, p=0.001), BMI (SM no: 24.554 vs. SM yes: 27.274, p=0.001); pre-HT hypertension (SM no:17 vs. SM yes: 47.9%, p<0.001), dyslipidemia (SM no: 37 vs. SM yes: 53%, p=0.023). Long-term survival was better for those who did not develop MS, but it did not reach significance on the long-term (SM no: 2,900110 vs. SM yes: 2,381110 days, p=0.339)
Conclusions: Early development of MS after HT is an important complication. Nevertheless, prognostic implication of this syndrome over global survival could appear in a very long-term.

DISEASE MANAGEMENT PROGRAMMES

60761
Hypoalbuminemia as a predictor of worst functional capacity recovery in patients attending cardiac rehabilitation after ACS

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Background: Hypoalbuminemia is a negative acute phase protein and a marker of poor prognosis in heart failure and acute coronary syndrome (ACS).
There are no data addressing the relation between hypoalbuminemia and functional capacity (FC).
This study aimed to evaluate the effect of admission serum albumin on the improvement of FC in ACS patients undergoing a cardiac rehabilitation program (CRP), as well as to access the prognostic impact of hypoalbumin in this population.
Methods: 249 consecutive patients were enrolled. Admission serum albumin measurements were collected. FC was measured in metabolic equivalents (METS) achieved during the initial and the final exercise sessions of the CRP. Improvement in FC was evaluated through the METS difference. Post-discharge follow-up was performed to determine the occurrence of a composite outcome (all cause mortality and new hospital admission for ACS, stroke and congestive heart failure).
Results: 222 (89.2%) patients were male and mean age was 53.9 ± 9.9 years. Mean serum albumin was 39.2 ± 7.5 and 56 (22.5%) patients had hypoalbuminemia (≤37mg/dL).
Patients with hypoalbuminemia were older (56.7 ± 10.4% vs. 52.9 ± 9.6%, p=0.012), more often women (19.6% vs. 7.9%, p=0.014) and diabetic (30.4% vs. 16.5%, p=0.023). There were no differences in other cardiovascular risk factors prevalence, admission diagnosis, left ventricular systolic function and severity of the coronary disease. Hypoalbuminemic patients had lower hemoglobin (13.2 ± 2.3 vs. 14.5 ± 1.3 g/dL, p=0.0001) and higher maximum BNP level (294.5 ± 298.2 vs. 155.6 ± 159.9 pg/mL, p=0.0001).
After the CRP, FC improved significantly in both groups: from 5.1 ± 1.4 METS to 8.3 ± 2.0 METS (p=0.0001) in hypoalbuminemia group, and from 5.6 ± 1.4 to 9.5 ± 1.8 METS (p=0.0001) in normoalbuminemia group. However, the degree of improvement was lower in the hypoalbumin group (3.2 ± 1.9 METS vs.3.8 ± 1.6 METS, p=0.033).
Follow-up was possible in 235 (94.4%) patients, for a mean time 24.4 ± 8.3 months. Composite outcome occurred in 23 (9.2%) patients at a mean time of 11.4 ± 8.6 months. After Cox-regression multivariate analysis, adjusted for relevant covariates, hypoalbuminemia was a strong and independent predictor of the composite outcome (HR 5.6, CI 2.0-16.0).
Conclusions: Admission hypoalbuminemia associates with poorer FC recovery and worse outcome in ACS undergoing CRP. A new, inexpensive, functional and prognostic marker might have been found.

60675
Long-term insights on exercise capacities in HF-patients enrolled in exercise based CR in the period between 1999 and 2010

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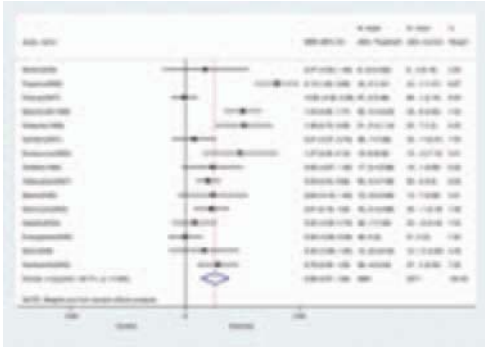
Purpose: Exercise capacities in HF-patients attending exercise based cardiac rehabilitation (CR) were significantly improved in previous meta-analyses without distinction between short- and long-term perspectives. The aim of the following meta-analyses was to evaluate a minimum follow-up of 6 months of exercise capacities in HF-patients attending exercise based CR.
Methods: Randomised controlled trials (RCTs) including HF-patients irrespective of left ventricular function attending exercise based CR in the period between 1999 and Aug 2010 were searched through 5 different databases: Medline, CENTRAL, EMBASE, CINAHL, and PsycINFO. Standard mean differences (SMD) for the exercise capacities measured through 6- minute walk test (6-MWT), exercise-time and -power (Watt), and peak oxygen uptake (PVO2) were calculated in separate meta-analyses. Heterogeneity was assessed by the heterogeneity index (I2). If heterogeneity was significant a random-effect model was applied, where a fixed-effect model was used elsewhere.
Results: Out of 14,875 trials, 15, 9, 10 and 9 trials were found eligible for PVO2, 6-MWT, exercise-time and -power, respectively. The SMD was improved significantly for PVO2 (SMD, 0.67; 95% [CI], 0.37 to 1.00; I2= 82.7%; P< 0.001) (Fig. 1), exercise time (SMD, 0.70; 95% [CI], 0.53 to 0.83; I2= 37.2%; P< 0.001), Watt (SMD, 0.83; 95% [CI], 0.27 to 1.40; I2= 88.6%; P< 0.001), but not on 6-MWT (SMD, 0.81; 95% [CI], -0.02 to 1.63; I2= 97.2%; P= 0.06).
Conclusion: Exercise based CR had significant improved exercise capacities of PVO2, exercise-time and -power in HF-patients participating in exercise based CR.



Forest plot of the CR effect on PVO2 (Abstract 60675 Figure)

61166
Improved clinical outcome in patients followed in a hospital-based heart failure center

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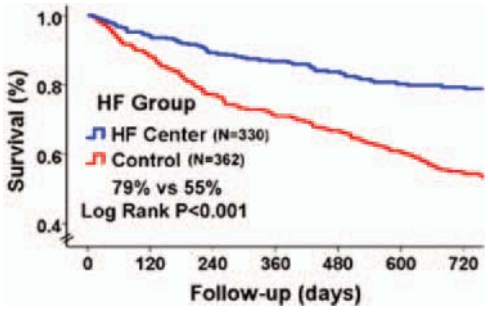
Background: Patients with heart failure (HF) have a poor prognosis. Heart failure centers (HFC) may improve prognosis.
Objectives: To evaluate the clinical outcome of patients with HF treated at a HFC operating in a tertiary referral hospital.
Methods: We evaluated all patients followed at the HFC managed by specialized nurse supervised care for clinical outcome.
Results: 330 patients were included and followed at the HFC. Mean age was 72 ± 1 and 58% were in New York Heart Association (NYHA) class III-IV. 58% had reduced left ventricular function. 54% had ischemic heart disease, 74% hypertension, 44% diabetes, 79% hyperlipidemia and 27% had atrial fibrillation. Mean creatinine was 138 ± 7 μmol/L and mean hemoglobin 11.9 ± 0.1 g/dL. The median follow-up was 792 days (Interquartile range 760 to 823 days). The estimated cumulative survival rate at 1 and 2 years was 87 ± 2% and 79 ± 2% respectively. Survival was influenced by NYHA class (Log rank P<0.01). The estimated cumulative survival rate at 1 year and 2 years were 91 ± 2% and 88 ± 3% in NYHA I-II and 84 ± 3% and 73 ± 4% in NYHA III-IV. Comparing to a similar HF control group from the same hospital before the establishment of the HFC (N=362), demonstrated an improved 2-year survival rate in the HFC: 79 ± 2% vs 55 ± 3%, P<0.001, Figure 1. Cox regression analysis after adjustment for significant predictors demonstrated that treatment in the HFC was a significant predictor of increased survival (Hazard ratio 0.52, 95% confidence interval 0.37-0.73, P<0.0001).
Conclusions: Survival rates of patients followed in a tertiary hospital HFC, including those with severe chronic heart failure, were better than a comparable control group. HFC should be part of the standard treatment of patients with symptomatic HF.



Kaplan Meier Survival in HFC patients (Abstract 61166 Figure)

DIURETICS AND FLUID STATUS MANAGEMENT

60161
Differential mortality association of loop diuretic dosage according to blood urea nitrogen and antigen carbohydrate 125 following a hospitalization for acute heart failure

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Purpose: In heart failure (HF), titration of loop-diuretics remains largely empirical. Recent observations in chronic stable HF, suggest high-dose loop-diuretics (HDLD) have detrimental prognostic effects in high-blood urea nitrogen (BUN) patients, but recent findings have also indicated that diuretics may improve renal function. Antigen carbohydrate 125 (CA125) has shown to be a surrogate of systemic congestion. The aim of this study was to explore whether BUN and CA125 modulate the mortality-risk associated with HDLD following a hospitalization for acute heart failure (AHF).
Methods: We analyzed 1389 consecutive patients discharged for AHF. HDLD ($\geq$120 mg/day in furosemide-equivalent dose) was interacted to a four-level variable according to CA125 ($>$35 U/ml) and BUN (above median), and related with all-cause mortality.
Results: At a median follow-up of 21 months, 561 (40.4%) patients died. HDLD was independently associated to increased mortality [HR=1.23 (1.01-1.50)], but this association was not homogeneous across CA125-BUN categories (p-for interaction$<$0.001). In patients with normal CA125, HDLD was associated with high mortality if BUN was above median [HR=2.29 (1.51-3.46)] but not in those below median [HR=1.22 (0.73-2.04)]. Conversely, patients with high CA125, HDLD showed an association with increased survival if BUN was above median [HR=0.73 (0.55-0.98)] but was associated with increased mortality in those with BUN below median [HR=1.94 (1.36-2.76)]. Conclusions: The risk associated with HDLD in patients after hospitalization for AHF was dependent on the levels of BUN and CA125. The information provided by these two biomarkers may be helpful in tailoring the dose of loop-diuretics at discharge for AHF.

61099

Strong correlation between intra- and transthoracic impedance in patients with chronic heart failure

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Background: Telemonitoring of vital parameters may improve the outcome of patients (pts) with heart failure (HF), but the data to be monitored must be adequately chosen. In fact, many of the parameters currently telemonitored (ECG tracing, blood pressure, body weight etc.) are poorly related to one of the key determinants of clinical events and prognosis in advanced HF, i.e. pulmonary congestion. Many ICD/CRT systems can nowadays detect intrathoracic impedance [Z0(IT)], whose changes with respect to a reference value seem to correlate with pulmonary congestion before symptoms appear. Hence, telemonitoring of intrathoracic impedance is currently being used in some programs of remote management of HF pts, with encouraging preliminary results. However, for a number of reasons many HF pts do not carry a device. Since also the measure of transthoracic impedance [Z0(TT)] and transthoracic conductance (TFC = 1/Z0) allowed prognostic stratification of HF pts in preliminary studies, we investigated whether a relationship existed between intra- and extrathoracic impedance.
Methods: During a 6 months period, we collected data from 50 HF pts carrying a ICD/CRT device with the Carelink function (Medtronic LdTt) [age 73$\pm$9 years; NYHA 2.6$\pm$0.4, EF 29$\pm$6%, BNP 561$\pm$192 pg/ml; optimal treatment]: 25 pts were studied during clinical stability, 25 during system alarms and after appropriate treatment (diurethics and/or vasodilators), so that a total of 75 measurements were obtained. We correlated intrathoracic impedance [Z0(IT)=Ω] and conductance [TFC(IT)=1/Z0(IT)=1/Ω] obtained with the Carelink system, with transthoracic impedance [Z0(TT)=Ω] and conductance [TFC(TT)=1/Z0(TT)=1/Ω] obtained simultaneously with a commercial system (Niccomo LdT).
Results: A strong relationship was found between intra- and transthoracic impedance (R^2=0.62, p$<$0.0001) and between intra- and transthoracic conductance as well (R^2 = 0.64, p$<$0.0001). Morevoer, changes in these variables after treatment were of the same direction and order of magnitude (for ΔZ0 intra- vs transthoracic: R^2=0.59, p$<$0.0001; for ΔTFC intra- vs transthoracic: R^2=0.60, p$<$0.0001). Finally, both intra- and transthoracic impedance were related to BNP levels obtained at the same time (R^2=0.62, p $<$ 0.0001).
Conclusions: Trans- and intra-thoracic impedance are mutually related in pts with chronic HF being telemonitored with the Carelink system, in particular during clinical instability. The value of transthoracic impedance and/or conductance alone, as a non invasive index of impending pulmonary congestion requiring treatment should be tested in the telemonitoring of HF patients.

61157

High furosemide dose is associated with worsening of renal function in patients with chronic heart failure independently of pre-existing chronic kidney disease

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Introduction: Heart failure (HF) patients with clinical signs or symptoms of congestion are routinely treated with diuretics. Despite symptomatic relief, there is still debate concerning the impact of diuretics on long-term prognosis. Deterioration of renal function secondary to high furosemide doses has been traditionally considered as one of the predominant mechanisms by which diuretics may adversely affect outcome.
Objective: To investigate the impact of the prolonged use of high dose furosemide on renal function in patients with stable chronic HF.
Methods: We retrospectively analyzed 173 consecutive HF patients followed in the outpatient HF clinic of our institute, clinically stable (no prior HF related hospitalization in the last 6 months, stable New York Heart Association(NYHA) class and diuretics dose during the past 3 months) with a minimum three year follow-up. Patients were divided into two groups based on the daily dose of furosemide (median dose 80 mg); group A consisted of 70 patients receiving $>$80mg of furosemide daily (high dose group) while group B of 103 patients receiving $\leq$80 mg daily (low dose).
Results: Patients' age, NYHA class, left ventricular ejection fraction, peak oxygen consumption and cardiac index were 56.2 $\pm$ 11.7 years, 2.1 $\pm$ 0.6 , 27.1 $\pm$ 7.3%, 18 $\pm$ 5.1 ml/kg/min and 2.5 $\pm$ 0.9 L/min/m^2 , respectively. In 73% of patients of group A vs 47% of patients of group B renal function worsened during the follow-up period (p=0.002).
The incidence of worsening of renal function during the follow-up period was 66.6% in patients with baseline estimated glomerular filtration rate (eGFR)$<$ 60 mL/min/1.73 m2 vs 50.6% in patients with preserved renal function, irrespectively of furosemide dose (p=0.062).
In the multivariate logistic regression analysis, high furosemide dose ($>$80 mg/daily) was identified as an independent risk factor for developing renal function deterioration during the 3-year follow-up. (Odds Ratio [95% CI]: 2.753 [1.282-5.909], p=0.009).
Conclusion: In patients with clinically stable HF, the prolonged use of high doses of furosemide is associated with worsening of renal function, independently of the prevalence of pre-existing chronic kidney disease

60010

The parabola-shaped relation between inferior vena cava collapsibility and estimated glomerular filtration rate in chronic heart failure treated with diuretics: results from a retrospective study

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Background: In chronic heart failure(CHF), collapsibility index of the inferior vena cava (IVCCI) is used for non-invasive echographic appraisal of central venous pressure(CVP), but it also may be related both to estimated glomerular filtration rate (eGFR) and renal outcome.
Objectives: In CHF patients undergone unloading intravenous (iv) treatment with furosemide(fur) we decided to retrospectively search for possible association between any clinical and hematochemical variables and development of short-term renal worsening; furthermore, we investigated whether a biphasic relation might be detected between eGFR and IVCCI, consistent with that already demonstrated by other Authors between eGFR and invasively measured CVP.
Methods: According to a retrospective cohort design, we analyzed 49 patients with right or biventricular CHF in III NYHA class, undergone iv intensive treatment with fur. Aggravated renal dysfunction (ARD) was defined by serum creatinine (Cr) increase $\geq$ 0,3 mg/dl from baseline. IVCCI was categorized in three layers (IVCCI $\leq$15%, IVCCI 16-40% and IVCCI $>$40%). The possible predictors of ARD were searched for as well as any relation between basal IVCCI and both eGFR at admission and occurrence of ARD.
Results: 15 cases and 34 controls were compared. Multivariate predictors of ARD were a lower basal eGFR (HR: 0,82 CI: 0,72-0,94 p=0,0045) and iv fur daily mean dose$>$80 mg (HR: 48,62 CI: 1,62-3841,5 p= 0,0430). A very significant positive correlation was found between IVCCI $\leq$15% at admission and basal eGFR (r = 0,96 p$<$0,0001),while a negative correlation with eGFR at admission was detected in the IVCCI highest ($>$40%) basal layer (r = - 0,696 p =0,0013). Furthermore, the category with basal IVCCI$>$40% showed a significantly higher rate of ARD compared to that with basal IVCCI 16-40% (p $<$0.05). Besides, in the layer with basal IVCCI estimated equal to 16-40%, the mean value of eGFR at admission was significantly higher with respect to both the layer with basal IVCCI $>$ 40% and the one with basal IVCCI $\leq$ 15% (p$<$0,05 for both).
Conclusions: In right or biventricular CHF pts undergone unloading iv fur therapy , high dosages of fur and preexisting decreased renal function predicted ARD. On the basis of the demonstrated u-shaped relationship between IVCCI and eGFR both the stratum with the highest ($>$40%) and the one with the lowest ($\leq$ 15%)basal IVCCI may be associated with increased risk of ARD.

60152

Effect of transfer from furosemide to torasemide on tolerability in patients with chronic heart failure NYHA II to IV

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Background: The hypothesis was that torasemide, due to more predictable pharmacokinetics/ pharmacodynamics, induces greater improvements in functional and social limitation than furosemide and reduces the frequency of hospitalisations in patients with chronic heart failure (CHF). Patients and methods: Prospective, randomized, unblinded study in 196 patients with CHF (NYHA II-IV), treated with furosemide in the past 6 months who were all transferred to torasemide on top of their concomitant therapy. Endpoints: Clinical efficacy, safety, tolerability, hospitalisations for a period of 6 months.

Results: Clinical improvement was observed in both groups, but the trend to improve by at least one NYHA class was significant only in torasemide- (P=0.014), but not in furosemide-treated patients. There were no differences with regard to adverse events and hospitalisation due to CHF. Overall, tolerability (P=0.0001) and improvement in daily restrictions (P=0.0002) were significantly higher, number of mictions at 3, 6 and 12 h after diuretic intake (P<0.001 at all time points) and urgency to urinate (P<0.0001) significantly lower in torasemide versus furosemide-treated patients.
Conclusion: CHF patients treated with torasemide gain a higher benefit in quality of life than furosemide treated patients, due to torasemide's dual effect on both clinical status and social function.

60153
Torasemide (Trifas) in clinical practice--own experience

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Background: Loop diuretics potently excrete water and electrolytes and therefore have been widely prescribed for the treatment of various kinds of edema for a long time. The potent diuretic action of loop diuretics, however, often causes hypokalemia, and therefore potassium sparing diuretics have also been supplied as a concomitant drug. Chronic heart failure (CHF) is the cause of significant morbimortality all over the world and its incidence and prevalence are increasing. Furosemide is the most commonly used loop diuretic. Torasemide is a loop diuretic belonging to the pyridine sulfonylurea class. It is a high-ceiling diuretic that has a longer half-life, longer duration of action and higher bioavailability compared to furosemide.
Methods: Demographic, clinical, and psychosocial data were collected by questionnaires and medical record review for 196 patients with HF (aged 64,1 ± 11 years, 56 % were male, 60% were in New York Heart Association class III/IV). Medication adherence was monitored objectively for 6 months. Cardiac event-free survival data were obtained by patient/family interview, hospital database, and death certificate review. A series of regression and Cox survival analyses were performed to determine whether medication adherence mediated the relationship between diuretic treatment and event-free survival.
Results: Cardiac event-free survival was worse in patients treated with furosemide than in patients treated with torasemide. Patients treated with furosemide were more likely to be nonadherent and 2 times more likely to experience an event than patients treated with torasemide (P = .017). Diuretic treatment with torasemide led to no change in the potassium levels with time. Diuretic treatment with torasemide was not a significant predictor of event-free survival after entering medication adherence in the model, demonstrating a mediation effect of adherence on the relationship of treatment with torasemide to survival.
Conclusion: Medication adherence mediated the relationship between treatment and event-free survival. It is important to design interventions to increase medication adherence. Torasemide has additional actions such as antialdosterone and vasodilatation effects. Thus, torasemide is recommended for CHF treatment instead of furosemide also because of its safety as far as diselectrolitemia is concerned.

60065
Eplerenone in refractory heart failure

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Background: Aldosterone blockade since RALES(1) for advanced heart failure has extended it use to a less severe forms (2). One of the limitations for its use is the grade of renal dysfunction and hyperkalemia (about 2% of patients) (1,2,3). The close monitoring would expand its use toward the most severe clinical scenarios.
Clinical Case: 85 year-old man with a history of Hypertensive Cardiomyopathy followed for the last 10 years, treated with atenolol and ibersartan. As a mark comorbidity he suffer myelodysplasia that ultimately requires monthly blood-lettings. ECG historically shows frequent monomorphic ventricular ectopies (20000/day) and the echo showed a progressive deterioration of the ejection fraction to 35% in the last 5 years. A first Syncope 2 year ago motivated a CDI- R implantation but the patient has a poor evolution with a decrease to a 18% EF at now and frequent admissions for congestive HF. In the last months he lived with signs of chronic low output syndrome and hypotensive state that forced discontinuation of beta blockers and ARAII. He has a moderate renal dysfunction with clearance of 50 ml/min and 4.7 mmol/l potassium. We decided to initiate eplerenone 25mg daily only associated with 20 mg furosemide and digoxine and two weeks later the patient significantly improved his status with reduction of dysphnea , ortophnea and better skin perfusion.
Discussion: Expanded indications of aldosterone blockade to mild symptomathic patients, maybe should also be consider to the most severe and refractory cases due to its power in the control of symptoms without forget the renal monitoring.
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DRUG THERAPY, OTHER

60226
Ivabradine treatment prevents dobutamine-induced increase in heart rate in patients with acute decompensated heart failure

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Purpose: Heart rate (HR) is a key determinant of myocardial oxygen consumption. There is an association between elevated HR and poor outcomes in heart failure (HF). Dobutamine (DOB) increases HR and myocardial energy consumption, and thereby may precipitate ischemia and myocardial necrosis. Ivabradine, a novel HR lowering agent, has been shown to improve clinical outcomes in chronic HF by reducing HR. The aim of this study was to evaluate the effect of ivabradine on DOB-induced increase in HR.
Methods: Twenty five patients with NYHA III-IV acutely decompensated HF, LVEF <35% and in sinus rhythm who were intended to be treated with DOB were included in the study. All patients underwent holter recording for 6 h before the initiation of DOB infusion. Following baseline recording, DOB was administered at three increasing doses, starting at a rate of 5 μgr/kg/min and up-titrating to 10 and then 15 μgr/kg/min, each step consisting of a 6-h infusion period. Holter monitoring was continued during 18 h of DOB infusion. Ivabradine 7.5 mg was given at the time of the initiation of DOB and readministered at 12 h of DOB infusion in 15 patients (ivabradine group). 10 patients did not receive ivabradine during DOB infusion (control group). Holter recordings were analyzed for mean HR change for each step of study protocol.
Results: There was no significant difference in baseline mean HR between two groups. In control group, mean HR significantly increase during the two highest doses of DOB infusion as compared with baseline mean HR (p=0.008 and p=0.025, respectively), while no significant elevation in mean HR was observed with increasing doses of DOB in ivabradine group (table). Two-way ANOVA analysis also showed a significant change in HR in control group (p <0.01) and no significant increase in ivabradine group.
Conclusions: The results of this study suggested that DOB-induced increase in HR with relatively higher infusion rates was blunted by ivabradine, which may be very important in reducing adverse effects of DOB.

	Control Group Mean HR, bpm	Ivabradine Group Mean HR, bpm
Baseline	81.1 ± 13.8	81.1 ± 15.1
DOB 5 μg/kg/min	87.1 ± 15.2	80.7 ± 15.0
DOB 10 μg/kg/min	92.1 ± 15.6*	83.0 ± 12.5
DOB 15 μg/kg/min	90.5 ± 15.8**	81.7 ± 9.6

*p=0.008 and **p=0.025 compared with baseline.

60479
SUrvey of Guideline Adherence for Treatment of Systolic Heart Failure in Real World (SUGAR)

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Background: In prior studies, clinical practice guidelines developed by several organizations were slowly and inconsistently applied in clinical practice, and certain evidence-based, guideline-driven heart failure (HF) therapies were significantly underused.
Objective: The purpose of this study is to survey the guideline compliance of the cardiologists in the treatment of systolic HF and to investigate the consequence of adherence to care by cardiologists on the rate mortality and hospitalization in Korea.
Method: The SUGAR trial is a multi-center, retrospective observational study on the clinical information of subjects admitted to hospital with systolic heart failure (EF<45%) from 23 university hospitals cross Korean regions (clinical trial registration, NCT01390935). Guideline adherence (GA) was defined as modified validated performance measures on the basis of the 2 or 3 proven pharmacological classes (ACEI or ARB, proven β-blockers and aldosterone antagonist) according to NYHA functional class and GA expressed as mean percentage of prescribed each drug. We divided 2 group as compliance (≥ 50%) and noncompliance group (<50%) based on overall adherence percentage.
Results: We included 1319 patients (male 56.5%, 68.0 ± 13.8 years) which subject to participate in the study recruit regional participants as a representative to standard population distribution from Korean national census in 2008. Adherence of proven drugs at discharge and 1 year was as follows: ACEI or ARB, 87.4% and 71.9%; β-blocker, 65.3% and 56.8%; aldosterone antagonist, 63.0% and 45.1%, respectively. The proportion of compliance group was 85.2% at discharge and 69.2% 1 year. The percentage of target doses at 1 year reached for ACE-I or ARB was 36.2%, for

β-blocker only 7.5%. Overall mortality and rehospitalization at 1 year was 6.9% and 37.3% respectively. In survival analysis by log rank test, there was a significant difference the rate of survival (at discharge, 92.5 vs. 68.5%, p<0.0001 and at 1 year, 93.5 vs. 78.8%, p<0.0001) and rehospitalization (at discharge 50.1 vs. 60.1, p=0.0015 and at 1 year, 45.9 vs. 65.5%, p<0.001) between compliance and noncompliance group.
Conclusions: This trial was powered to provide robust clinical information for guideline adherence for treatment of systolic heart failure in real world. Guideline adherence for prescription of proven drugs was associated with improving clinical outcomes and this result showed further room for improvement of quality care and outcome.

60356
Drug treatment in the elderly with heart failure: where is the evidence?

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Most patients with heart failure are older than 75 years. Unfortunately little evidence based information is available to guide drug treatment in elderly patients. We performed a systematic review to investigate to what extent patients (aged 75 years and older) are included in clinical trials on drug therapy considered the cornerstone of heart failure treatment. All randomised controlled trials assessing the effects of diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, or mineralocorticoid receptor antagonists in chronic heart failure included in the MEDLINE and Embase databases, were eligible when they evaluated either the effect on mortality and hospitalizations ("hard" endpoints) or quality of life ("soft" endpoint) or both. Seventy two different trials including a total of 72,164 patients (mean age 65 years, 27% female) fulfilled the inclusion criteria; 43 trials evaluated mortality/hospitalization (67,528 patients, mean age 65 years, 27% female) and 33 trials evaluated quality of life (14,539 patients, 66 years, 34% female). Four trials evaluated both endpoint categories. None of these studies exclusively included patients of at least 75 years. In only three (3,128 (4.6%) patients) studies evaluating the effect on mortality/hospitalization and two (314 (2.2%) patients) studies evaluating the effect on quality of life the mean age of the participants was at least 75 years. Subgroup analyses in elderly patients were only reported in a minority: 16 mortality trials, 10 hospitalization trials, and 1 quality of life trial. The mean age of patients included in heart failure trials increased slightly (from 62 years before 1990 to 66 years between 2000 and 2010). Although the majority of chonic heart failure patients are older than 75 years they remain largely underrepresented in clinical trials evaluating essential heart failure drugs.

60640
Statin therapy is associated with reduced content of Monocyte-Platelets-Aggregates in patients with aortic stenosis

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Background: An increased platelet activation is known to be associated with the risk of thrombotic events like myocardial infarction, which is known to be one of the main reasons of chronic heart failure. The pro-thrombotic Monocyte-Platelet Aggregates (MPAs) could be identified as reproducible and valid markers of platelet activation. Anti-thrombotic agents like aspirin, clopidogrel and vitamin K antagonists had shown to have contradictory effects on MPA content. Several studies in patients with atrial fibrillation showed a reduction of CD40 expression on platelets due to the use of statins as parameter of reduced platelet activation. In this study we examined the effect of statins on the content of MPAs in patients with severe aortic stenosis.
Methods: Platelet and monocyte activation were determined by flow-cytometric quantification of MPAs and CD 11b (MAC-1) on monocytes in 35 patients with aortic stenosis. The MPA content was detected by co-expression of the platelet specific marker CD 41 and the monocyte marker CD 14. Plasma concentrations of soluble CD40Ligand was measured with the Cytometric Bead Array assay.
Results: Elderly patients with severe aortic stenosis had high levels of MPAs. Patients were divided into two groups depended those with statins (n=19) and those without statins (n=16). There were no differences between the two groups regarding chronic use of aspirin, age, Euroscore and haemodynamic parameters including left ventricular function. Patients on chronic statin therapy had significant reduced circulating MPAs compared to patients without statin therapy (46,3% vs. 60,5%, p<0,05). In patients without atrial fibrillation this difference was even higher (40,7% vs. 61,5%, p<0,01). The use of statins further resulted in a significant lower CD11b expression as marker of a decreased monocyte activation (p<0,05). Furthermore there was a positive correlation of solCD40L with the MPA content (p<0,01) which was also significantly reduced in patients on chronic statin therapy (p<0,01).
Conclusion: Especially elderly patients with severe aortic stenosis have high levels of MPAs and are therefore at high risk of thrombotic events. Beside the known beneficial effect of statin therapy in heart failure and atherosclerosis, chronic statin therapy seems to be able to reduce monocyte-platelet aggregation. The use of statins may have an additional anti-thrombotic effect.

61025
Red-light drugs: using the Delphi method to reach consensus on inappropriate medicines in heart failure

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Purpose: Heart failure (HF) patients may have multiple co-morbidities requiring pharmacotherapy. This is problematic as the literature suggests that a number of commonly prescribed medicines, such as non-steroidal anti-inflammatory drugs and thiazolidinediones, are contraindicated or cautioned for use in HF patients. Therefore the need for a consensus on potentially inappropriate HF medicines was identified.
Methods: A guideline and literature review was carried out in order to select the medications to be considered. A list of 19 potentially inappropriate medicines or medicinal classes was prepared as a questionnaire. The Delphi consensus method was used to assess these medicines. Forty-seven specialists consisting of cardiologists, clinical nurse specialists, general practitioners and pharmacists were approached to participate in the process. Questionnaires were distributed electronically. Each medicine was scored on a Likert scale to establish the likelihood of it causing harm in a HF patient (1 = very unlikely, 5 = very likely). The mean score and 95% confidence interval were calculated for each statement and used to assess whether the medicine was considered likely to cause harm. All analyses were carried out in SPSS v18.
Results: The questionnaire was completed by 22 specialists (46.8%). A consensus was reached on 13 medicines. Eleven potentially inappropriate medicines were agreed upon, 2 were rejected and no consensus was reached on 6 medicines. Medicines and medicinal classes considered likely to cause harm were as follows: non-steroidal anti-inflammatory drugs (mean score = 4.45), COX-2 inhibitors (4.25), metformin in HF patients with poor renal function (4.06), medicinal products with high salt content (4.05), thiazolidinediones (4.00), non-dihydropyridine calcium channel blockers (3.95), decongestants (3.89), oral corticosteroids (3.70), oral beta2-agonists (3.72), pregabalin (3.47) and itraconazole (3.37). Aspirin at doses <300mg daily was considered unlikely to cause harm however there was no consensus reached on aspirin at doses ≥300mg daily. Although metformin in patients with poor renal function and oral beta2-agonists were considered likely to cause harm, metformin in patients with adequate renal function and inhaled beta2-agonists were considered safe in HF patients.
Conclusion: The Delphi consensus method can be used to assess specialist opinion on inappropriate medicines in HF. However some classes of medicine remain controversial including aspirin, beta2-agonists and metformin.

60801
The one-stop heart failure clinic, evidence of improved rates of prescribing evidence-based medical therapy in primary and secondary care

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Purpose: Early treatment with beta-blockers (BB) andangiotensin converting enzyme inhibitors (ACEI) is paramount in patients withheart failure (HF) caused by left ventricular systolic dysfunction (LVSD). Thisis to reduce the high 6-month risk of hospitalisation and mortality. Weestablished a one- stop HF clinic on the 1st May 2009.
Methods: Generalpractitioners (GPs) refer their patients suspected of HF for an echocardiogram.If there is LVSD, the patients are invited to the one-stop HF clinic to beassessed by a HF cardiologist. We evaluated data on all patients with HF-LVSDseen in the clinic between 1st May 2009 and 31st December2009 (group A), and publicised the results locally. A second evaluation wasmade of those seen from 1st January 2010 until 31st July2011 (group B). The management of the two groups was compared to assess servicedevelopment.
Results: There were 229 patients with HF-LVSD seen in the clinic. There were nodifferences between the two groups' gender distribution (64% male). The meanage of the patients was 72.4 years [26-88 years] in group A, and 74 years [24-95years] in group B (NS).
The GP's commenced BB therapy in 46% of group Apatients, and in 54% of group B patients. Similarly, the GP's started ACEI in56% of the patients in group A, and in 61% of the patients in group B. The HFcardiologist added BB to the treatment of a further 25% of group A patients,and to 37% of group B patients. The HF cardiologist introduced ACEI to afurther 21% of group A patients, and to 29% of group B patients. Furtherinterventions (including further investigations) were carried out in 84% ofgroup A patients and to 90% of group B patients
Conclusion: There is evidence of improved rates of prescribing evidence-basedmedical therapy to patients newly diagnosed with heart failure due to leftventricular systolic dysfunction, by primary and secondary care physicians.

HORMONES / NEUROHUMORAL REGULATION

60586
The association of glucagon-like peptide 1 (GLP-1) with resting energy expenditure and endothelial function in chronic heart failure

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Purpose: Glucagon-like peptide 1 (GLP-1), an insulinomimetic and insulinotropic peptide, exerts beneficial effects on cardiac function. In healthy subjects, it is correlated with resting energy expenditure (REE). Elevated REE may be associated with weight loss in patients with chronic heart failure (CHF). We sought to investigate whether GLP-1 and REE are linked in patients with CHF and aimed to examine the interrelationship between GLP-1 and endothelial function in these patients.
Methods: We prospectively enrolled 58 patients with stable systolic CHF (age [mean ± SD] 65.5 ± 11.2 years, male 81%, left ventricular ejection fraction[LVEF] 31.0 ± 6.5%, NYHA class 2.5 ± 0.6, serum creatinine 1.23 ± 0.54 mg/dL) and 21 controls (age 61.5 ± 12.1, male 38%, creatinine 0.80 ± 0.11 mg/dL). Fasting plasma levels of GLP-1 were measured by ELISA. REE was assessed by indirect calorimetry, and its values were compared with predicted REE as calculated by the Harris-Benedict formula and expressed as REE%. Endothelial function was measured by peak forearm blood flow and flow mediated flow (FMF) using strain-gauge plethysmography.
Results: Plasma GLP-1 was detectable in all CHF patients (5.3 ± 4.4, range 2.2-11.8 ng/mL) and all healthy controls (5.2 ± 1.5, range 3.0-7.5 ng/mL). Patients' REE% ranged between 84-142% (108 ± 13%), and was not different in controls (109 ± 12%, range 89-147%, p=0.70), nor did it correlate with GLP-1. REE% was correlated with body weight (r=+0.26), creatinine (r=-0.31), blood urea nitrogen (r=-0.38), and uric acid (r=-0.32), and estimated glomerular filtration rate (r=+0.31, all $p<0.05$). Diabetic CHF patients presented with higher REE% than those without (115 ± 12% vs. 105 ± 13%, p=0.02). Among CHF patients with ischaemic heart disease (n=41), REE% was correlated with GLP-1 (r=+0.32, p=0.04). Patients' GLP-1 correlated with serum sodium (r=+0.28, p=0.04) and chloride (r=+0.27, p=0.04), but not with age, measures of body composition or disease severity (NYHA, peakVO2, 6-minute walk). Patients' peak forearm blood flow ranged from 6.7 to 33.3 with a mean of 17.1 ± 6.7 mL/min/100mL and FMF ranged from 1.2 to 21.1 with a mean of 6.6 ± 4.3 mL/min/100mL. Patients' GLP-1 levels correlated with peak forearm blood flow (r=+0.35, p=0.009), even more strikingly in the ischaemic group (r=+0.45, p=0.005), but not with FMF (r=+0.04, p=0.74).
Conclusions: Clinically meaningful associations exist between GLP-1 and REE%, particularly so in the subgroup of ischaemic CHF patients. Higher basal levels of GLP-1 appear to be associated with better endothelial function. Further studies in larger cohorts are necessary to evaluate these findings.

60419
Chronic heart failure disrupts the physiological age-related decline of serum testosterone

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Background: Low plasma levels of TotalTestosterone (TT) have been reported in patients with Chronic Heart Failure(CHF). It has been hypothesized that hypotestosteronemia might impair exercisetolerance in patients with CHF and appears associated with an adverse outcome .AlthoughTT decline with age in the general population is widely accepted (andropause),no systematic evaluation has been reported regarding TT age-related changes inpatients with CHF.
Methods: 178 male CHF patients and 178 age and BMI-matched male Controls were selected from a large cohort participatingin an Italian multicenter observational trial. TT was detectedby RIA.
Results: Means TT serum level were lower in CHF than Controls (respectively: 395.2 ± 20.2ng/dL vs 437.9 ± 17.4 ng/dL; p=.032).Moreover Testosterone deficit, defined as a serum level less than or equal to 300 ng/dL ,was detected in 26% of CHF patients vs 5% of Controls (p= .002).
Both: A slight increaseper decade (>6%/10 years) of TT levels was observed in CHF patients (see Table 1).
Conclusions: CHF disrupts the physiological age-related decline of TT levels.

Testosterone status in CHF and Controls

	<45 years (n=12)	46-55 years (n=24)	55-65 years (n=58)	>65 years (n=84)
CHF patients TT (ng/dL)	332.2 ± 38.3	353.5 ± 42.8	397.3 ± 40.8	421.5 ± 27.9
Δper decade(%)	(tot +26.8)	+6.3	+12.3	+6.1
Controls TT (ng/dL)	521.2 ± 29.3	475.2 ± 37.5	437.7 ± 42.5	415.5 ± 28.5
Δper decade(%)	(tot -20)	-9.9	-8.0	-5.3

Data shown as mean ± SEM

METABOLISM / DIABETES MELLITUS

60370
In heart failure patients with type 2 diabetes myocardial lipid content correlate inversely with left ventricular function

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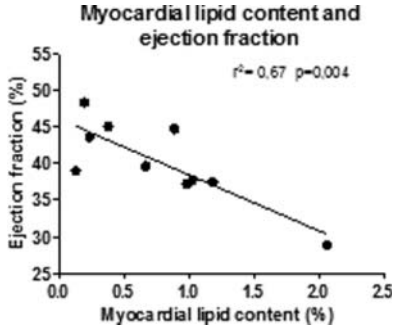
Background: In type 2 diabetic (T2D) patients with normal left ventricular ejection fraction (LVEF) myocardial lipid (MLIP) accumulation is associated with reduced left ventricular systolic strain and diastolic function. It has been suggested that lipotoxicity promotes heart failure (HF) in these patients. It is unknown whether a similar correlation exists in heart failure (HF) patients with T2D. In the present study we investigated whether MLIP content was associated with left ventricular dysfunction in T2D patients with HF.
Methods: 10 patients with T2D, HF (LVEF ≤45%) and NYHA class 2 or 3 were enrolled. To standardize whole body metabolic status all patients underwent a hyperinsulinaemic euglycaemic clamp at plasma glucose of 5-7 mM for 8 hours. MR-proton-spectroscopy was used to measure myocardial lipid content expressed as percentage of myocardial water content. Left ventricular function was determined by speckle tracking, Doppler, tissue Doppler and contrast enhanced echocardiografic evaluation.
Results: P-glucose levels decreased from 10.1 ± 1.4 mM to 5.5 ± 0.2 mM (mean ± SEM) and circulating free fatty acids from 0.45 ± 0.06 mM to 0.05 ± 0.01 mM during the clamp. MLIP content was 0.77 ± 0.19% and LVEF 40 ± 2%. MLIP content correlated inversely with LVEF (r^2=0.67, p=0.004, figure 1) and borderline significantly with strain (r^2=0.34, p=0.08) and Doppler derived measurements of stroke volume (r^2=0.38, p=0.06). No correlation was found between myocardial lipid content and E/A ratio, E/e', Hba1c or fasting plasma glucose levels.
Conclusion: In T2D HF patients MLIP correlated inversely with LVEF. Future studies should investigate whether reducing MLIP content has beneficial effects in TD2 HF patients.



Abstract 60370 Figure

61143
Monoamine oxidase activity promotes oxidative stress and mitochondrial dysfunction in cardiomyocytes exposed to high glucose

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Oxidative stress is well known to occur and contribute to the development of diabetic cardiomyopathy. Mitochondrial respiratory chain and NADPH oxidase are described as major sources of reactive oxygen species (ROS) in this setting. Whether monoamine oxidase (MAO) activity also plays a role in the onset/progression of diabetes-induced cardiac alterations has not been investigated yet. These mitochondrial flavoenzymes are responsible for oxidative stress and cell death in failing and ischemic/reperfused hearts. Here we assessed whether MAO contributes to high glucose (HG) induced cell damage. Neonatal rat cardiomyocytes were cultured in HG (30 mM) for 48 hours in the absence or presence of MAO inhibitor pargyline and compared to those cultured in normal glucose (NG, 5 mM) or high mannitol (HM, 30 mM) containing media. Mitochondrial ROS production, detected by Mitotracker Red, was significantly higher in HG myocytes (+30%, $p<0.005$) as compared to other cells. Pargyline completely prevented this increase. Mitochondrial membrane potential was unchanged under the same experimental conditions. However, when myocytes were co-incubated with ATP synthase inhibitor oligomycin, HG-treated cells started depolarizing immediately, whereas NG- or HM-treated cells were able to maintain their membrane potential longer (> 50 minutes). Pargyline offset this change suggesting that MAO activation triggered by HG induces a latent mitochondrial dysfunction causing mitochondria to hydrolyze ATP. Our data shows that MAO are chiefly involved in redox changes and

mitochondrial dysfunction observed in cardiomyocytes upon exposure to HG. Although in presence of HG MAO expression remains unchanged, it may still amplify ROS generation from other sources and/or HG may directly enhance MAO activity. Both phenomena are likely to be relevant for the onset and progression of diabetic cardiomyopathy.

60373

Depressing of diabetes induced endogenous protective mechanisms in membranes of heart mitochondria due to hypercholesterolemia

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Purpose: It is well documented that diabetes (DIA) induced remodeling of subcellular membrane systems in the myocardium has not exclusively pathological character, it also reflects the outcome of endogenous protective mechanisms (EPM). Aim of the present study is to elucidate those functions of the diabetes (DIA)-remodeled mitochondrial (MIT) membranes, which are associated with EPM in acute DIA hearts, with reference to the impact of additional pathological stimulus such as elevated cholesterol.
Methods: Male Wistar rats (229 $\pm$ 20g) were used in the experiment. Diabetes mellitus was induced by a single dose of streptozotocin (80 mg/kg, i.p.). For the first 24 h following streptozotocin application the rats obtained for drinking 5% glucose solution. Hypercholesterolemia (HCH) was induced by application of a fat—cholesterol diet consisting of 1% cholesterol, 1% coconut oil, 20 g/day (HCH rats).
Mg2+ -dependent and 2, 4-dinitrophenol-stimulated ATPase activity was estimated by measuring the Pi liberated from ATP splitting. Membrane fluidity was assessed spectrofluorometrically by means of 1, 6-diphenyl-1, 3, 5-hexatriene and the content of conjugated dienes was determined spectrophotometrically at 230 nm.
Results: At termination of experiment, on the 8th day after streptozotocin application, the DIA rats exhibited elevated levels of glucose, total cholesterol, HDL, LDL and triacylglycerols. Increase in these variables was even more expressed in the DIA+HCH group ($p<0.05$). In acute DIA hearts MIT exhibited significant elevation in MF and Mg-ATPase activity ($p<0,05$) and non-significant increase in CD. HCH animals exhibited only non-significant changes in all parameters investigated. In respect to controls the DIA+HCH rats exhibited increased-, but in comparison with the DIA group lower fluidization of MIT membranes. MIT ATPase activity in the DIA+HCH group was slightly depressed in comparison to the control and DIA groups while the changes in contents of CD showed an opposite trend.
Conclusions: Fluidization of MIT membranes is a positive effect attributed to EPM. It was most expressed in the DIA group. Significantly increased cholesterol found in the DIA+HCH group antagonized the EPM, it increased the rigidity of MIT membranes. Consequently, the MIT ATPase activity in DIA+HCH group became also depressed. This study reveals the trends in changes of membrane properties and activities that will occur in heart MIT influenced simultaneously by DIA and HCH. VEGA: 2/0101/12, 2/0054/11, 1/0638/12, 1/0620/10, APVV-LPP-0393-09.

HEART FAILURE IMAGING

60861

Left atrial function changes from the very early stage of hypertension: evaluated by strain imaging

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Background: We tried to assess the effects of dipper and non-dipper status of hypertension on LA function in untreated dipper and non-dipper hypertension.
Methods: A total 19 untreated dipper hypertension patients (male 68%, mean age 46 $\pm$ 10) and 19 untreated non-dipper hypertension patients (male 58%, mean age 47 $\pm$ 10) were included. The patients whose night time systolic and diastolic BP did not decrease less than 10% were classified as non-dippers. Atrial strain and strain rate imaging were obtained at narrow sample volume. Peak strain rate were measured in late diastole in the basal septal, inferior, lateral and anterior walls of the atrium from the apical 4 and 2-chamber views.
Results: Maximal LA volume (Dipper:Non-dipper 24.61 $\pm$ 3.51: 27.15 $\pm$ 3.30 mL/m2, p=0.03), LA active emptying volume (Dipper:Non-dipper 4.48 $\pm$ 1.90: 6.03 $\pm$ 1.16 mL/m2, p=0.01), and LA active emptying fraction (Dipper:Non-dipper 29.43 $\pm$ 10.21: 35.74 $\pm$ 8.39 %, p=0.04) were increased in non-dippers. LA peak strain and late diastolic peak strain rates were significantly increased in basal septal and lateral wall. They also increased in inferior and anterior wall but not statistically significant. But the average of strain and strain rates in four segments were increased in non-dipper patients (Table).
Conclusion: The peak strain and late diastolic peak strain rate of LA were increased in non-dipper hypertension patients. These findings demonstrated that atrial reservoir and booster pump function is increased in non-dipper hypertensives. And strain imaging is useful method for the evaluation of LA function.

	dipper (n=19)	non-dipper (n=19)	p value
Septal SR (s^{-1})	-1.31 ± 0.32	-1.61 ± 0.23	<0.01*
Lateral SR (s^{-1})	-1.16 ± 0.53	-1.54 ± 0.36	0.01*
Inferior SR (s^{-1})	-1.87 ± 0.73	-2.13 ± 0.45	0.20
Anterior SR (s^{-1})	-1.51 ± 0.48	-1.94 ± 0.57	0.10
Average SR (s^{-1})	-1.46 ± 0.37	-1.81 ± 0.29	0.01*
Septal strain (%)	15.80 ± 5.00	20.20 ± 5.61	<0.01*
Lateral strain (%)	13.68 ± 5.98	19.70 ± 7.58	0.01*
Inferior strain (%)	27.35 ± 9.54	29.74 ± 11.31	0.61
Anterior strain (%)	22.20 ± 11.50	22.23 ± 8.65	0.85
Average strain (%)	19.76 ± 4.75	22.97 ± 3.52	0.037*

60968

Submaximal dobutamine echocardiograms : which prognostic significance?

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Purpose: The presence of inducible ischemia in dobutamine stress echocardiograms (DSe) has been shown to be a potent predictor of cardiac events; on the other hand the absence of ischemia is associated with good outcomes. The prognostic significance of submaximal DSe is unknown. The aim of this study was to estimate the prognostic value of submaximal DSe on major cardiac events.
Methods: We identified patients (pts) undergoing DSe and divided them into two groups based on predicted maximal heart rate (PMHR): group A (PMHR > or equal to 85 %) and group B (PMHR < to 85%). A test was considered positive for ischemia if it showed new segmental changes and/or worsening of baseline segmental changes. Pts in group B were subdivided into four groups: B1 (no segmental changes), B2 (segmental changes in the test), B3 (only basal segmental changes) and B4 (basal segmental changes and in the test). Groups were compared in their clinical, echocardiographic, previous use of beta blockers and/or calcium channel blockers, clinical reasons for the DSe, mean dobutamine dose, atropine use and occurrence of significant cardiac events - death, hospitalization, or revascularization - at 6 and 12 months.
Results: Of the 325 pts identified, 80 (25%) joined group B. In this group pts were younger (p = 0.002) and more often treated with beta-blockers (73%). The mean doses of dobutamine and atropine were 38.5 ug/kg/min and 0.37 mg, respectively. Pts in group B had more segmental changes (p <0.0001) and symptoms - chest pain and / or dyspnea (p <0.0001) during DSe. At 6 months, pts in group B had more significant cardiac events (p = 0.003) — they were more frequently hospitalized (p = 0.004) and revascularized (p = 0.029); at 12 months, pts in group B had more cardiac events (p = 0.008) and were more revascularized (p = 0.035). Groups A and B did not differ in a previous history of ischemic heart disease, previous use of calcium antagonists, ventricular dimensions and function, reason for the DSe, dose of dobutamine and atropine use. When we compared B subgroups we found that the frequency of significant cardiac events, at 6 months, was tendentiously higher in groups with tests positive for ischemia (p <0.0001).
Conclusions: In our study, tests submaximal and positive for ischemia were associated with a worse prognosis. It is possible that the greater frequency of adverse events observed in the overall analysis of all tests in group B is dependent on the occurrence of tests positive for ischemia. We assume that further studies are needed to assess the prognostic value of DSe submaximal and negative for ischemia.

61032

Can left atrial longitudinal peak diastolic strain predict cardiac resynchronization therapy response?

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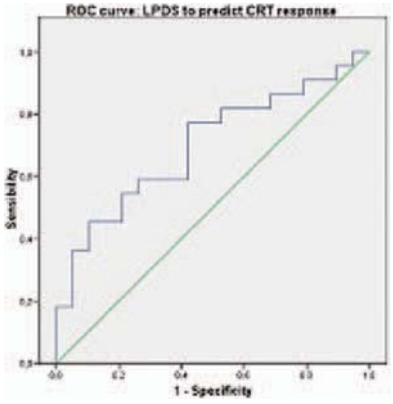
Background: Recent studies showed improvement of left atrial (LA) geometry following cardiac resynchronization therapy (CRT), but little is known about the impact in LA function.
Purpose: To assess LA function response to CRT.
Methods: Prospective, longitudinal study of 62 consecutive patients undergoing CRT between October 2009 and March 2010 in a single centre. Fourteen patients were excluded due to atrial fibrillation and 11 due to low quality pictures. Standard echocardiographic evaluation and LA deformation analysis by two-dimensional speckle-tracking echocardiography (2DSE) was performed prior to and up to 12 months after implantation. Left atrial longitudinal late peak diastolic strain (LPDS) was used as a surrogate of LA function. Response to CRT was defined as $\geq$15% reduction in left ventricular end-systolic volume.
Results: Mean age was 65.5 years, with a male predominance (64.9%). Regarding etiology, 73% were idiopathic and 27% were ischemic. Tha majority of the population was in NYHA class III, the mean basal QRS duration was 140.9 $\pm$ 22.1 ms and the mean left ventricular ejection fraction (LVEF) 23.9 $\pm$ 7.1 %. Pre-CRT, LPDS was -0.21 $\pm$ 0.64% and improved with the device (-0.93 $\pm$ 1.21, p<0.001). There was no correlation between LA volume, LVEF and LPDS. LPDS was a predictor of CRT response (AUC= 0.70, p=0.03). A -0.24% LPDS cut-off value had a 74% specificity and 60% sensitivity to predict a CRT echocardiographic response.

Conclusions: In our population LPDS improved with CRT, and was a predictor of CRT response. It can be theorized that such improvement in LA function may translate in better LV filling, less atrial arrythmias and less events in the long term. Further studies are warranted to evaluate these findings.



ROC curve (Abstract 61032 Figure)

60234

Is there distinctive echocardiographic predictor of severity of diastolic dysfunction in patients with diabetes mellitus?

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Objectives: Left atrial (LA) enlargement has been suggested as a marker of the severity and duration of diastolic dysfunction (DD). DD has been described as an early sign of diabetic cardiomyopathy. We wanted to determine if there is distinctive echocardiographic predictor of severity of DD in pts with diabetes mellitus (DM) irrespective of its duration.
Methods: 197 pts (69.9% men, 38, 1% women) with LA enlargement (44.7 $\pm$ 2.9 mm), enlarged LA volume index (42.1 $\pm$ 13.ml/m2) and average EF% of 64.8 $\pm$ 15.6 were selected for participation in this study. All pts were divided according to the presence of DM. LV systolic and diastolic function were evaluated by traditional, TDI and colour Doppler M-mode echocardiographic methods. The overall degree of diastolic function and specific parameters were analyzed.
Results: There was no difference between pts with (40,1%) and without DM (59.9%) regarding gender, BMI, presence of hypertension, dislipidemia, presence of CAD, LVEF and/or LA dimension and volume, only pts with DM were significantly older ($p=0.045$). Assessment of diastolic function revealed insignificant difference between pts with and without DM for degree of DD ($p=0.419$), but pts with DM showed significantly worse septal, lateral and average early diastolic velocity (Ea) ($p=0.031$; $p=0.033$; $p=0.018$, respectively) as well as significantly worse peak septal and average E/Ea ratio ($p=0.022$; $p=0.024$, respectively) which was confirmed with existence of significant negative correlation for septal, lateral and average Ea velocity ($p=0.037$; $p=0.042$; $p=0.022$, respectively) and significant positive correlation for septal and average E/Ea ratio ($p=0.012$; $p=0.017$, respectively). In a stepwise logistic regression model septal E/Ea ratio was independently associated with DM ($p=0.025$).
Conclusion: In pts with DM and already affected diastolic function, E/Ea ratio appears as a distinctive marker of severity of diabetic cardiomyopathy. Its assessment should be part of standard procedure in pts with DM.

60832

Assessment of left ventricular function by two-dimensional echocardiography speckle tracking in a group of type 2 diabetic asymptomatic patients

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Background and Objectives: Patients with diabetes mellitus (DM) with normal left ventricular ejection fraction (LVEF), often have diastolic dysfunction(DD). However, there are three factors we have to consider in these patients: first LVEF by two-dimensional transthoracic echocardiography (TTE) is not a sensitive marker for the detection of subclinical left ventricular systolic dysfunction (SD), second the early onset of SD in patients is due to the involvement of the longitudinal myocardial fibers and thirdly the associationof comorbid conditions in DM introduce biases in the evaluation of ventricular function. The development of Speckle Tracking Echocardiography (STE) appears to allow a more accurate assessment of the deformity of the LV myocardium. We have studied this degree of deformity by STE in a group of uncomplicated and normotensive diabetic patients and compared with a healthy control group.
Methods: 21 patients cardiologically asymptomatic with type 2 DM were studied (12 male, mean age 64 $\pm$ 9). Patients with severe or moderate-hypertension, history of coronary disease, valvular disease or significant renal failure were excluded. Control group consisted of 16 healthy subjects (9 males, mean age 63 $\pm$ 10 years). Complete TTE was performed and M-mode measurements, systolic function by modified Simpson method, cavity volumes and diastolic function (DF) by pulsed transmitral Doppler, pulmonary veins and tissue Doppler annular velocities were obtained. Furthermore, both ventricular functions were evaluated using STE.
Results: By Doppler, in the diabetic group 12 patients had normal DF, 6 type I DD and 3 type II DD. LVEF was normal in both groups. However it should be noted that the mean global longitudinal systolic strain (S) in the diabetics was -11,3 $\pm$ 2,7%($P<0.001$), the mean global longitudinal systolic strain rate (SR) was -0.90 $\pm$ 0.25s-1 ($P<0.001$) and a mean global early diastolic SR of 0.89 $\pm$ 0.42 s-1($P<0.001$).
Conclusions: We found discrete differences in LV wall thickness, in LV mass index and the classical Doppler parameters to evaluate DF between groups. There was no difference in the parameters to evaluate SF when measured by classical TTE, but if measured by STE. In conclusion, the assessment of LV SF by STE allows to identify patients with subclinical SD at an early stage.

60013

Atrial work on diastolic disfunction

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Background: Diastolic heart failure is associated with poor prognosis and increased mortality. Early diagnosis can help in the treatment of the condition and set goals terapeutics. We know that at rest, less than 30% of left ventricular filling due to atrial contraction. With chronic myocardial infarction, ventricular relaxation changed the mechanics of the involvement of the left atrium and it becomes more important. The study of Dopplermitral flow velocity time integral (VTI) of E and A waves for the same mitral orifice shows the proportion of flow at each stage ofventricular filling.
Methods: We studied 640 patients, no significant differences in age and body mass index), 440 patients (58% men and BMI: 28 $\pm$ 7) with normal echocardiography and without cardiovascular disease and compared with 220 patients (62% men and BMI: 26 $\pm$ 8) with abnormalities on the echocardiogram as dilated, hypertrophic and / or systolic dysfunction, but more than 140mswhen atrial depressurization.
Results: The estimated percentage of active atrial left ventricular filling in for the tests were below 30% (25.75% $\pm$ 0.7029 N = 420)echocardiography in patients with normal and abnormalechocardiography were above 30% (36 , 00% $\pm$ 0.8335 N = 220), $p<0.001$.
Conclusion: The calculation of the dependence of left ventricular filling to atrial contraction is useful to quantify diastolic dysfunction.

60111

Are there specific MPI SPECT study variables that can distinct ischemic from nonischemic cardiomyopathy?

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Aim of the study: To identify MPI SPECT variables distinctive for nonischemic dilated cardiomyopathy (NIDCM).
Material and methods: We analyzed 47 patients with DCM who underwent MPI SPECT, divided in two groups: with IDCM (27), and NIDCM (18). We analyzed clinical

Comparative MPI SPECT characteristics

	ICM (N=29)	NICM (N=18)				
Variable	Frequenciesmean $\pm$ SD	Frequenciesmean $\pm$ SD	sig	Chi square/Rsquare	OR or beta	sig OR
ST deniv.	18/29	1/18	0.000	17.20	9.17	0.002
LBBB	2/29	8/18	0.004	9.36	3.34	0.002
L/H stress	0.43 $\pm$ 0.04	0.35 $\pm$ 0.03	0.001	0.55	$-$0.74	0.001
L/H rest	0.44 $\pm$ 0.03	0.35 $\pm$ 0.02	0.000	0.69	$-$0.83	0.000
TID categorical	10/29	11/18	0.069	3.20	2.98	0.078
Fixed perf. defect	26/29	7/18	0.000	13.90	0.43	0.001
Reversible perf. defect	12/29	0/18	0.001	14.06	0.13	0.000
Patchy distribution	0/29	8/10	0.000	23.92	23.25	0.005

EF-ejection fraction; EDV-enddyastolic volume; ESV-endsystolic volume; L/H-lung to heart ratio; TID-transient ischemic dilatation; OR-odds ratio.

and MPI SPECT hemodynamic, ECG, functional response to pharmacologic stress with dipyridamol, left ventricular functional and myocardial perfusion variables.
Results: No differences were found for clinical except for LBBB (table), nor for LV functional variables. Variables with differences are presented in the table.
Significant correlations with NIDCM: LBBB (r 0.446/p 0.002); patchy distribution (r 0.660/p 0.000); ST deniv. during stress (r -0.560/p 0.000); fixed (r -0.540/p 0.000); reversible defect (r -0.461/p 0.001); L/H ratio (stress r -0.805/p 0.000 and rest r -0.858/p 0.000).
Multivariate logistic regression analysis (R square 0.700, sig = 0.000) identified five independent predictors of NIDCM: patchy distribution (OR 1.97, p=0.056), ST denivelation (OR -4.34, p=0.000); extensive fixed defect (beta -0.264, p=0.031); reversible defect (OR -4.22, p=0.000) and increased L/H ratio (beta -0.833, p=0.000) of NICM.
Conclusion: Patient with DCM who are not experiencing anginal symptoms, have LBBB, have no ST-denivelation nor chest pain during dipyridamol stress, with small fixed perfusion defects (especially in the presence of LBBB) or patchy distribution are more likely to have NIDCM. Increased H/L ratio is typically associated with ICM, rarely present in NIDCM even with severely depressed LV function.

60070
Ventricular tachycardia due to pectus excavatum

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A 19-year old boy with pectus excavatum presented at the adult congenital heart disease clinic for his yearly follow-up. During adolescence his exercise tolerance was decreased. Sometimes he suffered from lightheadedness while extensively exercising, but he never experienced palpitations or syncope. Previous tests revealed a slightly restrictive lung function and an incomplete right bundle branch block on ECG, which were both explained by the deformation of the chest wall and the mild rotation of the heart. Transthoracic echocardiography was normal. Despite completely normal exercise tests in the past, this time a short non sustained ventricular tachycardia of 4 beats was seen during bicycle test at 60 Watt. On the 12-lead ECG it was clear that the ventricular tachycardia originated from the right ventricle free wall. A cardiac CT and an MRI with late enhancement were performed. On the dynamic analysis of the MRI and the images of cardiac CT it was found that during diastole the distal part of the sternum impinged in the free wall of the right ventricle. Since there was no familial history of sudden cardiac death and no other structural anomalies of the heart, coronary arteries or myocardium could be detected, we assume that the impingement triggered the arrhythmia. Whether this process was mediated by fibrosis of the right ventricular free wall could not be determined. A bicycle after the start of a betablocker couldn't trigger the ventricular tachycardia anymore. A documented ventricular tachycardia as a complication of pectus excavatum has never been described in literature so far. Since it is suggested that symptomatic patients with pectus excavatum remain symptomatic after adolescence, the patient was referred for surgical repair.

61016
In natriuretic peptide era chest X-ray still useful in the evaluation of pulmonary congestion in a pretransplantation heart failure outpatient clinic?

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Introduction: Patients with heart failure are often evaluated with some degree ofuncertainty, even by highly skilled clinicians. Optimal evaluation includesbalance of symptoms, physical examination and adjunctive testing. Chestradiograph (CXR) has been a reliable, inexpensive tool commonly used, but itmay have a low accuracy for congestion evaluation.
Objective: Define moreclearly the relationship between the information provided by the CXR and thenatriuretic peptide (NT-proBNP) test as part of the evaluation of pretransplantheart failure patient in an outpatient clinc.
Methods: Cohort of 38 patientswith advanced systolic heart failure in a pretransplantation clinic. Clinicalcharacteristics and diagnostic performance for each test were compared,focusing on blinded NT-proBNP and CXR interpretation by 2 blinded radiologists.
Results: 38 patients, 65.5% men, age 48.53 $\pm$ 10.93y, 47.2% with idiophatic and 29.3% withisquemic dilated miocardipathy. NYHA class 2 was present in 41.4%. Congestionwas present in 51.7% estimated by a clinical congestion score, 44.8% byNT-proBNP>1000 and 44.7% by CXR evaluation. The performance of CXR findswere in the following table. A combination of 2 CXR abnormal finds wasassociated with a 76.5% of sensitivity and a 82.4% of specificity (95%CI).
Conclusion: Chest radiography is a crutial part of the complete evaluation and an useful test to evaluate pulmonary congestion. The strategy of grouping signs into an overall radiological impression did outperform individual radiographicsigns and achieved a similar accuracy to that provided by NT-proBNP.

CXR comparative diagnostic performance

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%)	NPV (%)
Cardiomegaly	84.2	76.9	64	52.6
Left atrial enlargement	36.8	89.5	77.8	58.6
Cephalization of vessels	68.4	78.9	76.5	71.4
Interstitial edema	73.7	84.2	82.4	76.2
Alveolar edema	5.3	100	100	51.4
Overall Evaluation	73.7	84.2	82.4	76.2

60035
Myocardial acceleration during isovolumic contraction in the routine evaluation of right ventricular function

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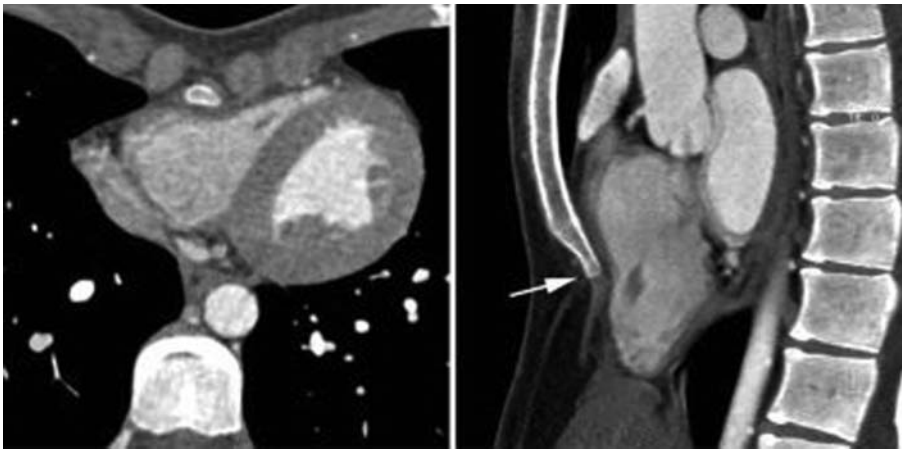
Introduction: The evaluation of the right ventricular systolic function (RVF) is complicated, because of its complex geometry. Methods like MRI or 3D echocardiography have been used for this evaluation but are still hardly available and time consuming. The acceleration myocardial acceleration during isovolumic contraction (IVA) is an index poorly studied that in previous works showed to correlate with the severity of illness in conditions affecting right heart function and to be relatively load independent. Still it is not recommended as a screening parameter for RV systolic function in the general echocardiography laboratory population.
Aim: To evaluate the utility of AIV as a measure of RVF in the general echocardiography population when compared with objective parameters used routinely: tricuspid annular plane systolic excursion (TAPES) and pulsed doppler velocity at the annulus (S′) and subjective parameters such as eyeball.
Methods: Prospective study of 313 patients (pts) with inpatient and outpatient sent to echocardiographic study, included from October/2011 to June/2011. AIV was made by Doppler tissue imaging at the lateral tricuspid annulus at the level of the lateral tricuspid annulus as the peak isovolumic myocardial velocity divided by time to peak velocity;



Cardiac CT images : short and long axis (Abstract 60070 Figure)

TAPES and S′ were obtained as previously described in the literature. The presence of RV dysfunction was considered for AIV<2.2 m/s2,TAPES<1.6 cm and S'<10 cm/s. We evaluated the validity of this new index considering TAPES and S′ as the benchmarks in the routine evaluation of FVD. Tests of correlation were performed between the variables and kappa coefficient was used to study the agreement.
Results: The average age of the sample pts was 62.7 ±14.75 years, 56.9% were male. The presence of RV dysfunction was identified in 13% of all pts and 26.5% had left ventricular dysfunction. Average heart rate of 73 bpm. The AIV showed low agreement values (k<0.4) when compared with all other parameters evaluated: TAPES vs. AIV; k= 0.06(p=0.257), S′ vs AIV; k=0.18(p=0.002); eyeball vs AIV: k = 0.22 (p=0.001). The AIV correlated moderately with S′(rs = 0.47, p <0.001) and weakly with the TAPES (rs =0.30, p =<0.001). We obtained a sensitivity of 0.31, specificity of 0.84, a positive predictive value of 0.34 and a negative predictive value (NPV) of 0.81.
Conclusion: In the population studied AIV showed apparently to be an index of low utility in the routine evaluation of the RVF, when compared with other benchmarks. It can, however, be an important exclusion discriminator of RV dysfunction given the relatively high NPV and high specificity.

BIOMARKERS (OTHER)

60072
Correlation between biomarkers levels and types of postinfarction remodeling according to cardiac magnetic resonance imaging

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Purpose: To evaluate correlation between biomarkers levels characterizing development of inflammation, degradation and synthesis of an extracellular matrix in myocardium with a type of postinfarction remodeling according to cardiac magnetic resonance imaging (MRI).
Methods: 60 patients with ST-segment elevation acute myocardial infarction (STEMI) admitted to cardiac clinic were taken to the study. High-sensitivity C-reactive Protein (hsCRP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), pro-matrix metalloprotease-1 (proMMP-1), matrix metalloprotease-9 (MMP-9), tissue inhibitor of the matrix metalloprotease-type 1 (TIMP-1) were evaluated on the 4-5th day. All patients underwent coronarography followed by angioplasty and stenting of the infarct-relating coronary artery. MRI with contrasting by gadolinium was performed on the 10th day and over 3 months after STEMI attack. All patients got a standard therapy.
Results: A direct correlation was revealed between levels of MMP-9 and the following indicators of MRI (on the 10th day of illness): the left ventricle end-diastolic size (LVEDS) and left ventricle end-systolic size (LVESS) and their indices, the index and percent of the affected myocardial mass (iAMM, %AMM). An inverse correlation with the left ventricle ejection fraction (LVEF) was revealed too. Over 3 months assessing MRI results the direct correlation with AMM, LVESS and inverse correlation with LVEF were kept. The levels of proMMP-1 had inverse correlation with a left ventricle stroke volume on the 10th day and over 3 months. Indices of TIMP-1 were correlated with iAMM and %AMM on the 10th day and over 3 months; the inverse correlation dependence on LVEF was also detected over 3 months. Besides, the inverse correlation between levels of hsCRP and LVEF was revealed. In patients with a microvascular obstruction phenomena according to MRI results the levels of hsCRP were significantly higher then in patients without this phenomena - 25,3 [6,3; 28,7] mg/L and 22,8 [5,9; 25,6] mg/L correspondently (p<0.05). Levels of NT-proBNP correlated with LVEDS, LVESS, the left ventricular end-diastolic and end-systolic volume (LVEDV, LVESV) and their indices, iAMM, %AMM according to MRI results performed on the 10th day and over 3 months.
Conclusions: The linear correlation was revealed between levels of biomarkers on the 4-5th days and cardiac MRI indicators on the 10th day and over 3 months in patients with STEMI. This fact showed the correlation between inflammatory process, degradation, synthesis of the extracellular matrix and postinfarction remodeling of the heart.

60837
Functional impairment and angiogenesis biomarkers in chronic heart failure

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Purpose: Though advances in the treatment of chronic heart failure (CHF) has led to significant improvement in prognosis, morbidity and mortality remain high. A better understanding of CHF mechanisms might result in new therapeuthic opportunities. Angiopoietin-2 (Ang-2) has been implicated in endothelial angiogenesis and homeostasis, while Endostatin (End) provokes a hypertrophic response in cardiomyocytes, and Thrombospondin-2 (Tsp-2) is a regulator of cellular responses for tissue repair, and inhibits angiogenesis.
Methods: ELISA tests were used for quantification of serum/plasma levels of Ang-2, End, Tsp-2 and pro-Brain Natriuretic Peptide (pro-BNP) in 43 patients aged (mean ± SE) 59 ± 3 years with CHF of increasing severity according to New York Heart Association (NYHA class I, n=6; II, n=18; and III, n=19) and in 7 healthy subjects (66 ± 2 years). Differences betwen groups were analysed using analysis of variance (ANOVA). The Kruskal Wallis test was applied for serum/plasma levels data, followed (when differences were significant) by the Mann-Whitney U test for comparison between groups. Correlation coefficients were calculated using Spearman's rank method. Values of p< 0.05 were considered as significant.
Results: pro-BNP levels were higher in NYHA III patients (Median(range) 6633 (829-35000) pg/ml compared to NYHA II (1685 (134-12676), p<0.0001), NYHA I (803 (5-3822), p<0.0001) and controls (17 (5-73), p<0.0001). Ang-2 levels were higher in CHF patients in NYHA III (Median(IQR), 4.67(2.6) ng/ml compared to NYHA II (2.63(0.9), p<0.0004), NYHA I (3.0(1.8), p<0.001) and controls (1.9(1.8), p<0.001). End and Tsp-2 were higher in NYHA III (106(59) and 29.4(22) ng/ml, respectively) compared to NYHA II (74(30) and 23(7), p<0.05), NYHA I (54(75) and 22(1.8), p<0.05) and controls (58(18) and 23(9), p<0.05). Only Ang-2 and End correlated significantly with pro-BNP levels (r=0.65, p<0.0001 and r=0.58, p<0.0001, respectively).
Conclusions: Our preliminary data on a small CHF population show that the regulation of the complex balance between hypertrophic, angiogenetic and anti-angiogenetic molecules may be involved in the pathophysiology of CHF. Further studies are needed for a better comprehension of the interaction between these molecules, potentially leading to the development of new prognostic informations and therapeutic opportunities.

60384
In-vitro stability of novel bio-markers at room temperature

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Background: Plasma concentrations of a variety of bio-markers have been found to predict morbidity and mortality in patients with heart failure. In most studies, samples are processed with great care under controlled conditions. In routine clinical practice, it may take hours or even days for a sample to reach the laboratory for assay, leading to sample degradation and unreliable results rendering the bio-marker useless for clinical practice.
Aims and methods: We assessed the in-vitro stability of plasma concentrations of five bio-markers [mid-regional pro-atrial natriuretic peptide (MR-proANP), C-terminal pro-endothelin-1 (CT-proET-1), mid-regional pro-adrenomedullin (MR-proADM), procalcitonin (PCT) and copeptin]. Samples were centrifuged at 4°C and stored at -80°C within 30 minutes of collection, compared to keeping whole blood at room temperature for 4 hours, 24 hours or 72 hours before centrifugation. Samples were obtained from 19 patients with chronic heart failure of varying severity.
Results: All bio-markers were stable at 4 hours and 24 hours. When sample preparation was delayed for 72 hours, plasma concentrations of CT-proET-1 were substantially lower. Mean difference and limits of agreement from ideal conditions for each bio-marker at all time points are shown in table 1.
Conclusions: These novel bio-markers are stable in-vitro at room temperature for long periods and appear suitable for use in a routine clinic or community setting provided there are no undue delays in preparation.

Table 1

Bio-markers	Median (IQR) of samples at 0 hrs	0 hrs vs 4 hrs		0 hrs vs 24 hrs		0 hrs vs 72 hrs	
		bias	±2SD	bias	±2SD	bias	±2SD
MR-proANP [pmol/l]	286 (198-404)	−1.08	9.64	1.39	9.28	−3.29	12.90
MR-proADM [nmol/l]	0.82 (0.72-1.14)	0.004	0.065	−0.010	0.071	−0.063	0.126
CT-proET-1 [pmol/l]	83 (71-109)	−2.00	5.45	−5.78	10.46	−20.65	21.82
Copeptin [pmol/l]	13.2 (8.1-24.8)	1.13	5.98	0.63	7.49	1.14	5.58
PCT [ng/L]	32 (24-47)	2.8	12.0	3.3	15.8	−0.6	16.8

60177
Short term effect of CRT on biomarkers of cardiac remodelling and fibrosis

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Effective cardiac resynchronization therapy (CRT) is associated with reverse ventricular remodelling.
Study objective: To assess short-term effect of CRT on biomarkers of cardiac remodelling and fibrosis (sST2, galectin-3, NT-proBNP) together with marker of oxidative stress (ceruloplasmin).

Population and methods: Serum levels of soluble ST2, galectin-3, NT-proBNP and ceruloplasmin were measured before and two months after CRT device implantation in 18 CRT candidates (15 men, 3 women). Mean age was 68 years, mean LV EF was 29%, ischemic aetilogy of CHF had 66% patients and 33% had atrial fibrillation. Mean interval between first and second measurment was 66 days.
Results: mean galectin (GAL) level was 1,26 ng/ml before and 0,67 ng/ml after CRT ($p = 0,0002$), sST2 level was 38,15 ng/ml, and 35,88 ng/ml after CRT, ($p = 0,55$), mean NT-proBNP was 1927 pg/ml, and 1996 pg/ml after CRT ($p = 0,75$), ceruloplasmin level was 0,24 g/l and 0,27 g/l after CRT ($p < 0,0001$). ST2 levels corrrelated significantly with NT-proBNP ($r = 0,66$, $p = 0,004$) and ceruloplasmin ($r = 0,77$, $p < 0,001$) at baseline, correlation of galectin-3 with other biomarkers was not significant. Ceruloplasmin level correlated with NT-proBNP ($r = 0,579$, $p = 0,015$).
Conclusion: short-term CRT was associated with significant decrease of GAL, but not with significant change of sST2 and NT-proBNP. Short-term CRT was associated with consistent increase of ceruloplasmin level, which correlated with NT-proBNP and sST2 singificantly. The results of this pilot study should be verified in the study with more subjects and longer-term follow-up.

61173

Markers of coagulation, B-type natriuretic protein levels and their possible interrelationship with aortic valve stenosis

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Aortic valve stenosis is a progressive disease of aging with serious complications, among which heart failure is most dramatic and usually addresses bad prognosis.
We aimed to investigate markers of coagulation (fibrinogen and d dimmer) in patients presented with aortic stenosis (AS), their possible interrelationship and interrelationship with echocardiographical findings and BNP levels.
Patients and results: The study included a total of 82 patients with both heart failure and aortic stenosis (68 ± 5.3 years of age, 51% females) admitted to our Clinic due to progressive heart failure. Blood was sampled for analysis (fibrinogen, d dimmer, BNP). In addition troponin I and C reactive protein were determined, echo study was performed (aortic valve stenosis was graded by gradient as mild, moderate and severe). Majority of the patients had moderated AS with hemodynamic gradient between 36 and 64 mmHg. Markers of coagulation were elevated in AS: fibrinogen 5.8 ± 2.1 g/l and d dimmer 320 ± 89. BNP levels were above 300 pgr/ml (up to 2500 pgr/ml) and further graded heart failure as mild, moderate and severe. Tropnin I levels were slightly elevated and correlated with BNP levels. There was no correlation between BNP levels and hemodynamic gradient of valve stenosis, but there was a correlation with ejection fraction. Also, there was no association between D dimmer levels, fibrinogen and AS. Our results suggest the linear correlation between C reactive protein and echocardiographically determined gradient of valve stenosis.
Conclusions: Our results suggest that inflammatory pathways might be involved in pathogenesis of aortic valve stenosis, but not pathways of coagulation. Progression to heart failure is not related to degreed of stenosis — determined by using BNP levels.

60194

Hyperglicemia and insuline resistance predict neurohormonal activation and prognosis at early stage of chronic heart failure

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Purpose: Metabolic alterations like hyperglicemia and insulin resistance are common in heart failure (HF), beyond overt diagnosis of type 2 diabetes mellitus. These alterations could affect, above all at early stage of heart failure, the functionality of several autonomic cardiovascular feedbacks, possibly promoting neurohormonal imbalance, a major determinant in the clinical evolution and outcome of HF. We evaluated whether hyperglicemia and insuline resistance (respectively evaluated with glycated haemoglobin (Hb1Ac) and HOMA index) could be related to biomarkers of neurohormonal activation and to outcome, also according to different degree of systolic dysfunction.
Methods: We prospectively studied 813 patients with HF (mean age of 65 ± 12 (mean $\pm$ SD), left ventricular ejection fraction (LVEF) 33 ± 9.8) on optimal treatment. DM was diagnosed in 235 patients (29.3%). All patients underwent echocardiography and neurohormonal evaluation. For subgroups analysis patients were divided according to tertiles of EF. The end-point of cardiac death was considered for survival analysis.
Results: Patients with Hb1Ac > 7 % showed higher levels of PRA, (3,66; 0,62-6,13 vs. 2,34; 0,34-4,68 ng/ml/h, $p<0.01$) and NT-proBNP (1602; 826-3498 vs. 1199; 368-3222 ng/L, $p<0.01$). Patients with higher values of insuline resistance (i.e. > 2.5), showed higher values of PRA (5.1 ± 7 vs. 3 ± 5 ng/ml/h, $p<0.01$) aldosterone (205 ± 177 vs. 172 ± 138 pg/ml, $p=0.021$) and norepineprhine 679 ± 569 vs. 623 ± 544 ng/L, $p=0.024$), but, interestingly, lower values of NT-proBNP (2723 ± 5527 vs. 3382 ± 5547, ng/L, $p=0.015$).
When population was stratified according to LVEF, these differences in neurohormonal activation were evident only in the upper LVEF tertile.
During a median follow up of 41.8 months, 124 cardiac deaths occurred. At multivariate analysis Hb1Ac $> 7\%$ predicted cardiac mortality in general population (Exp (B) 1.720 95% C.I. 1.11-2.65) and particularly in upper LVEF tertile (Exp (B) 8.1 95% C.I: 1.9—33.2), independently by NT-proBNP and PRA values. An higher HOMA index predicted cardiac mortality only in LVEF upper tertile (Exp (B) 1.2 C.I.1.4-1.3), independently by NT-proBNP and PRA values.
Conclusions: Hyperglicemia and insuline resistance impact on neurohormonal activation and prognosis, seem relatively more pronounced at early stage of HF. A more aggressive therapeutic approach in early stage of CHF (with maximal up-titration of anti-neurohormonal medical therapy, different recommendations for cardiac devices, strict metabolic control) could be appropriated in these patients.

60368

Use of cardiorenal biomarkers Cystatin-C and NT-proBNP in the early follow up after AHF hospitalisation

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Purpose: There is evidence both for NT-proBNP measurement at discharge for risk evaluation and repeated measurement after discharge. In addition, cystatin-C measurement has been used in long-term mortality and HF rehospitalisation risk evaluation. In this study we demonstrate sequential measurement of cardiorenal biomarkers in combined mortality and HF hospitalisation risk evaluation.
Methods: This study is a FINN-AKVA substudy. 146 patients were recruited in this early follow up arm. Laboratory samples were collected at day 2 (D2) and week 5 (W5). Patients were followed for 6 months after the W5 point. 18 patients were rehospitalised or died before W5 control point and 3 more patients lacked cystatin-C measurements, and these were excluded. 125 patients were included in this study.
We used IBM SPSS software in statistical analysis. Cox regression analysis and Log Rank analysis were used. In all analysis the point of statistical significance were set at $p < 0.05$.
Results: 11 patients deceased during follow up and 33 patients obtained combined mortality and HF hospitalisation end point. In multivariate Cox regression analysis the strongest predictor of high combined mortality and HF hospitalisation risk factor was Day 2 cystatin-C followed by lack of at least 30% decrease in NT-proBNP from D2 to W5 and patient age at admission (Table). In Log Rank analysis risk was significantly higher if cystatin-C at D2 was $\geq$ median (1.22 mg/l) (34.9% vs 17.7%, $p=0.025$) and at W5 $\geq$ median (1.33 mg/l) (35.9% vs 16.4%, $p= 0.012$). In Log Rank analysis the importance of at least 30% decrease in NT-proBNP from D2 to W5 was observed (37.9% if decrease was $< 30\%$ vs 16.4% if decrease was $\geq 30\%$, $p=0.006$).
Conclusion: Our results supported the use of cardiorenal biomarkers cystatin-C and NT-proBNP also in the early follow up after AHF hospitalisation.

Independent predictors of 6-month risk

Factor	HR	95% CI	p
D2 cystatin-C	2.90	(1.64-5.13)	<0.001
Lack of ≥30% decrease on NT-proBNP	2.39	(1.14-5.03)	0.022
Patient age on admission	1.04	(1.00-1.08)	0.043

Analysis included variables with p-value less than 0.10 in the univariate Cox regression, and age and sex.

60775

Combined use of low levels of neutrophil gelatinase-associated lipocalin, CA125, troponin, and natriuretic peptides improves the risk stratification in outpatients with chronic heart failure

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High levels of biomarkers (BM), signaling different pathophysiological mechanisms, have demonstrated an important prognostic role in heart failure. We assessed the hypothesis that the combined use of neutrophil gelatinase-associated lipocalin (NGAL), carbohydrate 125 antigen (CA125), cardiac troponin I (cTnI), and type B natriuretic peptide (BNP) could have additive impact to stratifying risk in outpatient with chronic heart failure (CHF).
Method: Between January and August 2011, 100 outpatients with CHF were prospectively enrolled. Samples obtained during the visit were assayed for urine NGAL, and serum CA125, cTnI and BNP with a chemiluminiscent microparticle immunoassay using an ARCHITECT I 1000 SR automatic analyzer.

Results: Mean age was 66 ± 12 years, 74% were male, 22% had LVEF ≥50% and 50% had ischemic etiology. During the follow up (200 ± 86 days) the incidence of the combined end point (hospitalization for acute heart failure or death) was 25%. The area under ROC curves for predicting end points for NGAL, CA125, cTnI, and BNP was 0.67, 0.66, 0.67 and 0.69 (p=ns for all comparisons), and cut-off were ≥10 ng/ml; ≥ 16 U/ml, ≥0.005 ng/mL, and ≥55 pg/mL, respectively. According to status of biomarkers above or below cut-off, the population was classified as (+) or (-). The prevalence of (+) for NGAL CA 125, cTnI and BNP was 41, 36, 59 and 65%. In univariate analysis, variables associated with events were diabetes (p=0.007), anemia (p=0.036), functional class (p=0.010), sodium (p=0.011), ischemic etiology (p=0.011), NGAL (+)(p=0.026), CA125 (+)(p=0.004), cTnI (+)(p=0.003) and BNP (+)(p=0.045). In Cox-proportional hazard model, the variables independently associated with events were diabetes (HR=3.7, 95%CI=1.6-8.4, p=0.002), NGAL (+) (HR=2.5, 1.1-5.6, 0.027), CA125 (+) (HR=2.9, 1.3-6.8, 0.012), and BNP (+) (HR=3.8, 1.1-13, 0.036). The 1-year free events survival was 94% in patients with 0-1 BM (+), 67% with 2-3 (+) and 23% with 4 BM (+) (p<0.00001). Compared with subjects with 0-1 BM (+), the presence of 2-3 (+) was associated with a risk of events of 4.7 (95%CI=1.1-20.7), whereas all positive biomarkers increased the risk 26.1 times (95%CI=5.6-120).
Conclusion: The combination of low levels of NGAL, CA125, cTnI and BNP is a powerful tool to identifying CHF outpatients at risk of poor outcome. These findings suggests that the risk-stratification in this setting should include BM of kidney failure, congestion, myocardial damage and ventricular overload.

60891
Prognostic value of increased CA-125 circulating levels in stable heart failure patients

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CA-125 is a high-molecular weight glycoprotein used as tumor marker. Recently, increased levels of CA-125 have been documented in heart failure (HF) patients (Pts). To assess the prognostic value of increased circulating levels of CA-125, 114 pts diagnosed of HF were studied. Pts were in stable condition and followed in a HF Unit. New HF episodes, hospital admissions and death were evaluated and considered as a combined end-point. NT-proBNP values were also assessed on the same day.
Results: Pts mean age was 72 ± 12 years, 61% were men. Atrial fibrillation was present in 48% of pts. The etiology of HF was hypertension in 29%, ischemic heart disease in 37%, dilated cardiomyopathy in 8%, valvular heart disease 15%, congenital 2% and others 14%. Mean ejection fraction (EF) was 50 ± 18% with 68% of pts having preserved EF. Pts were treated with ACEI or angiotensin antagonists in 78%, diuretics in 88%, beta-blockers in 55% and aldosterone antagonists in 43%. During follow-up (15 ± 8 months), 57 pts (50%) presented with new episodes of mild decompensated HF, 76 pts required a hospital admission (67%) and 16 died (14%). Pts with new HF episodes had higher CA-125 values 79 ± 100 vs 40 ± 81 KU/L (p<0.02) and higher NT-proBNP values 4587 ± 5167 vs 1382 ± 1362 (p=0.001). CA-125 circulating levels higher than the 75% percentile (50 KU/L) were associated with a higher incidence of the combined end-point 86% vs 62% (p=0.02). CA-125 circulating levels higher than the 75% percentile was identified as the most powerful predictor of combined events by multivariant Cox regression analysis (p=0.008) Conclusions: 1. Circulating levels of CA-125 are a useful biomarker in HF patients. 2. Increased levels of CA-125 identified patients with higher incidence of the combined end-point: death, hospital readmission and new HF episodes.

60004
Prognostic value of biochemical stress markers in patients with q-wave myocardial infarction

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Background: Not all arterial hypertensive patients after myocardial infarction with chronic heart failure respond to conventionally treatment are equal. Traditionally, NT-pro-brain natriuretic peptide (BNP) variations could be useful in predicting the therapeutic efficacy of CT. However, it has been considered some limitations for predicting value of NT-pro-BNP concentrations among population of arterial hypertensive patients. Some biochemical stress markers have been proposed as a possible marker of severity of cardiovascular remodeling and survival after myocardial infarction.
Aim: To evaluate value for 1-year survival of matrix metalloproteinase's (MMP-3 and MMP-9) plasma level in comparison to NT-pro-BNP concentration in arterial hypertension patients after Q-wave myocardial infarction
Methods: 85 arterial hypertension patients (male and female) with documented Q-wave myocardial infarction (MI) were observed during 1 year after hospitalization period due to mentioned above indications. In has been identified hard end-point included all fatal and non-fatal atherotrombotic events, new cases of both urgently angioplastic and stenting, all newly diagnostic cases of heart failure and hospitalization ratio due to mentioned above reasons. MMP-3, MMP-9 plasma levels and NT-pro-BNP were measured at the study entry by ELISA.
Results: Univariant analysis has been shown that increase of MMP-3 plasma level above optimal cut-point (9.7 ng/ml) was closely associated with up of 1-year cardiovascular mortality risk in arterial hypertension patients after Q-MI. Prognostic model of compromise with both MMP-3 and MMP-9 is tightly related with positive prognostic value of 70% (prognostic sensitivity and specify are 84% and 82% respectively). Additionally assessment of pre-discharge NT-pro-BNP cannot improve of summary predispose capacity of both MMP-3 and MMP-9, especially there is pre-admission Killip class acute HF >1.
In conclusion, we believed that obtained data can be helpful to be prescreen patients with high risk of unfavorable clinical outcomes associated with atherothrombotic events, heart failure and death.

60583
Hyponatremia and its prognostic value on heart failure; one year of clinical follow-up data

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Purpose: In the context of acute HF, to appraise the predictive value of hyponatremia on the severity of the cardiac condition, by monitoring the combined but mutually exclusive endpoints defined either by death or re-admittance, due to HF, along a clinical follow-up of 3, 6 and 12 months after hospital release.
Methods: 600 patients - of which 53% were women - with a global mean age of 76.5 years (± 10.2) were prospectively scrutinized from April 2009 onwards; a subgroup of 355 patients was incorporated in the analysis due to the fact that they have being given a complete clinical follow-up. All those patients were admitted to a Cardiology infirmary due to HF of different etiologies. All patients have been divided accordingly to their relative levels of natremia: group (G) A presented a natremia of less than 135mmol/L, whereas GB presented a natremia ≥ 135mmol/L. At this stage, clinical, analytical and echocardiographic parameters were duly assessed. Subsequently to hospital release, patients were followed all through a 12 month period. The resulting set of acquired data was then inspected using chi-square and Student t tests, together with Kaplan-Meier log-rank test survival curves. Statistical significance was attributed if p <0.05.
Results: On admission, GA presented lower systolic and diastolic pressures (for p<0,001, GA vs. GB of 128mmHg vs. 144mmHg, and of 74mmHg vs. 82mmHg, respectively). GA presented a higher value of BNP both on admission (p<0.01) and on hospital release (p=0.01). Levosimendan was more widely utilized by patients of the GA (6.1% vs. 1.7%, p=0.04). Echocardiographic examinations demonstrated both a higher LA diameter (p=0.04) and an elevated pulmonary artery systolic pressure (p=0.001) within GA. Hospital internment times were also lengthier within the GA (11.1 days vs. 8 days, p<0.01). Down the yearly follow-up, it was verified that GA actually reached the composite 3, 6 and 12 months endpoints with a statistically effective difference when compared to GB (43.9% vs. 22.5% , p<0,001; 47.0% vs. 34.6%, p=0,04; 59.1% vs. 43.9%, p=0,02, correspondingly). Kaplan-Meier curves showed that hyponatremia is coupled to a linear increasing in mortality and re-admission at 3, 6 and 12 months (3 months log-rank with p<0.01; 6 months log-rank with a p=0.03; 12 months log-rank with a p= 0.01).
Conclusions: Hyponatremia on hospital admission seems to be correlated with a poorer long-term prognosis and this naturally seems to show congruency with the growing evidence that hyponatremia may in fact act as a marker of a worse survival rate.

60706
The role of NT-proBNP and glomerular filtration rate in the prediction of fatal and non fatal cardiovascular events in asymptomatic diabetics

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Purpose: Several trials have shown limited usefulness of NT-proBNP in screening ventricular dysfunction or subclinical coronary artery disease in asymptomatic diabetics (Dts). This study aims to evaluate the role of NT-proBNP in cardiovascular risk (CVR) stratification.
Methods: Retrospective study of 105 consecutive asymptomatic Dts (without dyspnea or chest pain) from our diabetes clinic with a previous assessment of NT-proBNP and CVR scores (CRS: Framingham and SCORE): 48.6% men, 60 ± 10 years, 94.3% hypertensive, mean diabetes duration of 13 ± 9 years and hemoglobin A1c 8.2 ± 1.8%. They were evaluated regarding demographics, CVR factors (CRF), CRS and analytical parameters. Patients (P) were followed for 45 ± 13 months to identify fatal and nonfatal cardiovascular(CV) events (CVev: CV death, acute coronary syndrome and stroke/TIA). A comparative analysis of Dts with and without CVev was performed in order to evaluate potential predictors.
Results: There was a prevalence of 14.3% CVev . By univariate analysis, P with CVev were older (68 ± 7 vs 59 ± 10 years, p=0.001), had lower glomerular filtration rate (GFR, by MDRD: 76 ± 16 vs 100 ± 27mL/min/11.73m2, p=0.002) and higher NT-proBNP (241.9 ± 204.8 vs 105.2 ± 116.6pg/mL, p=0.002), Framingham (29 ± 15 vs 19 ± 11%, p=0.01) and SCORE (4 ± 2 vs 3 ± 2%, p=0.017). By multivariable regression, only GFR (OR 0.95, 95%CI 0.92-0.99, p=0.02) and NT-proBNP (OR 1.004, 95%CI 1.001-1.008, p=0.05) were independent predictors of CVev. On the ROC curve analysis there was a clear association between these variables and CVev (GFR: AUC 0.77, 95%CI 0.67-0.85, p<0.001, best threshold ≤99.2 mL/min/11.73m2 with 100% sensitivity (SE) and 52.4% specificity (SP); NT-proBNP: AUC 0.70, 95%CI 0.59-0.80, p=0.029, best threshold >205.6pg/mL with 63.6%SE and 89.9%SP), resembling the CRS curves (Framingham: AUC 0.69, 95%CI 0.59-0.78, p=0.034, best threshold >24% with

66.7%SE and 68.7%SP; SCORE: AUC 0.74, 95%CI 0.64-0.83, p=0.004, best threshold >3% with 57.5%SE and 72%SP). Based on GFR and NT-proBNP, a predictor model of CVev was created and its ROC curve analysis showed an excellent predictive value (AUC 0.86, 95%CI 0.76-0.92, p<0.001, best threshold >10% with a 81.8%SE and 76.8%SP).
Conclusions: According to these data, the NT-proBNP and the GFR proved to be independent predictors of CVev in asymptomatic Dts. They revealed a predictive ability similar to the classical CRS, with a high SP for NT-proBNP and a high SE for GFR. The predictor model built with these variables showed a better profile of SE and SP to identify the asymptomatic Dts that may benefit from a closer monitoring.

60639
Predictors of left ventricular reverse remodeling and subsequent outcome in nonischemic dilated cardiomyopathy

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Objectives: We sought to identify the clinical predictors of LVRR and their prognostic role, and to measure the midterm level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients with NIDCM.
Background: Optimal medical therapy can lead to left ventricular (LV) reverse remodeling (LVRR) in nonischemic dilated cardiomyopathy (NIDCM). However, the clinical variables associated with LVRR are poorly defined.
Methods: We evaluated 331 consecutive hospitalized patients with NIDCM by reviewing the records in the heart failure database of our institute. Clinical and echocardiographic data were available for 255 (77%) patients at the midterm follow-up (16±7 months). The patients were followed thereafter until the combined endpoint of cardiovascular death, heart transplantation, or hospitalization for heart failure; the mean duration was 29±22 months.
Results: LVRR was noted in 98 (38%) of 255 patients at mid-term. The baseline predictors of LVRR were higher systolic blood pressure, QRS duration <120 ms, use of a beta-blocker, and a small indexed LV end-systolic dimension. In landmark survival analysis from the midterm evaluation, LVRR, low midterm NT-proBNP level, and continuous use of a beta-blocker were independently related to good long-term results.
Conclusions: Monitoring of patients with NIDCM using both cardiac imaging of the LV structure and by assessing neurohormonal status (NT-proBNP level) at the midterm follow-up might be clinically useful for predicting the long-term clinical prognosis of NIDCM.

60302
Relationship between serum N-Terminal Pro-B-Type natriuretic peptide and echocardiographic parameters in elderly adults without known history of heart failure: the Shanghai Heart Health Study

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The aim of this study was to determine whether higher serum NT-proBNP was associated with the changes of parameters of color flow Doppler echocardiography in healthy elder subjects. We studied the relationship between circulating concentrations of NT-proBNP and echocardiographic parameters in participants aged>=65 from Shanghai Heart Health Study (SHHS). Participants age>=65 and without known history of heart failure were eligible for this investigation. Serum NT-proBNP was measured with the Roche Diagnostics Elecsys assay. Echocardiographic parameters included left ventricular ejection fraction (LVEF), left ventricular end diastolic volume index (LVEDVI), and the ratio of onset of early transmitral flow velocity (E) and that of early diastolic mitral annular velocity (e') (E/E'). Relationship between NT-proBNP levels and echocardiographic variables were analyzed using generalized linear model after adjustment for age and sex. Subgroup analyses were conducted in healthy normal (was defined as the absence of traditional clinical cardiovascular risk factors and echocardiographic structural cardiac abnormalities) and stage A heart failure subjects (was defined as subjects with >=1 traditional clinical cardiovascular risk factors and absence of echocardiographic structural cardiac abnormalities). Participants (n = 1,326) had a mean age of 71.4 ± 5.7 years, and 60.8% were women. The 25th, 50th, and 75th quartiles of NT-proBNP in women were 79.4 , 136.8 and 237.7 pg/ml, respectively; whereas in men were 52.0, 85.4 and 157.1 pg/ml, respectively. We identified 593 (44.7%) healthy normal participants and 733 (55.3%) in stage A heart failure subgroup. The level of NT-proBNP in stage A heart failure subgroup was significant higher than that in healthy normal group, P<0.0001 (25th, 50th, and 75th quartiles: 67.2, 120.6 and 245.2 pg/ml vs. 65.2 , 107.2 and 177.6 pg/ml). Overall, logarithmically transformed NT-proBNP concentration (log NT-proBNP) was significantly associated with LVEF (β=-0.026, P<0.001), LVEDVI (β=0.019, P=0.050) and E/E' (β=0.063, P=0.038). In healthy normal group, the results were similar; however, in stage A heart failure subgroup, only LVEF (β=-0.028, P<0.001) were significantly correlated with log NT-proBNP, we did not detect a statistically significant association between log NT-proBNP and LVEDVI (β=0.0262, P=0.1327), E/E'(β=0.046, P=0.1354). Conclusion: In our community-based study, higher concentrations of NT-proBNP were associated with increased LVEDVI and E/E' and decreased LVEF, but the relation was attenuated in stage A heart failure subjects.

60521
Role of B-type natriuretic peptide in outpatients with new onset heart failure

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Purpose: B-type natriuretic peptide (BNP) usefullness in new onset heart failure outpatients is unclear. Heart failure (HF) with preserved systolic function is highly prevalent in this population. The aim of this study is to assess the role of BNP for diagnosis of new onset heart failure in outpatients and to determine BNP cutoff in this population.
Methods: We designed an observational, prospective and longitudinal study in a cohort of outpatients who had new onset symptoms of HF. These patients were visited in a one-stop cardiology clinic for diagnosis. A clinical evaluation, elctrocardiogram, chest X-ray, determination of BNP and echocardiography were performed. The diagnosis of HF with preserved ejection fraction (HFPEF) or reduced ejection fraction (HFREF) was confirmed or ruled out. Baseline characteristics were analyzed. With BNP values a receiver operating characteristics (ROC) curve was performed.
Results: 143 patients were included from April 2009 to December 2011. Mean age was 75±10 years, 64% were females and 75% were hypertensive. HF was the final diagnosis in 66% of patients (67% HFPEF and 33% HFREF). NYHA class I-II was observed in 74% and III-IV in 26%. Median time from onset of symptoms to diagnosis was 90 days. The BNP values (pg/ml) were higher in HF patients compared to those without HF (234 ± 363 vs. 20 ± 26, p<0,001), and higher in patients with HFREF compared to HFPEF (401 ± 580 vs. 153 ± 123, p=0,025). Using ROC curve analysis BNP was a significant predictor for HF (AUC=0,898; 95% CI 0,848-0,948; p<0,001). A cutoff of 60.12 pg/mL for BNP provided 83% sensitivity and 84% specificity for predicting HF.
Conclusions: Outpatients with new onset HF, most of them with HFPEF, have significantly higher BNP levels than those without HF. We propose a cutoff of 60.12 pg/mL for BNP with 83% sensitivity and 84% specificity for predicting HF in them. Thus, BNP could be a good biomarker also to identify outpatients with HF.

60228
Role of peptide natriuretic to detect cardiac abnormalities in transthyretin amyloidosis

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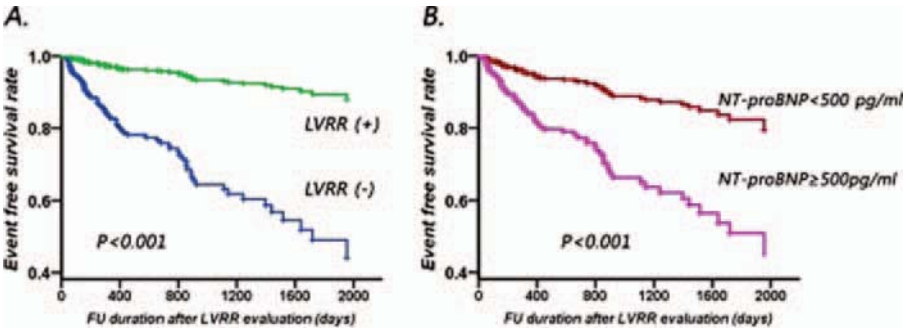
Background: Familial amyloid polyneuropathy (FAP) is an autosomal dominant neurodegenerative disease. FAP is characterized by the systemic deposition of transthyretin in the peripheral nervous system and the heart. Individuals begin to exhibit neurologic symptoms followed by heart symptoms between the third and seventh decades of life. Early non invasive detection of cardiac impairment is of importance for the therapeutic management.
Aim: Our aim was to assess if natriuretic peptide (NT-proBNP) could predict cardiac abnormalities in a wide variety of TTR patients.



Kaplan-Meier analysis of Events, ProBNP (Abstract 60639 Figure)

Methods: 36 patients with TTR amyloidosis had clinical, biological (NTproBNP) and echocardiographic assessment with left ventricle systolic function (LV2Dstrain), LV mass indexed (LVmassind) and LV filling pressure (LVFP) measurement
Results: In the all cohort, the median (IQR) age, NT-proBNP, LVEF were respectively 59 (41-74), 323pg/ml (58-1960) and 60% (51-66). TTR gene mutations prevalence was 50% for Val30Met, 11% for Ser77Tyr, 8% for Ile107Val and Val122Ile. 4 patients were asymptomatic, 6 had isolated neurologic disorders and 26 had cardiac LV abnormalities (systolic dysfunction, hypertrophy, increase in filling pressure) with or without neurologic disorders with respectively a median NT-proBNP value of : 33 (19-50), 54 (37-154) and 747(253-2840). Using received-operator curve, NTproBNP identified significantly patients with cardiac abnormalities (Area : 0.92;(0.83-0.99), p=0.001) with a threshold of 82pg/ml and sensitivity of 92% and specificity of 91%.
Conclusion: In FAP, NT-proBNP is elevated in presence of cardiac abnormalities. This test can be useful to follow patient with FAP and decided the good time to start the echocardiography follow-up.

60028
The association between coronary spasm and BNP and PWV

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Background: Coronary spasm causes transient left ventricular dysfunction and consequently may increase B-type natriuretic peptide (BNP) by chance. However, the correlation between coronary spasm and BNP has not been verified. We investigated the association between coronary spasm and BNP and pulse wave velocity (PWV) in patients with preserved left ventricular function.
Methods: Patients with chest pain who have ejection fraction $\geq$ 50% underwent both diagnostic coronary angiography with acetylcholine provocation and NT- proBNP measurement simultaneously were enrolled for the study. PWV test was done in all patients. Significant coronary artery spasm was defined as focal (>70%) or diffuse severe transient luminal narrowing (>90%) with or without chest pain or ST-T change of electrocardiogram.
Results: Among total 1,342 patients, 793 patients with heart failure, arrhythmia, coronary artery disease or valvular heart disease were excluded and 549 patients were enrolled. Thirty five percent (192/549) of enrolled subjects showed positive results at acetylcholine provocation test. Baseline characteristics were well balanced between the spasm group and control group. In the univariate analysis, the BNP levels of spasm group were lower than control group (146 $\pm$ 363 pg/ml vs. 197 $\pm$ 532 pg/ml, p= 0.050). But in the multivariate analysis, there was no significant difference of BNP between two groups. Also there was no difference of PWV value between the groups.
Conclusion: There is no significant relationship between BNP, PWV and coronary spasm. These finding suggest that coronary spasm with normal left ventricular systolic function is not associated with BNP or PWV.

60948
Alarmins S100A8 and S100A9 aggravate the inflammatory immune response in acute myocarditis and inflammatory cardiomyopathy

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Background: Various Toll-like receptors (TLRs) are a part of the innate immune system and involved in cardiac immune response after viral infection. Potential endogenous ligands of TLRs and their function in viral myocarditis still remain unclear. In the present study we investigated the role of the alarmins S100A8 and S100A9, identified ligands of TLR4, in Coxsackievirus B3 (CVB3)-induced myocarditis in mice.
Material and methods: S100A8/A9 knockout mice and their wild-type controls were infected with CVB3 to induce myocarditis. Seven days after viral infection left ventricular (LV) function was estimated by conductance catheter technique as well as cardiac fibrosis, inflammatory response and cardiac apoptosis by immunohistochemistry or PCR. In addition, we examined serum and endomyocardial expression levels of S100A8 and S100A9 in patients with myocarditis, inflammatory cardiomyopathy and controls.
Results: Seven days after infection WT-CVB3 mice displayed an impaired systolic (dP/dtmax -39%, SV -41%, SW -42%, CO -56%, EF -34%; P<0.05) and diastolic LV function (dP/dtmin -28%, LVEDP +66%, Tau +25%; P<0.05), associated with a significant increase in virus load, cardiac fibrosis, inflammation and cardiac apoptosis. In contrast, S100A8/A9 deficient mice showed a definite improvement in systolic (dP/dtmax +26%, SV +30%, SW +42%, CO +63%, EF +29%; P<0.05) and diastolic (dP/dtmin +31%, LVEDP -62%, Tau -44%; P<0.05) LV function. In addition, in S100A8/A9 deficient mice, virus load (P<0.05), inflammatory immune response (e.g. IL-6 2.5-fold, IL-10 2.7-fold, IL-12 2.1-fold, IFN-γ 2.6-fold; P<0.05), cardiac fibrosis (Col I 7.5-fold, Col III 1.4-fold; P<0.05) and cardiac apoptosis (TUNEL 6.4-fold, RACK1 8.1-fold; P<0.05) could be normalized to levels almost similar to uninfected control animals. Exogenous substitution of homodimer S100A8 in S100A8/A9 knockout mice led in turn to an exazerbation of CVB3-induced myocarditis. Moreover, patients with myocarditis or inflammatory cardiomyopathy (n=50 per group) displayed significantly increased serum and endomyocardial expression levels of S100A8 and S100A9 when compared to controls (P<0.05).
Conclusion: The identification of S100A8 and S100A9 proteins as key factors in the pathogenicity of experimental myocarditis might offer a new molecular target and biomarker for treatment of viral cardiomyopathy.

61006
Evaluation of myeloperoxidase activity in chronic heart failure

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Purpose: Increased oxidative stress has been recognized as an important contributory mechanism for the development and progression of cardiovascular diseases. Recent studies suggest that plasma myeloperoxidase (MPO) levels are elevated in patients with Chronic Heart Failure (CHF). However, nothing is described about quantification of MPO activity in CHF. The aim of our work was to evaluate MPO activity in ambulatory outpatients with CHF.
Methods: Fifty four patients with CHF (NYHA functional class I to IV) were selected from the Heart Failure Clinic of our Hospital. On the day of the visit, patients were examined and blood and urine samples were collected. Plasma total antioxidant status (TAS) was evaluated using commercial Kit and H2O2 and isoprostanes in 24-hour urine using also commercially available kits. Plasma MPO concentration was determined by an ELISA assay kit and plasma MPO activity was evaluated by monitoring the oxidation of tetramethylbenzidine at 655 nm. Serum uric acid (UA), urinary creatinine and plasma B-type natriuretic peptide (BNP) were also determined by an automated biochemical analyzer. Data from the last echocardiogram of the patients was registered from their clinical process and categorized according to ejection fraction.
Results: Patients were stratified into mild (NYHA classes I and II) and severe (NYHA classes III and IV) CHF. Patients with severe CHF had significantly increased levels of plasma TAS (3.90 ± 0.12 vs 3.19 ± 0.16 mM Trolox, n=9-21, p=0.011), serum uric acid (91.11 ± 10.13 vs 67.37 ± 2.86 mg/l, n=8-19, p=0.0069) and plasma MPO activity (41.87 ± 11.69 vs 16.46 ± 3.04 micromol/min/mg, p=0.034, n=16-18) but not MPO concentration (28.22 ± 8.00 vs 36.55 ± 7.29 ng/ml, p=0.45). Urinary isoprostanes and urinary H2O2 levels were also significantly increased in severe CHF patients (isoprostanes: 2.58 ± 0.38 vs 1.62 ± 0.11 ng/mg creatinine, n=19-27, p=0.008; H2O2: 0.027 ± 0.009 vs 0.013 ± 0.002 nmol/mg creatinine, p=0.047, n=8-18). BNP analysis confirmed our clinical evaluation of the patients as described in literature (1296.0 ± 328.2 vs 456.8 ± 105.6, p=0.009, n=23-31) but we didn't find any correlation between BNP levels or echocardiogram classes and redox markers.
Conclusions: Severe CHF patients have higher levels of redox status markers, namely plasma MPO activity compared to mild CHF patients. However, we haven't found significantly MPO raised levels in the more severe stratified patients as previously described in literature and all these measures did not correlate with already validated and routinely used biomarker BNP or with echocardiogram parameters as recently described.

61060
Prospective evaluation of endothelin-1 blood levels in pulmonary hypertension

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Purpose: Endothelin-1 (ET-1) is a potent vasoconstrictor implicated in the pathophysiology of pulmonary arterial hypertension (PAH), whose action can be blocked by the endothelin receptor antagonists (ERA).
We aimed to find the clinical, analytical, structural and hemodynamic predictors of ET-1 in PAH.
Methods: We included 30 consecutive patients prospectively followed in the PAH clinic at an university hospital. Included patients had invasive confirmation of severe PAH. We carried out clinical, analytical (including ET-1) and echocardiographic evaluation (including conventional and speckle tracking echocardiography).
Results: ET-1 correlated with renal function parameters including urea (R=0.43; p=0.02), creatinine (R=0.50; p=<0.01) and cystatin C (R=0.73; p<0.01) and also NT-proBNP (R=0.67; p<0.01). It correlated with right (R=0.51; p=0.01) and left atrial dimensions (R=0.51; p=0.01). There was an inverse correlation between basal ET-1 levels and the distance walked in the 6MWT at baseline (R=-0.42; p=0.04) that remained true for the subsequent walk test evaluations at 6 and 12 months.
Patients previously treated with ARE (n=14) had higher baseline ET-1 levels (p=0.05) and patients that were subsequently treated with ERA had a 20% increase in ET-1 blood levels. When analyzing only the patients that were not treated with ERA we found correlation between ET-1 and left ventricular wall thickness (R=0.69; p=0.01), the E/A ratio of right ventricular inflow (R=0.85; p<0.01) and was inversely related to right ventricular fractional area change (R=-0.60; p=0.01).
Conclusions: ET-1 correlates with markers of prognosis and atrial dimensions in PAH patients. It rises after treatment with ERA. The quantification of ET-1 levels may be particularly relevant in stratifying patients with PAH not treated with ERA as it relates to ventricular function.

60087

Serum uric acid as a predictor of the six months left ventricle systolic function of patients with acute non-ST-elevation acute coronary syndromes

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Background: Raised serum uric acid (SUA) is related to mortality from heart failure (HF), but scarce data are available on its predictive value for the future left ventricular remodeling in patients with non ST-elevation acute coronary syndromes (NSTE-ACS).
Aim: To determine the predictive value of SUA in patients with first NSTE-ACS on six months left ventricle systolic function.
Methods: Using hospital informational system database, we evaluated 157 patients (68.5% men; age 61.5 $\pm$ 9.8 years) with NSTE-ACS. SUA, cardiac troponin I (cTnI), C-reactive protein (CRP), fibrinogen, glucose, lipids and creatinine were determined once daily for the first 4 days, and heir maximal levels were analysed. All patients underwent coronarography at the index hospitalisation. Transthoracal echocardiography was done on 4. day and six months after admission. Patients with previous ACS, renal insufficiency and gout were excluded.
Results: The mean SUA was 326.56+/-94.18 μmol/L. The initial left ventricle ejection fraction (LVEF) was 54.8% $\pm$ 9.9%. Left ventricle end-systolic diameter (LVESD) $\geq$5cm initially had 2.8% ($p<0.001$), and after six months 5.4% patients. Patients with initial LVESD $\geq$5cm had SUA 487.20+/-81.73μmol/L, while mean SUA in patients with LVESD $<$5cm was 321.92+/-91.31 μmol/L ($p<0.001$).51% of patients had a hystory of hypertension ($p=0.21$). SUA corelated with trygliceride ($p<0.001$), creatinine ($p<0.001$), and ESD ($p=0.042$), but not with a number of hemodynamically significant coronary stenoses, body mass index (BMI), initial LVEF and left ventricular wall and ESD, cTnT, CRP and fibrinogen ($p>0.05$). In a simple logistic regression SUA (relative risk(RR)1.02;95% confidence interval(CI)(1.01-1.03);$p=0.001$) and serum creatinine (RR 1.01;95%CI(1.00-1.02);$p=0.045$) were associated with LVESD $\geq$5cm after six months, while age, gender, BMI, number of haemodynamically significant coronary artery stenoses, glucose, lipids, cTnI, CRP, fibrinogen and blood pressure were not ($p>0.05$). In a multiple logistic regression SUA (RR1.02;95%CI(1.01-1.03);$p=0.001$) was the only independent predictor of six months LVESD $\geq$5cm. The best SUA cutoff for predicting six months LVESD $\geq$5cm based on receiver-operating characteristics analysis was 410 micromol/L (area under the curve 93.9%;$p=0.01$). SUA above 410micromol/L was registered in 7.6% of patients ($p<0.001$).
Conclusion: In studied patients with NSTE-ACS, SUA was the only independent predictor of the left ventricular size increment after six months. Monitoring of a SUA concentration can be useful to identify patients with NSTE-ACS, who could be at risk for the development of heart failure.

NURSING

61076

Knowledge about heart failure among Slovenian nurses

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Purpose: The course of heart failure depends on patients' knowledge and skills related to self-care. Patients seek information about their disease, lifestyle and self-care management advice primarily from nurses. There is limited information whether nurses have sufficient knowledge about non-pharmacological heart failure interventions and how do they estimate burden of chronic disease. We therefore aimed to evaluate knowledge about heart failure and perception of chronic disease among Slovenian nurses.
Methods: During European Heart Failure Awareness Day 2011, nurses from Slovenian hospitals were invited to complete the questionnaire consisting of 15-item Dutch Heart Failure Knowledge Scale and questions about prevalence, survival and economical burden of heart failure, cancer, chronic obstructive pulmonary disease and stroke.
Results: Our sample included 310 nurses (9% men) with median age of 35 years. Median Dutch Heart Failure Knowledge Scale score was 12 points and 31 (10%) participants scored maximum of 15 points. Overall, 81% of all answers were correct and no differences between men and women or between those reporting to work with heart failure patients routinely or occasionally were observed. Lowest rate of correct answers were recorded for questions about daily fluid volume (42%), physical activity (62%) and action to be taken when thirsty (67%). All nurses correctly answered question about importance of taking heart failure medication regularly. Heart failure was percepted as the most common chronic disease (65%) and 73 (25%) nurses reported heart failure is normal consequence of ageing. Worst survival and highest costs were attributed to cancer (52% and 70%, respectively), followed by heart failure (29% and 20%), stroke (15% and 3%) and chronic obstructive pulmonary disease (2% and 5%).
Conclusions: Knowledge about heart failure among Slovenian nurses is suboptimal, particularly in issues related to daily fluid management and physical activity. Nurses perceive heart failure as most common chronic disease, which however has less socio-economic impact when compared with cancer.

60692

72 years old, advanced heart failure patient, with preserved function, multi-pathology, social and cultural conditioning issues

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Purpose: This case study reflects an advanced Heart Failure (HF) patient admitted in hospital with multiple previous admissions. He is at high risk of early admission and even risk of death. Discharge planning and follow up was made by a HF nurse.
Main Problems: Having had multiple hospital admissions, involving great Social and Health System impact. The difficulty of management of complexity: CV Diseases (advanced HF NYHA III, stage C, preserved function, hypertension its etiology). Multi-morbidity (Renal Dysfunction, Hyper- K, Anaemia, Chronic Obstructive Pulmonary Disease , Pulmonary Hypertension, Sleep Apnoea , Diabetes Mellitus, low albumin and proteins. He walks with stick, previous stroke, falls, and venous ulcers). Poly-medication
The Probable underlying Reasons: Poor education and self management. Smoker, sedentary, obese. Probable social risk (older, gypsy, low income, caregiver fatigue, dependence). Inadequate close follow up
Management: Nursing management supported by a multidisciplinary team. The Diferential diagnosis of signs and symptoms in a patient with several diseases. Evidence for preserved function patients was reviewed, co-morbidities, analytical alterations, drug contraindications and poly-pharmacy. His anaemia treated by the nephrologist with erythropoietin. His chronic obstructive pulmonary disease made difficult the up-titration of BB . Gout acute attacks were self-managed with advised colchicine. Avoiding hypoglycemic episodes, maintaining HbA1c $<$ 7. Education for self management emphasizing the precipitating factors for worsening HF. Na and fluid restriction. Obesity paradox precluded weight reduction. Hyper-K managed by restriction of K in diet. Exercise to manage obesity, diabetes, risk of falls and dependence. Cardiologist consulted for treatment and nephrologist for hypertension.
Results: Very positive progression, not re-admitted any time, despite several worsening episodes. Adherent to medication and self management. BP not completely controlled but improved. He Regularly walks, not feeling dyspnea. Long periods without smoking, currently some smoking. His relationships improved .Future plans reinforcing management of blood pressure, smoking and exercise.
Conclusions: A a HF nurse with Multidisciplinary support comprehensive assessment and close follow up, using guidelines and education for self management , taking into account social and cultural issues, can improve prognosis, quality of life and avoid admissions of a HF complex patient.

POPULATION STUDIES / EPIDEMIOLOGY

60249

Prevalence and outcomes of patients with chronic HF with moderate-severe mitral regurgitation: data from the IN-HF Outcome database

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Background: Several observational studies on heart failure (HF) have been conducted, but very few detailed information exist on the real burden of mitral regurgitation (MR). For this clinical condition, a new device (MitraClip) has been recently introduced to minimize the pathophysiological consequences of MR. In this context, we compared characteristics and outcomes of patients with or without moderate-severe MR. To achieve this goal, an ancillary analysis of the IN-HF Outcome database was performed.
Methods: Of the 3755 patients with chronic HF included in the registry, only those patients in NYHA Class III-IV or those in Class II with a hospitalization for HF in the previous year, all with echocardiographic data available, were considered for this analysis. Baseline characteristics and outcomes at 1 year have been evaluated in this population of patients with or without MR.
Results: 1190 patients were identified according to the above criteria. 151 (12.7%) had a moderate-severe MR. Patients with MR had a significantly lower BMI, a more frequent renal dysfunction, lower systolic BP, higher heart rate, lower ejection fraction and were more frequently implanted with CRT/ICD. There were no significant differences in terms of age, gender, etiology and other comorbidities. Patients with MR were more frequently treated with aldosterone antagonists, diuretics and digitalis, while no differences were observed for ACE-I/ARBs and betablocker treatments. The patients' outcomes at 1 year are reported in the Table.
Conclusions: Patients with chronic HF and concomitant moderate-severe MR are relatively frequent in clinical practice and present a worse 1-year outcome profile than those with the same severity of HF symptoms but without MR. Specific strategies addressed to these high risk patients should be the focus of future research.

Events at 1 year	MR(151 pts)	No MR(1039 pts)	p
All-cause mortality, %	18.0	6.3	<.0001
CV mortality, %	12.6	4.1	<.0001
HF hospitalization, %	24.0	11.2	<.0001
All-cause mortality/HF hsopitalization, %	33.3	15.0	<.0001

61049
Real world management of chronic systolic heart failure in Spain - Results of VIDA-IC

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Purpose: Chronic systolic heart failure continues to have a poor prognosis although recent randomized controlled trials have shown considerable progress. Real world treatment however usually slowly adopts these findings. It was therefore our aim to document the current real world treatment of chronic systolic heart failure management in Spain.
Methods: VIDA-IC is a national, prospective registry conducted by 120 investigators across Spain that included 1200 consecutive patients with chronic heart failure and left ventricular ejection fraction (LVEF) $\leq$ 40% in 2011.
Results: A total of 400 patients were available for this preliminary analysis. Patients' mean age was 71 $\pm$ 10 years, 68% were male and 62.5% had their follow-up with a cardiologist (37.5% internists).
The mean LVEF was 34 $\pm$ 7% and 44% had a NYHA class III/IV assigned. The most common etiologies were ischemic (49%) or hypertensive heart disease (26%), 50% of patients presented non-sinus rhythm, 41% had had prior MI and 49% coronary revascularization. 65% had had prior heart failure related hospitalizations. Only 21% were controlled in heart failure units. Non-pharmacological treatment included ICD in 9% and CRT in 6% of patients. 95% of patients received either ACEi or ARBs (59% and 36% respectively), 91% diuretics, 74% betablockers, 72% aldosterone blocking agents (51% eplerenone; 21% spironolactone), 27% digoxin and 9% ivabradine. A high proportion of patients received antithrombotic drugs (61%) or oral anticoagulation (42%). Only 52% of patients receiving optimal medical heart failure therapy (defined as betablocker, ACEi / ARBs and aldosterone blockers each). This low rate was not based on absolute contraindications (these were present for betablockers in only 3.2%). On the other hand, doses were lower than those recommended (bisoprolol 5.05 $\pm$ 3.3 mg/day; carvedilol 21.7 $\pm$ 15 mg/day).
Conclusions: These real world data suggest that there is sub-optimal transfer of clinical trial evidence into clinical practice. Only about half of chronic systolic heart failure patients were receiving optimal therapy of aldosterone blocking agents and betablockers in particular. This suggests that there is room for improving prognosis of patients with heart failure in Spain.

61145
Pathophysiological analysis of clinical characteristics and outcome of patients with chronic heart failure

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Purpose: Heart failure (HF) is a syndrome encompassing various cardiac diseases but these are not considered separately in current cohort analysis. In this study we compare a conventional and a pathophysiology-based cohort analysis
Methods: Clinical characteristics and 4-year outcome of 2,254 patients with symptomatic HF were comparatively analyzed using a conventional global analysis and a pathophysiological approach based bon three pathophysiological categories (LV necrosis, LV dilation, and LV hypertrophy) defined by ECG and echocardiographic criteria.
Results: As compared with the global analysis, the pathophysiological approach identified four populations with different ($p<0.001$) clinical profile and outcome. The LV necrosis group (n=567) included younger males, more often diabetics, with lower LV ejection fraction, received more β-blockers and presented more readmissions for ischemia. The LV dilation group (n=672) were the youngest with highest incidence of mitral valve regurgitation, wide QRS, LBBB, increased LV mass, large LA diameter, and received more ACEI drugs, diuretics, cardiac resynchronization and implantable defibrillators and had a lower survival rate. The LV hypertrophy (n=455) were the oldest, most often females with arterial hypertension, central obesity, high body mass index, atrial fibrillation, signs of right HF, wide range of LVEF values, and received less β-blockers, resynchronization therapy, and ICD. The three categories showed comparable functional class, signs of left HF, and mortality for HF progression. The remaining 560 patients formed a heterogeneous group with intermediate clinical and outcome profiles.
Conclusion: A pathophysiological analysis of a cohort of HF patients identifies populations with different clinical profile and outcome. This new approach affords a more comprehensive knowledge of HF and emerges as a potential methodological tool for more accurate assessment of the efficacy of the applied therapies.

60836
Heart failure and early hospital mortality in patients with acute myocardial infarction with st-segment elevation

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Introduction: Coronary artery disease, with its predominantly recognized acute clinical manifestation - Acute myocardial infarction remains the leading cause of death in developed, but even more in transition and developing countries. In 2000, cardiovascular diseases are the cause of death for> 4 million people in Europe and myocardial infarction predicts that 2020 will be the main cause of death worldwide.
Purpose: To monitor early hospital morbidity, intra-hospital complications and mortality in patients with acute myocardial infarction with ST-segment elevation (STEMI) treated without reperfusion therapy, in patients who receive pharmacological reperfusion therapy and in patients treated with mechanical reperfusion therapy .
Methods: The study included patients diagnosed with STEMI within three years from the eastern region of the Republic of Macedonia. Patients were divided into three groups: Group 1 - patients treated without reperfusion therapy, Group 2 - patients who receive pharmacological reperfusion therapy Group 3 - patients who were treated with mechanical reperfusion therapy (PKI). Early hospital morbidity, intra-hospital complications and mortality were observed in all three groups.
Results: From 2008 to 2010 registered a total of 543 patients with STEMI. In 2008 registered 156 (28.7%) patients, 196 (36.1%) in 2009, and 191 in 2010 (35.2%) person. Of the total 543 patients, 161 (29.7%) were women and 382 (70.3%) were male, with average age of 60,43 $\pm$ 11,76 years. Most patients with STEMI - 320 (58.93%) were treated conservatively. With pharmacological reperfusion therapy were treated 17 (3.13%) patients, and with mechanical reperfusion therapy (PKI) were treated 206 (37.94%) patients. In terms of early morbidity and intra-hospital complications, the most recorded complications were rhythm disorders and conduction - in 34 (6.26%), mechanical complications in 25 (4.60%) and haemodynamic complications - in 25 (4.60%) patients. There is a correlation between the kind of treatment and hospital morbidity, it is more established in patients on conservative treatment (2 test = 58,33 df = 24 p = 0,00011). The type of morbidity, heart failure carries the highest hospital mortality, followed by malignant rhythm disorders and conduction. (2 test = 56,98 df = 1 p = 0,00011).
Conclusion: The conservative treatment of patients with STEMI carries a higher risk of developing intra-hospital complications. Haemodynamic complications, which include heart failure, by frequency is on the third place. However, heart failure carries the highest hospital mortality.

60336
Heart failure in old peoples - gender differences

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Background: The prevalence of heart failure (HF) is similar in women and men, increasing with age. However men are diagnosed earlier, whereas in women the disease generally occurs after 75 years. This aspect was not studied until now in Romania.
Methods: The study include a representative urban sample of 515 old people (264 women) aged >55 years, in Cluj-Napoca, Romania. The cardiovascular profile was assessed by using the general practitioner's files and clinical examination, including echocardiography.
Results: The mean age of the entire study population was 73.41=- 6.44 y, with no relevant gender specific difference (77.35+-6.63years women vs 76.07+- 6.32years men, p=NS). Heart failure was diagnosed in 10.48% patients — 26 (9.8%) women, namely 28 (11.2%) men (p=NS). The prevalence of HF increased in women over 75 years, as compared to those under (15.3% vs 5.9%, p=0.011), as well as in men (20.2% vs 7.5%, p<0.01). The measurements showed an ejection fraction (EF) less than 40% in 34.3 % of women and 59.4% of men, p< 0.05. There are gender specific differences when assessing the mean values of risk factors (by using the Mann Whitney test). The entire cohort displayed a relevant difference between men and women in what concerned the ratio of patients with diabetes mellitus (21.2% vs 7%, p< 0.05), and there was a higher number of dyslipidemic (48.5% vs 32.3 % p<0.001), obese (29.5% vs 23%, p=0.02), hypertensive (91.3% vs 84.9% p=0.02) women. On the contrary, smoking habits prevailed in men (7.4% women 18.1% men, p=0.008). In case of most women and men it was identified an ischemic etiology of HF but for those with preserved EF, aging heart and hypertension represented the principal etiology. Treatment was similar, as categories of drugs used in men and women but ACEI (62.3 vs 78%) and BB (37 vs 59%) were less used in women, suggesting they are undertreated.

In conclusion, in old heart failure patients, there are no significant differences in clinical profile between men and women, but women have a higher EF and are undertreated in comparison with men.

60101
Psychological status in patients with recurrent (post-operational) angina pectoris complicated by heart failure

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Study objective: to assess psychological status in patients with recurrent (post-operational) angina pectoris complicated by heart failure in long term after bypass surgery.
Materials and methods: Forty eight patients with recurrent (post-operational) angina pectoris (FC II-III) complicated by heart failure (FC III) aged 45-64 were examined. The mean age was 55,2 $\pm$ 1,24 years. Mean post-CABG time was 18,7 $\pm$ 1,22 months. Drug therapy represented standard antianginal therapy. The clinical depression rate was evaluated the depression scale by A.Beck (Beck Depression Inventory), state and trait anxiety level was performed using C. Spielberg and L. Khanin test.
Results and discussion: Based on the A. Beck depression scale results it can be noted that most of patients did not demonstrated depressive disorders, the mean-rate of depression was 9,2 $\pm$ 6,6 scores which is above the norm. Only 10.8% of patients showed clinically pronounced depression above 20 scores more (mean score 25,5 $\pm$ 4,52) which is indicative the need to correct the treatment administered. The assessment of anxiety level showed the following data: high level of state anxiety was revealed in 10,4% of patients, trait anxiety was noted in 33,3% of patients. The mean evidence of the state anxiety was registered in 83,3%, trait anxiety - in 60,4% of patients, the low level of state and trait anxiety — in 6,3% of patients. The high level of trait anxiety correlated with neurotic and emotional breakups, high state anxiety — with impaired fine coordination and attention. The mean and high levels of state and trait anxiety in most of patients contributed to the progressing of angina.
Conclusion: The changes revealed suggest the necessity to correct psychovegetative impairments during the complex treatment of patients with recurrent (post-operational) angina complicated by heart failure to improve the clinical state and life quality for these patients.

PSYCHOSOCIAL / ETHICAL CONCEPTS / EDUCATION

60956
Single centre study examines self management and coping styles in an ambulatory Irish heart failure population - a single centre experience

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Background: How well patients adjust to living with HF is largely influenced by their individual coping strategies when confronted with the challenges of living with a chronic condition. The following study investigated the impact of patients' illness beliefs and coping styles on their health-related quality of life and self-management behaviour in HF.
Method: A cross-sectional design was employed examining the self-management behaviours and coping styles in a cohort of 86 patients (65% male; mean age 75 years). Participants were predominantly in NYHA class III diagnosed with ischaemic cardiomyopathy and HF-preserved attending a heart failure service for >3 months. Questionnaires used included the COPE, the Illness Perception Questionnaire (IPQ), the HeartQoL and the Self-care of Heart Failure Index (SCHIFI).
Results: Patients' use of maladaptive coping styles of denial (p= 0.027), behavioural disengagement (p= 0.042), venting (p=0.003) and self-blame were strongly linked with poorer health-related quality of life. Patients experiencing greater symptom load (p< 0.0001) and a greater emotional impact (p< 0.0001) of their heart failure reported poorer quality of life. Moreover, patients were more likely to engage in active coping when they understood their illness better (p= 0.007) and viewed their condition as personally controllable (p< 0.0001). These patients also reported greater confidence in implementing self management recommendations and reported a better quality of life (p = 0.001).
Conclusions: Patients' coping styles and illness perceptions significantly impact on their self-management behaviour and quality of life. Accordingly, patients employing maladaptive coping strategies require greater input in learning alternative healthier coping methods through tailored HF self-management programmes.

60461
Self-esteem and suicidal risk among subjects with heart failure in a west-african cardiology clinic

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Purpose: Self-esteem is an important psychological factor in health and diseases. Low self esteem, characterized by inner turmoil and a perception of negative changes in the self and its functions can impact negatively on the pathophysiology of chronic illnesses such as heart failure (HF). The increased risk of suicide associated with low self esteem and the dearth of relevant research in our environment prompted this study.
Method: Consenting, stable HF patient were recruited from the cardiology clinic of our hospital. Socio-demographic data was obtained, clinical and echocardiographic parameters were retrieved from their clinical notes and the subjects filled out the self esteem evaluation questionnaires (ISE) by WW Hudson. Scores were first transformed by reverse coding of some items and then indexed by subtracting 25 from the total scores. Scores were coded as abnormal if they were $\geq$ 30.89 for males and $\geq$32.04 for females.
Result: Data set for 190 HF patients, 91 males and 99 females was analysed. The mean age of the subjects was 51.90 $\pm$ 13.21yrs, duration of illness 35.82 $\pm$ 44.56 months, number of admissions 1.22 $\pm$ 1.41 and ejection fraction 45.93 $\pm$ 18.0%. About 66% of the subjects had post primary education and about 75% of them were in the low income bracket. Most were married, 81.6% and Christians, 80.5%. The mean ISE score was 24.38 $\pm$ 12.47 and 26 (27.45%) subjects had abnormal ISE scores. There was no difference in age, p=0.24; number of hospitalizations, p=0.45 and ISE scores 24.70 $\pm$ 12.38 vs. 24.10 $\pm$ 12.61, p=0.75 between males and females. There was no gender difference in the distribution of occupation, marital status and religion however the females had significantly longer duration of HF, p=0.01 and higher ejection fraction, p=0.005. There was no difference in the frequency of abnormal ISE scores among the educational levels, occupation and religion of subjects and it was not affected by age. However there was a significant difference in the frequency of abnormal scores by marital status with single patients having a frequency of 47%, p=0.04 and also higher levels in patients with poor QoL sores, 38.5%. p=0.02. A negative correlation was seen between ISE and QoL scores, r = -203, p=0.005.
Conclusion: We conclude that a quarter of the HF patients in our environment have low self esteem which is also related to their QoL. This aspect of their illness should be given proper attention as low self esteem has been shown to predict risk of suicide.

EXERCISE TESTING & TRAINING

60617
Compliance to a cardiac rehabilitation program: what benefits and prognosis impact?

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Background: Cardiac rehabilitation programs (CRP) have consistently demonstrated the ability to improve cardiac risk factors and reduce morbi-mortality.
Objective: To assess the clinical benefits and CRP compliance impact on prognosis, in a coronary heart disease population.
Methods: We evaluated a total of 241 patients referenced to a CRP after an acute coronary syndrome (ACS), recruited between September 2008 and November 2010. Information on socio-demographic, clinical and functional data was collected pre and post CRP. Functional capacity was assessed in metabolic equivalents (METS), determined by exercise stress testing. Telephonic interview to patients with at least 12 months of follow-up after index event was performed to assess the occurrence of composite endpoint of overall mortality and nonfatal cardiovascular events.
Results: Study population consisted of 241 patients, mostly male (89%), aged 54 $\pm$ 10 years (range 28-80). Non compliance was found in 24 (10%) patients and it was more common in women than men (23% versus [vs] 8%; p=0.030) and in obese patients (18% vs 8%; p=0.024). No significant differences were found in other baseline characteristics, including ACS type and severity indicators. At 6 to 12 months post index event, health status comparison between the 2 groups demonstrated that compliers achieved better control of cardiovascular risk profile: higher smoking cessation rate (70% vs 18%, p=0.001) and higher rates of adequate physical activity [82% vs 25%, p=0.022]. A significant improvement was found, only in the compliant group (CG), regarding functional capacity (+0.8 (1.6) METS, p<0.001 vs -0.6 (0.9) METS, p=0.208) and lipid profile (LDL-cholesterol [LDL-C]: -39.1 [39.6], p<0.001; HDL-C: +3.2 [8.7], p <0.001 and triglycerides [Tg]: -38.7 [102.7], p<0.001 vs LDL-C: -9.6 [37.1], p=0.434; HDL-C: +3.6 [6.4], p=0.096 and Tg: -10.8 [58.6], p=0.554). Follow-up data was available in 227 (94%) patients, with a mean follow-up time of 25 $\pm$ 7 months. Composite endpoints were found in 23 (10%) patients and tended to be more frequent in non-CG (17% vs 9%; p=0.182). With Cox regression analysis, non-compliance behavior was associated with a higher likelihood of composite endpoint occurrence, although no statistical significance was achieved (HR: 2.2, 95% CI: 0.7-6.4).
Conclusion: CRP compliant patients have a significant higher improvement in cardiovascular risk profile, functional capacity and tend to suffer less cardiovascular events than non compliant patients. Specific strategies are needed, in order to prevent drop-out and maximize the benefit of CRP.

60858
Presence of exercise oscillatory ventilation (EOV) during cardiopulmonary exercise testing (CPET) predicts cardiovascular (CV) death in patients with non-ischemic heart failure (HF)

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Instability of breathing, detected as exercise oscillatory ventilation (EOV) during CPET, is a possible marker for severity of HF. In the present study, we characterized HF patients with EOV, comparing with those without it.
Methods: Seventy-one stable patients with non-ischemic HF (NYHA functional class 3 or 4) were referred for CPET and other clinical evaluations, then followed up for 21 month in average in Hiroshima University Hospital.
Results: Patients with EOV (EOV group, n=23), compared with those without EOV (non-EOV group, n=48), had increased left atrial dimension, mitral E-wave velocity, and right heart pressures in ultrasonography and decreased exercise tidal volume response, rest, exercise end-tidal carbon dioxide, and increased ventilator equivalent for carbon dioxide and dead space ventilation in CPET (all $p < 0.05$). Multivariate analysis revealed that the presence of EOV was significantly associated with NYHA class, rest end-tidal carbon dioxide, and peak heart rate. During the follow-up period, the CV morbidity (9.6 vs. 4.8 per 100 patients years in EOV vs. non-EOV group, $p < 0.05$ by Kaplan-Meier analysis) and mortality (3.0 vs. 1.6, $p < 0.05$) were both higher in EOV group.
Conclusions: Presence of EOV was associated with impaired respiratory performance and was an independent risk factor for CV deaths in patients with advanced HF.

60038
Maximum heart rate among heart failure patients receiving beta-blocker therapy

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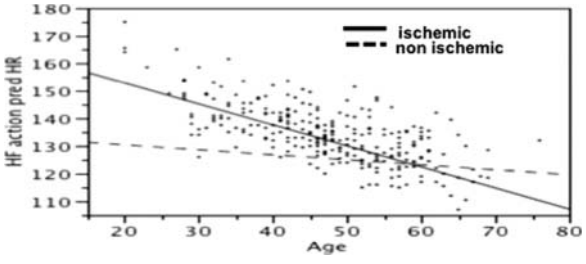
Background: At thesetting of evaluation of functional capacity, heart failure (HF) patients mustbe evaluated under optimized clinical therapy, including beta-adrenergicblockade (BB). Predicted maximum heart rate (HRmax) based on 220 - age iswidespread used, but it is not applicable to patients receiving BB therapy. Fewstudies suggest other equations which estimate HRmax in patients receiving BBtherapy with and without heart failure. However, these studies do not considerthe etiology in HF. The purpose of this study was to determine an equation topredict HRmax in patients with ischemic and non ischemic HF who are receivingBB therapy.
Methods: We includedpatients with heart failure who were being considered for heart transplantationand underwent treadmill cardiopulmonary exercise testing between 1999 and 2010,using Naughton protocol. All patients were taking BB at maximum tolerated doseat the discretion of the treating physician. We excluded patients withpacemaker and/or implantable defibrillator, ejection fraction greater than 0.50or peak respiratory exchange ratio (RER) less than 1.00 and chagas disease. Weused linear regression to develop the equation that predict HR max, based onage in ischemic and non-ischemic patients.
Results: We analysed 278patients, age 47 ± 10, ischemic (n=75) and onischemic (n=203). The left ventricleejection fraction was 30.8 ± 9.4 and $28.6 \pm 8.2\%$ ($p = 0.04$), peak VO2 was $16.9 \pm 4.7$and 16.9 ± 5.2 ml/kg/min (p = NS) and the HRmax was 130.8 ± 23.3 and 125.3 ± 25.3 bpm($p = 0.051$) in ischemic and non-ischemic respectively. We have found theequation HRmax = 168 - 0.76 x age for ischemic and HRmax = 134 - 0.18 x age fornon- schemic HFpatients.
Conclusion: Our results suggest that equations to estimate HR max should consider the etiology in heart failure patients.



(Abstract 60038 Figure)

PROGNOSIS

60686
How important is ventricular rate in heart failure patients with atrial fibrillation

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Background: A slower heart rate is associated with better survival in patients with heart failure (HF) due to left ventricular systolic dysfunction (LVSD) in sinus rhythm (SR). The relation between heart rate and mortality in patients with HF and AF is unclear.
Methods: We present data from a cohort of patients who attended a community heart failure clinic at baseline assessment (visit one) and at 1 year follow-up (visit two). All patients had an ejection fraction $\leq$50%. Two thousand and thirty nine patients were included at visit 1, of whom 24% (n=488) had AF. At visit 2, 841 patients were included, 22% (n=184) of whom had AF. From visit one, the median survival for patients in AF was 2,238 days versus 2,660 days for patients in SR. Cox regression models explored the relation between i) heart rate and survival and ii) heart rhythm and survival.
Results: A lower heart rate was strongly associated with better survival in patients with SR but not in patients with AF. After adjusting for multivariates, AF compared to SR was not associated with worse survival, (Table 1).
Conclusions: Ventricular rate is strongly associated with survival in patients with heart failure in SR but not for similar patients in AF. Heart rhythm is not a significant predictor of worse survival.

Table 1. Mortality Analysis

Cox Regression Analysis	Visit One HR (95% CI)	P Value	Visit Two HR (95% CI)	P Value
Univariable				
Sinus Rhythm vs AF	1.26 (1.08-1.47)	0.003	1.46 (1.16-1.83)	0.001
Heart Rate (per 10 bpm increase), SR	1.14 (1.10-1.18)	0.0001	1.12(1.03-1.21)	0.008
Heart Rate (per 10 bpm increase), AF	0.97 (0.87-0.99)	0.002	1.00 (0.89-1.12)	0.84
Multivariable (univariable with p value <0.05)				
Sinus Rhythm vs AF	0.94 (0.77-1.15)	0.56	0.98 (0.74-1.32)	0.91
Heart Rate (per 10 bpm increase), SR	1.09 (1.04-1.14)	0.001	1.10 (1.01-1.20)	0.03
Heart Rate (per 10 bpm increase), AF	0.94 (0.87-1.00)	0.07	0.97 (0.99-1.01)	0.61

60412
Inferior vena cava dimension in patients with chronic heart failure; relationships and prognostic significance

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Introduction: The inferior vena cava (IVC) distends as right atrial pressure rises. Its relationship with other prognostic markers and its prognostic significance in patients with chronic heart failure has not been explored.
Methods: Out-patients attending a community heart failure service in 2009/10 were enrolled. Heart failure was defined as the presence of symptoms and signs of heart failure supported by evidence of important cardiac dysfunction: either left ventricular ejection fraction (LVEF) $<$45% or the combination of both left atrial (LA) dilatation ($>$4cm) and raised NT-proBNP ($>$400 pg/ml).
Results: Amongst the 470 patients included, median age was 73 years, 34% were women and 373 had heart failure (HF). In the patients with HF, and compared with those in the lowest tertile, those in the highest tertile of IVC diameter indexed to body surface area (IVC/BSA) were older, had lower BMI, were more often women, were more likely to have atrial fibrillation and to be treated with diuretics. They had larger LA volumes and more right ventricular dysfunction. LVEF, global longitudinal strain and systolic blood pressure were similar across tertiles. IVC/BSA correlated with NTproBNP ($r=0.69$ ($p<0.001$)). During follow up of 456 (IQR: 381 — 550) days, 54 patients with HF died. In a multivariable Cox regression model, including NTproBNP, only increasing IVC/BSA, urea and the trans-tricuspid systolic gradient by echocardiography independently predicted a poor outcome.
Conclusions: In patients with chronic heart failure with or without a reduced LVEF, increasing IVC/BSA identifies patients who are at increased risk of an adverse outcome.

60780
Prognosis impact of ischemic mitral regurgitation of acute coronary syndromes without st-segment elevation

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Introduction: Ischemic coronary disease by remodeling of left ventricle can cause mitral regurgitation even without intrinsic valvular disease. Ischemic mitral regurgitation is a dynamic pathology which evolution is hard to predict. Isolated coronary revascularization could be insufficient to a favorable clinical outcome.
Purpose: Our purpose was study incidence, clinical predictors and prognostic implications of this specific valvular disease in acute coronary syndromes without st-segment elevation. To avoid confound factors, patients with known history of cardiac ischemic disease, mitral valve disease, hypertrophic cardiomyopathy or those with mechanical

complications during hospital stay were excluded. A total of 236 patients (69,9% males, mean age of 63,4 ± 12,7 years) consecutively admitted during a period of 2 years were included and followed for a mean period of 202 days.
Results: We identified 40 patients (16,9%) with significant ischemic mitral regurgitation (moderate to severe). In this group, advanced age (71,0 ± 11,2 vs 61,8 ± 12,4 years, p<0,0001), female sex (50,0 vs 26,0%, p 0,003), diabetes mellitus type 2 (40,0 vs 21,4%, p 0,013) and history of atrial fibrillation (17,5 vs 6,6%, p 0,033) prevailed. Three-vessel disease (OR 2,93, IC 95%, 1,14-7,51) and left systolic ejection fraction inferior to 40% (OR 3,25, IC 95%, 1,35-7,81) were independent predictors of mitral regurgitation. Significant mitral regurgitation was associated with heart failure during hospital stay (65,0 vs 23,0%, p<0,0001) and follow-up periods (48,4 vs 19,2%, p 0,001) and with mortality during total period of follow (16,2 vs 3,9%, p 0,012). In multivariate analysis, ischemic mitral regurgitation was also an independent predictor of major adverse cardiovascular events which included death, heart failure, angina or re-infarction in the follow-up period (OR 4,08, IC95% 1,32-12,64).
Conclusion: In the studied population, ischemic mitral regurgitation was associated to various comorbidities and worse cardiovascular stratification risk, with prognostic impact after an acute coronary syndrome without st-segment elevation, whether in the acute event or follow-up.

60068
The prediction of one-year mortality in congestive heart failure patients: a clinical score

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The indication of implant of ICD in primary prevention in heart failure CHF) patients should consider subjects with a reasonable expectation of survival with good functional status>1 year. The aim of this study was to assess the utility of a score designed for discharged CHF patients.
Methods: 317 consecutive patients (196 males, age 72) with CHF were analysed. All pts were discharged after an acute episode of cardiac decompensation and an one-year clinical follow-up was obtained. A comparison with the Seattle Heart Failure Model was also performed. CHF patients underwent transthoracic echocardiography, plasma determination of BNP and the hydration analysis using a biompedence technique (Akern).
Results: at 1-year follow-up 24(7.5%) died for any cause. The comparison between the population of alive patients vs patients with worse prognosis demonstrated a clear impairment of renal function (creatinine 1.3±0.8 vs 1.6±0.7 mg/dl , p=0.003), left ventricular ejection fraction (LVEF) (44.2±15.8 vs 34±15.7% , p=0.002), NYHA class (2.8±0.7 vs 3.4±0.6 , p=0.001). A significant elevation of plasma BNP at admission (532.5±670.7 vs 1029±655.1 pg/ml, p=0.001), a fluid overload measured using a bioimpedence analysis (74.4±2.8 vs 79.7±5.6% , p=0.007) and a higher degree of frailty (Barthel index 86.2±24.5 vs 71.3±28 , p=0.01; ADL 5.7±6.3 vs 4.2±1.8 , p=0.006) emerged. According to the Seattle Score the 1-year survival probability sensitivity and specificity were 93.5% and 66.6%, respectively; the PPV and NPV proved to be 99% and 16.7%. A simple clinical score was created including creatinine plasma level (0 point <1.3 mg/dl; 1 point 1.3-1.5 mg/dl and 2 points >1.5 mg/dl), LVEF (0 point >45%; 1 point 35-45% and 2 points <35%), NYHA class (0 point I-II; 1 point III and 2 points IV), Barthel index (0 point >80; 1 point 50-80 and 2 points <80) and finally plasma BNP (0 point <500 pg/ml; 1 point 500-900 pg/ml and 2 points >900 pg/ml). A clinical score ≥6 points identified a 1-year probability of survival with a sensitivity of 73%, a specificity of 81%, a PPV 35% and a NPV 95%. A ROC curve was obtained with an area under the curve of 0.854 (p=0.0001).
Conclusions: in a single-centre heart failure clinic, a reasonable life expectation>1 year might not be extrapolated by Seattle Score. In a large population discharged after acute CHF, a clinical score including renal dysfunction, disability and plasma BNP gained a better specificity and NPV.

60659
Influence of microalbuminuria and inflammation markers on in-hospital and six-month prognosis after acute myocardial infarction

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Introduction and aim: Microalbuminuria develops in acute myocardial infarction (AMI) as a consequence of endothelial dysfunction, heart failure and general vascular inflammation.
The aim of our study was to investigate the correlation of microalbuminuria (measured as urinary albumin creatinin ratio — UACR: 2.5-25 mg/mmol in men and 3.5-35 mg/mmol in women) with markers of inflammation (C-reactive protein -CPR, fibrinogen and white blood cell count-WBC) and theirs' influence on in- hospital and 6-months prognosis in patients (pts) with AMI.
Methods and results: In our prospective study we enrolled 130 consecutive pts with AMI (63% men, 37% women; age 62.48±12.02 years). Markers of inflammation were measured at admission (CRP=25.6±50.9 mg/L; fibrinogen=5.3±2.4 g/L; WBC=10.9±3.8x10 9/L). Left ventricular ejection fraction (LVEF) (52.65±12.22%) and UACR (8.16±21 mg/mmol) were measured on the 3rd day after hospital admission. Microalbuminuria (MA) was found in 27.7% pts, and it had significant correlation with LVEF (r= - 0.259, p<0.01). We found positive correlation between UACR and CRP level (r=0.28, p<0.01), UACR and fibrinogen level (r=0.28, p<0.01) and UACR and WBC (r=0,18, p<0.05). Patients with MA had a 4 fold increased risk of total mortality rate (in-hospital and 6-months after AMI) in univariant regression analysis (OR=4.051; 95%CI: 1.149-14.283; p=0.03). Risk of development of pulmonary oedema during hospitalization was increased in pts with higher levels of fibrinogen (3 fold for 1 increased unit) and CRP (1% for one increased unit) [fibrinogen (OR=3.304;95% CI:1.051-10.383); CRP (0.1-2%)]. In multivariant analysis fibrinogen had stronger influence on pulmonary oedema development, independently of LVEF. Use of statins reduced the risk for more than 15 fold for in-hospital mortality (OR=0.07; 95%CI: 0.005-0.959; p=0.046).
Conclusion: Microalbuminuria frequently occurs in AMI patients and can be used to identify subjects on high in-hospital and 6-month risk. Developement of MA is associated with high markers of inflammation. Microalbuminuria in AMI pts is useful not only as an easily measurable and low-coast prognostic marker, but also could have influence on therapy. Use of statins in higher doses could lead to better outcome in AMI patients with microalbuminuria, since they have anti-inflammatory effects.

61116
Prognostic value of multimarker diagnostic coefficient for adverse events and heart failure in patients with acute coronary syndromes

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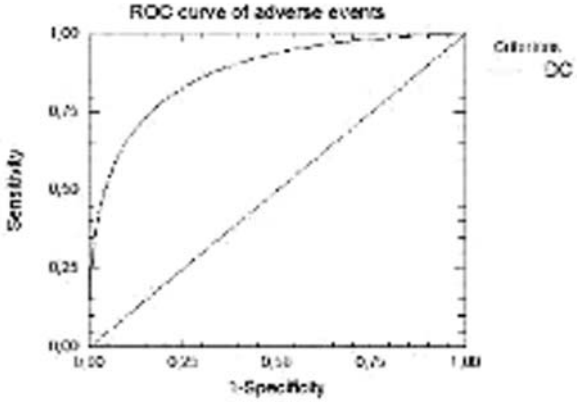
The aim of this study was to define the utility of the measurement N-terminal pro-brain natriuretic peptide (NT pro-BNP) and other clinical and biochemical markers to predict adverse events (death, stroke, reinfarct, unstable angina, revascularization or heart failure (III-IV NYHA class) at 1 year in patients with ACS.
Methods and results: We included 114 consecutive patients admitted in hospital for both non-ST-elevation and ST-elevation acute coronary syndromes. After one year-of follow-up, 18 patients (15,7%) died. Parameters with significant differences in patients with and without adverse events were taken for analysis: age, heart rate at admission, levels of hemoglobin and NT-proBNP. Curves of sensitivity and specificity were used based on the method of ROC analysis and cut-off values were chosen for each variable. Ball scoring was performed for each parameter regard to the cut-off value and a scale for calculating the summarized diagnostic coefficient (DC) by the method of Gubler was offered. Negative value of diagnostic coefficient was associated with adverse outcome in ACS patients. The summarized diagnostic coefficient has a sensitivity of 87.5% and specificity of 75.6% for the prediction of adverse outcome in patients with ACS within 1 year of follow-up.
Conclusion: A multimarker approach included on NT-proBNP, hemoglobin, heart rate at admission and age and the summation of balls based on offered scale and calculating diagnostic coefficient provides information in terms of ACS prognosis at 1 year, with a worse outcome for those with diagnostic coefficient has negative value.



Diagnostic coefficient in ACS (Abstract 61116 Figure)

60348
A prognostic index for heart failure after ICD implantation in ischemic cardiomyopaty. A new index for non arrhythmic death and heart failure

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Purpose: To evaluate a new prognostic index (PI) based on simple clinical parameters in patients (pts) with low EF and ischemic cardiomyopathy with ICD.
Methods: A total of 192 pts with previous myocardial infarction (MI) and ICD implantation for MADIT II criteria were enrolled. A PI was built with a single measurement of systolic blood pressure (PAS), obtained with oscillometric method (Spacelab 90207),

age, and creatinine levels according to the formula: IP= 120 − age + mean 24hPAS − (creatinine levels x 10). The end points of the study were death and new admissions for HF during one year follow-up. The PI, hemoglobin levels, EF, sodium levels, diabetes, biventricular pacing, heart rate (HR) and diastolic blood pressure (PAD) were evaluated in multivariate analysis.

Results: During the FU a total of 48 adverse events occurred (25%), 7 pts died for HF and 41 pts underwent a new admission for HF. Among the predictors only low PI values were associated with a higher incidence of events (HR=0.97, IC 95% 0.95-0.99; p<0.002). The ROC curve identified the PI value at 153 as the best cut-off (AUC 0.75, p<0,001, sensibility 67%, specificity 71%, positive predictive value 44%, negative predictive value 87%). Survival curves for PI confirmed low risk of events for pts with PI >153 (p<0.0001).

Conclusions: Although further studies are needed, the new PI index using only a simple clinical variable (single PAS measurement) can identify low risk patients with ischemic cardiomyopathy and ICD.

60019

Six minute walk distance and raised filling pressures predict mortality in patients with systolic heart failure

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Background and Aim: Six minute walk test (6-MWT) assesses exercise capacity in heart failure patients. We investigated the prognostic value of 6-MWT in a group of heart failure patients with left ventricular (LV) ejection fraction (EF) <45%.

Methods: We studied 77 consecutive patients (age 60 ± 12 years, 33.3% females) with stable heart failure who underwent 6-MWT and Doppler echocardiographic examination in the same day. LV dimensions, systolic function, myocardial velocities and spectral Doppler velocities were measured. Patients were divided into two groups based on the 6-MWT distance; limited exercise performance (≤ 300m) and good exercise performance (>300m). The primary outcome was mortality. Mean follow-up was 46 ± 15 months.

Results: During the follow-up period 31 died (40.3%). The NYHA class>2 (65% vs. 39%, P=0.025), restrictive filling pattern (61% vs. 37%, P=0.03) and 6-MWT≤ 300m (71% vs. 35%, P=0.002), were more frequent, E/E′ ratio (P=0.005) and blood urea (p=0.04) higher, LV end systolic dimension larger (p=0.026), LV shortening fraction (p=0.003) and EF (p=0.006) lower, total isovolumic time (t-IVT) and Tei index higher (p=0.014 and p=0.034, respectively), in the died patients compared to survivors. Multivariate analysis including age, gender, NYHA class, blood urea, T-IVT, E/E′ ratio, LV EF, restrictive filling pattern and 6-MWT, identified 6-MWT short distance (OR=0.987, 95% CI 0.977-0.997; P=0.011) and restrictive filling pattern as independent predictors of mortality.

Conclusion: In medically treated patients with non-rheumatic chronic heart failure and left ventricular systolic dysfunction, short 6-MWT distance and the presence of restrictive filling pattern independently predict mortality.

60405

Comparison of the effectiveness of different prognostic scales (Seattle Heart Failure Model, EFFECT, Heywood's model) in patients treated in out-patient heart failure clinic

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Relevance: Comparison of the evaluation effectiveness of the risk of death in patients with systolic chronic heart failure using the models, developed on the population of the U.S. and the EC countries, in Russia has not yet been conducted.

Purpose: To evaluate the prognostic significance of Seattle Heart Failure Model (SHFM), scale EFFECT, Heywood's model in patients with systolic chronic heart failure.

Methods: A retrospective study of medical charts and outpatient charts was conducted with estimation of the survival potential (SP) of the patients within 1 year using the above methods. Inclusion criteria were the following: patients with CHF II-IV FC and EF less than 30%, age less than 60 y.o.

Results: 89 patients with history of CHF were studied, 80% (n = 71) of them were male, 20% - female (n = 18). Severity of chronic heart failure at hospital discharge was 2,9 ± 0,7 FC, FC distribution of CHF (II: III: IV) - 29%:56%:16%; EF by Simpson was 23,7 ± 7,8%. Ischemic etiology of chronic heart failure was diagnosed in 49% of patients, 35% (n = 28) had a history of myocardial infarction. Regarding comorbidity, in 44% were observed cerebrovascular diseases, in 28% were cognitive impairments, in 25% were hepatic disorders, in 15% - Chronic Obstructive Pulmonary Disease, cancer occurred in 7% of cases. SP was assessed using Seattle Heart Failure Model, scale EFFECT and Heywood's model in the stable CHF status of the patient before discharge. Data on actual survival (AS) were obtained during a telephone interview. 20 patients died during 1 year, system EXCOR was implanted to two of them, two of the patients had heart transplantation. 30% of patients (n = 24) underwent implantation of devices for cardiac resynchronization therapy. AS of patients within 1 year of follow-up was 77%. SP, estimated in accordance with the scale EFFECT, was 77.3% (pAS — NS (difference is not significant)), for Heywood's model - 97,95%, which is 20.95% higher than AS (pAS <0.001), for SHFM - 90.8%, it is 13.8% higher than AS (pAS <0.05).

Conclusion: 1. The scale EFFECT demonstrated the most accurate assessment of SP within 1 year in patients with CHF in condition of the maximum possible compensation at the time of discharge from heart failure clinic.2. The risks of adverse outcome, calculated by Heywood's model and SHFM, significantly overestimate the survival potential in the studied patients. 3. Prognostic scales Heywood's model and SHFM are unsuitable for estimating of survival in patients from Russian Federation with systolic CHF receiving treatment and follow-up in an in out-patient heart failure clinic.

60567

Meta-analyses of survival and hospital readmission in HF patients enrolled in exercise based CR in the period between 1999 and 2010

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Purpose: The evidence of reduced mortality and hospital admissions in HF-patients attending exercise based cardiac rehabilitation (CR) is according to existing systematic reviews unclear. Our aim was to determine the benefits of exercise based CR programmes on deaths and hospital admissions in HF-patients.

Methods: Randomised controlled trials (RCTs) including patients with either systolic-HF (S-HF) or HF with normal ejection fraction (HFNEF) attending exercise based CR in the period between 1999 and Aug 2010 were searched through 5 different databases: Medline, CENTRAL, EMBASE, CINAHL, and PsycINFO. Baseline characteristics were calculated as means according to a weight of the sample size in each included trial (table 1). The primary outcomes were the relative risk ratios (RRs) of death and hospital readmission in HF patients attending CR synthesized by meta-analyses with a minimum follow-up of 6 months.

Results: Overall, 14,875 trials were yielded through the search strategy. Out of these, 18 trials were eligible for the meta-analysis of mortality versus 9 for hospital readmissions. The relative RR for death was not significantly decreased (RR, 0.90; 95% [CI], 0.79 to 1.03; P = 0.14) in contrast to the relative RR for hospital readmissions (RR, 0.64; 95% [CI], 0.48 to 0.87; P< 0.001).

Conclusion: Exercise based CR had a beneficial effect in HF-patients resulting in significantly decreased hospital readmissions, but not on mortality.

Baseline characteristics

Variables	Mean (Range); N= 18; Mortality	Mean (Range); N= 9; Hospital Readmissions
Comprehensive (%)	0.16 (0-1)	0.44 (0-1)
Age, years	61.7 (54.0-80.5)	62.8 (53.7-71.9)
Follow-up time, months	31.7 (6-72)	17.8 (6-60)
LVEF (%)	25.9 (23.5-41.0)	32.7 (25.0-51.0)
IHD (%)	0.57 (0.16-0.85)	0.36 (0.21-0.50)
≥3 times/week (%)	0.83 (0-1)	0.67 (0-1)
Exercise duration, months	21.1 (1-30.1)	7.9 (2-12)
Sample size, patients	219.6 (20.0-2331)	122.2 (25-200)
Combination of resistance and aerobic	0.35 (0-1)	0.67 (0-1)

Table 1. Baseline characteristics from studies including mortality and hospitalization. LVEF, Left ventricular ejection fraction; IHD, Ischemic heart disease.

60705

The determination of prognosis in heart failure patients with devices

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Introduction: The identification of patients at high risk of heart failure and death is an important issue for cardiac resynchronisation devices, influencing the decision to implant a pacemaker (CRT-P) or defibrillator (CRT-D).

Objective: To assess whether the Seattle Heart Failure Model (SHFM), validated in the United States, would be useful in a population of UK heart failure patients to determine suitability for CRT-D or CRT-P.

Method: A retrospective, cross-sectional study of 102 heart failure patients with CRT devices implanted between 2008-2011 was undertaken. The SHFM was used to predict the mean life expectancy and survival rates for each patient. The predicted results were compared with the real-world observed results.

Results: Five deaths were observed. The correlation coefficient between the predicted and observed 1- year and 2-year survival rate by quartiles were 0.07 (± 7.00) and 0.34 (± 11.18). The paired t-test between the predicted and observed mean life expectancy had a correlation coefficient of 0.127 and a p value of <0.05.

Conclusion: No correlation was found between the predicted and observed 1-year survival rates and mean life expectancy, and only a weak correlation between the predicted and observed 2-year survival rates. The SHFM may not be useful in deciding

which patients may receive additional benefit from CRT-D over CRT-P. Larger studies are needed to verify these results.

SHFM predicted versus actual survival

	Procedure CRT-P			
SHFM Annual Mortality %	Quartile 1 (n=13, 2.0-5.0)	Quartile 2 (n=15, 6.0-9.0)	Quartile 3 (n=13, 10.0-12.0)	Quartile 4 (n=13, 13.0-42.0)
Post CRT-P 1-year predicted survival %	96.2 ± 0.3	92.7 ± 0.3	88.8 ± 0.2	78.5 ± 2.9
Actual 1-year survival %	100	100	91.7	100
Post CRT-P 2-year predicted survival %	92.5 ± 0.6	85.7 ± 0.6	78.8 ± 0.4	62.8 ± 4.2
Actual 2-year survival %	100	88.9	83.3	90.0
	CRT-D			
SHFM Annual Mortality %	Quartile 1 (n=13, 2.0-4.0)	Quartile 2 (n=14, 5.0-8.0)	Quartile 3 (n=9, 9.0-12.0)	Quartile 4 (n=12, 13.0-47.0)
Post CRT-D 1-year predicted survival %	96.7 ± 0.2	93.6 ± 0.4	90.0 ± 0.4	82.4 ± 2.7
Actual 1-year survival %	100	100	100	100
Post CRT-D 2-year predicted survival %	93.6 ± 0.3	87.8 ± 0.7	81.2 ± 0.7	68.6 ± 3.8
Actual 2-year survival %	100	100	87.5	100

PATHOPHYSIOLOGY

60116

Neurogenic control of circulation in patients with severe heart failure: interconnection between efferent potential and baroreflex regulation of heart rate (study SICA-HF)

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Disturbed cardiovascular autonomic regulation is part of the heart failure (HF) syndrome and may reflect baroreflex dysfunction as well as reduced neurogenic reactivity.
Objective: To investigate chronotropic regulation of the heart in severe chronic heart failure.
Patients and methods: We examined 40 patients with CHF II-IV functional class, with ejection fraction (EF) <35%, mean age 56±8 years. 55% had HF due to coronary artery disease (CAD), In addition to standard clinical tests patients underwent autonomic function tests including evaluation of arterial baroreflex sensitivity (BRS) and the Valsalva index (VI). Haemodynamic variables were recorded continuously using the Finometer Pro device (FMS) with simultaneous ECG recording and subsequent spectral analysis of heart rate (HRV), blood pressure (BP) variability. The control group was age and sex matched healthy volunteers (n=33). Brain natriuretic peptide (BNP) was measured by immunoassay.
Results: Compared to the control group, patients with HF had reduced BRS (6.1±2.8 vs 10.1±5.4 ms/mm Hg, p <0.001) as well as VI (1.41±0.26 vs 1.84±0.37, p<0.001). HRV was also low in all frequency bands. In patients with HF, total HRV and VI were correlated (r = 0.56, p <0.001), but HRV was not associated with BRS. At the same time VI was associated with HF functional class (F = 8.27, p <0.001), EF (r =47, p <0.005), systolic and diastolic left ventricular volume (r =- 0.47, p=0.002 and r=- 0.46, p=0.003, respectively), as well as plasma BNP concentration (r=- 0.49, p=0.001). Interestingly, the VI was inversely related to the number of ventricular extrasystoles on Holter monitoring (r =-0.41, p=0.01). BRS was also associated with functional class of angina (F=2.6, p <0.05) and the number of significant coronary stenoses (F=3.8, p<0.01).
Conclusions: In HF, efferent chronotropic dysfunction is associated with decrease of myocardial contractility and severity of HF, whereas the arterial baroreflex dysfunction is mostly associated with the severity of CAD.
The research leading to these results has received funding from the European Union Seventh Framework Programme [FP7/2007-2013] under grant agreement n° 241558 (SICA-HF).

The research leading to these results has received funding from the Russian Ministry of Science and Education within the FTP "R&D in priority fields of the S&T complex of Russia 2007-2012" under state contract °02.527.11.0007.

60250

Circulating endothelial progenitor cells, cytokines, growth factors and NT-proBNP in patients with ischemic heart disease and chronic heart failure

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Endothelial Progenitor Cells (EPCs) were first described in 1997 and have since been the subject of numerous investigative studies exploring the potential of these cells in the process of cardiovascular damage and repair. Circulating EPCs are capable of differentiating into mature endothelial cells to assist in angiogenesis and vasculogenesis.
Purpose: To investigate EPCs mobilization during chronic heart failure (CHF) and their correlation with the severity, cytokine activation, growth factors and other clinic indicators.
Methods: Peripheral blood EPCs assessed both as CD133+ cells and CD133+ cells coexpressing CD34 and vascular endothelial growth factor (VEGF) receptor-2 cells, plasma tumor necrosis facror-α (TNF-α), C-reactive protein, NT-probrain natriuretic peptide (NT-proBNP), VEGF were studied in 106 men with ischemic heart disease and CHF I-IV class (NYHA), who were compared with 21 age-matched men with ischemic heart disease without CHF and 10 age-matched healthy control subjects.
Results: There was an decrease CD133+, CD34+/CD133+/VEGFR2+ cells in men with CHF compared without CHF (P<0.05) and healthy controls (P<0.05). Men with more severe CHF (class III–IV) had lower CD133+, CD34+/CD133+/VEGFR2+ cells (P<0.05), than class I-II. TNF-α (P<0.001), C-reactive protein (P<0.05), NT-proBNP (P<0.0001) were elevated in patients with CHF. A significant decrease levels of CD133+, CD34+/CD133+/VEGFR2+ cells (P<0.05) were detected with left ventricular ejection fraction (< 40%). CD34+/CD133+/VEGFR2+ cells negative correlated to age, smoking, New York Heart Association class, left ventricular ejection fraction, number of myocardial infarctions, NT-proBNP, and positive – to VEGF, CD34+, CD133+ cells.
Conclusions: EPCs mobilization was decreased in patients with ischemic heart disease with CHF, especially with more severe NYHA class, left ventricular systolic dysfunction and can be related to the myelosuppressive role of cytokine activation.

RIGHT VENTRICULAR FUNCTION

61024

Assessment of right ventricular systolic function by M- mode and tissue Doppler echocardiography in patients with pulmonary stenosis

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Objectives: To evaluate rightventricular (RV) systolic function in patients with RV pressure overloadanalyzing longitudinal tricuspid annular motions by M- mode and Tissue Doppler Imaging (TDI).
Methods: Study populationconsisted of 68 children divided into two groups: Group I (Control group): 43healthy children and Group II: 25 asymptomatic children with moderate to severepulmonary stenosis (PS). There were not significant differences in age, weightand sex between groups. Average pressuregradient across RV outflow tract in PS group was 81,3 ± 33,7 mmHg. Systolic RVfunction was assessed using following parameters derived from tricuspid annularmotion: amplitude of Tricuspid Annular Plane Systolic Excursion (TAPSE)measured by M-mode echocardiography, longitudinal tricuspid annular systolicvelocity (Sm) and isovolumetric contraction time (ICT) determined by TDI.
Results: Table shows results ofthe study:
Systolic longitudinal velocity(Sm) and amplitude of the tricuspid annulus (TAPSE) were significantly reducedin patients with RV pressure overload versus control group, but there was nodifference in duration of ICT.
Conclusions: Asymptomaticchildren with moderate to severe pressure overloaded RV have signs of impairedlongitudinal RV systolic function. Indices derived fromtricuspid annular motion are ease to obtain and appear to be sensitive andimportant tools for assessing right ventricular systolic function.

Results of the study

	TAPSE (mm)	Sm (cm/s)	ICT(msec)
Healthy children	22,1 ± 3,4	15,1 ± 2,3	42,8 ± 26,6
Pulmonary stenosis	17,4 ± 3,7	12,1 ± 3,0	48,7 ± 22,1
P value	< 0,005*	< 0,005*	0,432

Legend: *= statistically significant difference.

60067

Right bundle branch block as predictor of mortality after Chronic Right Heart failure. Right ventricle stress wall

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Introduction: The prognosis of patients with left bundle branch block after an acute myocardial infarction is known for everybody. What happen in a patient with heart failure and pulmonary arterial hypertension?
Patients with left bundle brunch block present injury in the conducting system of myocardium of left ventricle leading to delayed conduction.
Objectives: In our group we performed a follow-up with 100 patients with right heart failure, pulmonary arterial hypertension and studied 1000 thousand electrocardiograms with right bundle brunch block of these patients. All patients had right heart failure or diagnosed pulmonary hypertension. Diagnostic was made for clinical exploration and echocardiography study.
We realized a 3- and 6- month assesments fo cardiopulmonary treadmile test, echocardiography doppler procedures.
Results: All patients presented RBBB had affected the systolic right heart function. They presented high NT-pro BNP levels. Right heart failure was present in 83%. Echo parameters showed the progressive dilation of right cavities. Right catheterization showed high pressure in right ventricle and atrium. Treatment with diuretics and nitroglycerine gave positive results. Mortality: 35% of patients died after 5 years right heart ventricle disease.
Conclusions: RBBB is a good predictor of long-term mortality following chronic heart failure, right myocardial infarction, pulmonar arterial hypertension.
In patients with RBBB as a consequence of many episodes of heart failure with systolic heart dysfunction in echo, prognosis long-term mortality is the same in patients with LBBB. The difference is the affecting conducting system of left ventricle that represents the most important force to the heart. The mortality at 1,5,10 and 15 years is showed in table 1. RBBB in patients without coronary disease the first 10 years changes into LBBB not by the coronary affection, but for the combination of bilateral dysfunction, pulmonary dysfunction.

Table 1. Mortality at 1,5,10 and 15 year

Mortality	Year 1 (%)	Year 5 (%)	Year 10 (%)	Year 15 (%)
Non-BBB	21	42	61	73
LBBB	47	75	86	95
RBBB	39	61	79	89

(L)- and(R)BBB, left and right bundle branch block

LEFT VENTRICULAR FUNCTION

60627

Left ventricular rotation in hypertension with or without left ventricular diastolic dysfunction

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Purpose: The aim of our study was to asses the impact of increased arterial blood pressure (BP) values on the parameters of left ventricle (LV) rotation, both systolic and diastolic (diastolic recoil) in subjects with mildly or moderately elevated BP.
Methods: Our study included 45 patients (pts) with normal systolic function divided into 2 groups based on the presence of arterial hypertension (HA): Group 1 (30 pts) with HA (first and second degree) and Group 2 (15 pts) with normal BP. All patients underwent ambulatory blood pressure monitoring (ABPM). We performed standard two-dimensional echocardiography (2DE). Analysis was performed offline, using EchoPAC Workstation.
Results: There was no difference between Group 1 and Group 2 regarding age (49 ± 11 vs. 45 ± 10 years; p= 0.279) and gender (male: 41.7% vs. 56.7%; p = 0.296). There were significant differences between groups in left atrial dimension (LA) (36.47 ± 3.85 vs. 34.92 ± 3.06, p=0.001), interventricular septum diastolic thickness (IVSd) (10.97 ± 1.59 vs. 9.5 ± 1.0, p=0.005), posterior wall diastolic thickness (PWd) (10.8 ± 1.35 vs. 9.67 ± 0.99, p=0.012) and relative wall thickness (RWT) (0.44 ± 0.08 vs. 0.39 ± 0.03, p=0.047). Both groups were similar regarding the degree of basal and apical systolic rotation and LV torsion, but there was significant difference between groups in early diastolic recoil rate from LV base (RotRE) (41 ± 19 deg/s vs. 49 ± 14 deg/s, p=0.05). Also, comparing means, we didn't find differences in RotRE between pts with or without first/second degree diastolic dysfunction (post-hoc test Bonferroni). We established negative linear correlation between RotRE and: IVSd (r=-0.343, p=0.015), PWd (r=-0.411, p=0.003), isovolumetric contraction time (IVCT) (r=-0.286, p=0.044). RotRE correlated with ABPM measurements: total average systolic BP (r=-0.381, p=0.012), average daily systolic BP (r=-0.385, p=0.011) and percentage of systolic BP deviation (r=-0.356, p=0.019). According to Regression Model, total average systolic BP (β=-0.382, p=0.018) and IVSd (β=-0.304, p=0.050) were selected to be the strongest independent predictors of RotRE.
Conclusion: Our data showed that parameters of LV diastolic rotation differ according to total average systolic BP (measured by ABPM) and IVSd thickness. Subjects with higher systolic BP and greater IVSd thickness had downsloping in early diastolic rotation rate indepedent of the presence or absence of diastolic LV dysfunction.

60099

Effect of l-citrulline on endothelial and ventricular function in patients with systolic heart failure

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Background: The utility of l-arginine and l-citrulline in treatment of arterial hypertension, by increase vascular oxide nitric (ON) availability has been demonstrated. The photopletysmography, a simple and low-cost optical technique allow to assess the vascular function and is able to detect changes in blood flow, pulse and swelling of the microvascular space of tissues.
Objective: To evaluate the effect of L-citrulline on functional class, ejection fraction and peripheral blood flow in patients with systolic heart failure.
Methods: In a controlled clinical trial we included 35 outstanding patients with stable systolic heart failure and optimal treatment. The mean age was 68.2 years, with functional class NYHA I-III. They were divided in two groups: experimental group, with oral L-citrulline supplementation (3gr/day) and control group. They were followed during 4 months. Two measurements were made; basal and at the end of study, including clinical evaluation, photopletismography, recording maximal amplitude of the blood flow wave and evaluating the index Maximum Amplitude Time/Total Time (MAT/TT) in pre-ischemic and post-ischemic periods, as well as a radioisotopic ventriculography.
Results: Left ventricular ejection fraction (LVEF) increase 20.3 % at rest and 12.7% at effort, as well as in the right ventricle 15.10% and 14.88% at rest and effort, respectively, in the experimental group vs. control group, where decreased -6.47% at rest and -12.6% in effort .in LVEF and RVEF -10.7%. All of these changes except RVEF were statistically significantive. Functional class in the experimental group improvement of 35% (p=0.02); patients referred less dyspnea, compared with the control group in which there was no change. The MAT/TT index improved in the experimental group (-23.3% compared with the controls that increase 15.99% ($p<0.001$).
Conclusions: Citrulline supplementation can be an important co-adjuvant in the stable systolic heart failure treatment, improving functional class, endothelium dependent vasodilatation (share stress), and ejection fraction of both ventricles.

61165

Heart failure with preserved ejection fraction in hypertensive overweight and obese patients

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Background: The relevance of both hypertension and obesity, as important public health challenges, is increasing worldwide. Obese and overweight persons are at increased risk of heart failure. On the other hand, left ventricular (LV) diastolic dysfunction is an asymptomatic condition associated with future advanced heart failure events. We aimed to investigate possible effects of increased body size on left ventricular diastolic function in hypertensive patients with preserved ejection fraction.
Patients and methods: The LV diastolic function was evaluated in 207 hypertensive patients ($61+$ 5.7 years of age, 53% males) without coronary artery disease with preserved ejection fraction by traditional and tissue Doppler imaging. Peak early transmitral diastolic flow velocity (E), late transmitral diastolic flow velocity (A), and early diastolic mitral annulus velocity(E′) were measured, and E/A and E/E′ were calculated. Patients' data were noted and ECG was performed. The study participants were divided into 3 groups: normal weight (body mass index [BMI] $<$25.0 kg/m2) — a total of 24%, overweight (BMI 25.0 to 29.9 kg/m2) — 22%, and obese (BMI 30 kg/m2) - 54% .
Results: The results of our study indicated that there was no difference in systolic and diastolic blood pressure between normal weight, overweight and obese subgroups. Also there was no difference in left ventricular mass, septum and posterior wall tickness. BMI was associated with higher E, A, and E/E′, an indicator of LV filling pressure (all p 0.01). Overweight and obese had lower E′ (both $p < 0.01$) and higher E/E′ (both $p < 0.01$) than normal weight participants. The E/A was lower in obese subjects than in normal weight subjects ($p < 0.01$). The risk of diastolic dysfunction was significantly higher in overweight subjects.
Conclusions: Our results indicated that increased BMI was associated with worse LV diastolic function independent of LV mass and other risk factors. Further treatment is needed to reduce weight, but also to improve diastolic function and prevent disease progression.

60433

Predictive factors for the occurrence of mitral regurgitation in patients with left bundle branch block and its impact on left ventricular function

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Purpose: To identify the variables which predict the occurrence of functional mitral regurgitation in patients with complete left bundle branch block (LBBB) and its impact on left ventricular function.
Methods: A number of 50 patients aged 45-80 years with hypertension and LBBB without symptoms of heart failure or history of myocardial infarction, without known mitral regurgitation, other valvular or congenital heart disease, in sinus rhythm performed an initial echocardiographic exam and were evaluated after 1 year for the presence of mitral regurgitation and changes in LV dimensions, systolic and diastolic function.
Results: 16 patients had at the initial examination an EF $<$40% with moderate LV dilation (left ventricle end diastolic diameter LVEDD= 63,5 mm), the other 34 patients had normal EF (45-50%) and LV dimensions (LVEDD =52,3 mm). Coronarography was performed in pts with low EF and 3 pts had coronary stenoses of intermediate severity (50-70%), the rest had normal coronary vessels. The second examination after 1 year identified functional mitral regurgitation in 14 patients, 10 form the group with low EF. Mitral regurgitation correlated with QRS length (168 ms in pts with mitral regurgitation versus 124 ms in pts without valvulopathy p$<$0,04), low EF (71,4% versus 28,6% of patients, p$<$0,04), high blood pressure values (165/94 mmHg versus 143/92 mmHg), prolonged time interval between peak contration of LV walls (TDI) (60ms versus 45 ms, p$<$ 0,04) and more severe LV diastolic dysfunction (pseudonormal type in 78% versus 44% of patients). The presence of mitral regurgitation produced a slight increase in LV end- diastolic diameter (+3,5%), no change EF and correlated with deterioration of diastolic function (restrictive pattern in 42% versus 6% , p$<$0,04).
Conclusion: Functional mitral regurgitation appeared in 28% of pts with LBBB correlated with QRS length, low EF, high blood pressure and intraventricular dyssinchrony.

HYPERTENSION / LV HYPERTROPHY

60208

The genetics of echocardiographically measured left ventricular size in diabetes: a genome wide association study

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Purpose: Development of left ventricular hypertrophy (LVH) is a key pathophysiological step in diabetic cardiomyopathy and is associated with poor prognosis. There may be a genetic component to developing LVH. To investigate this we have conducted a population-based genome wide association study (GWAS) to identify genetic variants predictive of echocardiographically defined LVH in a large diabetic population case-control study recruited from the Tayside region of Scotland, United Kingdom.
Methods: This study was conducted using a prospective cohort of individuals with type 2 diabetes participating in the Go-DARTS (Genetics of Diabetes Audit and Research in Tayside, Scotland) study, which includes genetic and clinical information of patients with diabetes within the Tayside region of Scotland. A GWAS of echocardiographically defined-LVH was conducted in 973 cases (mean age=67 years; 461 females and 512 males) and 1438 controls (mean age=62 years; 591 females, 847 males) in which the DNA was analysed by the Affymetrix SNP array. Diabetic patients were defined as having LVH according to the American Society of Echocardiography criteria based on significantly increased direct 2D measurements (mean intraventricular septal thickness=1.35cm +/- 0.48cm, mean left ventricular posterior wall thickness=1.22cm +/- 0.354cm), relative wall thickness (mean=0.52cm +/- 0.290cm) or LV mass indexed to both body surface area (mean=135 g/m^2 +/- 82.8g/m^2) and height (mean=66.2 g/m^2.7+/- 39.5g/m^2.7). The GWAS was performed with adjustment for blood pressure, age, gender, height and weight.
Results: Initial analysis revealed several SNPs referenced in previous genomic studies were important here. These included rs1780324 (p value=1.86*10^-4), rs2008242 (p value=7.97*10^-4) and rs17421627 (p value=5.74*10^-4).
Further analysis also showed SNPs in close proximity to 2 loci previously implicated in LVH development also appeared to be important in this study. Further analysis and replication are required to determine whether these gene loci are truly significant at genome wide levels.
Conclusions: The datasets described above provide extensive scope to analyse the genetic basis of variation in echocardiographic variables, including LVH. Replicating any findings in other populations will be required to gauge the significance of any findings.

60494

Effect of spontaneous hypertension on membrane properties and function of rat heart and liver mitochondria: influence of treatment with captopril and nifedipine

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Purpose: Investigation the effect of hypertension and its treatment on membrane properties and on capability of rat heart and liver mitochondria (MIT) to maintain adequate oxidative ATP production.
Methods: Male spontaneously hypertensive rats (SHR) were treated with nifedipine (NIF, 10mg/kg/day, 4 weeks, p.o.) and/or captopril (CAP,80mg/kg/day, 4 weeks, p.o). We monitored systolic blood pressure (BP), heart rate (HR) and heart/body weight ratio of animals. Respiration of isolated MIT in state 3 i.e., in presence and state 4 in absence of exogenous ADP, respiratory control index, rate of oxidative phosphorylation (OPR) and ADP/O were assessed using the Clark oxygen electrode. Succinate and glutamate + malate were used as substrates. Fluidity and the content of conjugated dienes as well as Mg2+ -ATPase activity in membranes of MIT were also registered.
Results: Elevated BP, HR and developing cardiac hypertrophy, characteristic for hypertension, were accompanied with significant increase in O2-consumption and OPR of heart MIT. The latter results point to an adaptive response to hypertension-caused increase in energy demands of the myocardium. Liver MIT, like the heart MIT, also exhibited an elevated ATP production. Nevertheless, the increase in values of O2-consumption and OPR was much less expressed than in the heart. Treatments with CAP or with CAP+NIF prevented the increase in BP, HR and heart hypertrophy to a similar extent. Both antihypertensive therapies yielded to decrease in O2-consumption as well as OPR values to- or even below the levels registered in heart and liver MIT of normotensive control animals (p$<$0.05 — 0.01). MIT from SHR heart and liver exhibited moderate increase in membrane fluidity which was further potentiated by both types of treatment. Neither hypertension nor its treatments led to considerable changes in content of conjugated dienes in heart and liver MIT. This finding points to minor influence of free radicals on membranes of MIT in our experimental conditions.
Conclusions: ATP production in heart and liver MIT from SHR exhibited a certain degree of adaptation to increased energy demands resulting from increased work-load of the organ. Four weeks treatment either with CAP or with CAP+NIF decreased the arterial BP to approximately similar extent. Decreased workload of the heart might, at least in part, reverse the adaptation-increase of oxidative ATP production in both organs. VEGA: 2/0101/12, 2/0054/11, 1/0638/12, 1/0620/10, 2/7126/27, APVV-LPP-0393-09

60133

Assessment of left atrial volume and function in hypertensive patients with diastolic dysfunction: volumetric and speckle-tracking analysis

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Introduction: In hypertensive patients left ventricular diastolic dysfunction (LVDD) may result in left atrial (LA) morphophysiologic and functional changes.
Objectives: The aim of this study was to investigate the impact of LVDD on left atrial volumetric remodelling and function.
Methods: 106 hypertensive patients, with preserved ejection fraction, were divided in three groups according LVDD: normal (n=35), abnormal relaxation (Grade I, n=38) and pseudonormal (Grade II, n=33). Left atrial volume (LAV) was measured at three time points (maximal LAV, pre-atrial contraction volume and minimal LAV) and the following left atrial (LA) emptying volumes were then derived: LA passive emptying volume (LAPEV), LA conduit volume (LACV), LA active emptying volume (LAAEV) and LA total emptying volume (LATEV). All LA volumes were corrected for maximal LAV, which was indexed to body surface area (LAVI). We measured coresponding velocities from tissue Doppler at the level of the septal mitral annulus (e,a,s), including E/e. Global LA strain and strain rate parameters were assessed by two-dimensional speckle-tracking echocardiography as the average of six segmental values. Peak LA strain and strain rate during ventricular systole (S-LAs and SR-LAs), peak early diastolic LA strain and strain rate (S-LAe and SR-LAe), and peak LA strain and strain rate during atrial systole (SLAa and SR-LAa, respectively) were measured as LA function parameters.
Results: There was significant correlation between of LAVI and S-LAs (r=-0.340; p=0.0003), S-Lae (r=-0.296; p=0.002), SLAa (r=-0.371; p=0.0009), SR-LAs (r=-0.343; p =0.0003), SR-LAe (r=0.363; p=0.0001) and SR-LAa (r=0.362; p=0.0001) and between E/e and LAPEV (r=-0.349; p=0.0002) and E/e and LATEV (r=-0.334; p=0.0005). Significant diference of LAPEV (0.51 $\pm$ 0.21 vs 0.37 $\pm$ 0.18 vs 0.37 $\pm$ 0.28; p=0.009), LACV (3.28 $\pm$ 0.91 vs 2.86 $\pm$ 0.78 vs 2.66 $\pm$ 0.80; p=0.005), LAAEV (0.40 $\pm$ 0.16 vs 0.40 $\pm$ 0.14 vs 0.32 $\pm$ 0.11; p=0.008) and LATEV (1.01 $\pm$ 0.22 vs 0.93 $\pm$ 0.25 vs 0.85 $\pm$ 0.21; p=0.011) were found between groups, levels of atrial emptying volumes decreased from normal through Grade I and Grade II groups.
Conclusion: In hypertensive patients left atrial volume was expression of left ventricular diastolic dysfunction and coused impaired LA function assessed by Speckle-tracking echocardiography, wich may be considered a promising tool for the early detection of LA functional abnormalities in these patients. Functional left ventricular changes resulting in lower atrial emptying volumes as expression of diastolic dysfunction severity.

61095

The changes of viscosity and deformability indexes of erythrocytes in the patients with arterial hypertension and congestive heart failure after long-term usage of ramipril and losartan

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Purpose: to analyze the changes of erythrocytes' viscosity and deformability in patients with arterial hypertension (AH) of the III stage with congestive heart failure (CHF) II functional class after long-term therapy of ramipril and losartan.
Methods of research: We have inspected 93 patients with AH III and CHF II functional class according to the ESC Guidelines for diagnosis of heart failure (2008) and management of arterial hypertension (2007). The index of deformation (ID) and coefficient of viscosity of erythrocyte suspension (CVES) were estimated due to the method of Z.D. Fedorova, M.O. Kotovshchikova. Ramipril 5-10 mg (n=44) per day and losartan 50-100 mg (n=49) per day were prescribed by randomization. The period of supervision was 24 weeks.
Results: We have marked the reliable increase of ID of erythrocytes (31,7%, $p<0,05$) and decline to the CVES (16,3%, $p<0,05$) during using of ramipril. In relation to the estimation of changes of functional properties of erythrocytes during the use of losartan it is possible to mark an analogical change: an increase of ID (37,2%, $p<0,05$) and decline of CVES (6,8%, $p<0,05$). For comparison of clinical efficiency both ramipril and losartan in relation to influence on functional properties of erythrocytes we amount the patients with the expected effect, and number of patients was counted up also wherever a desirable effect wasn't got. A desirable result in relation to functional properties of erythrocytes was considered by increase of ID and decline of CVES. The attributable risk (AR) in relation to ID was established in 76,0% by ramipril and 65,0% by losartan, with therapeutic benefit of ramipril in 11,0%, and relative risk (RR) — 1,17 (0,89-1,51) and odds ratio (OR) — 1,69 (0,69-4,15). These data means high efficiency of both preparations identically, without advantage of relative risk (RR) and odds ratio (OR) relatively to ramipril. At the same time, AR in relation of decreasing CVES in 77,0% for ramipril and 51,0% for losartan, with therapeutic benefit (change of AR(CAR)) of ramipril in 26,0%, with advantage of relative effect (RR) and odds ratio (OR) relatively to ramipril (RR — 1,51 (1,1-2,1), OR — 3,26 (1,32-8,04).
Conclusions: Due to prescribing of preparations which influence on activity of the renin-angiotensin system, it was set an improvement of indexes of functional properties of erythrocytes ($p<0,05$). The influence of ramipril and losartan on the index of deformation of erythrocytes is identical, however ramipril had greater advantage in improving the coefficient of viscosity of the erythrocyte suspension.

60020

Health evaluation of hypertensive patients with heart failure using screening program of the center of health (russia)

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Cardiovascular diseases (CVD) remain the leading cause of death worldwide. Chronic heart failure (CHF) occurs in 5% of people under 65 and in 10% - over 80 years old, the prognosis and outcome of heart failure is greatly influenced by renal function. Centers of Health (CH) in Russia were created to examine working population for early detection of latent diseases.
Aim of this study was to evaluate health status of hypertensive patients, to identify signs of CHF and renal tubulointerstitial tissue (TIT) injury. Materials and Methods: From January to June 2011 4210 patients visited Moscow CH for complex examination. 36 healthy and 4174 people with insignificant and significant functional disorders were identified. Disease charts were analised with developed algorithm (age, sex, primary diagnosis and comorbidities, CVD risk factors, results of examination, etc.). All patients received comprehensive examination (dispersion heart mapping — the map of dispersion characteristics of "Cardiovisor - 06c" device was projected onto the surface of the three-dimensional computer model of the anatomical heart, so-called "Portrait of the heart", bioimpedansometry, angiologic screening with measurement of ankle-brachial index (ABI), cholesterol, complex "Health Express").
Results: The group of 250 patients (aged 54,3 $\pm$ 10,3 years, 183 female) was divided into 2 groups according to age (group 1 - 40 - 60 and Group 2 - 61 - 70 years). Increased index of "myocardium" was revealed in 30% (16% in group 1, 14% - in 2), signs of myocardial hypertrophy in 39% (18 and 21%, resp.), fluid retention - 44% (24 and 20% , resp.), excessive amount of adipose tissue-in 93% (48 and 45%, resp.), elevated BMI in 88% (44% in both groups), cardiovascular anamnesis in 72%, increased ABI in 15% and cholesterol - 59%, smokers - 15%. Using Spearman's rank correlation relationship between these parameters was evaluated. The highest correlation was observed between "myocardium"index, myocardial hypertrophy, fluid retention and amount of adipose tissue. First identified CHF was in 23 people in 1 group, and 24 - in group 2. Very high CV risk (SCORE scale) was in 2% of patients. The average GFR was 75,04 $\pm$ 17,3 ml/min/1, 73 m2. Spectrophotometric analysis of urine chloride-ion (which is equal to sodium excretion) showed delay of $Na+$ in 93.6% of subjects, that is responsible for TIT injury.
Discussion: High prevalence of newly diagnosed CHF and signs of TIT injury even with preserved GFR among people who visited CH and considered themselves to be healthy, says about importance of such screening programms for early disease detection.

HFPEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

60581

Specialist heart failure clinics: do we reassure patients by giving them a label?

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Introduction: Heart failure (HF) can be challenging to diagnose, especially for the primary care (GP) doctors. Specialist HF clinics have been advocated to provide efficient means of diagnosis and initiating evidence based treatment where appropriate. Usually only 30% patients referred to HF clinics have left ventricular systolic dysfunction (LVSD) by echocardiography. Patients diagnosed as non HF are reassured and discharged back to GP care. There is paucity of data on the long term outcome of patients labelled as non HF. We report on a cohort of patients referred to specialist HF clinic.
Methods: In a UK hospital, patients are referred from primary & secondary care to a one stop diagnostic HF clinic. By clinical assessment & echocardiography, patients are diagnosed either having LVSD or Non HF. LVSD patients are started on evidence based treatment. Non HF patients are referred back to their GP's. Among the non HF patients, a group was identified having HF with preserved ejection fraction (HFPEF), using the following criteria: Ongoing NYHA class II-IV symptoms & EF $>45\%$ on Echo, plus any two abnormal investigations. 1) Pulmonary oedema or cardiomegaly on Cxr. 2) LVH, LA diameter >40 mm, or E/A ratio <0.5) on Echo, and 3) LBBB, LVH or AF on ECG. Patient data was obtained from hospital & GP records, & cause of death from death certificates.
Results: From Jan 2002 to Dec 2007, 1034 patients were referred. 270 (26%) were diagnosed with LVSD. Of the 764 (74%) patients labelled as non HF, 242 (23%) fulfilled the criteria for HFPEF. Compared to LVSD, HFPEF group had more female & older patients, more had hypertension, AF & diabetes. Average number of admissions per patient to the hospital (2.38 v/s 2.85), & days spent in hospital (26.75 v/s 25.87) were equal in both groups. After a mean followup of 5.5 yrs mortality was high in both HFPEF and LVSD (50% v/s 60%), but strikingly different causes. LVSD had more HF deaths while HFPEF had more non-cardiovascular deaths (68 v/s 52, $P=0.0001$).
Conclusion:
1. HF clinics would mislabel upto 23% patients as non HF.
2. HFPEF patients had more cardiovascular co-morbidities, equally high 5 year mortality(50%), but significantly more deaths from noncardiovascular causes.
3. Cost of caring for both groups is equivalent as average admissions & days spent in hospital were equal.

60691

Proteomic analysis reveals a protein with anti-fibrotic potential

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Purpose: Heart failure with preserved ejection fraction (HFPEF) contributes to 20-50% of the heart failure population. Excessive fibrosis in the cardiac interstitium results in stiffness and reduced compliance of the left ventricle which leads to diastolic dysfunction (DD) and eventual HFPEF. In an effort to discover novel biomarkers and potential therapies to treat this condition, we performed 2D-DIGE proteomic analysis of at risk hypertensive patients and identified an interesting protein.
Methods: In order to understand the role of this protein (cryptonym: protein X) in relation to cardiac fibrosis further, we analysed serum and atrial tissue from 39 patients undergoing cardiac surgery for ischaemic and valvular heart disease. Protein X concentrations were measured using ELISA and compared with a comprehensive selection of fibro-inflammatory markers. The distribution and concentration of the protein in atrial tissue was estimated by immunohistochemistry (IHC). We also performed an animal study to investigate its therapeutic potential. Ten week old spontaneously hypertensive rats (SHRs) (n=10) were treated with recombinant protein X for a period of 12 weeks and echocardiographic findings were compared on completion of therapy with control SHRs (n=10) and wistar kyoto rats (n=10) treated with vehicle.
Results: Significant correlations were found between protein X and the collagen metabolic markers procollagen III N-terminal propeptide (PIIINP) and carboxy-terminal telopeptide of collagen type-I (CITP) (r: 0.62, $P<0.0001$ and r: 0.58, $P=0.0001$ respectively). It also correlated with the inflammatory cytokine interleukin 6 (IL-6) (r: 0.4, $P=0.0112$). IHC demonstrated that protein X was predominantly present in the myocardial interstitium and perivascular region, hence co-localising with collagen. Echocardiographic analysis of left ventricular mass index revealed a significant ($p=0.0004$) reduction in hypertrophy in treated SHRs compared to untreated SHRs. There was no effect of treatment on blood pressure.
Conclusions: Fibro-inflammatory correlations and immunohistochemical findings suggest that protein X expression may increase to combat cardiac fibrosis. This hypothesis is supported by the finding that augmentation of protein X in SHRs significantly reduces left ventricular mass. Our results indicate that protein X may have potential as an anti-fibrotic therapy in DD and HFPEF.

60105

The effect of perindopril treatment on echocardiographic diastolic and systolic functional parameters and serum NT-proBNP values in diastolic heart failure patients

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Purpose: In this study, we investigated the effects of perindopril treatment on echocardiographic diastolic and systolic functional parameters and serum NT-proBNP values in patients presenting to the Cardiology Depart. of Izmir Ataturk Education and Research Hospital with diastolic heart failure (DHF).
Methods: We included 108 patients who presented between May 2008 and March 2009 with HF symptoms. They were ≥50 years old, had EF ≥ 50% and echocardiographic diastolic dysfunction. The patients were randomised to 2 groups (54:54 patients). Perindopril treatment(10 mg/day) was started to the first group, whereas the second group had standard DHF treatment. Blood was drawn for NT-proBNP.The patients were followed for 11 months on average (3-16 months). 17 patients quitted the study and 3 patients died.Totally 88 patients completed the study. At the end of the follow-up period, NT-proBNP values and echocardiography were reassessed.
Results: Mean basal NT-proBNP level was 296 pg/ml. Average basal E′(mean) velocity was 6.5cm/s, E/E′(mean) ratio was 11.2. Patients in the first group used calcium antagonist drugs more frequently than patients in the second group (76% vs. 54%). At the end of the follow-up period, mean NT-proBNP value was 249 pg/ml, E′(mean) velocity was 6.9 cm/s, E/E′(mean) ratio was 11.4. At the end of the study, NT-proBNP values were not significantly different between the two groups (mean values 263 pg/ml vs. 238 pg/ml). Perindopril treatment increased A'(septal) velocity (+0.61 cm/s), Sm(septal) velocity(+0.99 cm/s) and Sm(mean) velocity (+0.9 cm/s). But A'(septal) velocity decreased in the second group (-0.28 cm/s).
Conclusion: Perindopril treatment did not improve important echocardiographic diastolic parameters and NT-proBNP values, but it increased tissue doppler A'(septal) and septal systolic myocardial velocities in DHF patients.

Comparison of echo parameters

	Group 1 (n=37)	Group 2 (n=51)	P value
E′(mean) velocity (cm/s)	7.0 ± 0.5	6.8 ± 0.7	0.165
A′(septal) velocity (cm/s)	10.8 ± 2.4	9.9 ± 1.2	0.036
E/E′(mean) ratio	11.2 ± 2.4	11.6 ± 2.7	0.487
Sm(septal) velocity (cm/s)	8.5 ± 2.2	7.6 ± 1.4	0.016
Sm(mean) velocity (cm/s)	8.3 ± 1.6	7.7 ± 1.1	0.034

Comparison of some echocardiographic parameters between two groups at the end of 11 month follow-up period.

60967

Phenotype of pulmonary hypertension in patients with heart failure and preserved ejection fraction

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Background: Because pulmonary hypertension (PH) seriously worsens prognosis of patients with Heart failure and preserved ejection fraction (HFPEF), new drugs are currently being tested to improve hemodynamic and outcomes. The purpose of this work is to establish the prevalence and determinants of PH in patients with HFPEF.
Methods: Between 01/12/2008 and 06/12/2011, we prospectively included patients with HFPEF recently discharged from hospital for worsening heart failure (Framingham criteria, BNP>100, EF>50%). Two months later, all patients underwent a full echocardiography study. Patients were dichotomized from the tricuspid regurgitation peak velocity (TRV < 3m/s or TRV > 3m/s i.e. high prevalence of PH).
Results: From 67 patients with HFPEF, 7 patients had undetectable TRV. Of the 60 remaining patients, 20 (33 %) had TRV< 3m/s and 40 (67%) had TRV> 3m/s. Weight (p=0,03, r =-0,27) , E velocity (p=0,002, r =+0,38), E/A (p=0,02, r=+0,38) both septal (p=0,02 , r=-0,29) and posterior wall (p=0,04 , r =-0,26)thickness, hemoglobin (p=0,02, r =-0,30), calcium blocker (p=0,05, r =-0,25) were univarietely but not independently correlated to TRV. From multiple regression analysis, the four residual determinants of TVR were weight (p=0,003), E velocity (p=0,03), parietal thickness (p=0,03) and calcium blocker administration (p=0,03).
Conclusion: Pulmonary hypertension is prevalent in patients with HFPEF. Pulmonary hypertension in HFPEF is correlated to weight, E velocity, parietal thickness and calcium blocker prescription.

ANIMAL MODELS AND EXPERIMENTATION

60139

Restoring cardiac gene expression and function by myocardin gene silencing in the porcine model of heart failure

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Background: Myocardin (MYOCD), a potent transcriptional activator of smooth muscle (SM) and cardiac genes, is upregulated in failing myocardium in animal models and human end-stage heart failure (HF). However, the role that myocd gene activation plays in HF conditions has yet to be determined.
Aim: To study if targeted inhibition of upregulated expression of myocd could influence failing heart gene expression and function.
Methods: The myocd short hairpin (sh) plasmids were delivered (using our catheter-based, video-assisted protocol) into left ventricular (LV) myocardium of neonatal piglets with diastolic HF (DHF) induced by Doxorubicin (Dox). Conventional molecular biology (RT-qPCR, Western blot) and cardiac parameter (ECG, cardiac output, LV end-systolic/diastolic pressure) measurements were used to examine the expression and functional consequences of transient myocd silencing in piglet failing myocardium.
Results: To meet the requirements in respect of specificity and knock-down efficiency of myocd-silencing and to control off-target effects, the following experimental design was applied. Piglets were injected with Dox or PBS. Two weeks later, Dox-treated animals with mid stage DHF received intramyocardial injections of sh-plasmids against myocd (Dox/sh-myocd group, n=12) or sh-scramble vector (Dox/sh-scr group, n=10), whereas PBS-treated piglets were intramyocardially injected with sh-scr vector (PBS/sh-scr group, n=10). In the Dox/sh-scr group, the development of severe diastolic dysfunction (with ECG-signs of ischemic changes) was associated with a significant upregulation of myocd and its SM-targets (CNN1, MYH11, ACTA2, ACTG2 and TAGLN) in failing myocardium as compared with myocardium of PBS/sh-scr-injected animals. In the Dox/sh-myocd group, myocd silencing resulted in a decrease in endogenous myocd and SM-gene expression in failing LV-myocardium, reaching the levels comparable with those in non-failing PBS/sh-scr-injected animals. Such adjusting of MYOCD and SM-target levels to the scores measured in non-failing controls was associated with restoring of impaired diastolic function and amelioration of ischemic symptoms. These effects of myocd silencing were transient (lasting 4-5 days) followed by a return to elevated myocd expression levels that was associated with the redeterioration of diastolic function (on day 6-8 after sh-myocd delivery).
Conclusions: The results strongly suggest that a moderate inhibition of exaggerated myocd expression in HF settings is sufficient to restore, at least partly, deteriorated cardiac gene expression and function.

60569

Electrophysiological remodelling and defective calcium handling are associated with alternans in rats with right ventricular failure

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Purpose: Electrical alternans is a recognised risk factor for sudden cardiac death in patients with heart failure. Although sudden death is a prominent feature of right ventricular (RV) failure, the electrophysiological remodelling associated with this pathological condition remains relatively understudied. Here we investigated the presence and the mechanisms underlying alternans in a rat model of pulmonary artery hypertension (PAH) and RV failure.
Methods: Wistar rats were injected intraperitoneally with monocrotaline (60 mg/kg) to induce PAH and RV failure within 4 weeks (MCT) and compared to age-matched saline-injected animals (CON). ECGs were monitored in unrestrained rats by radiotelemetry. Animals were sacrificed upon showing clinical symptoms of heart failure. RV electrical activity was optically mapped in Langendorff-perfused hearts loaded with the voltage-sensitive dye di-4-Anepps. RV myocytes were enzymatically isolated and loaded with either Fura-4F to monitor cytosolic Ca2+ level or with Fluo-4 to record spontaneous Ca2+ release.
Results: In vivo ECG recordings performed in MCT rats showed prolonged QT interval (P<0.001), time from peak to end of the T-wave (P<0.001), shorter RR interval (P<0.01) and alternans in 3 out of 7 MCT rats. Discordant action potential duration (APD) alternans was also observed in the RV of MCT perfused hearts when electrically stimulated above 10Hz (P<0.05). A profound electrophysiological remodelling was found in the RV of MCT hearts, including a prolonged APD (APD80 CON 52.3 ± 2.8 ms vs. MCT 89.0 ± 4.8 ms, P<0.001), greater APD dispersion (P<0.001) and altered APD and conduction velocity restitution properties (P<0.001). Ca2+ transient alternans were observed in MCT RV myocytes paced at 9Hz but not in CON (P<0.001) and are likely to be associated with mechanisms responsible for the increase in sarcoplasmic reticulum (SR) Ca2+ spark leak (CON 17.75 ± 1.22 $\Delta F/F0.\mu m^3.s\text{-}1$ vs. MCT 58.75 ± 5.48 $\Delta F/F0.\mu m^3.s\text{-}1$, P<0.001), SR Ca2+ release fraction (CON 0.51 ± 0.03

vs. MCT 0.66 ± 0.02, P<0.001), and the slowed SR Ca2+ uptake (CON 15.96 ± 1.17 s-1 vs. MCT 12.03 ± 0.48 s-1, P<0.01) observed in these cells.
Conclusion: Altered restitution properties, together with Ca2+ handling abnormalities lead to the generation of electrical alternans in PAH-induced RV failure. Electrical alternans in the presence of a marked APD heterogeneity put MCT rats at a high risk of developing re-entrant arrhythmias.

60213
Novel rat model reveals important roles for beta-adrenoreceptors, the Gi-protein-pathway and disturbed metabolism in stress-induced cardiomyopathy

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Background: Stress-induced cardiomyopathy (SIC), also known as takotsubo cardiomyopathy, is an acute cardiac syndrome with substantial morbidity and mortality. The unique hallmark of SIC is extensive ventricular dysfunction (akinesia) involving apical segments with preserved function in basal segments. Adrenergic overstimulation plays an important role in initiating SIC, but the pathophysiological pathways and receptors involved are unknown.
Methods: Sprague Dawley rats (300 g) were injected with the β-adrenergic agonist isoprenaline (25, 50, 100, 150, 300, 450 mg/kg) i.p. Echocardiography was performed to quantify the degree of left ventricular akinesia and global cardiac function. A subset of animals was pretreated with a selective Gi-protein or β2 receptor inhibitor. Cardiac tissue was obtained from SIC patients in the acute (n=4) and recovery (n=2) phase and from rats two hours post ISO. Histological assessment of intramyocardial lipid and glycogen content was performed.
Results: Isoprenaline at doses ≥50 mg/kg induced severe SIC-like regional akinesia in rats. Gi inhibition was associated with significantly increased acute mortality post ISO (p<0.05) whereas β2 receptor blockade was associated with a non-significant trend towards less severe apical akinesia. In patient and rat cardiac tissue, severe intracellular lipid accumulation could be observed in akinetic but not in normokinetic myocardial segments (p<0.05).
Conclusions: We provide a novel rat model of SIC that supports the hypothesis of circulating catecholamines as initiators of SIC. We propose that the Gi-pathway may be protective in the setting of severe catecholamine overstimulation and that perturbations of cardiac metabolism occur in SIC.

60380
Anti-inflammatory effect of intravenously administered bone marrow cells in a rat model of myocardial infarction

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Objectives: Using human placental alkaline phosphatase (ALPP) as a genetic cell tracking marker, we aimed to investigate the contribution of endogenous bone marrow cells (BMC) in post-ischemic cardiac repair as well as engraftment and therapeutic efficacy of intravenously administered BMC in experimental myocardial infarction (MI).
Methods: Human placental ALPP was used to track genetically labeled cells in histochemical tissue preparations enabling high sensitivity of detection without background staining. Lethally irradiated wild-type (wt) F344 rats were reconstituted with bone marrow from ALPP-transgenic (tg) F344 rats and subjected to coronary ligation for 30 minutes followed by reperfusion. Sham-operated animals underwent the same procedure except artery ligation. Nine days after sham/MI operation 10 million BMC from ALPP-tg donor rats or PBS was injected via tail vein. Engraftment of intravenously injected ALPP-tg BMC was histologically examined in marker-tolerant immunocompetent wt F344 rats. Cardiac function was evaluated by echocardiography and infarct size was measured after Masson-Goldner trichrome staining. Immune response and cytokine production were evaluated histologically, by ELISA, and by qPCR.
Results: Histochemical ALPP staining revealed that endogenous BMC gave rise to endothelial cells in the heart but provided no evidence that endogenous BMC contributed to cardiomyocyte regeneration in sham and MI rats. After MI, ALPP+ cells from bone marrow massively infiltrated the left ventricle. Interestingly, i.v. treatment with BMC reduced the number of ALPP+ infiltrating cells, mainly CD68+ macrophages, whereas the number of bone marrow-derived endothelial cells was not affected. Compared to PBS, BMC treatment decreased the serum levels of interleukin (IL)-1β and IL-6, and increased mRNA abundance of IL-2 in the myocardium. As a result, infarct size was reduced from 20.39 ± 9.09 in MI to 12.3 ± 3.24 one week after BMC treatment, expressed as a percentage of left ventricle area. Additionally, echocardiography indicated improved LV contractility in BMC-treated MI rats. We found no evidence for engraftment of intravenously injected BMC in the myocardium.
Conclusion: We propose that treatment with BMC in a model of established myocardial infarction exerts moderate beneficial effects on cardiac function by reducing post-ischemic myocardial inflammation.

60215
Absence of the androgen receptor is associated with increased mortality and impaired cardiac function in response to high doses of catecholamines

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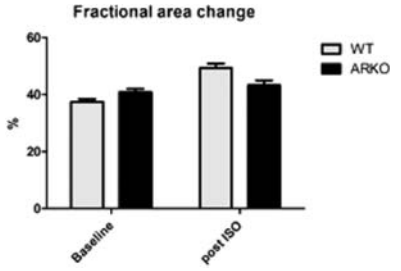
Purpose: Stress-induced cardiomyopathy (SIC), or Takotsubo cardiomyopathy, is an important differential diagnosis to acute myocardial infarction (AMI), as the patients present with chest pain, ST segment elevation and extensive myocardial wall motion abnormalities. This extensive ventricular dysfunction is frequently associated with potentially lethal complications, such as cardiogenic shock, malignant ventricular arrhythmias, cardiac rupture and death. Post-menopausal women are the most commonly affected group and a strong somatic or emotional stressor is thought to trigger an event. Catecholamines are believed to trigger cardiac dysfunction in SIC and estrogen has been shown to be protective. The question whether androgen receptors play a role in the gender disparity of SIC has not been addressed.
Methods: Androgen kockout mice (ARKO) and wildtype littermates (WT) underwent echocardiography at baseline and 90 minutes post a single dose intraperitoneal isoprenaline injection (450 mg/kg). ECG-gated Kilohertz visualisation technique (EKV) was used to acuire >1000 frames/s cine loops in which the endocardial area at end-diastole and end-systole was traced and fractional area change (FAC) was calculated.
Results: FAC was similar in ARKO and WT mice at baseline but was significantly worse in ARKO mice post isoprenaline. 10-day mortality was 55.6% in ARKO mice whereas no WT mice died (p<0.05).
Conclusions: In mice, the androgen receptor is protective in the setting of severe catecholamine induced cardiotoxicity. Androgens may partly explain the gender disparity observed in clinical SIC.



(Abstract 60215 Figure)

GENE AND CELL THERAPY

60739
Case of non-specific systemic inflammatory reaction after intracoronary infusion of bone marrow mononuclear cells (BMMCs) to patient with moderate chronic heart failure (CHF)

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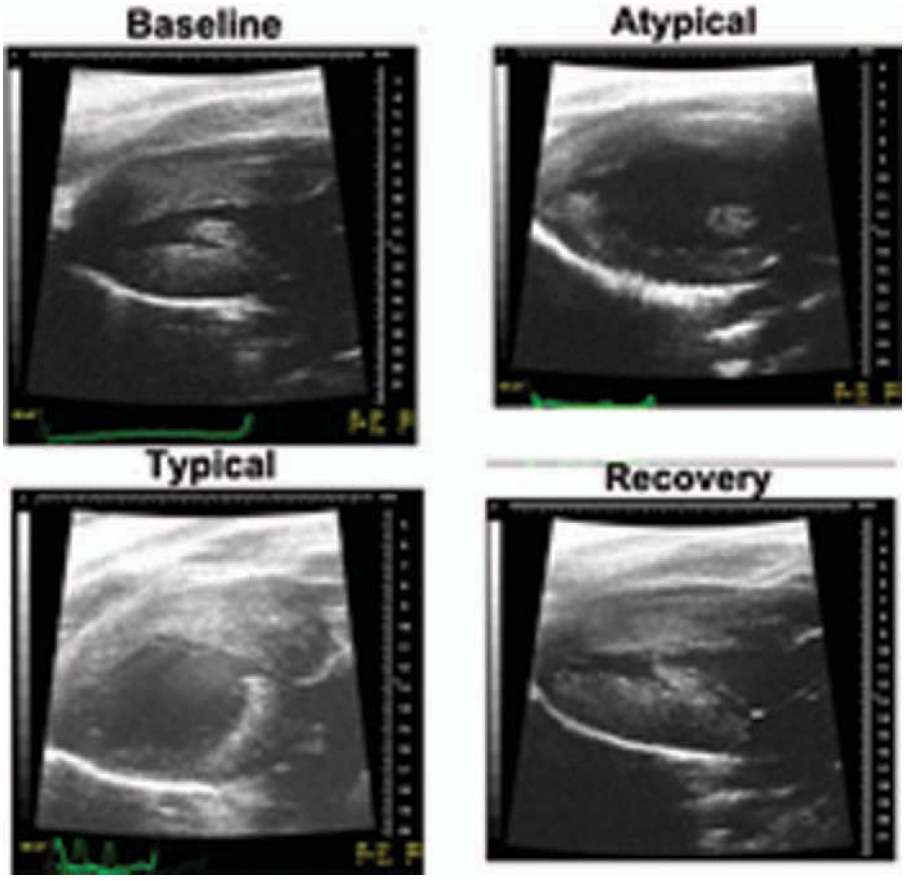
We've investigated the efficiency and safety of intracoronary BMMCs transplantation to patients with moderate CHF caused by myocardial infarction (MI). Here we'd like to present the case of non-specific systemic inflammatory reaction related to this procedure. We didn't find references on description of similar reaction after BMMCs infusion. Patient male 54 years old with history of pulmonary and bones tuberculosis in childhood survived after transmural MI 2 years before recruitment in this study. He was randomized in group of intracoronary infusion of BMMCs. Erratic pains, oedema and redness in different joints with elevation of body temperature till 39,8 C° emerged in 3 days after treatment. Leucocitosis till 13.4x103/ mcL and rise of C-reactive protein (CRP) till 6 mg/dl took place during first 7 days. Complex examination was performed to exclude infections, sepsis, acute rheumatic fever, rheumatoid arthritis, myeloproliferative disorder. Initial treatment with nonsteroidal antiinflammatory drug and antibiotics was ineffective — symptoms continue to persist, leucocitosis increased till 19.7x103/ mcL, CRP — 30 mg/dl, anemia developed. Two sessions of plasmapheresis was performed additionally. Condition was estimated like non-specific systemic inflammatory reaction, peroral treatment with methylprednisolone started. Joints pain resolved gradually during 7 days. Besides body temperature, account of leucocytes, erythrocytes and CRP level were normalized. Patient was discharged in satisfactory condition with recommendation of slow rejection of methylprednisolone within 1 month. Control examination lead in 3 months showed good general condition, non-specific systemic inflammatory reaction didn't relapse.
It was previously shown that after intracoronary infusion of BMMCs level of pro-inflammatory cytokines increased in more degree against control group. We propose that this patient with history of tuberculosis may had similar but more significant pro-inflammatory reaction on cells infusion probably due to some unknown initial changes in immune status. Further study of safety of cell therapy should be conducted.



End-systolic echocardiographic images (Abstract 60213 Figure)

60898

Genetic aspects of pharmacotherapy of arterial hypertension and chronic heart failure

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Research objective: Determine the value of genetic markers in the prediction of the flow and effectiveness of pharmacotherapy of arterial hypertension (AH) and chronic heart failure (CHF) on the basis of complex pharmakogenetic analysis.
Materials and methods: The study involved two groups of patients with AH and CHF in age from 27 to 83 years. 1 group: patients with AH and CHF (23 people) and patients with AH without CHF (22 people). In patients without CHF mainly observed AH 2 stage in 86,6% of patients, 1 degree in the 72,7%; in patients with CHF - AH 3 stages from 51,1% of patients; 3 degree in the 60,9%. Performed pharmakogenetic testing with the study of polymorphisms of genes (AGT: 704, AGT: 521; AGTR1: 1166, AGTR2: 1675). group 2: 129 patients with AH II stage, 1-3 degrees.In 26% of patients had a place AH 1st, on 56% - 2-th and 16% - 3-rd degree of gravity. Held pharmakogenetic survey with the definition of options in the genes of the ACE, NOS3, CYP2D6. Patients randomized into 3 groups of patients with different variants of genotypes.
Results and discussion: IN group 1 the frequency of occurrence of polymorphisms of genes responsible for the activity of the ACE (AGT: 704, AGTR1: 1166, AGTR2: 1675) in patients with CHF was higher than in patients without CHF and was within the range from 19,2% to 33,3%. In group 2 it was found that among the options ACE gene is the most common I/D genotype, he met in 50,5% of cases; among the variants of NOS3 gene of the most often met E298E genotype - in at 53,5% of cases, and among the options CYP2D6 gene - NON CYP2D6 *4/ NONCYP2D6 *4 genotype in 72% of the cases. Detection of polymorphism of the ACE in the form of genotype D/D in 29% of cases indicates that the risk of the development in this group of IHD, myocardial infarction, and stroke is higher in 1.5-2 times, than in the group with I/I genotype. In the group with the polymorphism of gene ACE in the form of genotype D/D fairly often met arterial hypertension of 2-3 degrees, and in the group with genotype I/D AH of the 2nd degree. In the treatment group 92% of patients achieved target figures: in the group with I/I genotype significantly more frequent in the monotherapy valsartani 80 mg; in the group with D/D genotype on therapy valsartani 160 mg + indapamidi 1,5 mg.
Conclusions: the genes responsible for the enzyme activity may be of value not only in the progression AH, but also in the development of CHF. It is necessary to apply different doses of valsartani to reach the target of AH in patients with genetically determined increase in the activity of the angiotensin-converting system.

61164

Inhibition of endogenous Wnt/beta-catenin following miR-29a upregulation mediates differentiation of cardiac stem cells into cardiomyocytes

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Adult cardiac stem cells (CSC) have the potential to differentiate into cardiomyocytes thereby contributing to the regeneration of the injured myocardium. However, the signaling mechanisms presiding in their induction into final differentiation are largely unknown.
We isolated, characterized and clonally expanded Sca-1+ CSC from murine adult hearts. These cells can differentiate into cardiomyocytes upon treatment with 5-Azacytidine (AZA, 5 μM) and transforming growth factor β1 (TGF-β1, 1ng/ml), as determined by a clear upregulation of mRNA encoding early and late cardiomyocyte markers (Nkx2.5; 230 $\pm$ 3.5%; n=3, $p<0.05$; cTnT; 40-fold over control). In parallel, we found that DETA-NONOate (1μM) stimulates the differentiation of Sca-1+ CSC into the cardiac lineage, as revealed by the increased number of cTnI+ cells (from 13.3 $\pm$ 9.3% to 37.3 $\pm$ 18.2%; n=5; $p<0.05$). We previously showed that cardiac differentiation was enhanced in Sca-1+ CSC isolated from mice with inducible deletion of β-catenin. In undifferentiated Sca1+ CSC, we detected a constitutive activity of canonical Wnt/β-catenin, nitric oxide-dependent, suggesting an inhibitory effect of NO on Wnt signaling (as confirmed in a β-catenin activity reporter assay with DETA-NONOate: 37 $\pm$ 4.9%; n=3; $p<0.05$). Consistent with our previous results, differentiation of Sca1+ CSCs with either AZA+TGF-β1 or Deta-NONOate induced a parallel downregulation of the Wnt target genes (AZA+TGFβ, Axin2: 59.7 $\pm$ 15.5%; Wnt 4: 53.7 $\pm$ 19.8%; Deta-NONOate, Axin2: 78.3 $\pm$ 3.8%; Wnt4: 70 $\pm$ 4.6% ; n=3; $p<0.05$). Accordingly, treatment of Sca-1+ CSC with pharmacological drug inhibiting Wnt signaling (Inhibitor of Wnt Response, 10μM) activated their cardiac differentiation (assessed by cTnI immunostaining), demonstrating a causal link between extinction of the Wnt pathway and differentiation. In search of endogenous molecular regulator(s) coordinating theses changes, we found that miR-29a was upregulated in CSC during cardiac differentiation (AZA+TGFβ: 444.1 $\pm$ 43.2%; Deta-NONOate: 189 $\pm$ 56%; n=3; $p<0.05$). This was associated with a decreased abundance of the DNA methyltransferase Dnmt3a, a bona fide target of miR-29a, and an upregulation of the Wnt antagonist HBP1, for which the promoter is enriched in CpG islands (AZA+TGFβ: 170.7 $\pm$ 37.7%; Deta-NONOate: 196 $\pm$ 17.5%; n=3; $p<0.05$).

We conclude that extinction of the endogenous canonical Wnt/β-catenin pathway promotes Sca-1+ CSC differentiation and involves miR-29a epigenetic control on Dnmt3a expression, relieving the inhibition of Wnt antagonists expression such as HBP1, possibly amenable to therapeutic modulation for cardiac repair.

60081

RhoA knockdown by RNA interference mediated by liposomal nanomedicine induces efferocytosis which activates death of apoptotic macrophage M1, and inflammation-resolution in advanced atherosclerosis

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Introduction: The aim of this research work is to prevent ATVD by repairing defective efferocytosis with antisense therapy which is facilitated by nanomedicine.
Methods: We formulate vasculature-endothelium targeted-pegylated colloidal nanoparticles composed of phosphatidyl-serine(PS),cationic and fusogenic lipids complexed with siRNA molecules for posttranslational gene silencing or RNAi of RhoA ,termed as EAS-PCNs.With these,we treat advanced atherosclerotic lesions of the intima where apoptotic macrophages that arise from ER-stress induced apoptosis(Mϕ) become secondarily necrotic coalescing into necrotic cores which form plaques vulnerable to rupture triggering acute luminal thrombosis and arterial occlusion due to impaired efferocytosis(Mϕs),and associated anti-inflammatory signaling.
Results: The nanoparticles are phagocytosed by the efferocytes after membrane rufling due to the eat-me signal which is derived from the externalization of phosphatidyl-serine (PS) which binds on receptors on the efferocyte surface including PSR(tether and tickle hypothesis), MFG-E8, Gas-6, thrombospondin, b2-glycoprotein-1, protein-S, and annexin-I.PS activates Rac-1/PI3-kinase /Cdc42/RhoG inducing NADPH oxidase, phosphorylating ERK1/2 p38/MAPK, enhancing the formation of cell ruffles,and activating efferocytosis that suppresses inflammatory cytokines,such as TNF-a,IL-6,IL-1b, chemokines such as IL-8 and MIP-2, and lipid mediators such as thromboxane-A2. Also, the PS-mediated efferocytosis suppresses adaptive immunity with its associated inflammation,and upregulates HGF, VEGF, TGF-b1, and b-catenin which regulates post-injury epithelial repair,and suppresses inflammation. Efferocytosis is further enhanced activating cell movement, phagocytosis, and actin cytoskeletal organization after the intracellular entry of the short,double stranded RNA effector molecules which cause post-translational silencing of RhoA.This RNA interference is caused after the dsRNA molecules are recognized and cleaved by the enzyme Dicer resulting in dsRNA duplexes that are incorporated into the multiprotein complex RISC where the antisense strand guides RISC to recognize,and cleave the target mRNA of RhoA. This inhibits production of ceramides, and downstream effector Rho-kinase blocking formation of stress-fibers, focal-adhesions, and cell-spreading.The activation of efferocytosis induced autophagy of apoptotic macrophages via overexpression of Beclin-1 reducing inflammation, and plaque necrosis which was correlated with URP markers including CHOP or DDIT3.
Conclusion: With antisense nanomedicine,we can reverse advanced atherosclerosis by inducing efferocytosis.

MOLECULAR BIOLOGY / GENETICS

61135

Oestrogen-dependent MYLIP regulation leads to reduced contractility in male rodent hearts

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High 17beta-oestradiol (E2) levels are a significant predictor of poor prognosis and higher mortality in men with heart failure. Recently, we showed that in E2-treated cardiac tissues of men the expression of the myosin regulatory light chain (Mrlc) interacting protein (Mylip) gene was increased compared to controls. Mylip has been shown to bind and target Mrlc for proteasomal degradation in neuronal cells. Mrlc modulates heart contraction and mutant mice for Mrlc phosphorylation show contractile defects. In the present study, we hypothesised that the induction of Mylip by E2 is associated with reduced Mrlc protein levels and impaired contractile function. One set of 11-month old male C57BL/6J mice were injected intraperitonealy with 0.2 mg/kg E2 (n = 6) or vehicle (Ctrl; n = 4). Five hours after injection, cardiomyocytes (CMs) were isolated for unloaded cell shortening measurements or RNA extraction. Another set of male mice with the same age and strain (n = 6 per group) were treated in exactly the same manner and left ventricles (LVs) were collected for protein extraction. Quantitative real-time PCR revealed that E2-treated CMs had higher Mylip levels than Ctrl CMs (49% induction, $P < 0.05$). Western blot analysis showed that E2-treated LVs had higher levels of Mylip protein than Ctrl LVs (37% induction, $P < 0.01$). As expected, Mrlc protein levels were decreased in E2-treated LVs compared to Ctrl LVs (56% reduction, $P < 0.05$). Immunoprecipitation assays revealed the binding of Mylip to Mrlc and the increased ubiquitination of Mrlc in LVs of E2-treated mice. Recordings of unloaded cell shortening at 1, 2 and 4 Hz demonstrated that the treatment with E2 impaired CM contractile function compared to Ctrl CMs (1 Hz: 31%, adjusted $P < 0.001$; 2 Hz: 30%, adjusted $P < 0.01$; 4 Hz: 25%, adjusted $P < 0.01$). Similarly, the rate of contraction of E2-treated CMs was significantly decreased compared to controls. Next, we assessed the effect of E2 on cardiac contractility ex vivo using Langendorff-perfused rat hearts. Although at baseline there were no significant changes, the response to isoprenaline was blunted in E2-treated hearts. E2 levels in elderly and/or obese men might increase considerably. Based on our present findings, we suggest that MYLIP could contribute to the association of high E2 levels and increased risk and incidence of cardiovascular disease in men. We propose that MYLIP could become a pharmacological target in this high-risk group.

61139

Sex differences in microRNA expression in cardiac hypertrophy. Role of ERbeta

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Sex differences (SD) in the development and progression of cardiovascular diseases have been described. The prognosis for HF patients is poor for both sexes, but with a better outcome in women than in men. Our global gene expression studies revealed SD in mitochondrial metabolism and myocardial remodeling. While metabolic genes belonging to the pathway of oxidative phosphorylation in mitochondria had a less pronounciated dowregulation in females than in males, the genes of matrix remodeling were stronger deregulated in male hearts. We confirmed SD in cardiac hypertrophy in a mouse model. Male mice with transverse aortic constriction (TAC) developed more ventricular dilatation and hypertrophy than females. These were at least partially mediated by direct effects of estrogens and estrogen receptor β. In addition, preliminary data suggest that mitochondrial metabolism is also sex differently regulated.
Over the last years, the importance of microRNAs in the regulation of gene expression in heart development as well as in diseases has been increasing. In spite of several studies analysed the regulation of microRNAs by estrogens, nothing is known about a sex-specific regulation of microRNAs in heart diseases.
Using microarray analysis we identified 81 expressed microRNAs in mouse hearts. 13 from those microRNAs exhibited a tendency for a sex-specific expression. On the other hand, search for putative microRNAs target sites in 80 genes, selected from sex-specific gene expression in mice, revealed 63 microRNAs as putative candidates contributing to sex-specific gene regulation in the heart. We chose these microRNAs for further analysis of their expression by qRT-PCR in left ventricles from male and female mice 9 weeks after TAC. We found some miRNAs exhibiting sexual dimorphisms after TAC compared to the sham operated animals, Using ERβKO animals we could observe that the sex-different expression of some of these microRNAs in wild type mice was abolish in the ERβKO animals, where females and males presented a similar expression pattern. A functional characterization of the putative target genes for selected miRNAs as well as further characterization of the role of estrogen and the estrogen receptors is under investigation. Knowing the mechanisms regulating the sex-different expression of microRNAs and the corresponding target genes is an important requirement for developing new therapeutic strategies specific for women and men.

60435

Features of ACE gene polymorphism in uzbek patients with myocardial infarction

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Purpose: to study the ACE gene polymorphism in Uzbek patients with Q-MI.
Material and Methods: 97 Uzbek male patients with primary Q-wave myocardial infarction at the age of 25 to 75 years (mean age 53 $\pm$ 9.5 years) were investigated. All patients at the10-14 day of MI were carried echocardiography (EchoCG) test and 24h Holtermonitoring of ECG. All patients were also genotyped on I/D polymorphism of ACEgene.
Results: In analysis of I/D-polymorphismof the ACE gene, frequency of I-allele carriage was 46.9% and frequency of D-allelecarriage — 53.1%. 26.2% (n=26) of patients were carriers of I/I homozygous genotype,41.4% (n=41) of patients have heterozygous I/D genotype and 32.3% (n=32) ofpatients have D/D homozygous genotype. Carriage of I-allele was associated withmore frequent development of anterior location of MI, as well as the subsequentdevelopment of left ventricular aneurysm in compare with carriers of D-allele.Presence of D-allele in genotype was associated with a higher frequency ofhypertension than carriage of I-allele ($\chi 2$=8.19, p=0.004). In addition, the carriage of D-allele weresignificantly more associated with one of the complications of acute period ofMI — potentially dangerous ventricular rhythm disturbances ($\chi 2$=3.63, p=0.05) and with the development of MIand heart failure in compare with I-allele carriers (8 vs 16, $\chi 2$=5.3, p=0.02 and 6 vs 13, $\chi 2$=5.16, p=0.02, respectively). Comparativeanalysis of echocardiographic parameters in patients with I/I and D/D genotypesrevealed the predominance of the degree of interventricular septum hypertrophy andLVMM, its indexed values, as well as relative wall thickness parameter inpatients with carriage of D/D genotype, while the differences were significant($p < 0.02$).
Conclusions: 2/3 of patients with Q-MI are carriers of I/D and D/D genotypes. Carriage of D/D and I/D genotypes is associated with more frequent development ofhypertension. Left ventricular hypertrophy degree is significantly associatedwith carriage of D-allele and D/D genotype. Carriage of D-allele wassignificantly more associated with one of the complications of acute period ofMI — potentially dangerous ventricular rhythm disturbances and with thedevelopment of MI and heart failure in compare with I-allele carriage.

60946

Mutations in the beta1-adrenergic receptor gene in patients with heart failure with diabetes mellitus and without it in ukrainian population

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Purpose: To investigate the genotype and allle freguencies of Arg389Gly β1-adrenergic gene polymorphism in patients with severe chronic heart failure (HF). To compare the distribution of Arg389Gly genotypes in patients with HF and diabetes mellitus (DM) type II with that in HF.
Methods: Ninety nine patients (78 males and 21 females; mean age 61,7 $\pm$ 0,96 years) with HF and systolic dysfunction were examined. Genotyping was performed to identify the individual β1-adrenergic receptor Arg389Gly polymorphism by the restriction fragment length analysis of polymerase chain reaction products. The patients were divided into 2 groups depending on the abnormalities of the carbohydrate metabolism: 43 patients with HF and diabetes mellitus (DM) type II and 56 patients with HF without DM. All variables were tested for normal distribution with the Kolmogorov-Smirnov test. For nonparametric comparisons Mann-Whitney U test and Chi-square tests were used. All statistical tests were 2-tailed, and $p<0.05$ was considered statistically significant.
Results: Genotyping revealed a prevalence of homozygous patients with HF for Arg389Arg of 48,5% (n = 48), heterozygous for Arg389Gly of 42,4 % (n = 42) and homozygous for Gly389Gly of 9,1 % (n = 9). The prevalence of all these genotypes in patients with DM type II and patients with HF without DM was Arg389Arg - 53,5% (n=23) vs 44,6% (n=25), Arg389Gly — 37,2% (n=16) vs 46,4% (n=26) and Gly38Gly 9,3% (n=4) vs 8,9% (n=5), respectively. The frequencies of these polymorphisms on 389 locus showed no significant difference between patients with HF and patients with HF and DM type II, (χ^2=0,554, p=0,457 χ^2=0,884, p=0.643, respectively).
Conclusions: There was no difference in the prevalence of the Arg389Gly genotypes between patients with CH and DM type II and HF subjects without DM.

VASCULAR BIOLOGY

60158

Integrated investigation of the effects of adenosine on endothelial progenitor cells

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Purpose: Whether adenosine may positively affect cardiac repair is still a matter of debate. We previously reported that adenosine beneficially regulates inflammation, extracellular matrix turnover and angiogenesis, all processes involved in cardiac repair. Here, using a combination of in silico, in vitro, and in vivo approaches, we investigated whether adenosine affects endothelial progenitor cells (EPC), other key players of cardiac repair.
Methods: In silico: gene expression data from adenosine-treated EPC were obtained by microarrays. Gene-gene functional similarity was estimated with Gene Ontology-based information. In vitro: early endothelial progenitor cells (EPC) were obtained from peripheral blood mononuclear cells of healthy volunteers. In vivo: 18 rats underwent permanent occlusion of the left anterior descending coronary artery (LAD) and were treated by NaCl (n=6), CADO (stable analog of adenosine, n=6) and CADO with 8-SPT (pan-antagonist of adenosine receptors, n=6). Rats were injected ip twice daily for 2 months. 6 additional rats were sham-operated.
Results: Computational systems-based approaches allowed the implementation of a new integrative predictive model based on the combination of gene expression data and gene ontology-based similarity information. This model predicted that adenosine may regulate the expression of several members of the chemokine family in EPC (AUC = 0.92). This prediction was validated in cultured EPC, in which adenosine regulated the expression of multiple chemokines and chemokine receptors. Among these, CXCR4 was significantly up-regulated (3-fold increase, $P<0.001$). Pharmacology and RNA interference experiments implicated the A2B adenosine receptor in this effect. Adenosine stimulated EPC migration towards stromal cell-derived factor-1α and conditioned medium from cardiac fibroblasts. This effect was blocked by anti-CXCR4 neutralizing antibodies. In rats, 2 months after induction of myocardial infarction, the amount of EPC recruited to the heart was enhanced by CADO treatment and inhibited by 8-SPT. This was accompanied by increased vascularization in the border zone.
Conclusion: Systems-based approaches identified adenosine a major regulator of EPC. Adenosine up-regulates CXCR4 expression in EPC and stimulates their recruitment to the infarcted heart. Together with previous observations, these results suggest that adenosine has the potential to enhance cardiac repair.

60787

Atorvastatin treatment improves circulating numbers of endothelial progenitor cells and vascular function in ischemic heart failure

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Background: Ischemic heart failure (HF) is characterized by increased inflammatory status and impaired endothelial function. Endothelial progenitor cells (EPCs) contribute to the maintenance of endothelial integrity and function. Statins beyond its lipid lowering effect exert beneficial effect on endothelial function and inflammatory process in patients with atherosclerosis. In the present study we examined the impact, of atorvastatin treatment, on vascular function, inflammatory status and circulating EPCs in HF patients.
Methods: We studied the effect of 4 weeks atorvastatin treatment (40mg) in 23 patients with ischemic HF. Measurements were carried out at baseline and at the end of the treatment period. Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (AIx) as a measure of arterial wave reflections. Serum levels of tumor necrosis factor alpha (TNF-a), intracellular adhesion molecule-1 (ICAM-1) and brain natriuretic peptide (BNP) were measured by ELISA. The number of circulating CD34(+)/CD133(+)/KDR(+) EPCs were evaluated by flow cytometry in a randomly selected subgroup population (8 subjects).
Results: Compared to baseline, atorvastatin treatment significantly improved FMD (3.18 $\pm$ 3.03% vs. 5.98 $\pm$ 2.49%, p=0.001), AIx (25.98 $\pm$ 8.55% vs. 23.09 $\pm$ 8.87%, p=0.046) and marginally improved PWV (10.13 $\pm$ 3.87 m/sec vs. 9.42 $\pm$ 3.10 m/sec, p=0.058). Furthermore, compared to baseline, a reduction in logTNF-a levels (0.099 $\pm$ 0.323 pg/ml vs. -0.011 $\pm$ 0.247 pg/ml, p=0.012) and logICAM-1 levels (2.46 $\pm$ 0.13 ng/ml vs. 2.37 $\pm$ 0.16 ng/ml, $p<0.001$) was observed with atorvastatin treatment, while there was no statistically significant difference in logBNP levels (2.10 $\pm$ 0.36 pg/ml vs. 2.17 $\pm$ 0.38 pg/ml, p=0.57). Interestingly, compared to baseline, circulating EPCs were significantly increased with atorvastatin treatment [413 (334, 510) vs. 194 (151, 241), p=0.028].
Conclusions: Short term atorvastatin treatment increases not only the number of circulating EPCs but also improves endothelial function and arterial stiffness.

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Association of serum neutrophil gelatinase-associated lipocalin and cystatin-c with arterial wall properties in patients with heart failure

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Background: Patients with heart failure (HF) have a significant decline of renal function. Measurement of arterial stiffness is well validated in large population studies as strong predictor of adverse cardiovascular outcomes. In the present study we investigate the association between novel biomarkers of renal dysfunction and indices of arterial function in HF.
Methods: We enrolled 79 consecutive patients with HF (mean age 65) and 79 healthy subjects (CI) adjusted for age and sex. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (AIx) as a measure of arterial wave reflections. Serum levels of Neutrophil gelatinase-associated lipocalin (NGAL), Cystatin-C, Brain natriuretic peptide (BNP) and Matrix metalloproteinase-9 (MMP-9) were measured by ELISA. Creatinine clearance was estimated using Cockcroft-Gault formula (eCcl).
Results: In HF patients, logCystatin-C levels was negatively correlated with eCcl (r=-0.214, p=0.049) and logNGAL levels were positively correlated with serum creatinine levels (r=0.458, $p<0.001$). Patients with HF, compared to CI, had significantly higher PWV (9.95 $\pm$ 2.80 m/sec vs. 9.02 $\pm$ 1.78 m/sec, p=0.027) and higher AIx (23.35 $\pm$ 9.54% vs. 19.82 $\pm$ 8.04%, p=0.047). Interestingly, in HF patients, AIx was correlated with logCystatin-C levels (r=0.261, p=0.029) while, PWV was correlated with logBNP levels (r=0.304, p=0.049). Furthermore, in HF patients, regression analysis revealed that logNGAL levels were correlated with MMP-9 levels independently of other confounders such as age, eCcl, ejection fraction, and sex [b=784 95%CI:(314, 1253), p=0.002].
Conclusions: Elevated arterial stiffness is correlated with BNP levels in HF patients. Moreover novel biomarkers of renal function are associated with arterial stiffness and biomarkers of cardiac remodeling. These findings highlight a possible common pathogenetic mechanism of arterial, cardiac and renal dysfunction in HF.

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Uric acid, a causal mediator of vascular disease?

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Purpose: It is well established that elevated serum level of uric acid (UA) is correlated with the outcome of cardiovascular disease. However it remains unclear if this relationship is causal. The present study examines if a high concentration of UA has a direct effect on vascular cells, HUVEC (endothelial cells) and HCASMC (smooth muscle cells).
Methods: HUVEC and HCASMC (contractile and synthetic phenotype) were stimulated for 4 hours with 500 and 1000μM UA in a CO2 incubator at 37°C. mRNA was isolated and quantified by real-time polymerase chain reaction.
Results: Following 4 h stimulation with 500μM UA in HUVEC, mRNA expression for MCP-1, IL8 and ICAM1 were increased (by 6.5, 2 and 2 fold respectively). This effect of UA was only partly inhibited by probenecid (URAT1 inhibitor). Only the contractile

phenotype of HCASMC responded to UA (1000μM) stimulation, observed by enhanced levels of IL8 (5 fold increment) and MCP-1 (2x increment). This phenotype of HCASMC also demonstrated an increased expression (mRNA) of the UA transporter, Scl2a9 (GLUT9). We found this novel UA transporter to be expressed in HUVEC as well.

Conclusion: Vascular cells in culture respond to uric acid in concentrations comparable to what can be found in plasma in patient populations. Both HUVEC and HCASMC respond to UA stimulation demonstrated by an increased expression at the mRNA level of pro-atherosclerotic mediators. Interestingly, only the healthy phenotype (contractile) of HCASMC responded.