**NOVEL ASPECTS ON PROGNOSIS IN HYPERTENSION**

**3782** Relation between blood pressure lowering therapy and cardio vascular events and mortality in hypertensive patients with coronary artery disease and type 2 diabetes: the HIJ-CREATE sub-study

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**Purpose:** To explore the optimal systolic blood pressure target in hypertensive patients with coronary artery disease (CAD) and type 2 diabetes in the subsity of the HIJ-CREATE trial.

**Methods:** HIJ-CREATE was a multicenter, prospective, randomized, controlled study that compared the effects of candesartan-based therapy with those of non-ARB-based standard therapy on MACE in 2,949 hypertensive patients with angiographically documented CAD. Of the 2,049 participants, 780 (38.1%) were complicated with type 2 diabetes. In both groups, titration of antihypertensive agents was performed to reach the target blood pressure (BP) of <130/85 mmHg. The primary endpoint was the time to first major adverse cardiac events (MACE). Incidence of endpoint events in addition to biochemistry tests and office BP was determined during the scheduled 6, 12, 24, 36, 48, and 60-month visits. Achieved BP were defined as the mean value of systolic BP in patients who did not meet with MACE and the mean value of systolic BP prior to MACE in those who met with MACE during follow-up.

**Results:** During a median follow-up of 4.2 years (follow-up rate of 99.6%), the primary outcome occurred in 259 (33.2%) diabetic patients and in 293 (23.1%) non-diabetic patients (p<0.0001). The participants were divided into equal quartiles based on the mean systolic BP during follow-up. The relationships between achieved systolic BP and the incidence of MACE did not follow J-shaped curves in both groups (Figure).

**Conclusions:** The present study suggests that the excessive BP lowering regimen of the contemporary era causes no harm even in high-risk population. Nonetheless, along with BP lowering therapy, the establishment of an optimal management strategy for hypertensive CAD patients with diabetes is essential.

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**3783** The effect of visit-to-visit variability in blood pressure on stroke and coronary events in the TNT, IDEAL and CARDS trials

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**Purpose:** It has been proposed that visit-to-visit variability in systolic blood pressure (SBP) predicts CV risk independently of mean SBP. This study assessed the association between visit-to-visit variability in BP and the risk of CV events (CVE) among high-risk patients in the TNT, IDEAL and CARDS trials, and investigated whether BP and BP variability contributed to differences in clinical benefits observed with different statin treatment regimens.

**Methods:** We analyzed data from 2,952 patients in TNT, IDEAL and CARDS were calculated and analyzed to determine the risk of CVE in relation to visit-to-visit variability in BP and evaluate any impact of these BP parameters on the treatment effect in these trials.

**Results:** Visit-to-visit variability in SBP and diastolic blood pressure (DBP) were significant risk factors for stroke and coronary events after adjusting for treatment (Table) and/or other BP parameters (data not shown). The treatment effect (atorvastatin 80 mg [ATV 80] vs ATV 10 in TNT; ATV 80 vs simvastatin 20-40 mg in IDEAL; ATV 10 vs placebo in CARDS) for reducing risk of stroke (HR 0.81, 95% CI 0.69-0.945) and coronary events (HR 0.81, 95% CI 0.74-0.88) was not affected by adjustment for SBP or DBP variability or other BP parameters.

**Conclusions:** Higher visit-to-visit variability in BP is associated with significantly increased CV risk. The clinical benefit seen with intensive atorvastatin therapy in TNT and IDEAL, or atorvastatin therapy vs placebo in CARDS, in reducing CVE in high-risk patients is not mediated through reduction in BP or BP variability.

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**3784** Low attenuation coronary plaque on multidetector computed tomography predicts three-year acute coronary syndrome events in patients with hypertension

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**Purpose:** Arterial hypertension is an established risk factor for acute coronary syndrome (ACS). Multidetector computed tomography (MDCT) is an accurate and less invasive technique for assessment of the degree of coronary artery luminal narrowing and characterization of coronary atherosclerosis. We therefore aimed to investigate the predictive power of MDCT for ACS events and compared with traditional parameters in patients with hypertension.

**Methods:** One hundred and thirty-four patients (93 men, mean age 70 ± 11 years) with hypertension underwent MDC for evaluation of coronary artery disease. MDCT analysis focused on the presence of plaques, the degree of stenosis, and the plaque characteristics. Traditional parameters included Framingham risk score (FRS), carotid intima-media thickness (IMT), and left ventricular mass index (LVM).

**Results:** During a mean follow-up of 3.3 years, ACS events occurred in 10 patients. In the multivariate analysis, the number of low attenuation plaque (LAP) was identified as an independent predictor of ACS events (p = 0.001). Case examples are presented in Figure. Curved multiplanar reconstruction image of right coronary artery demonstrated the presence of LAP (arrows) (Figure A), which developed ACS event 3 years after MDCT examination (Figure B). Increased events rate was observed in patients with ≥2 LAP compared with those without LAP (p = 0.001) (Figure C). There were no significant differences between patients with and without ACS events in the FRS, carotid IMT, LVM, and any of the laboratory parameters.

**Conclusions:** We demonstrated that LAP on MDCT predicted more accurately future ACS events in patients with hypertension than traditional parameters.

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**3785** Pulse wave velocity as independent predictor of stroke in patients with essential hypertension: data from a Greek 6-year-follow-up study

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**Purpose:** Although arterial stiffening is related to atherosclerosis progression, its prognostic role in cerebrovascular events in hypertension is not fully elucidated. The aim of the present study was to assess the prognostic role of arterial stiffness for the incidence of stroke in a cohort of essential hypertensive patients.

**Methods:** We followed up 1128 essential hypertensives (mean age 56.1 years, 587 males, office blood pressure (BP) 144±91 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and at baseline underwent blood sampling for assessment of metabolic profile and arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior BP). The distribution of
PWV was split by the median (8.1 mm/sec) and accordingly subjects were classified into those with high (n=566) and low values (n=562). Stroke was defined as rapid onset of a new neurological deficit persisting at least 24 hours unless death supervened confirmed by computed tomography and magnetic resonance angiography and/or cerebrovascular angiography findings. 

Results: The incidence of stroke over the follow-up period was 2.03%. Hypertensives who had stroke (n=23) compared to those without stroke at follow-up (n=1105) were older at baseline (63.8±6 years vs 55±10 years, p=0.015), had higher office BP levels (155±13 vs 143±17 mmHg, p=0.018) and prevalence of high PWV levels (67% vs 43%, p=0.021). No difference was observed between hypertensives with stroke and those without stroke with respect to baseline renal function and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that high baseline PWV levels predicted stroke (hazard ratio=1.307, p=0.014). Moreover, in multivariate Cox regression model, baseline age (hazard ratio=1.098, p=0.03) and PWV (hazard ratio=1.125, p=0.017) but not baseline office BP levels turned out to be independent predictors of stroke.

Conclusions: In essential hypertensive patients, PWV predicts future development of stroke, independently of age and office BP. These findings support that PWV constitutes a potent prognosticator of cerebrovascular events and its estimation is essential in order to improve risk stratification in hypertension.

**Prediction of cardiovascular events and all-cause mortality with brachial-ankle pulse wave velocity: a systematic review and meta-analysis of cohort studies**

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**Purpose:** Brachial-ankle pulse wave velocity (baPWV) is increasingly recognized as a surrogate end-point for cardiovascular (CV) disease. We performed a meta-analysis of all longitudinal cohort studies for determining the ability of baPWV to predict risk of CV events and all-cause mortality.

**Methods:** The MEDLINE, Cochrane and EMBASE databases, and reviewing reference lists from retrieved articles and abstracts from large international cardiovascular conventions were searched until January 2012. Longitudinal cohort studies that reported relative risk (RR) estimates with 95% confidence intervals were included. Reviewers extracted data independently and summary estimates of association were obtained using a fixed- or random-effects model. Risk estimates between subgroups were compared with an interaction test.

**Results:** Of the 17 studies included (8,217 participants, mean follow-up 3.37 years), 14 reported results on total CV events (5,406 individuals), 6 on CV mortality (2,139 individuals) and 9 on all-cause mortality (5,132 individuals). The pooled relative risks (RRs) for total CV events, CV mortality and all-cause mortality were 2.77 (95% confidence interval: 1.91 to 4.01) (Figure), 7.37 (95% CI: 3.67 to 14.79) and 2.62 (95% confidence interval: 1.87 to 3.66), respectively, for subjects with high baPWV versus subjects with low baPWV. For total CV events, the RR was significantly higher in high baseline risk groups (heart disease, renal disease, hypertension, diabetes) compared with low-risk subjects (general population). An increase in baPWV by 1 m/s corresponded to an increase of 17% in total CV events.

**Conclusions:** baPWV is associated with increased risk of total CV events and all-cause mortality. Predictive value of baPWV for total CV events is increased in general population.

**Influence of family history of hypertension and hypertension per se on overall and cardiovascular mortality in the Seven Countries Studies: the 40 years’ follow up results**

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**Purpose:** The Seven Countries Study is one of the landmark epidemiological studies that encompassed 12 cohorts in 7 countries with a total of over 10,000 men in a follow up going beyond 4 decades with a response rate nearing 95% worldwide. Its meticulously detailed design and systematic follow up, enables us to assess different aspects of the presence and impact of traditional risk factors on a myriad of outcomes. In this particular case, we sought to determine influence of family history of hypertension and hypertension per se on overall and coronary artery disease (CAD) mortality.

**Methods:** All subjects enrolled in the 3 Serbian cohorts of the Seven Countries’ Study, were men aged 40-59 years at entry (1962-1964) who were subsequently followed every 5 years.

**Results:** Of 1565 men, aged 48.53 years, 1288 deaths of known cause (82.9%) were available for further analysis, while data on presence of hypertension and family history of hypertension was available for all. Looking at overall mortality, 992 participants were hypertension free at entry, out of which 82% were deceased at the closure of the 40 years’ follow up, with 27 years’ survival; while of the 573 participants with hypertension at entry, 92.7% had a 23 years’ survival (logrank=76.067, p<0.001). In those who had hypertension, but also carried a burden of family history of hypertension (118 participants), survival was 24 years for 93.2% of the deceased, while for those who were free of parental hypertension (124 participants), survival was 30 years for 74.2% of the deceased. When CAD mortality has been additionally looked into, 24.1% of the hypertension-free participants (992) had a 35 years survival, while for those with hypertension, 26.5% of the 573 participants had a 33 years survival.

**Conclusion:** In the Serbian cohorts of the Seven Countries Study, as a result of the 40 years follow up, we have shown that participants who were hypertension-free at entry, had a longer life expectancy, both for overall and CAD mortality – 4 and 2 years, respectively, while for those who had hypertension and whose family history was also remarkable for hypertension, survival was shorter for 6 years.

**Validation and clinical application of systolic and diastolic central pressures derived from pulse wave analysis**

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**Purpose:** The use of surrogate measures for central artery blood pressure (BP) is now commonplace, including radial artery pulse wave analysis (PWA). Prior studies have examined central augmentation index (cAI), defined as the systolic augmentation pressure (cAP)/pulse pressure. We sought to assess the validity, reproducibility and clinical utility of systolic and diastolic parameters.

**Methods:** Patients attending elective coronary angiography were pre-assessed with conventional sphygmomanometry and radial PWA. Direct aortic BP was taken during catheterisation in 346 participants of the ARM-CAD study.

**Results:** PWA-derived central systolic BP was closer to measured pressure (2.70mmHg lower; SE=1.18) compared to conventional BP (8.03mmHg higher; SE=2.70). However for diastolic BP, conventional and PWA measurement were similar and higher than aortic (9.93; SE=0.83 and 10.99; SE=0.83mmHg) resulting in significant differences in pulse pressure (see figure). cAP was linearly correlated with central pulse pressure (cPP) and the ratio of central to brachial pulse pressure (cPPr) (r=0.82) (p<0.001). cPP and cPPr were derived from PWA analysis using the Pwave Pro software. The correlation between central PP and cPPr was better than aortic PP and cPPr (r=0.76) (p<0.001).

**Central Blood Pressure and Peripheral Vessels in Hypertension**

Figure 1. Comparison of invasive & non-invasive BP
Central blood pressure: a possible powerful predictor of the development of hypertension

Central blood pressure and peripheral vessels in hypertension

Aims: Vascular mechanisms are known to have vital roles in the development of hypertension. We examined whether the central aortic systolic blood pressure, a marker of function in systemic arterial tree, might be a more powerful predictor of the development of hypertension as compared with the brachial-ankle pulse wave velocity (baPWV), a marker of stiffness in large to middle-sized arteries.

Methods and Results: In 1268 Japanese men without hypertension (43±6 years old), the relationships of the baPWV and second peak of the radial pressure waveform (SP2) measured at the first examination with the presence of hypertension at the second examination (after 3 years' follow-up) were examined. Hypertension was detected at the second examination in 154 men. Estimated area under the curve to predict the presence of hypertension at the second examination were as follows: brachial-ankle PWV at the first examination = 0.716 and SP2 at the first examination = 0.843. The best cutoff point of the baPWV and SP2 for predicting the development of hypertension than a baPWV of 12.7 m/s and 109 mmHg, respectively, with 11%, 15% and 4% of people showing CCS, IMT and AAD respectively higher with 11%, 38% and 38% of subjects, respectively; 13% were actual smokers, 31% past smokers. Median NT-proBNP was 59 ng/L (IQR range 33-101). CCS, IMT (bilateral sum) and AAD were, respectively, 156±521 U.A., 1.6±0.3 mm and 32±4.4 mm, with 11%, 15% and 4% of people showing CCS, IMT and AAD respectively higher than 400 U.A., 2 mm and 40 mm. CCS > 400 U.A., IMT > 2 mm and AAD > 40 mm were all predicted at ROC analysis by plasma NT-proBNP levels (AUCs 0.589, 0.591, 0.564 respectively, p<0.05 for all). NT-proBNP was higher in patients with a CCS > 400 U.A. (64, 42-128 vs. 57, 32-98, p<0.01), b) IMT > 2 mm (72, 38-139 vs. 58, 32-95, p<0.01), c) AAD > 40 mm (65, 36-171 vs. 59, 33-99, p<0.05), despite no differences in left ventricular ejection fraction, nor in cardiac mass; this findings were confirmed in the subset of hypertensives, while not in subject with diabetes, hypercholesterolemia, or with past/present smoking habit.

Conclusions: NT-proBNP level, within the upper normal range, predicts subclinical coronary atherosclerosis and vascular health, namely in asymptomatic hypertensive subjects, with no relation with heart structural and functional involvement, possibly reflecting a vascular source of production and secretion.

Selective serotonin reuptake inhibitors exert a negative effect on peripheral wave reflections

Purpose: In view of the high likelihood that hypertensives will have comorbid anxiety and depression, all hypertensives should be screened for concurrent psychiatric illnesses and treatment. We hypothesized that there is a relationship between the administration of selective serotonin reuptake inhibitors (SSRIs) and arterial stiffness, a hallmark of the cardiovascular aging process.

Methods: We studied 210 consecutive untreated stage I-essential hypertensive subjects (aged=62±9 years, 110 female, office blood pressure (BP) = 163±91 mm Hg). The participants were divided into group A (n=83), those receiving SSRIs and group B (n=127), those without any antidepressant therapy. Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (c-f PWV) by means of a computerized method (Complior SP). Venous blood sampling was performed for the estimation of routine metabolic profile.

Results: The two groups did not differ regarding age, gender, office systolic/diastolic BP as well as serum glucose and triglycerides levels (83±9 vs 84±7 mmol/dl and 128±8 vs 119±9 mg/dl, respectively, p=NS in all cases). Group A was characterized by increased levels of body mass index (32.4±3 vs 29.2±4 kg/m², p=0.015) and elevated cholesterol plasma levels compared to group B (231±3 vs 220±36 mg/dl, p=0.05). Group A compared to group B exhibited significantly increased c-f PWV (8.4±3 vs 7.2±5.0 m/sec, p=0.02) and this differ-
ence remained significant after adjustment for confounders (p<0.03). In the SSRIs treated-hypertensives, c-f PWV was correlated with age (r=0.35, p<0.015) and office systolic BP (r=0.33, p=0.02), while no significant correlation was demonstrated with cholesterol levels (p=NS).

Conclusions: The administration of SSRIs exerts an incremental effect on arterial stiffness, thus accelerating the vascular aging process.

Renin-angiotensin aldosterone system gene polymorphisms and their association with vascular impairment in patients with essential hypertension

Purpose: The angiotensinogen (M235T) and aldosterone synthase (CYP11B2) gene polymorphisms have been positively associated with vascular properties. Therefore, in the present study we examined whether these variants affect carotid-femoral pulse wave velocity (c-fPWV), flow mediated dilation (FMD), ultrasound measurement of the C-IMT, augmentation index and ankle-brachial index.

Methods: The study population consisted of 318 untreated essential hypertensives and a control group, consisted of 193 matched subjects. c-fPWV, FMD, ultrasound measurement of the C-IMT, augmentation index and ankle-brachial index were evaluated. The gene mutations frequencies were determined using polymerase chain reaction (PCR) technique. Serum cystatin-C levels and inflammatory biomarkers were measured by the ELISA method.

Results: TT homozygotes had significantly lower FMD compared with M allele carriers in controls (p=0.038). Carriers of M allele of c-fPWV was higher in TT homozygotes compared with MM+MT genotypes in hypertensive patients (p=0.025). With respect to other vascular properties we observed no other significant associa-
tions across genotypes. Regarding the CYP11B2 promoter genotype we have observed higher values of IMT in -344TT homozygosity, in the group of hyper-
tensives (712.5±16.2 vs 781.8±33.5 μm, p=0.03). Notably, it was observed that T allele-carriers was significantly associated with higher prevalence of atheroscle-
rotic plaques in the study population (OR: 0.32; CI 0.12 to 0.85, p=0.01), and

N-terminal fragment of brain natriuretic peptide predicts vascular health and subclinical atherosclerosis: results from MEHLP study

N- terminal fragment of brain natriuretic peptide predicts vascular health and subclinical atherosclerosis

Conclusion: In middle-aged Japanese men without hypertension, SP2 may be a more powerful predictor of the development of hypertension than the baPWV, independent of the conventionally known risk factors for the development of hyper-

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tensives (712.5±16.2 vs 781.8±33.5 μm, p=0.03). Notably, it was observed that T allele-carriers was significantly associated with higher prevalence of atheroscle-
rotic plaques in the study population (OR: 0.32; CI 0.12 to 0.85, p=0.01), and
similar results were obtained for hypertensives, though without reaching statistically significant (p=0.07). Moreover, after adjustment for co-variables, cystatin-C levels correlated significantly with PWV values both in total (r=0.27, p=0.03) and in hypertensive populations (r=0.23, p=0.006). Interestingly, in univariable analyses, increased levels of cystatin-C (above 75th percentile) correlated with higher PWV values (p=0.0019).

Conclusions: We have shown that TT homozygotes had significantly lower FMD in controls and c-IPWV was higher in TT homozygotes compared with MM+MT genotypes in hypertensive patients. In addition, we have observed higher values of IMT in 344TT homozygosity, in the group of hypertensives, while Tallei carriage was significantly associated with higher prevalence of atherosclerotic plaques in the study population. Our results suggest that angiotensinogen genotypes are associated with arterial stiffness, whereas CYP11B2 promoter variant potentially constitutes a marker of subclinical atherosclerosis in untreated hypertension.

**3797 Insulin resistance is associated with increased large artery stiffness in normotensive healthy adults**


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**Aim:** At present there is limited evidence on the relationship between insulin resistance (IR) and measures of large artery stiffness (AS) and wave reflections in normotensive healthy adults. Aim of the present study was to explore this issue in 90 normotensive (Systolic(S) blood pressure(BP) 107.1±6.1; diastolic(D) BP 69.6±7.7 mmHg), normoglycemic, non-obese, otherwise healthy adults (mean age 48.1±10 yrs, 50% female).

**Methods:** IR was assessed with HOMA-Index and subjects were classified into IR tertiles, based on the distribution of HOMA-index values. Recordings of pulse wave waveform were obtained by means of a previously validated oscillometric device for ambulatory BP monitoring with in-built transfer-function like method. Aortic pulse wave velocity (PWV, m/s) and other measures derived from pulse wave analysis such as augmentation index (AIx, %), central SBP (cSBP), central DBP (cDBP) and central blood pressure (cBP) were calculated. Peripheral SBP and DBP, and heart rate (HR) were recorded and pulse pressure (PP) calculated as the difference between SBP and DBP.

**Results:** After multiple regression analysis adjusting for age, sex, HR and BMI, there was a significant overall effect of IR on measures of large artery stiffness and in central and peripheral BP levels. IR was associated with increased aortic PWV, and with higher central and peripheral SBP and DBP levels. See table.

**3798 Multidisciplinary cardiac rehabilitation and survival in The Netherlands**

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**Purpose:** This study assessed the effects of multidisciplinary cardiac rehabilitation (CR) on survival in a large cohort of patients with coronary artery disease in The Netherlands.

**Methods:** The cohort consisted of persons insured with Achmea, a health insurance company in the Netherlands covering approx. 20% of the Dutch population (3.3 million insured persons). All patients with an acute coronary syndrome (ACS) with or without ST elevation and patients that underwent coronary revascularization in the period 2007-2010, based on insurance claims, were included. Patients were categorized as having received CR when an insurance claim for CR was made within the first 180 days after the cardiac event or revascularisation. Propensity score weighting was used to control for confounding by indication.

**Results:** A total of 35,919 patients were analyzed, of which 11,014 (30.7%) used CR. Median follow-up time after CR was 19.3 months (min. 0 months, max. 42 months). Crude mortality rates during the study period were 2.6% (287 patients) for CR users and 8.7% (2,160 patients) for nonusers (adj. HR 0.68, p<0.001). The table shows mortality rates among different patient categories. There was a non-significant difference (p=0.14) in survival between CR users receiving physical therapy (adj. HR 0.62) and CR users not receiving physical therapy (adj. HR 0.74).

**Conclusions:** Among patients with an acute coronary syndrome and/or coronary revascularisation in The Netherlands, the use of multidisciplinary CR was associated with a survival benefit of 32%.

**3799 Cardiovascular rehabilitation after a first acute coronary syndrome and the risk of recurrence and death in patients from the French MONICA registries**

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**Purpose:** Cardiovascular rehabilitation following the occurrence of an acute coronary syndrome (ACS) has become more and more commonly used over the past years. However, differences still remain in prescription rates, depending on age, gender or the severity of the event. The aim of this work was to assess the prognostic influence of rehabilitation after ACS in the current medical practice.

**Methods:** Our study was based on 2008 data from the French MONICA population-based registry which collects all cases of ACS occurring in people aged 35-74 in 3 French areas located in North, North-Eastern and South-Western France. The population consisted of 1869 acute and consecutive hospitalized ACS, after exclusion of those who died in the first 28 days of follow-up. The relationship between prescription of cardiovascular rehabilitation and composite outcome (ACR- recurrence or death) was analyzed using Cox models adjusted for living area, age, number of diseased vessels, diabetes, cardiovascular treatments and delays between symptoms and the first medical care.

**Results:** There were 171 ACS-recurrences or deaths during a median follow-up of 18.1 months. The population consisted of 23.6% of women. The rate of cardiac rehabilitation was significantly higher in men than in women (36% vs. 26%, p<0.0001) and decreased with age. After multivariate adjustment the risk of composite outcome occurrence was identical in men and women for STEMI but higher in women for UA/NSTEMI (adjusted HR 1.75, 95% confidence interval (1.10 to 2.77). Rehabilitation was associated with a decrease of ACR-recurrences and deaths whatever the definition of ACS (global adjusted HR 0.48, (0.32 to 0.73)). However a significant interaction between rehabilitation and gender has been found in UA/NSTEMI (p=0.04) but not in STEMI. A stratified analysis for gender in UA/NSTEMI showed a significant benefit of rehabilitation in women (adjusted HR 0.06, (0.01 to 0.44) but not in men [adjusted HR 0.82, (0.39 to 1.72)].

**Conclusions:** Whatever the definition of ACS, cardiovascular rehabilitation was associated with a reduction of ACS-recurrence and death, and benefits both sexes. However rehabilitation seems to be more beneficial in women presenting UA/NSTEMI in whom rehabilitation is less prescribed and in whom the rate of recurrence and death is higher.
Phase II comprehensive cardiac rehabilitation prevents readmission for heart failure in patients with chronic heart failure and high brain natriuretic peptide levels

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Purpose: The purpose of this study was to investigate the effects of phase II comprehensive cardiac rehabilitation (CR) in patients with chronic heart failure (CHF) and high brain natriuretic peptide (BNP) levels.

Methods: We studied 312 patients with CHF (215 males; age, 71±10 years) who were hospitalized for acute decompensated heart failure. Patients were classified into four groups according to BNP levels at the time of discharge and participation in phase II CR. The CR with low BNP group (n = 67) included patients who participated in CR and had BNP levels less than 200 pg/mL, and the CR group (n = 74) included patients who did not participate in CR and had BNP levels less than 200 pg/mL, and the non-CR with high BNP group (n = 104) included patients who did not participate in CR and had BNP levels more than 200 pg/mL and, the non-CR with low BNP group (n = 67) included patients who did not participate in CR and had BNP levels less than 200 pg/mL, and the non-CR group (n = 23) included patients who did not participate in CR and who had BNP levels less than 200 pg/mL. Kaplan-Meier survival analysis based on cardiovascular risk factors including age, medication, left ventricular ejection fraction, BNP levels, and participation in phase II CR was a significant predictor for readmission of heart failure (adjusted hazard ratio, 0.66; p < 0.001). There were no significant differences between the two groups regarding compliance to a cardiac rehabilitation program: what matters is the compliance of the rehabilitation program itself. Follow-up data was available in 227 (94%) patients, with a mean follow-up time of 25.7 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: 2.25; 95% CI: 0.76-6.4).

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.

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


Background: Cardiac rehabilitation programs (CRP) have consistently demonstrated the ability to improve cardiac risk factors and reduce mortality. Thus, compliance to CRP is an essential requirement to achieve the goals of secondary cardiovascular prevention.

Objective: To assess the clinical benefits and CRP compliance impact on prognosis in a cohort of heart disease patients.

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±10 years (range 28-80). Non compliance was found in 24 (10%) patients and it was more common in women than men (23% 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 (≥600 METS/minute/week) [82% vs 25%, p = 0.022]. A significant improvement was found, only in the compliant group (CG), regarding functional capacity (6.1 ± 0.8 (6.4 ± 0.6); p = 0.011) and lipid profile (total cholesterol: 189.1 ± 38.9 [196.6 ± 38.7]; p = 0.001; HDL-cholesterol: 32.7 ± 8.7 [33.9 ± 8.7]; p = 0.051). No significant differences were found between the two groups regarding compliance to a cardiac rehabilitation program. Follow-up data was available in 227 (94%) patients, with a mean follow-up time of 25.7 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: 2.25; 95% CI: 0.76-6.4).

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.

The effects of respiratory muscle trainings on systemic inflammation and fibrosis process in patients with heart failure


Background: Number of studies showed the effectiveness of Respiratory Muscle Trainings (RMT) as a part of comprehensive cardiac rehabilitation (CR). The mechanisms of their positive effects in cardiac patients are still not well known. Purpose: To study the relations of long-term effects of RMT started in patients with NYHA III-IV class heart failure (CHF), with the intensity of systemic inflammation and pleasmatic levels of aldosterone and collagen.

Methods: 61 patients 64±5±5 years old with NYHA III-IV CHF were randomized to either an exercise training group (EG) (30pts) or to a control group. The CG patients had standard CR according to the national guidelines. The EG participants additionally in a RMT with gradual increase of inspire and expire resistance.12-15 RMT were held at the hospital with following continuation at home for 12 months by patients themselves. Trainings were held for 20-30 minutes 1-2 times every day. Pleasmatic levels of C-reactive protein (CRP), aldosterone and the carboxyterminal propeptide of human type I procollagen (P) were studied at discharge point and in 12 months.

Results: In 12 months peak VO2 increased significantly in EG (11.5±2.5 ml/kg/min in EG vs 9.1±2.12 ml/kg/min in CG, p=0.05). EG patients showed significant decrease in CRP level (5.2±2.4 mg/dl in EG vs 8.1±2.1 mg/dl in CG, p<0.05). IP (67.5±7.8 mg/ml in EG vs 106.±11.2 mg/ml in CG, p=0.05). RMT helped to stabilize mean pulmonary pressure (33.5±4.7 mm Hg in EG vs 44.2±7.6 mm Hg in CG, p=0.05). Health related quality of life measured by SF-36 increased in both groups, but results in physical functioning, bodily pain, vitality, role emotional scales were significantly higher in EG patients. Conclusion: RMT in patients with HF are effective in decreasing the level of systemic inflammation and pleasmatic activation of collagen and fibrosis synthesis and thus reducing fibrosis, besides improving physical capacity, stabilizing pulmonary pressure and increasing health-related quality of life.

Beneficial effects of rehabilitation in comparison with resynchronization therapy in patients with NYHA III heart failure

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Background: Indications to cardiac resynchronization therapy (CRT) have been extended in 2010. However, there is large group of patients with ejection fraction -35%, severe heart failure (HF) and QRS≥120ms, who are not qualified to CRT. They are treated with optimal pharmacotherapy. We compared outcomes of rehabilitation of patients in NYHA III heart failure and patients with implanted CRT-D device without rehabilitation.

Methods: The study included 47 patients with NYHA III HF and EF<35% on optimal pharmacotherapy. 25 patients received rehabilitation (R) and 22 - CRT-D device (CD). We compared clinical and functional outcomes at discharge and 12 months.

Table 1. Comparison of clinical outcomes of patients with and without rehabilitation

<table>
<thead>
<tr>
<th></th>
<th>R (group)</th>
<th>CD (group)</th>
<th>Statistical significance</th>
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<tr>
<td>Age [years]</td>
<td>64.4±9.2</td>
<td>70.8±7.2</td>
<td>ns</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>27.3±4.7</td>
<td>27.6±3.8</td>
<td>ns</td>
</tr>
<tr>
<td>EF [%]</td>
<td>24.6±4.9</td>
<td>25.4±5.4</td>
<td>ns</td>
</tr>
<tr>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>[L/min/m²]</td>
<td>28.8±10.4</td>
<td>31.5±9.1</td>
<td>0.0729</td>
</tr>
<tr>
<td>LV/d (cm)</td>
<td>6.2±1.1</td>
<td>6.1±0.6</td>
<td>0.0169</td>
</tr>
<tr>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>[L/min/m²]</td>
<td>5.7±1.0</td>
<td>6.0±0.5</td>
<td>0.0444</td>
</tr>
<tr>
<td>Peak oxygen uptake (VO2) [ml]</td>
<td>10.9±3.8</td>
<td>13.3±4.6</td>
<td>0.0613</td>
</tr>
<tr>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>[L/min/m²]</td>
<td>11.9±4.0</td>
<td>15.7±5.9</td>
<td>0.0144</td>
</tr>
</tbody>
</table>

ns 0.0168

Downloaded from http://academic.oup.com/eurheartj/article-abstract/33/suppl_1/655/430798 by guest on 07 February 2019
eral pharmacotherapy. The etiology of HF was comparable in both groups. 27 patients with QRS $>120$ ms had CRT-D implanted and 20 patients with QRS $<120$ ms had ICD implantation and went through the training program (aerobic exercises on ergometer, 3 times a week for 3 months). All patients were optimally treated pharmacologically. They had echocardiography and cardipulmonary exercise test (CPX) performed at baseline and after 6 months.

Results: NOx results are presented in Table 1. Conclusions: Repaired patients with NYHA III heart failure have better outcomes when compared with CRT group. Rehabilitation is a noteworthy therapeutic option for patients with severe heart failure and no indications to CRT.

Biventricular filling impairment limits cardiac performance during exercise in healthy subjects

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Background: Constraints in current imaging techniques have resulted in considerable disagreement as to what constitutes normal changes in left and right ventricular (LV, RV) volumes during exercise. The aim of this study was to determine normal biventricular diastolic and end-systolic volumes (EDV and ESV) using a novel CMR methodology during strenuous exercise.

Methods: Twenty-two healthy and physically active subjects (19 male, 3 female, age $32 \pm 7$ years) underwent CMR at rest and during supine exercise on a programmable cycle ergometer. Biventricular volumes were obtained at rest (heart rate $63 \pm 11$ bpm) and whilst cycling at moderate ($115 \pm 14$ bpm) and strenuous ($155 \pm 11$ bpm) workload intensities. Images were acquired during exercise and free-breathing (12-18 contiguous $8$mm slices) using an unaged real-time CMR sequence. We developed software to enable retrospective synchronization of long- and short-axis images with compensation for respiratory phase translation. Thus, biventricular borders could be delineated in a bi-plane model.

Results: There was excellent inter-observer agreement for all volume estimations (e.g. intra-class correlation coefficients $r=0.97$ and $r=0.98$ for EDV and CO respectively, $p<0.001$). Biventricular cardiac output (CO) increased by $111 \pm 51\%$ from rest to moderate exercise ($7.7 \pm 1.4$ vs. $16.3 \pm 4.8$ l/min, $p<0.001$) and by a further $30 \pm 16\%$ to strenuous exercise ($16.3 \pm 4.8$ vs. $21.1 \pm 5.3$ l/min, $p<0.001$). The total $174 \pm 60\%$ increase in CO was due to a $146 \pm 23\%$ increase in HR and a $9 \pm 13\%$ increase in stroke volume (SV).

Interesting, SV increased during moderate exercise ($124 \pm 27$ vs. $141 \pm 34$ ml; $p=0.001$) but then decreased during strenuous exercise ($141 \pm 34$ vs. $135 \pm 30$ ml; $p=0.002$). The early increase in SV was due to augmentation of both systolic function (end-systolic volume (ESV)) $-15 \pm 11\%$, $p<0.001$) and diastolic filling (end-diastolic volume (EDV)) $+2 \pm 7\%$, $p=0.02$; although during strenuous exercise there was further augmentation of systolic function (ESV $-20 \pm 16\%$, $p<0.001$) and NT group from 2.9 $\pm 1.1$ to 5.1 $\pm 1.4$ μmol/l (ns). Different rate of increased RSNO in examined groups resulted in significantly higher RSNO in NT group from 0.5 $\pm 0.7$ to 2.3 $\pm 0.8$ μmol/l ($p<0.001$).

Conclusions: A novel CMR methodology of biventricular volume assessment was used to demonstrate augmentation of biventricular filling and ejection during moderate exercise in healthy subjects. However, at higher exercise intensities, diastolic filling is compromised and attenuates further stroke volume increases.

Biventricular filling impairment limits cardiac performance during exercise in healthy subjects

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Background: The advantages of a structured cardiac rehabilitation (CR) program are well known. However, participation in phase III CR is low. This problem could be overcome by implementing a home-based supervised CR, but new technology is needed to allow that supervision and improve adherence to CR.

Methods: A novel web tool (HeartCycle’s GEX-System) is intended as a closed-loop cardiovascular disease management tool with support for both the professional and the patient, focused on CR based on physical exercise. The patient side system comprises a wireless sensor attached to a shirt that senses vital parameters such as respiration and activity. Data collection and transmission are performed by a PDA which gives feedback and guidance to the patient during the exercise.

Results: Phase I study was performed to evaluate feasibility and function of the GEX-System devices for home-based CR used during actual physical exercise. 50 patients were included during CR 36-13 days after intervention (7 women, age: 69.9 years, BMI: 26.1±3.3, EF: 58±10% for different cardiac reasons (valve replacement: n=9, MI: n=29, CABG: n=25, others-n=2). A standard exercise test (bicycle test begin 25 Watt, increase 20 Watt/min) was performed. ECG, heart rate, breathing rate were monitored using standard equipment and GEX-device simultaneously. The heart rate was also reported to the patients on the PDA.

Results: Mean exercise performance was 90±32 Watts with a VO2peak of 13.4±4.1 ml/min/kg. There was an excellent correlation between heart rate measured by the GEX-device and standard 12-lead ECG ($r=0.97$). All occurring arrhythmia were detectable (e.g. atrial fibrillation, ventricular ectopic beat). Breathing frequency during exercise was evenly well correlated ($r=0.74$). Additional heart rate measurement with PDA also exhibited an excellent correlation for heart rate for training ($r=0.97$).

Conclusions: There was an excellent correlation between standard spiroergometry and the GEX-device measuring of heart rate, breathing rate and detection of arrhythmias. As this sensor in combination with a special shirt is easy to use and wear, it seems suitable for monitoring home-based CR. Further studies are needed to evaluate applied training prescriptions.

Exercise capacity in patients with coronary artery disease: what is beyond global left ventricular systolic function?

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Purpose: Exercise capacity is influenced by multiple factors and elucidating the mechanisms for cardiac-related exercise limitation has been technically difficult. In this study we sought to determine the effect of cardiac function on exercise capacity. Methods: Prospective study including patients admitted to an outpatient cardiac rehabilitation program (CRP) after suffering an acute coronary event between January 2011 and September 2011. Echocardiography data and exercise capacity were evaluated at the beginning and at the end of the CRP. All echocardiographic and activity data were collected at baseline and after 3 months training and activity were reduced according to current guidelines and exercise capacity assessed by estimated metabolic equivalents (METs) achieved on exercise stress testing.

Results: Forty-five patients were evaluated, 38 (84%) male, mean age of 54±9 years, 30 (67%) had QRS $>120$ ms and QRS $<120$ ms had ICD implantation and went through the training program (aerobic exercises on ergometer, 3 times a week for 3 months). All patients were optimally treated pharmacologically. They had echocardiography and cardipulmonary exercise test (CPX) performed at baseline and after 6 months.

Results: NOx results are presented in Table 1. Conclusions: Repaired patients with NYHA III heart failure have better outcomes when compared with CRT group. Rehabilitation is a noteworthy therapeutic option for patients with severe heart failure and no indications to CRT.
Exercise echocardiography - effects of endurance training and ageing

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Purpose: To study the effects of endurance training and ageing on echocardiographic measures of myocardial function at rest and during exercise.

Methods: Four groups of healthy, normal weight males; master athletes (running –<30 years old), young athletes with similar level of physical activity, and sedentary age-matched controls underwent exercise test determining VO2peak, and echocardiography at rest and during supine bicycle exercise test at 60% of maximum workload. Linear regressions were performed to simultaneously assess the effects of training (two groups) and age (continuous) on echo parameters.

Results: VO2peak differed considerably between young and old and between athletes and non-athletes. Dimensions of left atrium and ventricle as well as transmural flowpatteron at rest were affected by both training and age. See table. Effects of age were also found on systolic and diastolic tissue-Doppler measures both at rest and during exercise.

OPTIMISATION OF MYOCARDIAL REPERFUSION IN STEMI

Solute TNF receptors are associated with infarct size and ventricular dysfunction in ST-elevation myocardial infarction

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Objectives: The aim of the study was to investigate circulating markers of apoptosis in relation to infarct size, left ventricular dysfunction and remodeling in an ST-elevation myocardial infarction (STEMI) population undergoing primary percutaneous coronary intervention (PCI).

Background: Immediate re-opening of the acutely occluded infarct-related artery via primary PCI is the treatment of choice in STEMI to limit ischemia injury. However, the sudden re-inflation of blood flow can lead to a local acute inflammatory response with further endothelial and myocardial damage, so-called reperfusion injury. Apoptosis is suggested to be a key event in ischemia-reperfusion injury, resulting in LV-dysfunction, remodeling and heart failure.

Methods: We included 48 patients with STEMI undergoing primary PCI. Blood samples were collected prior to PCI and after 24 hours. Plasma was separated for later analysis of soluble tumor necrosis factor receptor (sTNFR) 1, sTNFR2, sFas and sFas ligand (sFasl) by ELISA. Infarct size, left ventricular (LV) function and remodeling were assessed by cardiac magnetic resonance imaging at five days and four month after STEMI.

Results: The levels of sTNFR1 at 24 h as well as the relative increases in sTNFR1 and sTNFR2 over 24 h showed consistent and significant correlations with infarct size and LV-dysfunction evaluated four months after STEMI. Moreover, both sTNFRs correlated strongly with Troponin I and matrix metalloproteinase (MMP)-2 measures. Solute Fas and sFasl did not overall correlate with measures of infarct size or LV-dysfunction. None of the apoptosis markers correlated significantly with measures of remodeling.

Conclusions: In STEMI patients, circulating levels of sTNFR1 and sTNFR2 are associated with infarct size and LV dysfunction. This provides further evidence for the role of apoptosis in ischemia-reperfusion injury.

Hemostatic and fibrinolytic profile in patients with ST-segment elevation myocardial infarction resistant to fibrinolysis


Despite primary PCI is the treatment of first choice in patients with ST-segment elevation acute myocardial infarction (STEMI) for accessibility reasons, the fibrinolysis continues being the first line treatment about 30-70% of these patients, however in 40% of them is ineffective for unknown reasons.

Aim: To analyze whether it exists some association between hemostatic and fibrinolytic factors determined in circulating plasma and if it correlates with the thrombosis and fibrinolysis resistance.

Methods and Results: 20 patients (age 57±13y; 10 female) who underwent PCI

<table>
<thead>
<tr>
<th>Results</th>
<th>Young</th>
<th>Senior</th>
<th>Master</th>
<th>Effect of training</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2peak [ml/kg/min]</td>
<td>45 (5)</td>
<td>59 (3)</td>
<td>46 (8)</td>
<td>***</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pulse (bpm)</td>
<td>68 (16)</td>
<td>61 (7)</td>
<td>74 (15)</td>
<td>57 (9)</td>
</tr>
<tr>
<td>LVDD [cm]</td>
<td>4.8 (0.5)</td>
<td>5.3 (0.4)</td>
<td>5.0 (0.4)</td>
<td>* ***</td>
</tr>
<tr>
<td>EF [%]</td>
<td>61 (6)</td>
<td>63 (6)</td>
<td>63 (5)</td>
<td>62 (4)</td>
</tr>
<tr>
<td>LV stroke volume [ml]</td>
<td>31 (9)</td>
<td>47 (11)</td>
<td>38 (18)</td>
<td>61 (19)</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>82 (18)</td>
<td>94 (13)</td>
<td>55 (15)</td>
<td>64 (15)</td>
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<tr>
<td>E/A</td>
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<td>2.0 (0.3)</td>
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</tr>
<tr>
<td>sTnT [ng/ml]</td>
<td>16.1 (3.5)</td>
<td>14.1 (1.8)</td>
<td>7.4 (1.7)</td>
<td>8.3 (2.4)</td>
</tr>
<tr>
<td>sFas [ng/ml]</td>
<td>9.1 (1.4)</td>
<td>9.9 (1.1)</td>
<td>9.4 (1.2)</td>
<td>8.2 (1.5)</td>
</tr>
<tr>
<td>E/e'</td>
<td>7.4 (2.1)</td>
<td>6.8 (1.5)</td>
<td>7.8 (1.4)</td>
<td>6.1 (2.7)</td>
</tr>
<tr>
<td>E/e' ratio</td>
<td>150 (27)</td>
<td>146 (19)</td>
<td>111 (19)</td>
<td>112 (23)</td>
</tr>
<tr>
<td>sTNFR1 [ng/ml]</td>
<td>20.6 (4.5)</td>
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<td>sTNFR2 [ng/ml]</td>
<td>16.1 (4.2)</td>
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<td>13.6 (2.0)</td>
<td>12.3 (2.3)</td>
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<tr>
<td>sFas [ng/ml]</td>
<td>7.5 (1.8)</td>
<td>7.3 (1.5)</td>
<td>8.4 (2.0)</td>
<td>8.3 (2.2)</td>
</tr>
</tbody>
</table>

Age is given as median (range), All other variables are given as mean (SD). **p<0.01, ***p<0.001, ***p<0.0001.
for a first STEMI with initial TIMI 0 flow were included. Of these, 10 underwent primary PCI (group A) and the other 10 were subjected to rescue PCI (group B) because of ineffective fibrinolysis (TNK). In all patients tissue factor activity (TfA), TF Ag and tissue factor pathway inhibitor (TFPI), von Willebrand factor (VWF), D-dimer, plasmin inhibitor activated (PAI-1) and tissue plasmin activator (t-PA) were determined. The coronary thrombus was obtained during PCI by aspiration catheter in all patients. Specimens were submitted to immunohistochemical analysis. In order to know if all patients underwent primary PCI a thrombus sensitive to lysis, thrombus formation by thrombin was induced “in vitro”, and an effective thrombolysis by r-TPA was observed in 100% of patients. There were no differences between both groups in terms of age, sex, car- diovascular factors, time symptoms onset to balloon, infarct localization and number of affected vessels. Patients who underwent rescue PCI showed a higher D-dimer plasma level regarding patients who underwent primary PCI (2234.3±706.5 vs.774.5±1339.8 mg/ml, p<0.03). In plasma, D-dimer levels were associated to Fxs (R=0.95, p=0.01) and FVW levels (R=0.63, p=0.04). In the thrombus, FVW plasma levels were correlated with PAI-1 (R=1,79, p=0.006), CD34 (R=0.85, p=0.004) and P-selectin (R=0.77, p=0.002). However, in patients who underwent primary PCI, D-dimer levels were associated with 1-t-PA (R=0.65, p=0.001) and FVW levels were inversely associated with TFPI (R=0.87, p<0.01) in plasma. In addition, in the thrombus the content of fibrin was associated with CD34 and FVW (R=0.71, p=0.03; R=0.73, p=0.02, respectively).

Conclusion: There are clearly different patterns of thrombotic and fibrinolytic fac- tors. Resistant patients to fibrinolysis show positive correlations between strongly thrombotic factors, while in no resistant patients to fibrinolysis there are a trend to haemostasis between prothrombotic and fibrinolytic factors.

There are clearly different patterns of thrombotic and fibrinolytic factors. It is unclear whether minimising PBT is maintained over the years.

Objectives: We sought to evaluate the influence of PBT on long term clinical re- sults in patients (pts) with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) at a high volume centre.

Methods: In a prospective “all-comer” registry clinical and procedural characteris- tics, PBT and 5-year mortality were determined in consecutive STEMI pts treated with pPCI in our tertiary centre between Feb 2001 and Oct 2002. We divided pts according to PBT into three groups: A) <180, B) 180-360 and C) >360 minutes.

Results: Among 1064 consecutive STEMI pts treated with pPCI, PBT and mor- tality were known in 957 (94%) pts. There were 350, 461, 196 pts in group A, B, C, respectively. Pts in group A compared to B and C were younger, more often were male and smokers, less frequently had history of CAD, more frequently had occluded (TIMI grade flow <2) infarct related artery. There were no differences in prevalence of renal failure, hypertension, Killip class ≥1, cardiogenic shock or multivessel disease. Overall 9-year mortality was 28% (294 pts). Multivariable log- istic regression models indicated that longer PBT were associated with a higher adjusted risk of mortality (A:20.6%, B:27.5%, C:37.1%, P<0.0005). A reduction in PBT from 360 to 180 minutes was associated with 16.5% lower mortality.

Conclusion: There are clearly different patterns of thrombotic and fibrinolytic factors. It is unclear whether minimising PBT is maintained over the years. Efforts should be made to shorten PBT in all pts.
Drug eluting stents are associated with lower MACE rates compared to bare metal stents in small coronary arteries treated by primary PCI for STEMI

Methods: 2170 consecutive patients underwent primary PCI for STEMI at a single high-volume centre between October 2003 and September 2010. Of these, 863 had culprit arteries with reference vessel diameter <3mm, which were defined as small coronary arteries. The primary end point was major adverse cardiac events (MACE), defined as death, myocardial infarction (MI), stroke and target vessel revascularization (TVR). Median follow-up was 2.0 years (IQR 0.7-3.6 years).

Results: 246 patients underwent PCI with DES and 637 with BMS. Patients undergoing DES implantation were older, more likely to be diabetic and more likely to have undergone previous PCI. Kaplan-Meier estimates (Figure 1) of medium-term MACE demonstrated a significant difference in favour of DES (21.1% vs. 14.6%, p=0.04). Age-adjusted Cox analysis demonstrated this benefit to be maintained with increased duration (hazard ratio 0.97 [95% CI 0.94-0.99]). In addition, this difference persisted after regression adjustment incorporating a propensity score (age, stent length, stent width, gender, ethnicity, previous MI, PCI or coronary artery bypass grafting, diabetes, hypertension, hypercholesterolaemia, smoking status, presence or absence of shock, and ejection fraction) into the hazards model as a covariate (hazard ratio 0.82 [95% CI 0.7-0.96]).

IMPORTANCE OF CO-MORBIDITIES IN HEART FAILURE

Prognostic impact of the timing/degree of acute kidney injury for Acute Heart Failure: an evaluation of the RIFLE Criteria

Background: Various studies have reported the relationship between the short- and long-term prognosis of acute heart failure (AHF) and acute kidney injury (AKI) based on the risk, injury, failure, and end stage (RIFLE) criteria. However, the relationship between the short-term and long-term prognosis and the timing of AKI during the first 7 days has not been reported.

Methods: Six-hundred twenty-five patients with AHF admitted to the intensive care unit were analyzed. The occurrence of AKI was evaluated by the RIFLE classifications during the first 7 days after admission. AKI presented upon admission in 170 patients (early-AKI) and occurred after admission in 174 patients (late-AKI), however no AKI occurred in 281 patients (no-AKI). Patients assigned into three categories by the severest degree of AKI during 7 days after admission: Class R (risk: n=214), Class I (injury: n=73), or Class F (failure: n=57). The study evaluated the relationships between the presence of AKI (its timing and degree) and outcomes, including short term prognosis (in-hospital mortality) and long term prognosis (any-cause death and HF events, including death and readmission for HF within 5 years).

Results: A multivariate logistic regression model found the presence of AKI during first 7 days to be independently associated with in-hospital mortality (p=0.002, OR: 3.633, 95%CI: 1.591-8.297). Kaplan-Meier survival curves showed that the prognosis, including any-cause death, was significantly poorer in early-AKI than in late-AKI and no-AKI, and was significantly poorer in late-AKI than in no-AKI. A multivariate logistic regression model found that Class I (p=0.003, OR: 4.804; 95%CI: 1.610-10.137) and Class F (p=0.001, OR: 6.427; 95%CI: 2.610-15.561) were independently associated with in-hospital mortality. The Kaplan-Meier survival curves showed the prognosis, including any-cause death, to be significantly poorer in Class I than in no-AKI and Class R, to be significantly poorer in Class F than in no-AKI, Class R and Class I. The presence of AKI and Class R during the first 7 days was independently associated with short-term prognosis; furthermore, the presence of AKI on admission was associated with long-term mortality for AHF. The presence of severe AKI (Class I and F) during the first 7 days after admission was associated with both short-term and long-term prognosis for AHF. The RIFLE criteria should, therefore, be developed into a clinically applicable and standardized method for AHF patients.

Incidence of impaired pulmonary function in men with systolic heart failure and its clinical significance

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±11 years, LVEF: 30±6%, ischemic aetiology: 49%, NYHA class III/IV: 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 inspiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were assessed according to American Thoracic Society/European Respiratory Society Guidelines, and expressed in litres (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 48 (24%) men with HF and a 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.
Are functional and absolute iron deficiencies equally detrimental in heart failure?

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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 ≥30 μg/L and transferrin saturation <20%]) in a real-life HF outpatient population.

Patients: 678 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%). Due to a significant increase in ferritin level between 2000 and 2010 in a database of 1300 patients, these results are not generalizable to a broader population.

Methods: To assess the prognostic significance of ID (both absolute [defined as ferritin <30 μg/L] and functional [defined as ferritin ≥30 μg/L and transferrin saturation <20%]) in a real-life HF outpatient population.

Discussion: Absolute ID was associated with higher mortality. The prognostic value of ID in patients with reduced LVEF is poorly known and there are very few data about AF pattern and prognosis in HF with preserved LVEF. This study evaluated the prognostic value of ID in patients suffering from HF.

Conclusions: Iron deficiency is an important predictor of adverse outcomes in heart failure, and its correction may improve clinical outcomes.

Glycemic control imbalance is a main determinant of neuroendocrine activation and cardiac mortality in mild systolic heart failure

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Purpose: To assess the impact of glycemic imbalance on neuroendocrine activation and outcome in chronic heart failure (CHF) patients with different degrees of left ventricular (LV) systolic dysfunction.

Methods: We enrolled 1007 consecutive patients with systolic CHF (age 65±12 years, mean±SD, males 72%, LV ejection fraction ≤EF; 33±10%, 274 [29%] with diagnosed diabetes, undergoing a comprehensive clinical, humoral (including glycaemic, haemoglobin A1c (HbA1c), echocardiographic and neuroendocrine evaluation. For subgroup analysis, patients were divided into tertiles of LVEF (50-38%, 38-28%, <28%). Endpoint was cardiac mortality.

Results: During a 5-year follow-up (median 36 months, range 0.3-60), 154 cardiac deaths occurred. In the whole population, no differences were evident in clinical, neuroendocrine, echocardiographic parameters, nor in outcome between diabetics and nondiabetics. Conversely, patients with HbA1c >7 showed higher plasma renin activity (PRA, 3.66, 0.62-6.13 vs. 2.28, 0.41-4.1 mg/ml/L, p<0.01), NT-proBNP (1602; 826-3498 vs. 1076; 401-3112 ng/L, p<0.01), and worse clinical status (43% of patients with HbA1c >7 being NYHA III/IV vs. 35% of patients with HbA1c ≤7, p<0.05), no difference in any other parameter. HbA1c >7 predicted cardiac mortality (events in 22% vs. 14% p<0.04). In the subgroup with slightly reduced LVEF patients with HbA1c >7 showed higher PRA and cardiac natriuretic peptides. In this group, HbA1c along with NT-proBNP (but not the diagnosis of diabetes) resulted the only independent predictors of outcome, whereas this did not occur in patients with moderate-to-severe LV dysfunction.

Conclusions: Glycemic imbalance enhances neuroendocrine activation and worsen prognosis, in CHF patients, beyond diagnosis of diabetes. This association appears prominent at early stage of CHF, characterized by slight LV systolic dysfunction, when chronic hyperglycemia might have a specific impact on cardiac remodeling process, by eliciting neuroendocrine activation.

Surgical correction of valvular heart disease: predictors of outcome

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Purpose: The long-term survival of patients with severe compromised ischemic left ventricle and concomitant functional mitral regurgitation is reduced. We performed this study to understand how mitral valve replacement versus repair affects survival and reveal the predictors of mortality in this high-risk population.

Do mitral valve replacement versus repair in patients with severe ischemic mitral regurgitation affect survival?

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Purpose: The long-term survival of patients with severe compromised ischemic left ventricle and concomitant functional mitral regurgitation is reduced. We performed this study to understand how mitral valve replacement versus repair affects survival and reveal the predictors of mortality in this high-risk population.
Different surgical techniques of mitral valve repair for ischemic mitral regurgitation: predictors of efficacy

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Objective: Mitral valve annuloplasty is the standard surgical option for the management of ischemic mitral regurgitation (MR). However, after annuloplasty recurrent MR develops in some patients.

Methods of the Investigation: Preoperative echocardiographic data from 1215 patients who underwent MR repair for ischemic MR combined with revascularization were prospectively collected and reviewed. Of the 787 patients, 53 (8.1%) had residual MR ≥2 grade during even during hospital stay. The mitral valve and LV parameters, including tethering area and coaptation height of the mitral leaflets, were determined. SPSS 15.0 statistics was used.

Results: The type of annuloplasty (rigid ring, flexible ring or posterior annuloplasty) hadn’t influenced the efficacy of surgical treatment (occurrence of the residual MR ≥2 grade were 7.7%, 5.6% and 4.5% correspondingly, χ²=1.75, p=0.416). On ROC analysis and multiple logistic stepwise regression analysis from 227 patients, a larger LV (LVEDD >65 mm, OR 2.7, 95% CI 1.1-6.5, p=0.027; EDV >95 mm³, OR 2.5, 95% CI 1.3-6.0, p=0.042; EDD >105 mm², OR 3.41, 95% CI 1.42-6.29, p=0.007 and ISEV ≥66 mm², OR 2.63, 95% CI 1.12-6.24, p=0.03) were identified as independent predictors for failure of MR repair without rigid ring (flexible or semirigid ring, commercially available or xenopericardial posterior band and else). From 378 cases the higher tethering area for apic4ch viewer ≥2.5 sm² OR 1.81, 95% CI 1.01-3.43, p=0.049 and higher MR severity (for vena contracta ≥6.5 mm OR 1.56, 95% CI 1.02-2.3, p=0.02 and for ERO PISA >0.39 sm² OR 1.07, 95% CI 1.02-1.15, p=0.05) were identified as independent predictors for failure of MR repair.

Conclusion: In conclusion, these results demonstrated that preoperative findings of precise echocardiography can be used to identify patients with ischemic MR at increased risk of repair failure.

Comparison of risk scores for predicting early mortality after Aortic Valve Replacement for aortic stenosis


Background: Major risk scores of early mortality in cardiac surgery are the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) score. A new model of EuroSCORE, which is called EuroSCORE II, was launched at 2011. The aim of this study was to compare STS-PROM and EuroSCORE II after AVR for AS.

Methods: We analyzed the data from 258 consecutive patients who underwent AVR for AS at our hospital. The aortic valve was replaced by Carpentier, between 2002 and 2010. Observations versus expected (O/E) mortality rates were examined. Hosmer-Lemeshow goodness-of-fit test and receiver operating characteristics (ROC) curves were performed to assess the performance of these models.

Results: Observed early mortality was 4.2% (n=11). Predicted mortality rates for STS-PROM and EuroSCORE II were 4.7% and 3.5%, respectively, and thus the O/E ratios for STS-PROM and EuroSCORE II was 0.89 and 1.20, respectively. Pearson correlation coefficient revealed a good linear relationship between STS-PROM and EuroSCORE II (r = 0.76, p < 0.001). Hosmer-Lemeshow goodness-of-fit test indicated good accuracy for the prediction of mortality for both models (for STS-PROM p = 0.801 for STS-PROM and 0.588 for EuroSCORE II). The area under the ROC curve for STS-PROM was 0.79 (95% CI: 0.63 to 0.96) for STS-PROM and 0.69 (95% CI: 0.49 to 0.89) for EuroSCORE II, implying that the discrimination ability of STS-PROM was better than that of EuroSCORE II.

Conclusion: There was a slight trend toward overestimation in STS-PROM (O/E ratio; 0.89) and underestimation in EuroSCORE II (O/E ratio; 1.20). STS-PROM is better than EuroSCORE II in terms of discrimination ability. These results have implications for risk judgment in AVR for AS.

Aortic valve replacement: relationship between aortic stenosis severity and perioperative mortality risk scores

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Purpose: We assumed that perioperative mortality risk scores (Euro I and II and STS) were related with aortic stenosis (AS) severity assessed by aortic valve area (AVA).

Methods and results: We compared pre and postoperative clinical and echocardiographic parameters with perioperative mortality risk scores in 899 patients undergoing AV replacement according with AVA: group 1 (area>0.75 cm², n=78) with group 2 (area<0.75 cm², n=259). Mean age was 66±12 vs 73±9 years, men 56% vs 44% and EF 47±13 vs 36±12%. Mean gradients were 50±15 vs 60±18 mm Hg; mean AVA was 0.83±0.06 vs 0.61±0.09 cm² (p<0.001); index stroke volume was 41±11 vs 46±12 ml/m² (p<0.001). Mean Euro I, Euro II and STS mortality scores were 6.25±0.8, 3.7±1.7 and 2.6±1.2, respectively. Scores values were significantly greater in group 2 than group 1: Euro I 3.4±3.4% vs 6.5±9.3%, Euro II 1.5±1.1% vs 3.4±7%, STS 1.8±1.3% vs 2.9±2.4% (p<0.001). Postoperative mortality rate was 2.9%: 0% in group 1 and 3.4% in group 2 (p=0.062). All scores were negatively correlated (for Euro I vs Euro II, Euro I vs STS and Euro II vs STS, the coefficients were 0.75, 0.641 and 0.563, respectively; p<0.001) and were significantly greater in deaths vs survivors (Euro I 13% vs 2%, Euro II 11% vs 2% and STS 5% vs 2%; p<0.001). All scores were negatively correlated with ARA: r = 0.242 (Euro II), r = -0.235 (Euro II) and r = -0.292 (STS); p<0.001. Pre and postoperative left ventricular ejection fraction and postoperative systolic pulmonary artery pressure were significantly different by comparing deaths vs survivors: 46±13% vs 62±13%, 46±15% vs 57±10% and 37±5 mm Hg vs 31±10 mm Hg (p<0.001, 0.029 and 0.033, respectively).

Conclusion: Perioperative mortality risk and death rate seems to be related to AS severity in patients undergoing isolated AV replacement.

Predictors of persistent severe diastolic dysfunction after aortic valve replacement in aortic stenosis compared with aortic regurgitation

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Purpose: 1. To evaluate the effect of aortic valve replacement (AVR) on left ventricular (LV) diastolic function and LV remodeling, comparing patients with aortic stenosis (AS) to patients with aortic regurgitation (AR).

2. To identify the parameters appropriate for prediction of immediate and medium term evolution in these patients.

3. To assess the independent predictors for persistence of the restrictive LV diastolic filling pattern (LVDDF) after isolated AVR.

Methods: 5 years prospective study on 397 patients with restrictive LVDDF undergoing AVR for AS (Group A - 226 pts) or AR (Group B - 171 pts). Patients were evaluated preoperatively and at 10 days, 1, 3, 6 months, 1 year and yearly 5 years postoperatively. Depending on the LVEF, each of the two groups was divided into 2 subgroups: pts with LVEF<50% (Group A1-137 pts and group B1-102pts) and pts with LVEF>50% (group A2~99 pts and group B2-69 pts). Statistical analysis used SYSTAT and SPSS programs for the simple and multiple regression analysis and relative risk calculations.

Results: 1. The evolution of the LV diastolic function was different in AS group (after AVR diastolic filling improved) compared with AR group. At 1 year postsurgery the percent of the patients with persistent restrictive LVDDF was 23.01% in AS group and 60.23% in AR group.

2. At 5 years, cardiovascular event-free survival, including hospital visits caused by heart failure symptoms and sudden cardiac death was significantly higher in the patients with preoperative AS (87.1%) compared with AR group (64.9%).

3. The parameters appropriate for prediction of immediate and medium term evolution were age, preoperative NYHA class, LVEF, atrial fibrillation, coronary artery disease and smoking.

4. Simple and multivariate regression analysis identified as independent predictors for persistence of a restrictive LVDDF: AR (RR=19.2), E/A ratio >12 (RR=21.1), the LA dimension index >30mm/m² (RR=8.2, p=0.0017), LV enddiastolic diameter (LVEDD) >55mm (RR=6.6), severe pulmonary hypertension (PHT) (RR=8.7) and 2 degree MR (RR=12.6)
Conclusions: 1. Restrictive flow pattern is reversible mostly after AVR for AS than for AR, both in the early and medium postoperative term. 2. The parameters predicting fatal outcome and hospitalisation for heart failure on multivariable analysis were the presence of NYHA class, LVEF, atrial fibrillation, coronary artery disease and smoking.

The echocardiographic predictors for persistence of a restrictive LVFP and permanent pacemaker implantation (PPM) following transcatheter aortic valve implantation (TAVI) versus standard aortic valve replacement (SAVR), and to determine the factors associated with PPM following TAVI or SAVR.

Methods: We analyzed data from 340 patients (pts) with severe aortic stenosis (SAS) and no prior pacemaker who underwent TAVI with either the CoreValve (n=132) or Edwards-Sapien (n=208) prosthesis between 2007 and 2011 and from 210 patients (pts) undergoing SAVR between 2005 and 2010 at one centre. The incidence, reasons, and predictive factors for PPM following the procedure were compared between groups.

Regardless of age was similar in both groups (TAVI: 79.4±7.3 years; SAVR: 79.07±2.86 years, p=0.45), and the TAVI group exhibited a higher-risk profile (Log Euroscore 22.9±15.8% vs. 13.1±11.8% in the SAVR group, p<0.001). The rate of new PPM was higher following TAVI (n=50, 14.7%) compared to SAVR (n=2, 0.97%, p<0.001). The main causes of PPM implantation were: third-degree atriовentricular (AV) block (TAVI: 39pts, 78%; SAVR: 2pts, 100%), atrial fibrillation with a ventricular rate lower than 40/min (TAVI: 3pts, 6%), second degree atrioventricular block (TAVI: 3pts, 6%), and bradycardia-tachycardia syndrome (TAVI: 1pt, 2%). The median time from TAVI to implantation of a PPM was 2 days (interquartile range 1-7 vs. 3.5 days (interquartile range 12-15). Complete-AVB was the primary reason for PPM in the TAVI (78%) and SAVR (100%) groups (p<0.001). In the TAVI group, complete AVB was more common after implantation of a CoreValve than Edwards prosthesis (64.1% vs 35.9%, p<0.001). On multivariable analysis, the predictors of PPM for advanced AVB, after adjustment for age, were: presence of baseline RBBB (OR:2.3, 95%-CI:1.29-4.12), left ventricular ejection fraction (LVEF) ≤50mm²/m², and severe PH associated 2d degree M R.

Conclusions: TAVI was associated with a higher rate of complete-AVB and PPM compared to SAVR in elderly patients with SAS. The presence of baseline RBBB and Corevalve prosthes are correlated with the need for PPM in the TAVI group.

OUTCOMES AND COMPLICATIONS OF CATHETER ABLATION FOR ATRIAL FIBRILLATION

Five years follow up of patients undergoing catheter ablation of persistent atrial fibrillation using the stepwise approach: BLOC-AF study


Introduction: Data on long-term rhythm outcome after persistent AF (PsAF) ablation are limited. The BLOC-AF study (Bordeaux Long term Outcome after Catheter ablation for PsAF) was designed to prospectively collect long-term outcome data from 435 pts. (mean age 63,3 yrs., 340 m, 95 f) with ablation of long-lasting persistentRecent AF pulmonary vein isolation (PVI) is a well-established therapeutic option. In ablation of long-lasting persistent AF substrate modification is usually required. Adjunctive ablation of complex fractionated atrial electrograms (CFAE) has been used as an additional option in ablation.

Haut-Leveque, CHU Bordeaux, Bordeaux, France

Purpose: To compare the incidence of complete atrioventricular block (AVB) and permanent pacemaker implantation (PPM) following transcatheter aortic valve implantation (TAVI) versus standard aortic valve replacement (SAVR), and to determine the factors associated with PPM following TAVI or SAVR.

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Incidence and management of potentially fatal peri-procedural cardiac tamponade in patients undergoing pulmonary vein isolation for atrial fibrillation

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Purpose: Pulmonary vein isolation (PVI) has emerged as an effective treatment option for atrial fibrillation. However, it may be complicated by potentially life-threatening complications such as cardiac tamponade. We sought to assess incidence, circumstances, management and outcome of peri-procedural cardiac tamponade over the last 5 years in 2 high-volume interventional electrophysiology centres.

Methods: Since January 2007, a total of 4558 PVI procedures were performed in 3333 patients with AF (>65±11yo, 71% male, 39% persistent AF). Patients underwent (3D)-Lasso-guided wide circumferential PVI. Transseptal puncture was guided by TEE in 1950 procedures. Patient characteristics, comorbidities and procedure-related details of major adverse events were recorded immediately after procedure in a central database. We analyzed all tamponades with hemothorax occurred acutely (during procedure) in 29/27 patients and in 2/27 patients as an inflammatory reaction within the 2 weeks following the PVI. 

Urgent surgery was necessary in 6/27 cases (0.17% of all procedures; 29.6% of tamponades). In 2/8 cases pericardioctesis failed; in the remaining 6/8 cases immediate operation was necessary because of continuing bleeding, despite angiotensin of antiplatelet and successful pericardiocentesis. In all 8 cases surgical intervention was urgently necessary to overcome fatal outcome; in 3 cases the surgical intervention was performed in the catheter lab. The source of hemorrhage in 5/8 cases was perforation of the left atrial appendage and in 2/8 pop and perforation of anterior/anterolateral LA wall and remained undetermined in 1 case. The outcome was favourable in all 27 patients, hospital stay was delayed by 3±4 days.

Conclusions: Cardiac tamponade necessitating intervention occurs in 0.59% of PVI procedures. 29.6% of peri-procedural cardiac tamponades necessitate urgent cardiac surgery, in order to prevent fatal outcome. Late tamponade after hospitalisation due to an inflammatory reaction occurred in 2 patients (0.04% of procedures, 7.4% of tamponades).

Outcomes and complications of catheter ablation for AF

3868 Asymptomatic cerebral lesions in pulmonary vein isolation under therapeutic anticoagulation

Background: Left atrial radiofrequency ablation has been shown to carry a risk of asymptomatic cerebral lesions. No data exists in patients under full anticoagulation throughout the ablation procedure. The aim of this study was to quantify the amount of silent cerebral lesions assessed by preprocedural and postprocedural MRI in these patients and to identify clinical or procedural parameters that increase the risk.

Methods: A total of 111 consecutive patients undergoing catheter ablation for paroxysmal (n=69; 62.2%) or persistent (n=42; 37.8%) atrial fibrillation were included in the study. Pulmonary vein antrum isolation, roofline, mitral isthmus line, and CFAE ablation using 3.5mm open- irrigated tip catheters were performed, as needed. All patients underwent preprocedural and postprocedural cerebral MRI.

Results: Postprocedural MRI revealed new embolic lesions in 14 patients (12.6%), of them asymptomatic. The only clinical parameter showing a significant correlation with cerebral embolism was smoke in transesophageal echocardiogram (p=0.012). Type of atrial fibrillation showed a trend with 6/63 paroxysmal (9.5%) vs. 8/34 persistent patients (23.5%; p=0.098). Additionally, the CHA2DS2-VASc-Score revealed a trend to significance (p=0.057). Procedural parameters contributing to an increased risk were electrical cardioversion (p=0.026) and CFAE lesions (p=0.016). The only two factors showing a trend to significance in multivariate analysis remained CFAE ablations and smoke in TEE.

Conclusions: Radiofrequency ablation in patients under therapeutic anticoagulation is associated with a substantial risk of silent embolism detected by cerebral MRI. Significant risk factors for cerebral lesions are CFAE ablations and smoke in TEE and electrical cardioversion during the ablation procedure.

3869 Long-term results of transcatheter atrial fibrillation ablation in patients with impaired left ventricular systolic function
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Purpose: Aim of the present study is to evaluate sinus rhythm (SR) maintenance, clinical status and echocardiographic parameters over a long-term period following atrial fibrillation (AF) transcatheter ablation in patients with left ventricular ejection fraction (LVEF) <50%.

Methods: 196 patients (87.2% males, age 60.5±10.2 years) with LVEF <50% underwent radiofrequency transcatheter ablation for paroxysmal (22.4%) or persistent (77.6%) AF. Patients were followed for 46.2 (16.4-63.5) months concerning AF recurrences, functional class, and echocardiographic parameters.

Results: All patients underwent pulmonary vein isolation, while 167 (85.2%) required additional atrial lesions. Eleven (5.6%) patients suffered procedural complications. During follow-up 58 (29.6%) patients required repeated ablations. At follow-up end 15 (7.7%) patients died, while 74 (37.8%) documented at least one episode of AF, atrial flutter or atrial ectopic tachycardia. Eighty-three (47.2%) patients sustained antithrombotic drugs. During follow-up NYHA class improved by at least one class more frequently amongst patients maintaining SR compared to those experiencing relapses (70.6% vs. 47.5%; p=0.003). UEF showed a broader increase in patients maintaining SR (32.7% vs. 21.4%; p=0.047) and...
mortal regurgitation grading significantly decreased (p<0.001) only within these patients. At multivariable analysis SR maintenance emerged as an independent predictor of long-term clinical improvement (Odds Ratio 4.26 95%CI 1.69-10.74, p<0.002).

Conclusions: Although not substantially worse than in patients with preserved LV EF, AF ablation in patients with impaired LV EF is affected by high long-term recurrence rate. Amongst these patients SR maintenance is associated with greater clinical improvement.

**TRANSATHER VASCULAR AORTIC VALVE IMPLANTATION (TAVI) IN CURRENT AND FUTURE CLINICAL PRACTICE**

**3874 Early experience with the JenaValve transapical aortic valve implantation system**

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Transcatheter aortic valve implantation (TAVI) has become a well accepted clinical option for treating high risk patients suffering from severe symptomatic aortic valve stenosis. The self-expanding JenaValve prosthesis consists of a nitinol stent with a porcine root valve available in three different sizes. The stent is fixed in an orthotopic position by clipping on the cusps of the old diseased valve. The three-step implantation procedure can be performed under beating heart conditions avoiding hemodynamic compromise. The retrievable and repositionable system received CE-mark in September 2011. Three months results of all pre CE-mark implantations are summarized in this report. 79 patients (age 84.6±4.0 years, logistic EuroScore 28±7.3%) were included in the first-in-man and the consecutive CE-mark study. 76 patients underwent TAVI with the JenaValve System. In 69 patients the stent-valve was successfully implanted (valve-in-valve 6%, valve-in-ring 23%, TAVI only 70%). We observed a 30-day mortality rate of 6.6% (5 patients). Additional 10 patients died during the next 2 months resulting in a 3-month mortality rate of 19.7%. Pacemaker implantation was necessary in 7.9% due to conduction abnormalities after TAVI. No coronary obstructions occurred. Aortic regurgitation of grade I or less was present in 88.1% post procedure and in 93.0% at 3-months follow-up. Valve insufficiency grade II was described in 11.9% post procedure and in 7.0% after 3 months. Neither regurgitation of more than grade II nor signs of prosthesis dysfunction were observed in any patient during 3 months follow-up. Anatomically correct positioning and implantation without rapid pacing are favourable features of the JenaValve TAVI System. Implantation success was limited due to the learning curve when introducing the novel implantation technique. However, technical improvements of the delivery catheter will further increase the procedure success rate. First results of the self-expanding transapical JenaValve TAVI system showed promising result with respect to a low rate of aortic regurgitation at follow-up. Ongoing studies will further evaluate this TAVI device in high aortic root risk patients.

**3875 The impact of pulmonary hypertension on outcome in TAVI patients: a two-centre experience**

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Background: The prognosis of patients with aortic stenosis (AS) and pulmonary hypertension (PHT) is poor though not fully understood. Transcatheter aortic valve implantation (TAVI) facilitates treatment of patients in end-stage AS many of whom are suffering from severe PHT. The aim of our study was to elucidate the impact of PHT on outcome after TAVI.

Methods and results: Pre and 90 days post TAVI, pulmonary artery systolic pressure (PASP) was determined non-invasively by echocardiography in 326 patients undergoing TAVI. PASP was classified as absent (<30mmHg), mild-to-moderate (30-60mmHg), and severe (>60mmHg). 327 patients (logistic EuroSCORE: 26.9±6.7 years, ±4.0 years, log. EuroScore 28±7.3%) were included in the first-in-man and the consecutive CE-mark study. 76 patients underwent TAVI with the JenaValve System. In 69 patients the stent-valve was successfully implanted (valve-in-valve 6%, valve-in-ring 23%, TAVI only 70%). We observed a 30-day mortality rate of 6.6% (5 patients). Additional 10 patients died during the next 2 months resulting in a 3-month mortality rate of 19.7%. Pacemaker implantation was necessary in 7.9% due to conduction abnormalities after TAVI. No coronary obstructions occurred. Aortic regurgitation of grade I or less was present in 88.1% post procedure and in 93.0% at 3-months follow-up. Valve insufficiency grade II was described in 11.9% post procedure and in 7.0% after 3 months. Neither regurgitation of more than grade II nor signs of prosthesis dysfunction were observed in any patient during 3 months follow-up. Anatomically correct positioning and implantation without rapid pacing are favourable features of the JenaValve TAVI System. Implantation success was limited due to the learning curve when introducing the novel implantation technique. However, technical improvements of the delivery catheter will further increase the procedure success rate. First results of the self-expanding transapical JenaValve TAVI system showed promising result with respect to a low rate of aortic regurgitation at follow-up. Ongoing studies will further evaluate this TAVI device in high aortic root risk patients.

**3876 Is mitral regurgitation reversible in patients undergoing transcatheter aortic valve implantation?**

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Background: Significant mitral regurgitation (MR) is often present in pts with severe aortic stenosis (AS) undergoing transcatheter aortic valve implantation (TAVI). Detection of MR in such pts is crucial as it can independently affect functional status and prognosis.

Methods: To define the short term effect of TAVI on MR severity.

Results: In our department, 86 pts underwent successful TAVI since 2008. A balloon expandable valve was implanted (Edwards-Sapien- 79 pts, Medtronic- 7 pts); 70 by retrograde transfemoral, 14 by antegrade transapical and 2 by subclavian approach. Aortic peak/mean gradient in pre and post TAVI were 85.1±26.8/3.1±66mmHg and 32.4±10.2/9.9±7mmHg respectively (P<0.001 for both). Mild aortic incompetence (AI) post TAVI was observed in 27 (31%) pts, moderate in 18 (21%) pts. No patient had severe AI. Severity of MR: visual assessment (see Table). Mean VC was 0.41±0.17cm before TAVI and 0.38±0.16 af- ter procedure (P=0.003). Fifty-four (63%) pts had coronary artery disease (CAD), 66 (77%) had mitral annulus calcification (MAC) and 38 (44%) had organic mitral valvar disease (OMVD). No relation was found between presence of CAD, MAC or OMVD and improvement of MR degree or VC (p>0.2 for all). In 22 (26%) pts MR improved by 1 grade, 5 (6%) by 2 grades, 1 (1%) by 3 grades, no change in 45 (52%) and worsening in 13 (15%) pts.

**3877 Perivalvular aortic regurgitation: a major predictor of 1-year mortality after a successful TAVI procedure - Insights from the FRANCE2 registry**

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Background: A significant peri-valvular aortic regurgitation (AR) is observed in 15-20% of the cases after a successful transcatheter aortic valvular implantation
The impact of transcatheter aortic valve implantation on resource use. Results from the German transcatheter aortic valve interventions registry

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Purpose: Transcatheter aortic valve implantation (TAVI) has been shown to improve survival compared with standard therapy in patients with severe aortic stenosis who are ineligible for surgery. Especially older patients with aortic stenosis cannot always be offered conventional surgical aortic valve replacement at an acceptable risk. Therefore TAVI is currently an alternative treatment option. The effects of TAVI on health-related quality of life (HRQOL) have not been reported from a large scale cohort.

Methods: The prospective multicentre German transcatheter aortic valve interventions registry includes patients with symptomatic, severe aortic stenosis since 2008. A delay-enhancement MDCT study (GE) was randomized to manual thrombus aspiration (group I, N=44) or conventional use regarding inpatient hospital stays for a subset of patients who underwent TAVI and completed the one-year follow-up. These results refer to hospital stays one year after TAVI and before TAVI.

Results: Resource use data were eligible for 415 patients who survived 12 months after TAVI (average age 81.9 ± 9.5 years; men 73.7%). In the year before TAVI (2.2 in-patient hospital stays), 9.3% (p = 0.0001) of admissions were due to any cause. 12 months after the TAVI procedure 35.2% (142/403) of the patients had at least one hospital stay. The mean duration till rehospitalisation was 25.7 ± 17.5 weeks. The Kaplan-Meier estimation for the one-year rehospitalisation rate was 30.2%. Patients with rehospitalisation had on average 1.5 ± 0.9 admissions with a mean duration of 2.5 ± 2.9 weeks. Of those patients who give information about the number of hospital stays 70.4% reported one admission due to any cause (20.0%, 3.5%, ± 4.3%; ± 5.0%).

Conclusions: Among patients from the German transcatheter aortic valve interventions registry with severe aortic stenosis TAVI resulted in meaningful reductions in resource use regarding inpatient hospital stays one year after TAVI. The authors are grateful to the members of all clinics, which provided data to the German transcatheter aortic valve interventions registry, in particular H. Sieter/Frankfurt, S. Sack/München, U. Gerckens/Bonn, G. Nickenig/Bonn, K.E. Hauptmann/Trier et al for their support.

NEW INSIGHTS IN MYOCARDIAL INFARCTION BY MULTIMODALITY IMAGING

Effect of manual thrombus aspiration during primary PCI in acutely unstable coronary syndrome: evidence for a delayed enhancement MDCT study


Objectives: We sought to assess whether manual thrombus aspiration could reduce infarct size in patients with acute ST-elevation myocardial infarction (MI) undergoing primary percutaneous coronary intervention (PCI).

Background: The efficacy of manual thrombus aspiration during primary PCI for acute MI remains controversial.

Results: Between April 2009 and Mar 2011, 86 consecutive patients presenting with first acute STEMI (Killip-I/II) within 12 hours after the symptom onset underwent manual thrombus aspiration (group I, N=43) or conventional PCI without thrombus aspiration (group II, N=42). The use of glycoprotein IIb/IIIa inhibitor (GPI) was left to the discretion of the operator. All patients received aspirin 300 mg and clopidogrel 600 mg before PCI and underwent delayed enhancement (DE) multi-detector computed tomography (MDCT) immediately after PCI without injection of an additional contrast media for assessment of infarct size, determined as the total volume of myocardium showing DE. DE-MDCT was repeated at 2 months after PCI. The primary endpoint was infarct size reduction at 2 months. Baseline clinical characteristics and angiographic findings were similar between the 2 groups. There were no differences between group I and II in symptom-to-door-time (204 ± 205 min vs. 217 ± 168 min), door-to-balloon time (70 ± 42 min vs. 69 ± 25 min), PCI-to-MDCT time (17 ± 15 min vs. 13 ± 6 min), Pre-PCI TIMI 0/1, post-PCI TIMI 3, or the use of GPI. Markers of myocardial necrosis were not different between the 2 groups.

Conclusions: Thrombus aspiration resulted in a significant reduction in infarct size (by 73% vs. 65%) and corrected TIMI frame count (28 ± 31% vs. 24%). Initial infarct size determined by DE-MDCT and left ventricular ejection fraction (LVEF)
by 2-dimensional echocardiography were similar between group I and II (17±1.8 mL vs. 22±2.3 mL and 58±11% vs. 55±10%, respectively). At 2 months, there was no difference in infarct size and left ventricular ejection fraction between the groups; 14±1.6 mL vs. 17±1.2 mL and 62±1.2% vs. 60±1.2%, respectively. No adverse cardiac events occurred in either group during the 2-month clinical follow-up.

Conclusions: Manual thrombus aspiration was not associated with reduction in infarct size in patients with acute STElevation MI receiving timely reperfusion therapy.

3889 In vivo non invasive quantitative assessment of passive diastolic stiffness of infarcted myocardium using shear wave imaging

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Background: Quantitative imaging of myocardial stiffness is important for the evaluation of systolic (active) and diastolic (passive) LV function. No tool is available to quantify non-invasively myocardial stiffness, which is determinant in case of diastolic heart failure. Shear Wave Imaging (SWI) is a new non invasive ultrasound technique that can quantify the time-varying myocardial stiffness in vivo. In this study, we investigate the potential of this new technique to quantify the change of passive diastolic myocardial stiffness in ovine model of ischemic heart failure.

Methods: SWI was performed in vivo on five open-chest sheep. A linear conventional ultrasonic transducer (8 MHz) was positioned on the LV anterior wall. Shear waves were generated remotely in the myocardium using the acoustic radiation force induced by the ultrasonic probe. The shear wave propagation was imaged in real-time using an ultrafast scanner prototype (12 000 frames/s, Supersonic Imagine, France). The local myocardial stiffness was derived from the shear wave speed. Stiffness was calculated every 0.1 ms to measure the stiffness variation within one cardiac cycle. Myocardial stiffness was also assessed invasively in the same region using the pressure-segment length relationship obtained by sonomicrometers (Sonometrics, Canada). The ligation of one diagonal of the left anterior descending coronary artery was achieved to induce ischemia during 2 hours, and reperfusion was performed during 30 minutes. Measurements were made at baseline, during ischemia and after reperfusion.

Results: Diastolic stiffness of the ischemic myocardium was found to increase after 45 minutes of ischemia. The shear wave speed increased from 0.8±0.16 m/s to 1.5±0.4 m/s (p<0.01). After reperfusion, diastolic stiffness increased even more significantly and diastolic shear wave speed reached 2.8±1.1 m/s (p<0.002). The slope of the end-diastolic pressure-segment relationship, which increased from 10.3±4.2 to 31.6±16.2 kPa, confirmed the stiffening. The peak diastolic strain rate decreased (from 2.43±0.35 1/s to 0.82±0.13 1/s) demonstrating impaired relaxation of the ischemic segment. Finally, TTC staining performed on the explanted myocardium confirmed the presence of a large infarcted zone.

Conclusions: SWI was able to quantify non-invasively the increase of passive diastolic myocardial stiffness after myocardial infarction and reperfusion. We believe that this new non invasive real time ultrasound evaluation of passive myocardial stiffness opens the door to an improvement of early detection and treatment of patient with diastolic heart failure.

3890 Myocardial fibrosis and fat may be substrates of critical Association between left ventricular longitudinal function and neurohumoral activation after acute myocardial infarction. A two dimensional speckle tracking study

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Background: N-terminal pro-B type natriuretic peptide (NT-proBNP) is released in response to increased myocardial wall stress and is associated with adverse outcome in acute myocardial infarction. However, little is known about the relation between longitudinal deformation indices and NT-proBNP.

Methods and results: We consecutively included 611 patients with acute myocardial infarction admitted to a tertiary centre and performed echocardiography within 48 hours of admission. Global longitudinal myocardial function was assessed with 2D-dimensional speckle tracking imaging (DSTE) simultaneously with measurement of plasma NT-proBNP. A significant linear relation between NT-proBNP and global longitudinal strain (GLS) was found (p<0.0001, r=0.42). GLS emerged as the strongest predictor of log(NT-proBNP) (p<0.0001). In patients with preserved systolic function (LVEF >45%), GLS remained strongly correlated with NT-proBNP (p<0.0001, r=0.50). The C statistic associated with prediction of upper versus lower quartiles of NT-proBNP was significantly higher for GLS compared to LVEF (0.76 vs. 0.56; p<0.0001).

Conclusion: Left ventricular longitudinal function assessed by GLS exhibits a stronger association with NT-proBNP levels in acute myocardial infarction compared to LVEF. In patients with apparently preserved systolic function GLS is superior to LVEF in identifying increased neurohumoral activation.

3892 Two-dimensional longitudinal strain is more accurate than three-dimensional longitudinal strain to identify infarcted LV segments in STEMI patients


Purpose: To compare 2D vs 3D longitudinal strain (LS) in normal hearts and in patients with recent STEMI.

Conclusions: MF and MFC may be substrates of VF or sustained VT. 320 slice CT can evaluate coronary arteries and myocardium in subjects with arrhythmia and even with implantable cardioverter defibrillators which cannot be acquired on magnetic resonance imaging.
Methods: In 123 healthy subjects (aged 44-14 years, range 18-75) and 46 patients (58±13 years) with recent STEMI, three apical LV views for measuring 2D-LS (70±8 fps) and 4-beat LV full-volume data sets (31±4 fps) for measuring 3D-LS were acquired 8.3 days after primary PCI using Vivid E9 scanner and analyzed with dedicated software (BT11, GE Healthcare, Horten, N). All subjects were selected for good image quality, sinus rhythm and adequate 2D/3D speckle-tracking in at least 14 of all 17 segments. In pts, 2D-LS and 3D-LS were compared against 3D wall motion score (WMS) and delayed-enhancement at magnetic resonance (DE-MRI) performed 24±24h apart from echo study, both at segmental and global levels. 

Results: In healthy subjects, global 2D-LS values were significantly lower than 3D-LS (-2.5±1.9 vs -1.9±1.2, bias 1.3±2.2, p<0.001), with whom were also weakly correlated (r=0.37, p=0.001). In pts, global 2D-LS had closer correlations with infant size index at DE-MRI, 3D WMS index and EF (r=0.65, 0.70, -0.68) than global 3D-LS (r=0.36, 0.48, -0.56, respectively, p<0.01 for all). Segmental 2D-LS values showed a higher discriminative power (F ANOVA = 144 vs 50 for 2D-LS vs 3D-LS, p<0.0001) to separate normal segments from those with non-transmural and transmural necrosis (DE 0.50% and >50%, respectively). At ROC curve analysis, segmental 2D-LS had a greater predictive power than 3D-LS to identify segments with ady/skinesis (AUC 0.81 vs 0.70) or transmural necrosis (AUC 0.83 vs 0.73, p<0.0001). 

Conclusions: Significant differences were identified between 2D-LS and 3D-LS in both normals and STEMI patients. Between the two tested vendor-specific algorithms, 2D-LS was more accurate than 3D-LS to identify infarcted LV segments and to reflect global LV dysfunction in STEMI patients.

Necrosis and ischemia for risk stratification in patients with known or suspected ischemic cardiomyopathy. Study with stress cardiac magnetic resonance


Objectives: To determine the prognostic value of necrosis and ischemia analyzed with dipyridamole stress cardiac magnetic resonance (CMR) for predicting major events in patients with systolic dysfunction and known or suspected ischemic myocardial infarction.

Methods: 274 patients with depressed ejection fraction (<50%, 38±9%) referred for study with stress CMR for known or suspected ischemic cardiomyopathy. We quantified (number of segments, s) the presence of severe ischemia (dipyridamole-induced perfusion deficit and wall motion abnormalities) and the extent of necrosis (late gadolinium enhancement in >50% wall thickness). We considered abnormal if more than one segment was altered. 

Results: Ischemia and necrosis were ruled out in 89 patients (32%). Necrosis in 184 (67%) and severe ischemia in 22 (8%). During a median of follow-up of 329 days, 28 first events were detected (10%, death or infarction). Patients were excluded when suffered a major event or revascularization. More major events were detected in patients with necrosis (12% vs 7%, p<0.01) and specifically in those with severe ischemia (45% vs 7%, p<0.001). After adjusting for baseline characteristics and CMR indexes, predictors of major events were with (HR with 95% CI) end-systolic volume (1.01 [1.01-2.02] per ml/m², p=0.001), extent of necrosis (1.1 [1.01-1.1] per s, p=0.02) and extent of severe ischemia (2.1 [1.7-2.7] per s, p<0.001). Risk of major events was higher (p<0.01) in patients with severe ischemia (45%) compared with those with necrosis but without ischemia (8%) and those without necrosis or ischemia (6%). 

Conclusions: In patients with known or suspected ischemic cardiomyopathy, the presence of severe ischemia is the most powerful prognostic index. A simultaneous study of viability and ischemia is recommended for risk stratification.

MODIFIERS OF OUTCOME IN CORONARY ARTERY DISEASE

P3908 NSAI D use is associated with an increase in adverse cardiac events: 4-year results from the REACH registry

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Background: There have been conflicting results regarding the risk of non-steroidal anti-inflammatory drugs (NSAIDs) in high-risk patients or those with established atherosclerotic disease. These medications have been linked to salt and water retention, adverse ventricular remodeling, and heart failure (HF). For this reason, we sought to assess their impact on cardiovascular (CV) events, HF, and hospitalizations for ischemic events.

Methods: We analyzed 63,747 patients in the REACH registry who had information available on baseline NSAID use and were followed for 4 years. Baseline characteristics were compared using Chi-square tests and Cox proportional hazards models were constructed and adjusted for all baseline characteristics with p<0.05. In addition, the interaction was assessed between NSAIDs and aspirin or platelet-antiplatelet agents. 

Results: Among patients receiving NSAIDs, the median age was higher (71 vs. 65) and there was a higher percentage of females, whites, and patients who weighed >60kg. More of those on NSAIDs had cardiac risk factors (hypertension, dyslipidemia, diabetes), baseline HF and creatinine clearance <60 mg/ml (all p<0.001). There was a significant increased hazard associated with NSAID use for developing incident HF (HR 1.31, 95% CI 1.20-1.43, p<0.001), being hospitalized for ischemic events (HR 1.15, 95% CI 1.09-1.22, p<0.001), and in the composite endpoint of CV death/MI/Stroke/CV hospitalizations (HR 1.10, 95% CI 1.04-1.15, p=0.003) that persisted after fully adjusting for baseline differences in risk and for other clinical factors. There was no difference in CVDeath/MIs/Stroke (HR 1.03, 95% CI 0.96-1.12, p=0.40). Following multivariable adjustment, NSAIDs were not associated with statistically significant increases in bleeding leading to hospitalization and requiring transfusion (HR 1.14, 95% CI 0.92-1.41, p=0.22). There was also no significant interaction between NSAIDs and aspirin (p-interaction=0.22) or NSAIDs and antiplatelet agents (p-interaction=0.21).

Conclusion: Among patients with stable atherothrombosis, NSAID use at baseline is associated with a higher risk of CHF, hospitalizations for ischemic events, and major adverse cardiac events.

P3909 History of stroke in patients with coronary artery disease in the REACH Registry: impact on cardiovascular and bleeding event rates

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Purpose: Several recent randomized trials have identified prior stroke as a marker of increased bleeding risk in coronary artery disease (CAD) patients receiving novel antithrombotics. We sought to evaluate the impact of history of stroke/TIA in CAD patients within a large international registry.

Methods and results: From the REACH registry of atherothrombosis, 26,389 patients with a history of CAD (of whom 4460 (16.9%) had prior stroke/TIA) and 4-year follow-up were analysed. Patients with prior stroke/TIA were older (70.5±9.7 years vs. 67.6±10.0 years, p<0.0001), more frequently female (34.1% vs. 28.2%, p<0.0001), and had higher baseline risks of bleeding and CV events. Patients with a history of stroke/TIA had increased risks of all-cause death, MI and stroke relative to patients without history of stroke/TIA. While total bleeding was not increased, non-fatal haemorrhagic stroke (HS) rates were increased in Figure 1. Kaplan-Meier curves
these patients. In addition, among patients on dual antplatelet therapy, there was a 7-fold (95% CI: 1.7-29.3) crude and a 4.9-fold (1.1-20.8) adjusted increase in the risk of non-fatal HS in patients with vs. without prior stroke/TIA. The excess risk for HS was greatest in the 1st year following a stroke/TIA (adjusted HR: 3.62, 95%CI: (1.67-7.85, p= 0.0003), whereas beyond 1 year, risk was not increased (adjusted HR = 1.11, 95% CI: 0.47 - 2.61).

Conclusions: In CAD, a history of stroke/TIA is associated with an increased risk of death, MI, or stroke. However, it is also associated with a disproportionate increase in HS, particularly when patients receive dual antplatelet therapy and in the first year following stroke/TIA. This suggests that while these patients are at high risk of cardiovascular events, increasing antithrombotic therapy carries a specific risk of HS.

Methods: We retrospectively identified all patients from the Lund municipality on the population-based Rotterdam Study (2672 men and 3862 women), we determined the presence of unrecognized MI and recognized MI at the baseline (1990-1993). The cohort was followed for nearly two decades for all-cause and cause-specific mortality.

Results: During 82,268 person-years of follow-up (median 15.6 years) 3,412 persons died (1300 due to a cardiovascular cause). Both men and women with unrecognized MI had an increased risk of all-cause mortality (Hazard ratio [95% confidence interval] = 1.72 [1.43 – 2.07] and 1.36 [1.14 – 1.61] respectively). Having an unrecognized MI increased the risk of cardiovascular mortality by two-fold among men (2.19 [1.86 – 2.91]) and by approximately 30% among women (1.36 [1.03 – 1.81]), and by approximately 40-45% the risk of noncardiovascular mortality (1.46 [1.14 – 1.89]; 1.39 [1.10 – 1.75]) in men and women respectively. Recognized MI was associated with an increased risk of all-cause mortality in men and women (1.67 [1.45 – 1.94]; 1.87 [1.54 – 2.28]).

Conclusions: The long-term prognosis of persons with unrecognized MI is worse than that of persons without any type of MI. In men the prognosis is as unfavorable as that of persons with recognized MI. This adverse prognosis applies to both cardiovascular mortality and noncardiovascular mortality.

P3910

Triple anticoagulant therapy following an acute coronary syndrome: prevalence, bleeding rate and utility of the HAS-BLED score

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Purpose: The aim of this study was to evaluate the prevalence of triple anticoagulant therapy (TT; warfarin, aspirin and clopidogrel) and associated bleeding risk, compared to double antplatelet therapy (DAPT; aspirin and clopidogrel) in patients discharged from a Coronary Care Unit (CCU) following an acute coronary syndrome. Furthermore, we investigated the accuracy of the HAS-BLED risk score in predicting bleeding events in TT patients.

Methods: We retrospectively identified all patients from the Lund municipality on TT within discharge from the CCU at Skane University Hospital in Lund between 2005 and 2010. TT patients were compared with age- and sex-matched controls discharged from DAPT. Major bleeding was defined in accordance with the HAS-BLED derivation study. Any bleeding requiring hospital care or causing a decrease in haemoglobin level of more than 20 mg/dL or requiring blood transfusion.

Results: A total of 2423 patients were screened, of whom 159 (6.6%) were on TT. The mean age was 67.2 (+5.9) years. The most common indications for TT was atrial fibrillation (n=63, 39.6%) followed by apical akinisia (n=60, 37.8%), and the mean duration of TT was 3.7 (+0.3) months. Upon termination of TT, Warfarin was discontinued in 82 (52.2%) patients and clopidogrel in 57 (36.3%). The cumulative incidence of spontaneous bleeding events was significantly higher in the TT group at one year (10.2% vs 3.2%, p<0.01). The HAS-BLED score significantly predicted spontaneous bleeding events in TT patients (area under the ROC curve 0.67, 95% CI = 0.54 – 0.79, p=0.048).

Conclusions: TT was relatively common following an acute coronary syndrome and associated with a threefold increase in major bleeding at one year compared to DAPT. The HAS-BLED risk score predicted bleeding events with moderate accuracy. Careful patient selection and clinical follow-up for TT appears warranted.

P3912

Prognosis of unrecognized myocardial infarction in elderly men and women: the Rotterdam Study

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Background: Unrecognized myocardial infarction (MI) is frequent in the general elderly population. Its prognosis is reported at least as unpropitious as that of recognized MI, particularly in men. However, contemporary data with long follow-up are lacking.

Objective: To investigate the long-term prognosis of unrecognized MI with respect to all-cause and cause-specific mortality, and to investigate any sex-differences in prognosis.

Methods: In the population-based Rotterdam Study (2672 men and 3862 women), we determined the presence of unrecognized MI and recognized MI at the baseline (1990-1993). The cohort was followed for nearly two decades for all-cause and cause-specific mortality.

Results: Of the 6534 participants, 4460 (68.6%) had a prior history of stroke/TIA. The cohort was followed for nearly two decades for all-cause death. No differences were observed in the long-term prognosis of unrecognized MI with respect to all-cause or cause-specific mortality. Overall, the observed HR was 1.12 (95% CI: 0.86 – 1.46).

Conclusion: In patients with CAD and SDB, the use of PAP therapy improves long-term cardiovascular outcomes.

P3913

Impact of positive airway pressure therapy for cardiovascular outcomes in patients with coronary artery disease and sleep-disordered breathing

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Background: The aim of this observational study is to determine whether positive airway pressure (PAP) therapy affects the long-term outcomes of patients with coronary artery disease (CAD) and sleep-disordered breathing (SDB).

Methods: We studied 1693 consecutive patients who underwent polysomnography from November 2004 to July 2011, and enrolled 150 patients with SDB (apnea-hypopnea index [AHI] ≥ 15), who had been admitted to hospital because of CAD before polysomnography. They were divided into two groups: a PAP-treated group (AHI ≥ 15 and treated with continuous positive airway pressure or adaptive servo ventilation) and an untreated SDB group (AHI < 15 and untreated with PAP devices). The frequency of death and hospitalization due to cardiovascular events (acute coronary syndrome, coronary intervention, heart failure, stroke, and fatal arrhythmia) between the groups was analyzed using multivariate analysis.

Results: The mean follow-up period was 35.2±23.8 months and 36% of the patients died or were re-admitted to hospital due to CVD. Kaplan-Meier survival curve indicated that event-free survival was significantly higher in the PAP-treated group than in the untreated SDB group (Figure 1). Multivariate analysis showed that the risk for death and hospitalization was significantly higher in the untreated SDB group (hazard ratio [HR]: 2.62; 95% confidence interval [CI]: 1.09 to 6.64; p < 0.05) than the PAP-treated group.

Conclusion: In patients with CAD and SDB, the use of PAP therapy improves long-term cardiovascular outcomes.

P3914

Time course of depressive symptoms and first coronary heart disease and stroke in older adults. A prospective observational study cohort: the Three-City study

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Objective: To prospectively investigate the association between the course of depressive symptoms over time and the occurrence of coronary heart disease (CAD) and stroke events in older adults.

Setting: The Three City Study is a French multisite (Bordeaux (South-West), Dijon (East) and Montpellier (South-East) community-based prospective cohort. Participants: 7308 men and women aged 65 years and over with no history of CHD, stroke or dementia were recruited through the electoral rolls of these cities. Depressive symptoms assessed by the CESD questionnaire and other risk factors were quantified at baseline and after 2 and 4 years of follow-up. Incident CHD and stroke events were adjudicated by an independent expert committee. Depressive symptoms were assessed at baseline and after 2 and 4 years of follow-up. Incident CHD and stroke events were adjudicated by an independent expert committee.
symptoms were used as a time dependent variable in Cox proportional hazard model.

Results: At baseline, 2 years and 4 years of follow-up, depressive symptoms (CESD score $\geq 16$) were present in 22.7%, 18.8% and 18.5% of the patients, respectively. The corresponding rates for antidepressants use were 6.7%, 7.0%, and 7.5%. After a median follow-up of 5.25 years, 410 subjects had suffered a first CHD or stroke event including 82 fatal. At adjustment for study centre, sociodemographic characteristics and baseline conventional risk factors, the risk of CHD and stroke combined increased progressively with the percentage of time spent with depressive symptoms and was reflected in a selective association with fatal events. Compared to subjects who remained free of depressive symptoms during follow-up, those with persistent depressive symptoms had an increased risk of total vascular events (HR=1.38; 95% CI: 1.07–1.80), fatal CHD and stroke combined (HR=1.32; 95% CI: 1.21–1.45), and fatal stroke ($n=25$; HR=5.22; 95% CI: 2.07–13.3). The risk of fatal CHD and stroke combined was even higher in depressive subjects with impaired activities of daily life (HR=1.00, 95% CI: 0.93–1.88).

Conclusion: The current data support a dramatic increased risk of fatal CHD and stroke events associated with the course of depressive symptoms in older adults and emphasize the need to detect depressive symptoms in that population.

Prasugrel 5mg in the very elderly is non-inferior to prasugrel 10mg in non-elderly patients: the generations trial, a pharmacodynamic (PD) study in stable CAD patients


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Purpose: In the TRITON trial, prasugrel (pras) 10mg reduced ischemic events vs. clopidogrel (clop) 75mg but increased bleeding, notably in very elderly patients (VE, $\geq 75$). Pras 5mg is suggested in VE patients to reduce the risk of bleeding, but PD data are limited. We examined PD with pras and clop in a three-period, blinded, cross-over study involving VE or non-elderly (NE, 45-65y) stable CAD patients. Assuming that VE patients on pras 5mg would show lower platelet inhibition, the primary hypothesis was that the median of pras 5mg in VE would be non-inferior to the 75th percentile of pras 10mg in the NE.

Methods: After a run-in on low dose aspirin, VE patients ($n=73$, 79±2y) and NE patients ($n=62$, 56±5y) were randomized to pras (5 or 10mg) or clop 75mg during three 12-day periods. PD was measured by turbidimetric aggregometry (MPA to $20 \pm \mu$M ADP), VerifyNow®P2Y12 (VN), and VASP-PRIm at pre-dose and the end of each period.

Results: Median MPA during pras 5mg in VE was non-inferior to the 75th percentile of pras 10mg in NE (Figure). MPA was significantly lower for pras 5mg (57±14) vs. clop (63±14) in VE, but higher than pras 10mg NE (46±12), (mean±SD: p=0.001, Figure). The antiplatelet effect based on mean MPA during pras 5mg or 10mg or clop appeared similar between cohorts. Similar PD patterns were observed with VN and VASP-PRIm. Pras 5mg consistently resulted in fewer poor responders vs. clop in the VE, irrespective of definition. Higher rates of mild bleeding were seen in both VE and NE with pras 10mg, while being similar for pras 5mg vs. clop 75mg.

Conclusions: In patients with CAD, pras 5mg in the VE achieved pre-defined non-inferiority for PD by MPA compared to pras 10mg in NE while still providing significantly better PD and fewer poorer responders than clop 75mg in VE.

Twodimensional strain measures of left ventricular systolic function are new independent predictors of ventricular arrhythmic events in chronic heart failure patients

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The aim of this study was to evaluate the role of Two-dimensional (2D) speckle tracking measures of left ventricular systolic function in predicting the occurrence of ventricular arrhythmic events in chronic heart failure (CHF) patients. We enrolled 230 outpatients (75% males, 64±13 years, NYHA class 2.1±0.6, left ventricular ejection fraction 34±5% with CHF due to left ventricular systolic dysfunction, in conventional therapy (90% ACE-inhibitors and/or ARBs, 93% betablockers, 78% with implantable cardioverter defibrillator). At echocardiogram, by standard apical views left ventricular global strain (GS) and global strain rate (GSr) were measured by using 2-D speckle tracking analysis (Echo-PA, GE). NT-proBNP and presence of non-sustained ventricular tachycardia (NSVT) at ECG Holter were also evaluated. None of the enrolled patients had previously experienced major ventricular arrhythmias.

During follow-up (22±10 months), in 27 patients at least an episode of ventricular tachycardia and/or ventricular fibrillation requiring cardioverter defibrillator intervention (anti-tachycardia pacing and/or DC shock) occurred. At Cox univariate analysis GS (HR: 1.23; CI: 1.12–1.36; p<0.001) and GSr (HR: 1.48; CI: 1.15–1.91; p=0.011) were significantly associated to arrhythmic events. At multivariate analysis, after correction for NSVT, NYHA class and logNT-proBNP GS (HR:1.16; CI:1.01-1.33; p=0.035), but not GSr (HR: 1.18; CI: 0.88–1.59; p=0.270) remained significantly associated to the events. Figure shows Kaplan-Meier curves for arrhythmic events according to GS and GSr median values.

In conclusion, the results of this study support the possible clinical usefulness of the left ventricular systolic function 2-D strain measures in detecting CHF outpatients prone to experience major arrhythmic events.

Two-dimensional strain measures of left ventricular systolic function are new independent predictors of ventricular arrhythmic events in chronic heart failure patients

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Conclusion: The data from this study shows that quantitative LV flow vortex parameters are superior to conventional echo-Doppler measures to predict exercise capacity in patients with chronic compensated systolic heart failure.

**P3919**
The incremental prognostic value of inotropic contractile reserve combined with advanced mitral regurgitation in identifying responders to cardiac resynchronization therapy

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**Purpose:** Inotropic contractile reserve (ICR) during dobutamine stress echo (DSE) differentiates the viable myocardium from scar tissue according to inotropic response. Furthermore, low dose DSE provides information for the global left ventricular response. The aim of this study was to identify the role of inotropic contractile reserve, in combination with the presence of functional mitral regurgitation in patient selection for cardiac resynchronization therapy (CRT) and to compare it with other echocardiographic indices used in predicting CRT response.

**Methods:** 42 pts referred for clinically indicated CRT were evaluated. All patients underwent low-dose dobutamine stress echocardiography to assess inotropic contractile reserve, defined as an improvement of ejection fraction (EF) ≥ 5%. Mitral regurgitation (MR) severity was divided in four grades and advanced MR was defined as the presence of grade III or IV regurgitation. The interventricular mechanical delay index (by PW Doppler) and Opposing Wall Delay Index (by TDI) were used to assess interventricular and intraventricular dysynchrony respectively. Responders were defined by ≥ 15% reduction in left ventricular end systolic volume after CRT.

**Results:** 42 pts (mean age 68±7 years old, 28 men, NYHA III-II) were included. The mean GRS duration was 154±9.5ms. During a 12-month follow-up, 29 pts (69%) had responded. The ejection fraction before CRT was 24±5% and increased to 31±4% after CRT (p<0.05). The presence of ICR was the strongest predictor of response to CRT (area under the curve, 0.84; p<0.01) compared with interventricular dysynchrony index (area under the curve, 0.86; p<0.05) and intraventricular dysynchrony index (area under the curve, 0.74; p<0.05). The combination of ICR with the presence of advanced MR offered even greater predictive value (area under the curve, 0.89; p<0.00).

**Conclusions:** Inotropic contractile reserve was a stronger predictor of CRT response than conventional and TDI indices, and its diagnostic value can be further enhanced when combined with the presence of advanced functional MR. Dobutamine stress echocardiography may play a pivotal role in identifying responders to CRT, thus avoiding ineffective interventions and reducing the cost of desynchronous management.

**P3920**
Improved differential diagnosis between left ventricular non-compaction and dilated cardiomyopathy

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**Introduction:** Left ventricular non compaction (LVNC) is characterized by a two-layered myocardium consisting of a non-compacted inner and a compacted outer layer. Since left ventricles of many LVNC patients are dilated and exhibit poor systolic function, LVNC can be misinterpreted as dilated cardiomyopathy (DCM). This study assesses whether novel echocardiographic criteria may facilitate differential diagnosis between DCM and LVNC.

**Methods:** Transthoracic echocardiography was performed in 30 LVNC patients (mean age 36±3±17 years, 40 age-matched patients with DCM, and 42 age-matched controls. Maximal systolic thickness of “non-compacta” and “compacta” was measured in standard short axis views (2-D) at the apical or midventricular level in the segments with most prominent recesses (LVNC) or most prominent trabeculations (DCM and controls). The thickness of the basal septum was measured in parasternal long axis view (M-mode).

**Results:** LV ejection fraction was 37% (range: 10-59) in LVNC, 29% (16-51) in DCM, and 63% (range: 55-74) in controls. Maximal systolic thickness of “non-compacta” was 1.86±0.01 cm in LVNC compared to 0.4±0.02 cm in DCM (p<0.0001), and 0.2±0.01 cm in controls (p<0.0001). Maximal systolic thickness of “compacta” was lower in LVNC (0.83±0.02 cm) compared to DCM (1.0±0.02 cm; p<0.0001) and controls (1.1±0.03 cm; p<0.0001). Maximal systolic thickness of “compacta” was 8.2 mm (range: 3.5-8.2) in LVNC versus 8.5 mm (range: 8.5-14.0; p<0.0001) and 8.6 mm (range: 8.6-15.0; p<0.0001) in controls. The ratio of maximal systolic thickness of the indexed basal septum to that of the “compacta” was 0.64/m² (range: 0.641-1.90) in LVNC versus 0.61/m² (range: 0.29-0.61) in DCM and ≥ 0.57/m² (range: 0.28-0.57) in controls.

**Conclusion:** Maximal systolic “compacta” thickness > 8.2 mm and a ratio of indexed septal wall thickness to “compacta” thickness ≥ 0.64/m² is specific for LVNC. This observation may be particularly useful in patients with dilated ventricles and facilitates the differential diagnosis between LVNC and DCM.

**P3921**
Visual assessment of apical rocking predicts response and long-term survival following cardiac resynchronization therapy

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**Background:** Motion of the left ventricular (LV) apical myocardium perpendicular to the LV long axis (apical rocking), is an often observed phenomenon in asynchronously contracting ventricles. In this study, we tested if visual assessment of apical rocking can predict reverse remodeling and survival in cardiac resynchronization therapy (CRT) candidates.

**Methods:** A total of 201 patients eligible for CRT (63±11 years, ejection fraction ≥ 26±6%) underwent standard echocardiographic examination before and 12±2 months after device implantation. Three blinded physicians were asked to assess response to CRT (yes/no) by visually assessing the presence of apical rocking and extend and localization of infarct scar. Response was defined as LV end-systolic volume decrease ≥ 15%. Patients were followed for an average period of 37±19 months for the occurrence of cardiac death.

**Results:** Visually assessed apical rocking predicted reverse remodeling with a sensitivity, specificity and accuracy of 95, 85, and 90%, respectively. When corrected by CRT, visually detected apical rocking was the only parameter associated with favorable outcome, whereas worse functional class, a high scar burden (>6 segments) and atrial fibrillation were associated with poorer survival (Figure). Baseline LV ejection fraction and QRS duration did not predict outcome.

**Conclusions:** Simple visual assessment of apical rocking is a robust predictor of response and long-term survival after CRT. In patients with heart failure of ischemic origin, visual assessment of scar burden further enhances predictive power of visible LV dysynchrony.

**P3922**
Diagnostic and prognostic role of global longitudinal strain in patients with heart failure and normal ejection fraction

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**Introduction:** Many patients have clinical and bio-marker evidence of heart failure but normal left ventricular (LV) ejection fraction (EF) (<50%). More subtle abnormalities of systolic function may explain the syndrome. We measured global longitudinal strain (GLS) to identify LV systolic dysfunction in patients with HFNEF. Methods: 313 patients referred to our clinic with symptoms and signs suggesting heart failure (median age 74 years, 42% women, 40% in atrial fibrillation (AF)) with an LVEF >50% were recruited. Three different subgroups were identified: 1) pts with no substantial cardiac failure (atroventricular n=57); 2) pts with NT-proBNP ≥ 400ng/l, >40mm or NT-proBNP ≥ 400ng/l. All underwent echocardiography. Peak systolic strain was defined as the peak negative
value on the strain curve during the entire cardiac cycle. Values obtained from each of 16 LV segments were averaged.

Results: Median plasma NT-proBNP levels (IQ range) were 164 ng/l (59-268) in patients with no evidence of cardiac dysfunction, 414 ng/l (143 487) for grey cases and 1627 ng/l (868-2837) for definite HFpEF. Mean LVEF was 58% in each subgroup. Patients with HFpEF were older (78 years), more often had AF (73%) had more symptoms and signs of fluid retention, and were treated with higher doses of diuretics. They also had more right ventricular dysfunction and more mitral and tricuspid regurgitation. Mean GLS (SD) was higher (worse function) in patients with HFpEF (-15.9 (2.4) % vs -15.2 (3.1) % vs -13.6 (3.0) % vs -p<0.001). During a median follow of 647 days in survivors, 30 patients had an unplanned hospitalisation due to HF and 32 patients died from cardiovascular (CV) causes. In univariable Cox regression analysis, GLS but not LV EF predicted events. In multivariable analysis, urea, inferior vena cava (IVC) diameter, NT-proBNP and atrial fibrillation (AF) were the only independent predictors of adverse outcome.

Conclusions: GLS is impaired in patients with HFpEF compared to those with no evidence of heart failure, but does not add independent prognostic information to other simpler variables.

**P9023 Comparison of left ventricular discoordination and dys synchrony assessment by radial strain imaging in cardiac resynchronization therapy**

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Background: Patients with nonischemic etiology, left bundle-branch block (LBBB) and GLS and QRS duration >150 ms are more likely to derive benefit from cardiac resynchronization therapy (CRT) than those without. This study aimed to compare mechanical discoordination and dysynchrony in CRT candidates.

Methods: Speckle-tracking strain imaging was performed in 120 CRT candidates and 60 patients with LVEF <35% and QRS duration ≤120 ms. CRT candidates were divided into subgroups according to the etiology of heart failure (ischemic vs nonischemic), QRS morphology (LBBB vs non-LBBB) and QRS duration (>150 ms vs <150 ms), respectively. Dysynchrony indices based on time-to-peak radial strain of anteroseptal and posterior walls (AS-P delay) and standard deviation of time-to-peak radial strain (RS-SD) were measured. Dyscoordination was indexed using the mid-ventricular radial discoordination index (RDI-M).

Results: RDI-M could distinguish between patients in the narrow and wide QRS groups. Patients with nonischemic etiology were more likely to show dyssynchrony without significant differences between ischemic and nonischemic subgroups. CRT candidates with ischemic etiology were more likely to show dysynchrony without significant discoordination than nonischemic candidates.

Conclusions: Mechanical discoordination performed better than dysynchrony in differentiating CRT candidates with and without favorable characteristics.

**THE ENDOTHELIUM: KEY PLAYER IN VASCULAR CONTROL**

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Purpose: Asymmetric dimethylarginine (ADMA), competes with L-arginine to inhibit NO synthase (NOS), leading to a decreased NO bioavailability, increasing vascular oxidative stress and endothelial dysfunction. Recent data suggest that reduced leukocyte telomere length (LTL) could be associated with increased risk of acute myocardial infarction (MI). The aim of our study was to analyse the relationship between LTL and ADMA, as a biomarker of oxidative stress, in patients with acute MI.

Methods: Blood samples from 33 consecutive patients hospitalized ≤24 hours after symptom onset for acute MI were taken on admission. Serum levels of ADMA, SDMA (its biologically inactive symmetrical stereoisomer and L-arginine) were determined using high-performance liquid chromatography. LTL was assessed by extraction of leukocyte DNA from venous blood samples and performing real-time PCR. The L-arginine/ADMA ratio was used as a biomarker of vascular oxidative stress and endothelial dysfunction. Patients from the lowest L-arginine/ADMA tertile were compared with patients from the higher L-arginine/ADMA tertiles.

Results: Demographic data, chronic treatments, cardiovascular risk factors and history were similar for the 2 groups. Strikingly, in patients with the lower L-arginine/ADMA tertiles, LTL was markedly reduced when compared with the highest L-arginine/ADMA tertiles. LTL was negatively correlated with age (r=-0.356, p≤0.0042). Moreover, a trend for a positive correlation between LTL and L-arginine/ADMA ratio was noted (r=+0.339, p≤0.053) but not with SDMA (r=0.069, p=0.698).

Conclusions: Our study showed that, in MI patients, reduced LTL was associated with increased levels of vascular oxidative stress, as assessed by serum L-arginine/ADMA ratio levels. Further experimental studies are now needed to explore the relationship between L-arginine metabolism pathways, endothelial dysfunction and mechanisms of leukocyte telomere shortening.

**Circulating plasma free heme levels correlate with endothelial injury and atherosclerotic lesions extent in patients with stable coronary artery disease**

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Purpose: Spontaneous hemolysis is associated with plasma free heme release in that can increase oxidative stress phenomenon and enhance vascular cell apoptosis, leading to endothelial dysfunction and ultimately atherosclerosis. We investigated if free heme release could be related to endothelial injury and atherosclerotic lesion extent in patients with cardiovascular risk factors (CRF).

Methods: Patients with cardiovascular risk factors who underwent coronary angiography for suspected stable coronary artery disease were eligible for inclusion. Levels of endothelial (CD144+ EMPs), erythrocytes (CD235+ RBCMPs), platelets (CD41+ PMPs) and leukocytes-derived microparticles (CD11+ LMPs) were measured by flow cytometry methods on free platelets plasma samples. Levels of circulating free heme (CFH) were analyzed by absorption spectro-photometry methods.

Conclusion: CAD was angiographically defined as presence of at least 1 stenosis with >50% luminal diameter narrowing. The atherosclerotic lesions extent was evaluated by the Gensini score calculation.

Results: A total of n=97 subjects (63.6±1.1 y 78% male gender/32% diabetes) fulfilled the inclusion criteria. These patients had significantly higher levels of CFH compared to healthy subjects without CRF. We observed higher levels of CFH in diabetic patients compared to non-diabetic subjects (10.21±3.9 vs. 8.2±0.5 AU, p<0.03), whereas no significant influence of other risk factor (hypertension, dyslipidemia, active smoking) was noted. Moreover, CFH levels were correlated with CD144+ EMPs (r=+0.26, p=0.01), suggesting a potential link between hemolysis and endothelial dysfunction.

Significant CAD was diagnosed in n=71 patients in whom the Gensini score fulfilled the inclusion criteria. CFH levels were independently related to atherosclerotic lesion extent in patients with cardiovascular risk factors (CRF).

Conclusion: In circulating free heme levels are associated with endothelial injury in patients with cardiovascular risk factors and atherosclerotic lesions severity in stable CAD subjects. These results suggest that CFH might influence coronary artery disease development.

**Changes in blood flow determine endothelial vaso motor responses: insight into the meaning of flow-mediated constriction and dilation**

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Introduction: Flow-mediated dilation (FMD) is an accepted parameter of endothelial function. To date, it is unclear whether the FMD is a direct measure of vascular reactivity or a surrogate of more complex changes in the conduit arteries caused by the release of endothelial factors. This study aimed to assess changes in blood flow in response to FMD and the role of these changes in determining the magnitude of endothelial vasomotor responses.

Materials & Methods: Healthy volunteers (n=9) underwent FMD testing in the right brachial artery with a cuff placed on the upper arm. Blood flow was measured using laser Doppler velocimetry before and after FMD induction. The degree of FMD was calculated as the percentage change in diameter from baseline, and the peak negative blood flow was calculated as the maximum change in flow from baseline. The relationship between blood flow changes and FMD was assessed using Pearson’s correlation coefficient. The study protocol was approved by the local ethics committee, and all participants provided written informed consent.

Results: A significant negative correlation was observed between the peak negative blood flow and the degree of FMD (r=-0.78, p<0.01). This suggests that changes in blood flow during FMD play a critical role in determining the magnitude of endothelial vasomotor responses.

Conclusion: Changes in blood flow during FMD may be a key determinant of endothelial vasomotor responses, providing additional insight into the mechanisms underlying vasomotor responses in the conduit arteries.
The endothelium: key player in vascular control

Epigenetic regulation of cell adhesion and communication by enhancer of zeste homolog 2 in human endothelial cells

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Objective: Epigenetic modifications such as DNA and histone methylation have long-term effects on gene expression. The histone methyltransferase Enhancer of zeste homolog 2 (Ezh2) mediates trimethylation of lysine 27 in histone 3 (H3K27me3) which acts as a repressive epigenetic mark. Previous studies demonstrated an essential role for Ezh2 in different differentiation processes of human stem cells. In differentiated endothelial cells, however, information about the function of Ezh2 is missing. Therefore, the aim of our present study was to identify Ezh2 target genes in endothelial cells.

Methods and Results: Whole genome mRNA expression arrays identified 964 genes that were regulated by more than twofold after knock down of Ezh2 and ii) association with H3K27me3. Comparative analysis with our mRNA expression data identified 5,585 genes whose promoters were associated with H3K27me3. Notably, we observed a striking overrepresentation of genes involved in canonical and non-canonical Wnt signaling pathways. Epigenetic regulation of several genes by Ezh2 namely cadherin 13, integrin 4, fibroblast growth factor 21, transforming growth factor α, frizzled homolog 7, lymphoid enhancer binding factor 1, and wingless-type MMTV integration site family member 5B was specifically confirmed by PCR analysis of DNA enrichment after chromatin immunoprecipitation using the H3K27me3 antibody.

Conclusion: Combining mRNA expression arrays and ChIP-on-chip analysis after siRNA-mediated silencing of Ezh2, we identified 276 Ezh2 target genes in endothelial cells. Ezh2-dependent repression of genes involved in cell adhesion and communication contributes to epigenetic regulation of angiogenesis.

The effects of AdVEGF-B and AdVEGF-D on angiogenesis and arteriogenesis in a novel porcine model of percutaneous bottleneck stent induced chronic myocardial ischemia


Purpose: Purpose of this study was to develop a novel porcine model of chronic myocardial ischemia and test adenoviral (Ad) VEGF-B and VEGF-D gene therapy in this model.

Methods: Ischemia was induced by restricting coronary blood flow in either proximal left circumflex artery (LCX) or left anterior descending artery (LAD) by installing a bare metal stent covered by a bottleneck shaped tube in domestic pigs. One week after the stent placement, gene transfer was conducted. Collateral vessels wereelectrodegraphed, and myocardial microvascular resistance were assessed using coronary angiography, left ventricle-cineangiography, modified Miles assay, myocardial contrast echo-cardiography (MCE) and index of myocardial resistance (IMR) measurements, respectively.

Results: Notable collateral vessel formation to LCX and LAD area in the respective models was observed. Ejection fraction during stress decreased from 80% to 46% and 45% in the LAD and LCX models, respectively. Infarct scar covered 12% and 20% of the left ventricle and cardiovascular mortality was 20% and 50% in the LCX and LAD models, respectively. AdVEGF-B and AdVEGF-D induced sufficient capillary vessel enlargement, increased myocardial perfusion, and caused myocardial edema six days after gene transfer, but the effects were disappeared four weeks after gene transfer. The gene transfers on blood vessel growth in the ischemic heart will be presented in detail in the congress.

Conclusions: We have established a novel porcine model of chronic myocardial ischemia, which is minimally invasive, repeatable, and which offers multiple clinically relevant endpoints. The LCX model, which is not as severe as the LAD model, can be applied to studies concerning collateral vessel formation while the more severe LAD model can be applied to study treatments for ischemic cardiomyopathy.

Protection against stroke through preservation of vascular integrity by angiopoietin-like 4 (ANGPTL4)

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Aims: Timely recanalization of the occluded artery is the treatment for ischemic stroke, but has limited application. We demonstrated that ANGPTL4 has vasculoprotective effects in myocardial infarction by counteracting VEGF-induced permeability. Given the impact of vascular leakage and edema formation in tissue damage during stroke, preserving vascular integrity represents a pertinent strategy for brain protection. Therefore we hypothesized that ANGPTL4 might exert cerebral protection in stroke.

Methods and Results: In a mouse model of ischemic stroke, with 1 hour ischemia followed by 24 hour reperfusion, injection of ANGPTL4 at ischemia led to a decreased infarct size, as assessed by TTC staining (p < 0.0008) and cerebral MRI (p < 0.003). Brain edema was decreased in the ANGPTL4 treated group (p < 0.002). Using PECAM staining we showed that vascular network was preserved in ANGPTL4-treated mice (vascular density p < 0.0007 and branching points p < 0.002). We then assessed integrity of tight and adherens junctions using VE-cadherin and Claudin 5 immunostainings. We showed a significant increase in VE-cadherin and Claudin 5 areas (normalized to endothelial cell surface) in ANGPTL4-treated mice. Thus ANGPTL4 protects from global vascular damage, but also specifically protects from ischemia-induced junctions disruption. ANGPTL4 protective effect on junctions was further assessed in vitro using microvascular endothelial cells (HDMC) treated with VEGF/ANGPTL4 and stained with VE-Cadherin antibody. The straight and tight VE-Cadherin junctions were observed by immunofluorescence staining in treated cells. ANGPTL4 was also deposited by ANGPTL4 co-treatment: thus ANGPTL4 counteracts the effect of VEGF on junctions breakdown. Mechanistically, using VEGFR2 co-immunoprecipitation experiments, we showed a significantly decreased recruitment of phospho-ERK in angiopoietin-like 4 silenced in infarcted hemispheres of ANGPTL4-treated mice. Thus ANGPTL4 counteracts VEGFR2-induced Src signaling and protects VE-Cadherin junctions from Src-dependent disassembly. Moreover, ANGPTL4 protected neuronal loss after stroke, as assessed by the increased number of NeuN-positive cells (neurons) in treated mice (p < 0.001). Finally, mouse behavior was also significantly improved in treated mice (p < 0.01).

Conclusion: ANGPTL4 treatment counteracts the loss of vascular integrity in a mouse model of ischemic stroke, by restricting Src kinase recruitment downstream VEGFR2. Consequently, ANGPTL4 reduces edema, infarct size, neuronal loss and finally improves mouse behavior. These results show that ANGPTL4 is a relevant target for vascular protection, thus conferring cerebral protection during stroke.
DOPING IN HYPERTENSION

Antihypertensive and laxative effects by inhibition of NHE3-mediated sodium absorption in the gut

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Purpose: High intestinal sodium absorption is one important mechanism of hypertension and constipation. The sodium-proton-exchanger (NHE3) is an important mediator of sodium absorption in the gut. Inulin stimulates the NHE3-exchanger. We used senescent lean hypertensive rats (SHR-lean) and a hyperinsulinenic rat strain (crosstraining lepithin receptor deficient hypertensive rats, SHR-ob), and treated them orally with a non-absorbable specific NHE3-inhibitor.

Methods: Twenty-six-week-old 78 weeks old senescent SHR-lean were randomized in 2 groups (n=14 /group): placebo (PLAC) and NHE3-inhibitor SAR (1mg/kg/d in chow), treated for 14 weeks. Eight weeks old SHR-ob were randomized in two groups: PLAC (n=7) and SAR (n=8), treated for 6 weeks. Water and sodium content in the feces were measured via flame photometer, and systolic blood pressure via tail cuff. Gene expression of NHE3 in the gut and plasma renin activity and aldosterone were studied.

Results: SAR treatment resulted in a dose dependent increase of feces sodium and water content in normotensive Sprague Dawley rats. In senescent SHR-lean, inhibition of intestinal NHE3 increased sodium (33.5±3.4 mmol/L vs. 20.2±2.2 mmol/L in PLAC, p<0.01) and water-content (58% vs. 42% in PLAC, p<0.01) in the feces and reduced systolic blood pressure from 222±7 mmHg to 184±2.2 mmHg (p<0.01). Aldosterone plasma concentration or renin- and ACE plasma activity was not modified in SAR. Gene expression of NHE3 was up-regulated in the ileum and colon but not in the jejunum of SAR treated rats. Treatment did not cause hypokalemia or impairment of kidney function. In hyperinsulinenic SHR-ob, SAR treatment resulted in a more pronounced reduction of systolic blood pressure via tail cuff, gene expression of NHE3 in the gut and plasma renin activity and aldosterone were studied.

Conclusion: Reduction of intestinal sodium absorption by selective NHE3-inhibition in the gut reduces high blood pressure and increases feces water eXcretion. Intestinal NHE3-blockade could be a new treatment strategy for elderly patients suffering from high blood pressure and constipation.

DOPING IN HYPERTENSION

Predictive factors of adherence in uncontrolled hypertensive patients in France: results of the observational real life survey HBP-ADHERENCE

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Purpose: Despite antihypertensive treatment, the proportion of uncontrolled hypertensive patients remains high and the non adherence to treatment is a major issue. One of the aims of this study was to determine the predictive factors of antihypertensive medication adherence in uncontrolled hypertensive patients treated by general practitioners in France.

Methods: HBP-ADHERENCE observational study was conducted in France from March to September 2011. A population of 3560 hypertensive patients was included by 1049 French general practitioners. Hypertensive patients whose blood pressure was not controlled with at least two antihypertensive drugs were included. Adherence was determined according to a validated questionnaire. Comparative analyses were performed on two subgroups of patients: “adherent or minor non-adherent” versus “major non-adherent”.

Results: Mean systolic and diastolic blood pressure (SPP/DDBP) were 157.1±9.1/88±11.1 mmHg. The majority of patients (60%) were over 60 years old and nearly 40% were women. Patients were classified as “major non-adherent” in 28% of cases. Age and sex were unrelated predictive factors of adherence. Major non-adherent patients had a significantly higher number of drugs prescribed (5.4±2.6 versus 4.6±2.4 p<0.0001), larger number of daily medication intakes (3.6±2.9 versus 3.0±2.3, p<0.0001) and less knowledge about their treatments (73.7% versus 88% or <0.0001) than adherent or minor non-adherent patients. In multivariate analysis, independent factors strongly associated with risk of major non-adherence were (OR, 95% CI): fear of adverse effects (2.7, 1.23-4.3), presence of at least one symptom (1.93, 1.52-2.45), sedentarity (1.5, 1.21 1.87), excess alcohol intake (1.65, 1.24-2.20). The regular practice of home blood pressure measurement was the only factor inversely correlated to the risk of major non-adherence (1.9, 0.48-0.86).

Conclusion: In this real life study, we identified several modifiable factors to predict risk of non-adherence in uncontrolled hypertensive patients. Therapeutic education focusing on the expected benefits of antihypertensive drugs, their mechanisms of action and their adverse effects, as well as a wider use of long acting fixed-dose combinations would improve long-term effective care of hypertensive patients.

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Purpose: The risk of atrial fibrillation (AF) associated with left atrial (LA) remodeling is increasing in elderly hypertensive patients. Intensive BP lowering therapy would have a beneficial effect on LA structure and function and decreases the incidence of first AF in elderly HTN.

Methods: We studied 240 subjects ≥65 years, who were divided into 4 groups by mean office BP for past 2 years; normal (n=73, 75.5±5.9 yrs, 37 men), intensive BP (systolic BP>130 or diastolic BP>80 mmHg, n=74, 74.4±4.3 yrs, 43 men), poor controlled HTN (systolic BP>140 or diastolic BP>90, n=114, 73.4±6.5 yrs, 24 men) and good controlled HTN (130/80<BP<140/90, n=75, 72.4±5.3 yrs, 21 men). LA volume, emptying function (EF), strain rate (SR) and strain were measured by speckle tracking echocardiography at baseline and after 2 years.

Results: There was no difference in LV ejection fraction among 4 groups. LA volume, EF, SR and strain in intensive controlled HTN were more preserved and comparable to normal including diastolic function at baseline and after 2 years. The incidence of first AF was significantly lower in intensive controlled HTN for 2 years.

Table 1. parameters at baseline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Intensive HTN</th>
<th>Good HTN</th>
<th>Poor HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP, mmHg</td>
<td>126±8/75</td>
<td>128±8/75±14</td>
<td>136±26/5±37</td>
<td>144±29/2±11</td>
</tr>
<tr>
<td>Diastolic fraction (E/e')</td>
<td>10.0±1.4</td>
<td>8.3±1.4</td>
<td>8.8±1.6</td>
<td>10.4±1.8</td>
</tr>
<tr>
<td>LA dimension, mm</td>
<td>39±5</td>
<td>40±5</td>
<td>41±6</td>
<td>45±6*</td>
</tr>
<tr>
<td>Max. LA volume/ml²</td>
<td>41.1±11</td>
<td>44±11</td>
<td>53±14</td>
<td>66±18*</td>
</tr>
<tr>
<td>Min. LA volume/ml²</td>
<td>23±8</td>
<td>25±8</td>
<td>31±10*</td>
<td>44±14*</td>
</tr>
<tr>
<td>LA total EF, %</td>
<td>45.7±6</td>
<td>46±6</td>
<td>41±6*</td>
<td>33±5*</td>
</tr>
<tr>
<td>LA passive EF, %</td>
<td>22.8±7</td>
<td>20±7</td>
<td>17±6*</td>
<td>14±6*</td>
</tr>
<tr>
<td>LA active EF, %</td>
<td>30±8</td>
<td>30±7</td>
<td>28±7*</td>
<td>22±6*</td>
</tr>
<tr>
<td>Peak strain</td>
<td>24.0±6.3</td>
<td>24.0±5.6</td>
<td>22.1±6.4*</td>
<td>18.5±5.0*</td>
</tr>
<tr>
<td>SR-systole, s⁻¹</td>
<td>1.2±0.3</td>
<td>1.1±0.3</td>
<td>1.1±0.3*</td>
<td>1.0±0.4*</td>
</tr>
<tr>
<td>SR-early diastole, s⁻¹</td>
<td>-1.0±3</td>
<td>-1±0.3</td>
<td>-0.8±0.3*</td>
<td>-0.8±0.3*</td>
</tr>
<tr>
<td>SR-atrial contraction, s⁻¹</td>
<td>-1.4±0.4</td>
<td>-1±0.4</td>
<td>-1±0.5</td>
<td>-1±0.4*</td>
</tr>
</tbody>
</table>

* p<0.05 vs. normal, ** p<0.05 vs. intensive HTN, *** p<0.05 vs. good HTN.

Conclusion: LA structure and function were preserved in intensive controlled HTN associated with preserved diastolic function and comparable to normal. Intensive BP lowering therapy had a beneficial effect on LA structure and function and would be recommended to prevent LA remodeling and first AF even in elderly HTN.

3971 Pilot analysis of the effect of the SGLT2 inhibitor dapagliflozin on blood pressure in patients with type 2 diabetes mellitus: a pooled analysis of placebo controlled trials

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Purpose: Obesity and hypertension are common comorbidities in patients with type 2 diabetes mellitus (T2DM). The glomerular mechanism of dapagliflozin (DAPA), a selective sodium-glucose co-transporter 2 (SGLT2) inhibitor, is associated with improvements in hyperglycemia and weight loss. A modest reduction in blood pressure has been observed in development studies, potentially as a result of osmotic diuresis, and to some extent weight loss. The aim of this post-hoc analysis is to further characterise the BP effects of DAPA in patients with T2DM.

Methods: Safety data were pooled from 12 placebo (PBO) controlled phase IIb and III studies. Patients with T2DM (N=4545) received DAPA (2.5, 5 or 10 mg) or PBO daily for 12-24 weeks (wks). Background antihypertensive therapy was not controlled.

Results: Greater mean reductions from baseline (BL) BP levels were observed at each time point measured across the DAPA groups compared with PBO for systolic BP (SBP) and diastolic BP (DBP) (Figure). At 24 wks there was a mean change from BL in heart rate of ~ 0.4 to ~ 1.1 beats per min (BPM) across the DAPA groups and an increase of 0.5 BPM with PBO. AEs of hypertension/dehydration/hypovolaemia were slightly more frequent with DAPA (0.6-1.2%) versus PBO (0.4%) none of which were serious or resulted in discontinuation. The proportion of patients with measured orthostatic hypotension at any visit during treatment was 10.0%-12.5% with DAPA and 9.2% with PBO.

Conclusions: DAPA is associated with modest mean reductions in SBP and DBP in patients with T2DM, with no increased risk of orthostatic hypotension and without any clinically relevant changes in heart rate. These post-hoc observations are intriguing and further studies will be needed to evaluate potential clinical benefit in hypertensive patients.

SPORT CARDIOLOGY – PRE-PARTICIPATION SCREENING: CONSEQUENCES AND PITFALLS

3977 Exercise related out-of-hospital cardiac arrest: incidence, prognosis, and prevention of sudden death

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Purpose: Although regular physical activity has beneficial cardiovascular effects, exercise can trigger an acute cardiac event. We aimed to determine the incidence of exercise related out-of-hospital cardiac arrest (OHCA) and whether exercise-related OHCA are associated with higher survival rates than non-exercise-related OHCA in persons aged ≥35 years.

Methods: We analyzed all OHCA cases prospectively collected from January 2006 to January 2009. The relation between exercise during or within 1 hour before OHCA and outcome was analyzed using multivariable logistic regression, adjusting for age, gender, public location, bystander witness, bystander cardiopulmonary resuscitation (CPR), automated external defibrillator (AED) use and shockable initial rhythm. Incidence is shown per 100,000 person-years.

Results: Of 2517 OHCA cases, 145 (5.8%) were exercise-related, of whom 7 were ≤35 years. Most patients were men (93.1% and 85.7%, respectively). The incidence of exercise-related OHCA was 2.0 in all ages and 0.2 in those ≤35 years. Survival after exercise-related OHCA was distinctly better than after non-exercise related OHCA (44.8% vs. 15.4%) (unadjusted odds ratio 4.13; 95%CI 2.93-5.82; P<0.001), even after adjustment for other prognostic factors (odds ratio 1.57; 95%CI 1.04-2.37;P<0.03). Patients ≤35 years did not benefit from exercise: survival was 33.3% versus 34.5%, respectively (adjusted odds ratio 0.47; 95%CI 0.04-5.37;P=0.54). In hospital treatment did not differ between groups.

Conclusion: Exercise-related OHCA has a low incidence, particularly in the young and predominantly affects men. Cardiac arrests occurring during or shortly after exercise carry a markedly better prognosis than cardiac arrests that are not exercise-related in persons older than 35 years.

3978 Costs of cardiovascular screening with ECG in young athletes in Switzerland

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Purpose: Adding ECG to cardiovascular screening in young athletes remains controversial. One of the reasons refers to costs of the screening program and the subsequent cardiac examinations generated mainly by the false positive ECG. The aim of this study was to assess the total costs of a program of cardiovascular screening with ECG in young athletes in Switzerland using basically the 2010 recommendations of the European Society of Cardiology (ESC) for interpretation of ECG in athletes.

Methods: In this observational prospective study, competitive athletes from 14 to 35 years were examined following the 2005 ESC proposal. ECG was interpreted based on the ESC 2010 recommendations (adapted). Further examinations were proposed in cases of positive findings. The costs of the screening and of all subsequent examinations was calculated for each athlete according to the Swiss medical rates. We present the interim results of this study.

Results: From 02/2011 to 02/2012, 920 athletes were examined. Mean age was 19.9±6.5 years, 75% were men. Football (35%) and ice hockey (12%) were the sports most often represented. Mean weekly training’s hours were 7.9±4.8 for a
Concentric remodelling of the right ventricle in African football players

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Purpose: We have previously shown that male Caucasian athletes have a larger increase of both LV and RV size than Africans. African athletes, however, had similar LV mass but markedly more concentric remodelled LV than the Caucasian athletes. Thus, the aim of this study was to investigate if a similar remodelling between black and white athletes is present in the RV.

Method: As a part of the mandatory heart screening, 555 male elite football players (509 Caucasians and 46 Africans) and 46 Caucasian controls were examined. RV and diastolic wall thickness (RVDWT) were measured from a four chamber view. Measurements of RV free wall thickness (RVTW) in end diastole were performed by a subcostal view. Relative wall thickness on the right side (RVRWT) was calculated by dividing RVTW with RVDWT multiplied with two. Body mass index (BMI) and body surface area (BSA) were calculated, and all echo measurements were performed blinded.

Results: Compared to Caucasian athletes, Africans had a significantly higher BMI but similar BSA and a lower body mass index (BMI) (p<0.005). The prevalence of Brugada ECG-pattern was higher in Africans (p<0.005 vs. Caucasian athletes). The only diagnostic was a Brugada ECG-pattern recorded in 1 (1.5%) of the athletes and were also more common in endurance athletes (8.2% vs. 6.1%, p<0.005); right ventricular hypertrophy (RVTW+RVDWT ≥15mm) in 8 (1.7%); abnormal T-wave inversions in 7 (1.5%); RBBB in 2 (0.4%); left anterior fascicular block in 3 (0.6%); ST-segment depression in 1 (0.6%) and left atrial enlargement in 3 (0.6%). There were no cases of pre-excitation, long or short QTc, pathological Q waves or Brugada-like ECGs. No athlete with Group 2 ECG changes had features of underlying structural heart disease on further evaluation with echocardiography.

Conclusion: Preliminary data of this study indicate that cardiovascular screening in young athletes using strict criteria for interpreting ECG is feasible in Switzerland at low cost. These data should aid the implementation of this policy in our country.

Abstract 3980 – Table 1. Risk ratio for SCD (95% CI)

<table>
<thead>
<tr>
<th>Cardiorespiratory fitness:</th>
<th>High CRF (MET ≥over 8)</th>
<th>Low CRF (MET &lt;below 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular risk factor:</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Smoking cigarette (daily)</td>
<td>2.24 (1.91-2.64)</td>
<td>2.73 (2.19-3.40)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>1.99 (1.60-2.50)</td>
<td>1.57 (1.08-2.29)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>3.67 (3.32-3.69)</td>
<td>1.73 (1.20-2.47)</td>
</tr>
<tr>
<td>History of previous coronary heart disease</td>
<td>1.12 (1.00-1.26)</td>
<td>1.02 (0.89-1.17)</td>
</tr>
<tr>
<td>Resting systolic blood pressure</td>
<td>1.14 (1.04-1.26)</td>
<td>1.14 (1.04-1.26)</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>1.14 (0.86-1.54)</td>
<td>1.14 (0.86-1.54)</td>
</tr>
<tr>
<td>Myocardial ischemia during exercise stress test</td>
<td>1.91 (0.97-3.78)</td>
<td>2.91 (1.18-7.42)</td>
</tr>
</tbody>
</table>

1 type 2 diabetes: 1.99 = 1.57 = 2.98
1 smoking history: 3.67 = 1.73 = 4.60
1 history of coronary heart disease: 1.12 = 1.02 = 2.51
1 resting systolic blood pressure: 1.14
1 body mass index: 1.14
1 myocardial ischemia during exercise stress test: 1.91 = 2.91 = 4.83

Abstract 3981 – Prevalence of Brugada ECG-pattern recorded with V1 in the second intercostal space in young athletes

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Purpose: The prevalence of Brugada ECG-pattern is about 1/2000, mostly of type 2 and 3. In some circumstances, type 2 and 3 can convert in type 1 pattern, the only diagnostic. Recording ECG with V1 and V2 in the second intercostal space (3IC) can raise the sensibility of recording a Brugada ECG-pattern and the prognostic value of this tracing seems to be similar as the standard ECG. The aim of this study was to analyse the prevalence of Brugada ECG-pattern in a cohort of young athletes registering ECG also in the 3IC.

Methods: ECG was analysed as part of a prospective ongoing study about the impact of cardiovascular screening with ECG in young (14-35 years) competitive athletes. Besides a standard tracing, ECG was recorded with V1 and V2 in the 3IC. The prevalence of Brugada ECG-pattern type 1, 2 and 3 was analysed. Particular care was taken to distinguish an incomplete right bundle branch block pattern from a Brugada pattern.

Results: Of 556 athletes (72% males, aged 19.9±6.3 years) was analysed. In standard ECG tracing there was 3 Brugada type 2/3 pattern (0.5%). In ECG recorded in the 3IC there were 21 (3.8%) Brugada type 2/3, no type 1 was recorded. Of these 21 athletes, 20 were males (prevalence in males 4.8%), 1 female (0.4%). Of 20 males, 15 had a Brugada type 3 pattern (3.7% of males), 5 had a type 2 pattern (1.2%). The female had a type 3 pattern. No athlete took medications known to elicit Brugada ECG-pattern.

Conclusions: Brugada ECG-pattern type 2 and 3 in the 3IC is relatively common in young athletes, particularly males. This should be taken into account before drawing conclusion about risk stratification in this young healthy population.
Alteration of gene expression profiling of the murine intestine suffering from heart failure

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Background & Purpose: Association between hearts and other organs such as cardiovascular interaction has received a lot of attention in recent years. The gastrointestinal tract is an organ that produces a variety of hormones including ghrelin and glucagon-like peptide 1 which have been recently reported to improve cardiac functions. Although heart failure is thought to induce gastrointestinal dysfunction due to circulatory disturbances, little is known about gastrointestinal functions in heart failure. To clarify the function of intestines in heart failure, we analyzed global gene expression levels of intestines in mice with heart failure.

Methods: We constricted transverse aorta of eight-week-old male C57/BL6J mice to create the condition of heart failure. Sham operation was also performed as the control. We collected intestines from these mice 4 weeks after aortic constriction. RNAs extracted from these samples were hybridized to GeneChip Mouse Genome 430 2.0 array. We constructed global gene expression profiles of intestines in mice with heart failure and compared them with the control.

Results: Low CRF combined with all measured risk factors was associated with a higher risk of SCD (Table). The highest risk factor combination was low CRF with a smoking history of more than 10 packyears, the risk ratio for SCD was 4.6 (95% confidence interval 2.86-7.43).

Conclusions: By combining these previously known risk factors with CRF, more accurate SCD risk assessment can be made. This should be taken into account when considering treatment for patients in risk of SCD.

Obesity paradox in patients with acute heart failure: application of propensity score methodology in an acute heart failure database AHEAD

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Introduction: Obesity has repeatedly been identified as an independent risk factor for progress of heart failure. This may be given by several factors: presence of metabolic syndrome, increased diastolic blood pressure, or higher insulin resistance. In contrast to stated risk factors, recent studies reported overweight and obesity to be associated with a lower risk of death, even after multivariate ad- justment. This phenomenon is called “obesity paradox” (Curts et al. Circulation 2002). Aim of this study is comparison of mortality of acute heart failure (AHF) patients with normal weight (BMI <25), obesity (BMI ≥30) and normal weight (BMI <25) by means of the modern “propensity score” statistical method.

Methods: Of the 5,343 patients from the AHEAD database (4,153 AHEAD Main + 1,190 AHEAD Network), 4,523 patients hospitalised with AHF and with available BMI data were assessed. The propensity score method is based on selection of patients, who are comparable in their selected characteristics and parameters (difference <10%) and differ in BMI only – so called data set balancing. Based on a Hosmer-Lemeshow test, a model with 6 variables was chosen (sex, age, exercise stress test result, diastolic blood pressure, diabetes mellitus, and smoking).

Results: Normal weight was recorded in 27% of patients, 39.5% of patients had overweight and 33.5% of patients had obesity. In-hospital mortality was 10.3% and according to BMI 12.8%, 10.3%, and 8.3% (p < 0.05 for normal vs. overweight, p < 0.005 for normal vs. obesity). In the balanced cohort, the overall mortality was 10.6%, in overweight with overweight 12.2%, with obesity 7.6% (p = 0.051 for normal weight vs. obesity).

Conclusions: The propensity score method decreased the in-hospital mortality difference between patients with overweight and obesity; nevertheless, the obesity paradox was confirmed, since the patients with obesity had lower in-hospital mortality in comparison to patients with normal weight.
Thirty-two of the patients (4.8%) died in hospital. Patients dying in hospital were older, had lower admission systolic blood pressure, worse admission renal function and higher BNP. Patients with in-hospital death also had significantly lower total cholesterol levels (12.2% (91-145) mg/dl vs 150% (126-186) in those discharged alive; lower albumin: 32.0 (4.0) vs 35.4 (4.8) mg/dl; and lower pre-albumin: 13.2 (5.2) vs 18.2 (7.1) mg/dl. Higher pre-albumin predicted in-hospital survival with a HR of 0.96 (95% CI 0.92-0.99; P = 0.001). Association with outcome was independent of other variables also associated with outcome in an univariate approach (systolic blood pressure, age, blood urea, BNP, total cholesterol and albumin). An admission pre-albumin <18 mg/dl predicted in-hospital death with a HR of 5.64 (95% CI: 1.20-26.51; P = 0.03).

Conclusions: Malnutrition as assessed by lower pre-albumin predicted in-hospital death in patients admitted with acute HF. HF patients with admission pre-albumin <18 mg/dl have more than five-fold higher risk of in-hospital death than those with higher admission pre-albumin.

Are total cholesterol levels important for hospital and long-term prognosis of patients with acute heart failure?


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The purpose of this study was to evaluate if there is an association of total cholesterol levels with hospital and long-term mortality of patients admitted for acute heart failure.The AHEAD MAIN registry is a database conducted in 7 university hospitals, all with 24 hour cath lab service, in 4 cities in the Czech Republic. The database included 4,153 patients hospitalised for acute heart failure in the period 2006 – 2009. Median age was 73.8 years, 42.4% females, more than 70 years 60%, ejection fraction below 30% 37.9%. The data were collected prospectively using a database accessible via the internet website and were evaluated continuously (including in-hospital mortality). The long-term mortality was followed by the national centralised database of the Ministry of Health of the Czech Republic and recent data from the year 2010. The log rank test was used for the analysis of long term survival. The independent influence of total cholesterol level on mortality and survival was assessed using multivariate logistic regression and Cox proportional hazards model respectively. Of 4,153 patients, 526 (12.7%) patients died during hospitalisation. The median length of hospitalisation was 7.1 days (5.5 days for those patients who died and 9.7 days for those who were discharged home). 2,384 patients had complete records for total cholesterol levels – 946 females and 1,437 males were included in this analysis. The median total cholesterol level was 4.40 mmol/l. For the calculation of long-term mortality, the cohort was divided into three groups: total cholesterol levels below 4.50 mmol/l, 4.50-5.49 mmol/l and above 5.50 mmol/l. Total cholesterol levels were important for hospital mortality for both genders (p<0.001, respectively). In the long-term follow up (78 months) patients with total cholesterol level below 4.5 mmol/l had the worst prognosis (p<0.001). The independent influence of total cholesterol on hospital and long term mortality was confirmed in the multivariate analysis when total cholesterol levels below 4.5 mmol/l was combined with other predictors revealed in the univariate analysis. Total cholesterol levels are important for in-hospital mortality and long term survival of patients admitted for acute heart failure.

The prognostic importance of evaluating nutritional status in patients with chronic heart failure


Yamagata University School of Medicine, Yamagata, Japan

Background: Low nutritional status is one of the unfavorable prognostic factors in some clinical setting. However, the association between nutritional indicators and outcomes in patients with chronic heart failure (CHF) is unclear. The purpose of this study was to clarify the impact of nutritional status on cardiac prognosis in patients with CHF.

Methods and Results: We evaluated controlling nutritional status score (CONUT), prognostic nutritional index (PIN), and geriatric nutritional risk index (GNRI) in consecutive 388 patients with CHF (mean 69.6±12.3 years) admitted to our hospital. CONUT consists of 2 biochemical parameters (serum albumin and total cholesterol level) and 1 immune indicator (total lymphocyte count). PIN consists of 1 biochemical parameter (serum albumin) and 1 immune indicator (total lymphocyte count). GNRI consists of 1 biochemical parameter (serum albumin) and ratio of body weight to ideal body weight. Patients were prospectively followed with the endpoints being cardiovascular death or rehospitalization. There were 60 endpoints including 3 deaths and 97 rehospitalizations during 2 year follow-up of 37.7 months. Patients with cardiac events showed higher age, more severe New York Heart Association (NYHA) functional class, lower prevalence of valvular heart disease, lower body mass index, lower serum triglyceride level, lower serum high-density lipoprotein cholesterol level and higher serum brain natriuretic peptide (BNP) compared with those without cardiac events. Furthermore, patients with cardiac events showed higher CONUT score (6.3-8 vs. 2.1-3, P<0.001), lower PIN score (15.2, 26.4-35.7 vs. 38.6, 35.2-40.0, P<0.001), lower GNRI score (84.9, 76.8-92.3 vs. 95.3, 89.8-101.3, P<0.001) compared with those without cardiac events. In Cox proportional hazards analysis, CONUT (hazard ratio 40.9, 95% CI 8.4-154.8), PIN (hazard ratio 6.4, 95% CI 5.4-25.1), and GNRI (hazard ratio 11.6, 95% CI 3.7-10.0) were independently associated with cardiac events after adjustment of age, gender, NYHA functional class and serum levels of BNP. Among these nutritional indexes, CONUT had the highest hazard ratio. Kaplan-Meier analysis revealed a significantly higher cardiac event rate in patients with low nutritional indexes than in those without it.

Conclusion: Low nutritional status was associated with unfavorable outcomes in patients with CHF. It was suggested that evaluating nutritional status may provide a pivotal prognostic information in patients with CHF.

Impact of stent fracture on long-term clinical outcomes after sirolimus-eluting stent implantation


Purpose: Stent fracture (SF) is associated with adverse events after drug-eluting stent implantation. However, few data exist on its long-term clinical impact in real world practice. Therefore, we evaluated the impact of SF on long-term clinical outcomes after sirolimus-eluting stent (SES) implantation.

Methods: Consecutive 2494 patients who had undergone the first SES implantation from November 2002 to December 2007 and received follow-up angiography within 12 months were analyzed. Angiographic stent fracture was defined as apparent separation of stent segments. Some tips, including focus image, inverse image, and image without catheter or contrast media were used to obtain the exact prevalence of SF. The incidence of clinical outcomes, including all-cause death, myocardial infarction (MI), stent thrombosis (ST), target lesion revascularization (TLR), and major adverse cardiac events (MACE, defined as all-cause death, MI, and TLR) was compared between SF and non-SF groups.

Results: Because 446 of the 2494 patients were excluded because of no angiographic follow-up within 12 months, the entire study population consisted of 2048 patients (3218 lesions) and was classified into two groups: 243 patients with SF and 1805 without SF. The median duration of follow-up was 4.9 years. At 4-year follow-up, the rates of TLR, MI, and MACE were significantly higher in the SF group than in the non-SF group (38.3% vs. 17.2%, p<0.001; 2.1% vs. 0.6%, p<0.001; 42.4% vs. 25.0%, p<0.001, respectively), whereas the rate of all-cause death was similar between groups (6.6% vs. 10.0%, p=0.20). The figure shows the cumulative incidence of definite or probable very late ST.

Conclusion: Our study suggests that SF is associated with higher rates of late adverse events except all-cause death after SES implantation.

Stent fracture and restenosis at stent fracture site after sirolimus-eluting stent and everolimus-eluting stent implantations: impact of stented vessel

K. Miyake, K. Kadota, T. Tada, H. Tanaka, Y. Fuku, N. Oka, H. Kadota, H. Yamamoto, T. Goto, K. Mitsu, Kurashiki Central Hospital, Cardiology Department, Kurashiki, Japan

Background: Stent fracture (SF) and its related restenosis are concerns of sirolimus-eluting stent (SES) implantation. However, everolimus-eluting stent (EES) may have a potential for the reduced prevalence of SF. We assessed SF and restenosis at SF site in terms of stented vessel after SES and EES implantations.

Methods: A total of 8817 stent-implanted lesions (SES 6000, EES 2217) from...
November 2002 to March 2011 were analyzed at midterm follow-up. Stented vessels were classified into two groups: right coronary artery (RCA) and non-RCA. **Results:** The SF rate of EES was significantly lower than that of SES in both RCA and non-RCA. The restenosis rate at SF site of EES was significantly lower in the non-RCA, but it was similar in the RCA.

**Conclusion:** Although EES reduced the prevalence of SF, the effect of EES on SF related restenosis depends on the vessel site.

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**Decreased interleukin-33 serum levels after coronary stent implantation are protective against in-stent restenosis**

S. Demyanets1, R. Jaras2, K. Katasou2, S. Farhan3, A. Wornert4, G. Maurer1, W.S. Spedel1, J. Wojt1, K. Huber1, M. Medical University of Vienna, Vienna, Austria; 2Wilhelminen Hospital, Vienna, Austria

**Background:** Restenosis after stent deployment is an overreaction of the wound healing response after vascular injury and is characterized by the sequence of inflammation, granulation, and extracellular matrix remodeling. Interleukin-33 (IL-33) is a recently described member of the IL-1 family of cytokines and is a ligand for the ST2 receptor. Circulating IL-33 was increased in patients with inflammatory disorders such as rheumatoid arthritis, systemic sclerosis, inflammatory bowel disease and liver failure. However, the predictive value of IL-33 for the development of in-stent restenosis (ISR) is not known.

**Methods:** We included 387 consecutive patients undergoing percutaneous coronary intervention (PCI) of whom 193 had stable angina, 93 non-ST elevation myocardial infarction (NSTEMI), and 101 ST-elevation MI (STEMI), respectively. Blood was taken directly before and 24 hours after stent implantation. Plasma levels of IL-33 were measured by a specific ELISA. The presence of ISR was initially evaluated by clinical means. When presence of myocardial ischemia was suspected, coronary angiography was performed to confirm the suspected diagnosis of ISR.

**Results:** Bare metal stents (BMS) were used in 283 and drug eluting stents (DES) were used in 104 patients. Clinical ISR was present in total in 34 patients (8.8%). IL-33 was detectable in 185 patients and was below detection limit in 202 patients. In patients with decreased IL-33 (n=195), unchanged or non-detectable levels (n=210) or increased levels of IL-33 after PCI (n=82), ISR-rate was 2.1%, 4.5% and 21.7%, respectively. This association was independent from clinical presentation and risk factors as well as numbers and type of ISR.

**Conclusion:** In patients with both stable and unstable coronary artery disease, a decrease of IL-33 serum levels after stent implantation is associated with a lower rate of in-stent restenosis.

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**Efficiency of statin treatment on EPC recruitment depends on baseline EPC titers, and does not improve angiographic outcome in coronary artery disease patients treated with the Genous stent**

W. Den Dekker1, J.H. Houtgraaf1, S.M. Rowland2, S.P.M. De Boer1, R.J. De Winter2, P. Den Heijer3, F. Zijlstra1, W.P. Serruys1, C. Cheng1, H.J. Dukker1,1 Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, Netherlands; 2Orbis Necht, Fort lauderdale, United States of America; 3Academic Medical Center, Amsterdam, Netherlands; 4Amphia Hospital, Department of Cardiology, Breda, Netherlands

**Objective:** To assess the effect of high dose Atorvastatin treatment on endothelial progenitor cell (EPC) recruitment and angiographic and clinical outcome in coronary artery disease (CAD) patients treated with the GenousTM EPC capturing stent.

**Methods:** The HEALING IIB study was a multi-center, open-label, prospective trial that enrolled 100 patients. Patients were started on 80mg Atorvastatin qd, at least two weeks before index procedure and continued for at least 4 weeks after the index procedure.

**Results:** 87 Patients were included in this analysis. EPC levels significantly increased as early as 2 weeks after start of statin. Remarkably, among this group, 31 patients proved to be non-responder to Atorvastatin treatment (i.e. no increase in EPC levels) while 56 patients were responders (i.e. rise in EPC count between week -2 and 0). Compared to responders, non-had a significantly higher baseline EPC count (76.10 vs 41.5, p<0.01) with a lower LLL at 6 and 18 month FU (0.81±0.07 vs. 0.88±0.08 vs. 0.86±0.08 vs. 0.82±0.08 p<0.01 respectively, see figure). Furthermore, baseline EPC count inversely correlated with LLL at 6 month follow-up (FU) (R=−0.42, p<0.001).

**Conclusion:** Patients with higher EPC count at baseline showed no increase in EPC recruitment in response to statin treatment but had favorable LLL at 6 and 18 month FU, whereas patients with lower EPC count were responsive to statin therapy but EPCs might be less functional as they had higher LLL at 6 and 18 month FU. These data imply that, although statin treatment can enhance EPC titer in these patients with low baseline levels, there is no indication for a possible beneficial clinical effect with EPC capture stents.

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**Drug-eluting stents for the treatment of chronic total occlusion: a comparison with sirolimus, paclitaxel, zotarolimus, biolimusA9, EPC capture and everolimus-eluting stent: multcenter registry**

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**Aim:** The aim of this study is to compare the safety and efficacy of Sirolimus (SES), Paclitaxel (PES), Zotarolimus (ZES-R/ Endeavor Resolute), BiolimusA9 (BES), EPC capture (ECS) and Everolimus-eluting stent (EES) on the outcome of patients with chronic total occlusion (CTO).

**Methods:** A prospective analysis of 1576 patients with 1738 CTOs (396 SES, 526 PES, 219 ZES-R, 209 BES, 148 ECS, 240 EES) in six high volume Asian centers after successful recanalization of CTO was performed. The study endpoints were 30 days and 12 months major adverse cardiac events (MACE), 12 months angiographic restenosis and target lesion revascularization (TLR). **Results:** See table for clinical results.

<table>
<thead>
<tr>
<th>SES</th>
<th>PES</th>
<th>ZES-R</th>
<th>BES</th>
<th>ECS</th>
<th>EES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MACE (%)</strong></td>
<td>7.1</td>
<td>8.7</td>
<td>7.5</td>
<td>5.9</td>
<td>19.5*</td>
</tr>
<tr>
<td><strong>Restenosis rate (%)</strong></td>
<td>7.1</td>
<td>9.4</td>
<td>7.0</td>
<td>6.4</td>
<td>21.1*</td>
</tr>
<tr>
<td><strong>12 months MLD (mean: mm)</strong></td>
<td>2.50</td>
<td>2.30</td>
<td>2.49</td>
<td>2.66</td>
<td>2.10</td>
</tr>
<tr>
<td><strong>Proximal RD (mean: mm)</strong></td>
<td>2.86</td>
<td>2.80</td>
<td>2.85</td>
<td>2.84</td>
<td>2.92</td>
</tr>
<tr>
<td><strong>Procedural success (%)</strong></td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><strong>LAD/LCX/RCA (%)</strong></td>
<td>54/23/23</td>
<td>52/24/24</td>
<td>50/18/32</td>
<td>46/21/33</td>
<td>52/18/30</td>
</tr>
<tr>
<td><strong>Number of patients/lesions</strong></td>
<td>365/396</td>
<td>482/526</td>
<td>199/219</td>
<td>188/209</td>
<td>123/148</td>
</tr>
</tbody>
</table>

**Conclusion:** Patients with higher EPC count at baseline showed no increase in EPC recruitment in response to statin treatment but had favorable LLL at 6 and 18 month FU, whereas patients with lower EPC count were responsive to statin therapy but EPCs might be less functional as they had higher LLL at 6 and 18 month FU. These data imply that, although statin treatment can enhance EPC titer in these patients with low baseline levels, there is no indication for a possible beneficial clinical effect with EPC capture stents.

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**Differences in progression pattern of late restenosis after drug-eluting stent implantation**

S. Otsuru1, K. Kadota1, D. Hasegawa1, S. Habara1, T. Tada1, H. Tanaka1, Y. Fuku1, N. Oka1, T. Goto1, K. Mitsuoda1, Kurashiki Central Hospital, Kurashiki, Japan

**Background:** Recently, late restenosis after drug-eluting stent (DES) has been reported. However, the impact of DES type on the prevalence and progression pattern of late restenosis remains unclear. Thus, we evaluated the prevalence and progression pattern of late restenosis after sirolimus-eluting stent (SES), paclitaxel-eluting stent (PES), zotarolimus-eluting stent (ZES), and everolimus-eluting stent (EES) implantation.

**Methods:** From November 2002 to May 2010, 6811 consecutive patients (8879 lesions) were treated with SES, PES, ZES, and EES (SES, 6291 lesions; PES, 1519; ZES, 561; EES, 508) and performed midterm follow-up coronary angiography.
Regional differences in the use of antithrombotic therapy for stroke prevention in atrial fibrillation: European and Asian insights from the Global Anticoagulant Registry in the FIELD (GARFIELD)

S. Goto1, I. Mueller2, D.A. Fitzmaurice3, S. Haas4, G.Y.H. Lip5, A.G.G. Turpie6, S.Z. Goldhaber5, S. Rushton-Smith7, A.K. Kakkar8 on behalf of The GARFIELD Investigators. 1Tokai University, Kanagawa, Japan; 2The Thrombosis Research Institute, London, United Kingdom; 3Primary Care Clinical Sciences, The University of Birmingham, Birmingham, United Kingdom; 4Technical University of Munich, Munich, Germany; 5University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; 6McMaster University, Hamilton, Canada; 7Harvard Medical School, Brigham and Women’s Hospital, Department of Medicine, Boston, United States of America

Guidelines for antithrombotic therapy in atrial fibrillation (AF) recommend oral anticoagulation (OAC) for all AF patients at moderate/high risk of stroke and without contraindications. Clinical evidence suggests that intra- and extra-atrial haemorrhage in Asian patients occurs at a lower intensity of anticoagulation than in other ethnic patients. Little is known about real-world use of antithrombotic therapy for stroke prevention in Asia.

Aim: To compare use of antithrombotic therapy according to CHADS2 score in Asian and European AF patients.

Methods: GARFIELD is a worldwide registry that will enrol 55,000 patients as of May 2018. Overall, OACs were used in 43.7% of Asian and 50.5% of European AF patients. We analysed the dataset of the AMADEUS trial, which was a multicentre, randomised, non-inferiority study that compared fixed-dose idraparinux with adjusted-dose oral vitamin K antagonist (VKA) therapy in patients with AF. The principal safety outcome was any clinically relevant bleeding that was a composite of “major bleeding” and “clinically relevant non-major bleeding”.

Results: Data are shown in the table.

Conclusions: The progression pattern of late restenosis differs among various DESs. Although the mechanism of this phenomenon is unclear, different clinical follow-up may be necessary depending on DES types.

BALANCING STROKE PREVENTION VERSUS BLEEDING RISK IN ATRIAL FIBRILLATION

Regional differences in the use of antithrombotic therapy for stroke prevention in atrial fibrillation: European and Asian insights from the Global Anticoagulant Registry in the FIELD (GARFIELD)

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Conclusions: These international observational data indicate regional differences in OAC use for stroke prevention in AF in Asia and Europe, reflecting a potential overuse of OAC in Europe for patients at low risk for stroke according to existing risk scores and an underuse in Asian patients at higher risk.
and 5 strokes (0.99%/year) and 10 major bleeding events (1.97%/year) in the warfarin group (continuing on VKA), in the 30 days after stopping study drug with the majority of the imbalance after the first week (Table). This pattern mirrored the first 30 days of placebo where warfarin-naive patients starting warfarin had a higher rate of stroke or systemic embolism (5.41%/year) than warfarin-experienced patients (1.41%/year). No similar increase in event rate was seen in the apixaban group following study drug discontinuation before the end of the trial.

Conclusions: The excess in thrombotic and bleeding events in the apixaban arm after study drug discontinuation at the end of ARISTOTLE seems to be related to an increased risk associated with the new initiation of a VKA that extends over several weeks rather than a direct effect of apixaban.

4046 CHA2DS2VASc score and thromboembolic and bleeding complications after successful cardioversion of acute atrial fibrillation

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Purpose: It has been common practice to perform cardioversion of acute (<48 hours of fibrillation without anticoagulation). The objective was to determine the incidence of thromboembolic and bleeding complications related to cardioversion of acute atrial fibrillation in patients with and without perioperative anticoagulation.

Subjects and methods: A total of 5652 cardioversions were performed in 2569 consecutive patients with atrial fibrillation lasting <48 hours in three hospitals. For this analysis, embolic and bleeding complications were evaluated in 1632 cardioversions with and 4020 cardioversions with no perioperative anticoagulation.

Results: Cardioversions were successful in 5326 (94%) cases. Thirty-eight thromboembolic events (in 35 patients) occurred within 30 days after cardioversions. All were after successful procedures and 29 (76.3%) were strokes. One thromboembolic event (in 35 patients) occurred within 30 days after cardioversion with and 4020 cardioversions with no perioperative anticoagulation. The incidence of postcardioversion thromboembolic complications is high in patients with high CHA2DS2VASc score after cardioversion of acute atrial fibrillation when no anticoagulation is used. The present data supports the view that effective anticoagulation should be used in these patients also during cardioversions of short attacks of atrial fibrillation.

4047 Stroke prevention in non-valvular atrial fibrillation: long-term results after 6 years of the watchman left atrial appendage occlusion pilot study

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Background: Patients with non-valvular atrial fibrillation (NVAF) are at enhanced risk of embolic stroke; it has been reported more than 90% of left atrial thrombi in NVAF patients are found in the left atrial appendage (LAA).

Methods: The WATCHMAN LAA Closure device (Boston Scientific, Plymouth, MN) is made of nitinol, incorporates fixation bars around its perimeter and has a porous membrane on its atrial surface. A multi-center pilot study was initiated in August 2002. Patients were assessed at 45 days, 6 months and one year with transesophageal echo (TEE) and clinically assessed annually.

Results: Of 75 patients enrolled, the device was implanted successfully in 66. Anatomic limitations prevented implantation in 7. Failure of venous access and an earlier generation delivery cable problem resulted in the other 2 unsuccessful implants. Mean follow up was 73±25 months for all patients and 92±8 months for patients still actively followed. Mean age was 68±5 years at enrollment. The acute efficacy data have been published previously. After 6 months, 92% of patients were treated with apixaban therapy and at the present time, 91% remain on warfarin therapy. On routine 6 month TEE follow-up, 4 patients were noted to have a thrombus layer along the atrial face of the implant, one of whom developed a transient ischemic attack (TIA). Warfarin was restarted in these patients for 3 months without further evidence of thrombus. Two patients had an embolic stroke; one at 2 months and one at 39 months in the setting of severe concurrent carotid disease. These data reflect an overall stroke rate of 0.52% (2 events in 402 patients); the expected stroke rate given a mean CHA2DS2 Score of 1.8±1 would have been 5.75%. Fifteen patients have died (mean 49±21 months), all deaths were non-device and non-procedure related.

Conclusions: The long-term data suggest that WATCHMAN LAA Closure is safe and feasible, with two embolic strokes through more than 6 years of active follow up. This reflects a 90% lower stroke rate as compared with the expected stroke rate according to the CHADS2-score.
The present study demonstrated that the detection of ring-like sign on CCTA could help us to identify patients at high risk for future ACS events.

Conclusions: The present study demonstrated that the detection of ring-like sign on CCTA could help us to identify patients at high risk for future ACS events.

Purpose: Anomalous coronary arteries originating from the opposite sinus of Valsalva (ACAOS) are rare, but are associated with an increased risk of cardiac events. The clinical impact of ACAOS is still not clear and the natural history of ACAOS is unknown.

Methods: A total of 8,002 consecutive patients were evaluated with dual-source angiography (CCTA) at a single high-volume center.

Results: The incidence of ACAOS was 0.74% (59/8002). The origins and course of ACAOS were clearly visualized in all patients, including right-sided origin of the left main or the left anterior descending coronary artery (n=16), right-sided origin of the left coronary artery (n=28), and left-sided origin of the right coronary artery (n=16). Among analyzed subtypes of ACAOS, 19 (0.24%) had an interarterial course of which 11 (0.14%) showed a significant compression between the aortic root and the pulmonary trunk. The presence of both ACAOS was found in 5 (0.06%) right coronary arteries arising from the left sinus of Valsalva.

Conclusions: Dual-source CCTA allows accurate and noninvasive identification of ACAOS, which are found more frequently compared to previously published studies. The malignant characteristics of the proximal ACAOS might be exclusively associated with left-sided origin of the right coronary artery.

Purpose: Combined CT angiography and CT myocardial perfusion imaging to detect functionally significant stenoses in patients with suspected coronary artery disease - comparison with fractional flow reserve.

Methods: 40 patients with chest pain and suspected CAD underwent CCTA and CT perfusion imaging (CTP) which were acquired using 320-row detector CT. FFR was determined in all major vessels and assumed 0.5 in vessels with 50% stenosis on CCTA, CTP which were acquired using 320-row detector CT. FFR was determined in all major vessels and assumed 0.5 in vessels with 50% stenosis on CCTA. CT perfusion density was measured in the myocardial segment with CT perfusion imaging. The present study demonstrated that the detection of ring-like sign on CCTA could help us to identify patients at high risk for future ACS events.

Conclusions: Dual-source CCTA allows accurate and noninvasive identification of ACAOS, which are found more frequently compared to previously published studies. The malignant characteristics of the proximal ACAOS might be exclusively associated with left-sided origin of the right coronary artery.
were defined as cardiac death, nonfatal myocardial infarction, unstable angina requiring hospitalization, or coronary revascularization. Cardiac event-free survival was estimated using the Kaplan-Meier survival methods with log-rank statistics. The associations of selected variables with outcome were assessed in the multivariate Cox proportional hazard models.

**Results:** A very low, low, intermediate or high pre-test probabilities were observed in, respectively, 11.5%, 41.4%, 41.4% and 5.7% of study patients. During follow-up (736±337 days), a total of 12 (4.0%) cardiac events occurred involving nonfatal myocardial infarction in 1 (0.3%), unstable angina requiring hospitalization in 2 (0.6%), coronary revascularization in 9 (0.9%). In this study, of 12 patients with cardiac events, 5 patients (41.7%) with a high pre-test probability of CAD, 3 (25%) with an intermediate, and 4 (33.3%) with a low were observed. Kaplan-Meier event-free survival rate in patients with very low, low, intermediate and high risk pre-test probability of CAD was 0%, 3.3%, 2.4% and 29.4%, respectively. Patients with high pre-test probability had significantly more cardiac events as compared to patients with very low, low, intermediate and high pre-test probability (p < 0.001). The event rate was 0% among patients with very low pre-test probability. Multivariate model revealed that high pre-test probability was the only significant predictor of cardiac events (risk ratio 11.3: 95% confidence interval 3.5-36.8).

**Conclusion:** CAGS zero by MDCT did not predict future cardiac events completely. The prognostic value of pre-test probability of CAD for patients with very low risk, low, and intermediate was excellent. The cardiac event rate was 0% among patients with very low pre-test probability. Coronary CTA could be avoided for these patients, especially those with very low pre-test probability.

**4089 Impact of lipid lowering on prevention of plaque progression detected by coronary computed tomography angiography.**


**Purpose:** There are some reports that the severity of coronary artery stenosis by coronary computed tomography angiography (CTA) was associated with cardiac event rate. So, it would be important to find out the optimal treatment for prevention of plaque progression. Our previous study showed that serial CTA was useful to evaluate the plaque volume change of coronary arteries noninvasively. The aim of this study was to investigate the factors associated with the plaque progression of coronary arteries detected by CTA.

**Methods:** We studied 199 patients (84% male, mean age 66±10years) undergoing CTA twice for any purpose. The median period from 1st to 2nd CTA was 9 months. Coronary artery plaques were compared between 1st and 2nd CTA, and patients were classified into two groups; progression group (n=27) and non-progression group (n=172). The patients background and laboratory findings contributed to plaque progression investigated.

**Results:** Coronary risk factors were similar in two groups. There were no significant differences in high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), triglyceride, glucose level, and Hemoglobin A1c between two groups at baseline. In progression group, total cholesterol at baseline (209±37 mg/dl vs 193±37 mg/dl p=0.0359) was significantly higher, however, there was no significant different between 2nd CTA. Patients on statin was not significant difference both at 1st (44.4 vs 45.4%, p=0.9301) and 2nd CTA (59.3 vs 75.6%, p=0.0745) at 2nd CTA. Significant different proportions of plaque progression were investigated.

**Conclusion:** Plaque progression of coronary arteries by CTA was associated with poor control of LDL-C level at 2nd CTA. The present study confirmed that LDL-C <100mg/dl was significant for secondary prevention of coronary artery disease. CTA might have potential to provide the optimal strategies for improve of prognosis.

**POSTER SESSION 5 GENETIC ASPECTS/VENTRICULAR ARRYTHMIAS**

**4083 Outcome of screening of relatives to patients with long QT syndrome; a nationwide Danish study.**

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**Aims:** According to international recommendations relatives to patients with long QT syndrome (LQTS) are offered cascade screening. In this Danish study we assessed the outcome of clinical and genetic cascade screening of LQTS families nationwide.

**Methods and results:** Patients with LQTS were identified from Danish national registries and patient files were reviewed. A total of 286 patients with LQTS were identified in 79 families and included 209 relatives. The majority of diagnosed relatives identified by cascade screening were asymptomatic. Symptomatic probands and family members most often presented with syncope, followed by aborted cardiac arrest (abSCD), unexplained symptoms and sudden cardiac death (SCD). Syncope, abSCD and SCD most often occurred at rest. The most pronounced QTc prolongation was seen in probands and patients with serious cardiac events. A disease-causing mutation was found in 59 probands (81% of 73 probands tested). The majority of mutations were localized to the KCNH2 gene (63%). A total of 180 (63%) patients were on beta-adrenergic blocking agents (BB) and 67 (23%) patients had an implantable cardiac defibrillator (ICD). Appropriate ICD therapy was given to 12 (29%) probands and three (12%) family members. Fourteen (33%) probands and two (8%) family members experienced ICD complications.

**Conclusions:** By cascade screening we identified almost 3 affected relatives for each proband. Proband were notably more clinically affected compared to others relatives, but a considerable fraction of the diagnosed relatives were asymptomatic and 14 family members (7%) fulfilled guideline criteria for ICD implantation.

**4084 The australian national genetic heart disease registry.**

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**Purpose:** There are now over 40 cardiovascular diseases known to have a genetic cause. Current studies are limited by a lack of detailed clinical information and large patient cohorts, leaving many key clinical and genetic questions unresolved. The Registry aims to recruit every Australian family with a genetic heart disease, and will provide a valuable resource to better understand these conditions.

**Methods:** Patients are recruited from specialised cardiac genetic clinics and through self-referral. Written informed consent is required and clinical data are collected and entered into a central Registry database. Diseases included are the inherited cardiomyopathies (hypertrophic cardiomyopathy [HCM], familial dilated cardiomyopathy [FDC], arrhythmogenic right ventricular cardiomyopathy [ARVC], isolated left ventricular noncompaction [LVNC], primary arrhythmogenic disorders (long QT syndrome [LQTS], catecholaminergic polymorphic VT [CPVT], Brugada syndrome [BrS]) and familial valve diseases (bicuspid aortic valve disease [BAV]).

**Results:** To date 1032 individuals from 611 families have enrolled. The mean age of registrants is 46±20 years, 520 (50%) are males and 711 (69%) have clinical disease (remainder are at-risk relatives). There are 428 (41%) individuals with a clinical diagnosis of HCM, with a mean age of 52±18 years. Among these, 354 (58%) are HCM families, 117 (33%) have had gene testing with a gene mutation identified in 70 (60%) families, which includes 6 (5%) families with multiple gene mutations. There are 93 (9%) individuals with LQTS, 39 (4%) with DC, 25 (2%) with BAV, 23 (2%) with ARVC, 15 (1%) with CPVT, and 11 (1%) with BrS. Importantly, 813 (79%) registrants have consented to be approached for future research studies. The Registry aims to recruit every Australian family with a genetic heart disease, and will provide a valuable resource to better understand these conditions.

**Conclusions:** The Australian National Genetic Heart Disease Registry is a unique resource for the study of these diseases. The Registry will provide an accurate and up-to-date source of information for health professionals and families, and will emerge as an important resource for future research in genetic heart diseases.

**4085 A new MG01 transcript variant implicated in arrhythmias.**

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A missense mutation in the Mg01 gene has been recently identified in one Brugada syndrome (BrS) patient. This gene has been shown to interact with the clathroplasia loop II (between transmembrane domains DII and DIII) of Nav 1.5. This interaction plays a critical role in the regulation of sodium current density, increasing the whole-cell iNa current. In our study we screened a cohort of 161 BrS and 79 IVF (idiopathic ventricular fibrillation) patients by direct sequencing on all the three alternative transcript variants of the Mg01 gene. All patients were screened for mutations on the SCN5A, CACNA1c and GPD1L, associated with BrS.
Two different variations, L18F and D133N, have been identified in three unrelated patients. L18F located in a region common to all the three transcript variants of KCNJ2, has been identified in a BrS patient and in an IVF patient. Variation D133N, identified in a IVF patient, is positioned in the alternative exon 3 of the KCNJ2 protein. Our results describe the expression of different transcript variants c, not yet characterized, and performed a computational analysis of the alternative region that allow to distinguish the variant KCNJ2c from the other two variants KCNJ1a and KCNJ1b. Results show the expression of KCNJ1c in all the 16 tissues, including heart. Our screening discovered two novel, unreported amino acid variants on KCNJ1 gene in patients with a BrS or IVF phenotype. These findings also strengthen the role of the novel KCNJ1c transcript in the human heart and reinforce the hypothesis that KCNJ1c could play a role in the pathophysiology of BrS and IVF.

**P4089**

**Evidence for a heritable contribution to death from atrial fibrillation**

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**Background:** Using a unique population-based genealogy (Utah Population Data Base or UPDB) linked to over 100 years of death certificate data for the state of Utah, we have tested the hypothesis of a heritable contribution to death from atrial fibrillation.

**Methods:** We identified 14,335 Utah death certificates that included atrial fibrillation (AF) as a primary or contributing cause of death using ICD9 427.3 and ICD10 I48 codes. We tested the hypothesis of excess relatedness among the individuals dying from Atrial Fibrillation using the Genealogical Index of Familiality Method. We estimated the average pairwise relatedness between all possible pairs of the 4,335 deaths and compared it to the expected relatedness in 1,000 sets of 1:1 matched controls (with Utah death certificate: matched by 5-year birth cohorts, sex, and birthplace (Utah or not) selected randomly from the UPDB for an empirical significance. We estimated relative risk in first- to fifth-degree relatives by comparing the observed number of relatives dying from AF to the expected number of first- to fifth-degree relatives using cohort-specific death rates from the UPDB applied to all relatives of AF deaths.

**Results:** The overall average relatedness of the 4,335 AF deaths was significantly higher than expected (empirical p < 0.001). We also observed significant excess relatedness when close relationships (genetic distance closer than first cousins) were identified in both cases suffering from the above mentioned ICVDs. In most common ICVDs (HCM, LQTS, ARVC, BrS), the Mut(+)Phen(–)% of total tested relatives was 0.0% for AF deaths.

**Conclusions:** These results provide strong evidence that AF mortality clusters in families. The results also provide strong evidence that the excess relatedness among AF deaths has a strong heritable contribution, as it is observed in both close and distant relationships.

**P4098**

**Inherited cardiovascular diseases (ICVDs) in the every day clinical practice: diagnostic yield and genetic family screening**

A. Anastassakis

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**Purpose:** ICVDs have variable clinical expression and incomplete penetrance. The aim of this study is to identify the diagnostic yield of genetic testing on each disease in every day clinical practice and the response of family members to family screening. The diagnostic yield coming from ICVD clinic is satisfactory in most common ICVDs (HCM, LQTS, ARVC, BrS). The diagnostic yield on each disease is higher than expected (empirical p < 0.001) were obtained.

**Conclusion:** The diagnostic yield coming from ICVD clinic is satisfactory in most of the cases. The experience of a SD in a family motivates relatives to accept better the usefulness and the economic burden of genetic family screening. The importance of genetic testing as a prophylactic health approach should be further highlighted.

**P4088**

**A novel mutation affecting the transmembrane domain of the KCNJ2 protein is associated with high prevalence of life-threatening ventricular arrhythmias in a family with Andersen-tawil syndrome**

E. Fertund

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**Abstract:** A novel mutation in KCNJ2 (c.271_282del12[p.Ala91_Leu94del]) affecting the transmembrane domain of KCNJ2 has been identified in a family with Andersen-Tawil syndrome with high prevalence of any other extracardiac disease manifestation. 7 and 17 years of age in 5 of 10 mutation carriers. 3) All mutation carriers pre-dying from Atrial Fibrillation using the Genealogical Index of Familiality Method.

**Results:**

<table>
<thead>
<tr>
<th>Family</th>
<th>Mut(+)Phen(–)% of total tested relatives (%)</th>
<th>Mut(+)Phen(+)% of total tested relatives (%)</th>
<th>Mut(–)Phen(+)% of total tested relatives (%)</th>
<th>Mut(–)Phen(–)% of total tested relatives (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family 1</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 2</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 3</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 4</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 5</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 6</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 7</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 8</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 9</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Family 10</td>
<td>26.9%</td>
<td>67%</td>
<td>18.8%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

**Conclusion:** This family screening also highlighted the role of the novel KCNJ2 transcript in the human heart and reinforces the hypothesis that KCNJ2 is associated with mutations in KCNJ2 and relatively low prevalence of ventricular arrhythmias.

**References:**

1. Marfan syndrome (MfS) according to the latest diagnostic criteria for each disorder. The aim of this study is to identify the diagnostic yield of genetic testing on each disease in every day clinical practice and the response of family members to family screening.

**Results:** The diagnostic yield coming from ICVD clinic is satisfactory in most common ICVDs (HCM, LQTS, ARVC, BrS). The diagnostic yield on each disease is higher than expected (empirical p < 0.001) were obtained.

**Conclusion:** The diagnostic yield coming from ICVD clinic is satisfactory in most of the cases. The experience of a SD in a family motivates relatives to accept better the usefulness and the economic burden of genetic family screening. The importance of genetic testing as a prophylactic health approach should be further highlighted.

**Purpose:** ICVDs have variable clinical expression and incomplete penetrance. The aim of this study is to identify the diagnostic yield of genetic testing on each disease in every day clinical practice and the response of family members to family screening. The diagnostic yield coming from ICVD clinic is satisfactory in most common ICVDs (HCM, LQTS, ARVC, BrS). The diagnostic yield on each disease is higher than expected (empirical p < 0.001) were obtained.
The effect of corticosteroid, antiarrhythmic agents, and radiofrequency catheter ablation on ventricular tachycardia associated with cardiac sarcoidosis

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Purpose: Ventricular tachycardia (VT) and sudden death are commonly observed in cardiac sarcoidosis, however, the clinical impact of a multimodality therapy is still uncertain.

Methods: We enrolled 35 patients (55±12 years, 11 male) who had a diagnosis of sustained VT associated with cardiac sarcoidosis. All patients were initially treated with corticosteroids and antiarrhythmic agents unless they refused to take them. Steroid therapies were started with an initial dose of 30 mg/day, and the dose was gradually decreased over a period of 6 to 12 months to 5-10 mg/day as a maintenance dose. If the VTs recurred even on the antiarrhythmic and steroid therapy, radiofrequency catheter ablation (RF-CA) was performed. Patients who underwent RF-CA before being medicated, including with corticosteroids and antiarrhythmic agents, were excluded from this study. The clinical impact of both a steroid and antiarrhythmic therapy associated with RF-CA was evaluated.

Results: All patients received antiarrhythmic drugs and 32 patients received steroid therapy. During a 51±37 month follow-up, 22 (65%) patients were free from any VT episodes. The ejection fraction and prevalence of a Gallium-67 uptake was lower in those with VT recurrence than in those without (40±16% vs. 54±6%, p<0.05; 15% vs. 9%, p<0.01, respectively). The multivariate Cox regression analysis demonstrated that the absence of a Gallium-67 uptake in the heart was an independent predictor for a VT recurrence under the drug therapy (Hazard ratio, 8.89; 95% confidence interval, 1.86 to 42.43; p<0.01). After a mean follow up of 24±11 months, 6 of 13 patients experienced recurrent VTs. The number of induced and sustained VTs was higher in the patients with VT recurrences than in those without (9±2±5 vs. 2.7±0.8; p<0.05, 4.0±1.4 vs. 2.0±0.8; p<0.01, respectively). An ROC curve revealed that the number of induced VTs of more than 4 identified VT recurrences after RF-CA with a sensitivity of 83% and specificity of 86%.

Conclusions: The multimodality therapy for VT associated with cardiac sarcoidosis could successfully suppress VT recurrences in 85% of the patients.

Changes in NT-proBNP level after successful PVC ablation in patients without structural heart disease: evidence for PVC-induced chronic wall stress

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Purpose: NT-proBNP is synthesized in ventricular myocardium in response to increased wall stress. A high, chronic PVC burden has been associated with a reversible cardiomyopathy. However, the majority of patients with symptomatic PVCs presents with only slightly impaired or normal LV function. We evaluated NT-proBNP levels before and after ablation to determine the potential wall stress caused by PVCs in symptomatic patients with slightly impaired or normal LV function.

Methods: Eighty patients (42 male, 48.1±16 years) with a LVEF<50%, referred for ablation of PVCs (n=30; 14±4% PVC burden, 20±12% of PVC burden), underwent clinical echocardiography including standardization echocardiography, 24h Holter monitoring and assessment of NT-proBNP before and 3 months after ablation. Symptoms increased 1-year mortality risk (HR=1.9 CI 95% 0.85-4.35).

Conclusions: In this study early VT/VF was associated with increased risk of in-hospital death but not with increased post discharge, whereas late VT/VF was associated with increased risk of 30 day death and a trend for increased 1-year mortality risk.

Outcome of patients with acute coronary syndromes complicated by ventricular tachycardia or fibrillation in the acute coronary syndromes israeli survey (ACSIS)

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Background: Most of the data regarding the occurrence of VT/VF among patients hospitalized due to acute myocardial infarction (AMI) and its associated prognosis were obtained before the reperfusion era, whereas data on VT/VF in the era of primary percutaneous coronary intervention (PCI) are limited and conflicting regarding early and late prognosis.

Aim: To evaluate the incidence and outcome of patients with AMI presenting with early and late VT/VF.

Methods and results: We studied 7669 patients from the Acute Coronary Syndrome Israeli Survey (ACSIS) between the years 2002-2010 which included ST elevation (n=5673) and non ST elevation MI: ACS (n=4096). We divided them into 3 groups: patients with no VT/VF, early (<48h) VT/VF and late (>48h) VT/VF. Of the 7669 patients with ACS, 7369 (96%) had no VT/VF, 166 (2.1%) had early VT/VF and 194 (1.7%) had late VT/VF. Baseline characteristics were significantly different among the 3 groups; with higher number of coronary risk factors and comorbid conditions in the VT/VF groups and notably younger age (mean 60±12 years) in the early VT/VF group.

Patients with late VT/VF had a more complex hospital course with higher frequency of mechanical and arrhythmic complications other than VT/VF, and longer hospital stay.

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The characteristics of malignant premature extrasystoles originating from right ventricular outflow tract


Premature extrasystoles (PES) originating from right ventricular outflow tract (RVOT) are often observed in patients without structural heart diseases and are generally considered as benign ventricular arrhythmias. However, ventricular fibrillation (VF), and/or polymorphic ventricular tachycardia (PVT) are occasionally initiated by the PES. The aim of this study was to clarify how to differentiate malignant (M) PES from benign (B).

Methods: Consecutive 30 patients, in whom radiofrequency catheter ablation was conducted for PES originating from RVOT, were enrolled. Spontaneous VF and/or PVT initiated by the PES were showed in 9 patients (M-gr). Coupling interval, QRS duration, QRS morphology and optimal ablation site of the PES in M-gr were compared with them in the other 21 patients group (B-gr).

Results: There were no differences between M-gr and B-gr in coupling interval (419±30msec vs. 438±41msec, ns) and QRS duration (165±11msec vs. 153±15msec, ns). The prevalence of notch on QRS in inferior leads of PES was significantly higher in M-gr than in B-gr (9/9 vs. 3/21, p<0.01). Broad R wave (>150msec) in I was significantly more frequently observed in M-gr than in B-gr (7/9 vs. 1/21, p<0.01). The prevalence of aVF to aVL (the ratio of negative amplitude of aVF to aVL) >1 was not significantly higher in M-gr than in B-gr (7/9 vs. 4/21, ns). PES originated from posterior, free wall in 7 out of 9 patients in M-gr, and 1 out of 21 patients in B-gr (p<0.01).

Conclusion: In conclusion, PES originating from posterior side of free wall in RVOT, with notch in inferior leads and broad R wave in I, frequently initiate VF and/or PVT. Malignant form of PES in RVOT could partially depend on the localization of its origin.

Effect of vagal nerve on the monophasic action potential of ventricular outflow tract

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Objective: Vagal nerve may be related with idiopathic ventricular tachycardia. Its present study was aimed to investigate the effect of vagal nerve on the monophasic action potential (MAP) of ventricular outflow tract.

Methods: Eight adult mongrel dogs were involed. Bilateral vagosympathetic nerves were decentralized for stimulation. Metoprolol was given to block sympathic effects. Three MAP recording electrode were placed at the left ventricular outflow tract (LVOT), right ventricular outflow tract (RVOT) and right ventricular apex (RVA) respectively through right femoral artery and vein. MAP was recorded at the LVOT, RVOT, RVA with or without vagal stimulation (VS) respectively.

Results: MAPD at outflow tract was greater significantly than that at RVA. It suggested that VS could reduce MAPD significantly. With VS, the abbreviation of coupling interval is a marker of reversible cardiomyopathy. This suggest an association between early irritation of PVE in the preceding mechanical cardiac cycle and the development of LV dysfunction.

Conclusions: In pts referred for frequent PVC ablation, electromechanical coupling intervals are a marker of reversible cardiomyopathy. This association between early irritation of PVE in the preceding mechanical cardiac cycle and the development of LV dysfunction.

Figure 1. Coupling interval and basal LVEF

Digitalis use and multivessel disease independently predict ventricular fibrillation at reperfusion in PCI-treated patients with STElevation myocardial infarction

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Purpose: Ventricular fibrillation (VF) during reperfusion in STElevation myocardial infarction (STEMI) is an infrequent event, but confers increased in-hospital mortality. We assessed clinical characteristics associated with VF during reperfusion in an unslected population of STEMI patients treated with percutaneous coronary intervention (PCI).

Methods: It total, 1744 consecutive STEMI patients were admitted to a Swedish tertiary care hospital for primary PCI during 2007-2009. Clinical characteristics and information about presence of VF were obtained from the Register of Information and Knowledge about Swedish Heart Intensive care Admissions. Medical records were reviewed to determine VF timing in relation to the infra-arterial artery (IRA) opening. Clinical and angiographic characteristics were tested for association with reperfusion VF using logistic regression analysis.

Results: Acute IRA occlusion was present in 1127 patients (age 66±12 years, 72% male) at admission, of whom 26 (2.3%) developed VF at IRA opening. Increased risk of VF during reperfusion was observed for asprin, beta-blockers or digitals at admission, VF before reperfusion, inferior location of infarct and multivessel disease. In multivariate analyses, only multivessel disease and the use of digoxin remained independently associated with reperfusion VF (Table). Reperfusion VF was not associated with either age, gender, body mass index, history of hypertension, heart failure, diabetes, stroke, PCI, CABG, myocardial infarction, IRA or the presence of left main artery stenosis.

Clinical factors associated with VF during reperfusion in PCI-treated acute STEMI

<table>
<thead>
<tr>
<th>Characteristics at admission</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tr>
<td>Medications</td>
<td>HR 95% CI p-value</td>
<td>HR 95% CI p-value</td>
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<tr>
<td>Aspirin</td>
<td>2.75 1.27-6.21 0.015</td>
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<td>Beta-Blockers</td>
<td>3.43 1.52-7.74 0.003</td>
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<td>Digitalis</td>
<td>8.63 1.85-41.20 0.006</td>
<td>6.96 3.20-39.89 0.029</td>
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<td>VF before reperfusion</td>
<td>5.04 1.82-13.97 0.002</td>
<td>-</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>3.05 1.54-6.19 0.027</td>
<td>3.11 1.04-9.36 0.043</td>
</tr>
<tr>
<td>Inferior localization</td>
<td>2.82 1.11-7.14 0.029</td>
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</table>

Conclusion: Multivessel disease and digitalis use at admission independently predict VF at IRA opening in patients with acute STEMI. Our data further support a proarrhythmic effect of digitalis in the setting of acute coronary syndrome.

Electroanatomical substrate mapping guidance for left ventricle aneurysmectomy in patients after myocardial infarction

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Introduction: Left ventricle aneurysmectomy (LVAR) with peri-infarction cryoablation...
is an effective approach for the treatment of post-MI patients who present with VT. The purpose of this prospective study was to evaluate the efficacy of catheter-based electroanatomical mapping (EAM) prior to aneurysmectomy to identify the atherosclerotic regions as a guide for surgical resection and coronary artery bypass. Method: We included 35 pts (M/F: 28/7), average age 64 years (38 – 79). Mean LVEF prior the surgery was 23.5% (20-50%) and post MI aneurysms were documented by echocardiography or LV angiography. VT inducibility was confirmed prior to surgery and EAM was performed (CARTO, Biosense-Webster) to identify border zones and late/frac-tionated potentials. The surgeon used the EAM image during surgery, arrhythmic zones were eliminated by aneurysmectomy, endocardial resection and cryotherapy. An EP study and EA mapping were repeated at ~3 mo after surgery. Results: In 27 pts we performed LWAR + CABG, in 5 pts LWAR + mitral valvoplasty and in 3 pts LVAR + cryotherapy. The EF improved significantly to 48%. The end-systolic volume decreased from 142ml to 93ml. Pre-surgery, VT was inducible in 24 pts (68.5%), but after LWAR only in 4 pts (11%). Post-surgical EAM revealed reduction of late and fractionated potentials. When present, MRI revealed significant scar tissue reduction in all pts. Conclusion: EA mapping prior to LVAR can facilitate arrhythmogenic substrate elimination with significant reduction of VT induction – this minimizes the risk of life threatening arrhythmias.

P4099 Increased spatial dispersion of the ventricular recovery time in patients with idiopathic ventricular fibrillation
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Background: Diagnosis of idiopathic ventricular fibrillation (IVF) before its occurrence is very challenging, because cardiac arrest could represent the first or the only sign of the disease. Heterogeneity of ventricular repolarization has been considered important to be linked to ventricular tachycardia in patients with is- chemic and idiopathic cardiomyopathy. The purpose of this study was to test the hypothesis that IVF also might be associated with ventricular repolarization abnormalities.

Methods and Results: Spatial dispersion of recovery time as an index of heterogeneity of ventricular repolarization was assessed by means of a 107-lead high-resolution electric field electrocardiograph (187-ch SAVP-ECD) in a group of 14 consecutive patients (13 male, 48±17 year-old) who were diagnosed with IVF and who received ICDs for secondary pre- vention after an episode of resuscitated sudden cardiac death. A control group consisting of 22 healthy persons (22 male, 35±7 year-old) was set for compar- ison. Recordings took a maximum of 10 minutes and were obtained without any complication. The patients with IVF did not present with characteristic ECG ab- normalities. Spatial dispersion of corrected recovery time (defined as the time between the R wave peak and the first positive maximum derivative of T wave corrected by Bazett’s formula) was significantly higher in the IVF group compared with the control group (94±17 milliseconds versus 63±19 milliseconds P<0.001).

Conclusions: 187-ch SAVP-ECD is a simple and reliable method for the evalu- ation of ventricular repolarization. It may be useful to reveal patients with latent IVF.

P4100 Predictors and prognosis of ventricular fibrillation during acute coronary syndromes
Introduction: Different types of arrhythmias are originated in the setting of acute coronary syndromes (ACS) due to electrical instability and ischemia. The most important is ventricular tachycardia which degenerates in ventricular fibrillation (VF). VF during hospital stay is associated with a poor prognosis.

Objective: Assess the predictors and prognosis of VF during ACS.

Methods and results: We performed a prospective study involving 902 consecu- tive patients (P, aged 64±13.2 years, 77.5% male) admitted in a Coronary Unit for the period of 2 years, with a 6 month follow-up. The VF rhythm was identified in 51 P (5.7%) during hospital stay. This arrhythmia was not associated with any car- diovascular risk factor, relevant past medical history (including ischemic cardiomy- opathy or valvular heart disease) or previous medical therapy. At admission, the P with VF presented with higher heart rate (HR; p=0.014) and lower systolic blood pressure (SBP; p<0.001). ACS with ST segment elevation was the most common type of ACS in those P (p<0.001). During hospital stay, VF was more frequent in P with multivessel disease (2 or 3 vessels, p=0.008), higher maximum Killip class (KMax; p<0.001) and left ventricular ejection fraction ≤ 40% (LVEF; p<0.001). Acute myocardial infarction (AMI) occurred in 30% of these patients. VF was more frequent in patients with anterior location of myocardial infarction (MI) (p=0.001), and increased inducibility of monomorphic VT (p<0.001). Among the other characteristics, during hospital stay, patients with VF had higher blood levels of NT-proBNP (p=0.001). During hospital stay, patients with VF experienced more complications (p<0.001), including severe bradycardia with transient AV block during 24-hours Holter monitoring (3 cases) and aborted cardiac arrest (1 case). During the follow-up, 16 Pts (33%) experienced PDA during ICD follow-up: 15 pts. experienced sustained VF treated with IVF shocks: episodes of spontaneously terminated asymptomatic VF were registered in 7 pts, and unsustainable ventricular tachycardia -in 4 pts. Inappropriate shock (T oversensing) was registered in 1 patient. Among genotyped Pts the greater part of VF was found in patients with combination of mutations of ryanodine receptor and JLN. Furthermore multiple episodes of VF were registered in 3 pts with LQT1 and in 1 pt - with LQT2.

Conclusions: ICD implantation was needed in about 9% of children with LQTS,
who were exposed to a high risk of SCD. ICD appears to be an effective therapy option for primary (14 pts) or secondary (1 patient) prevention of SCD in 50% of pts. ICD monitoring allowed to reveal unsatisfactory efficiency of beta blockers in 53% of pts with severe course of disease. Nearly all children with QTDS were not exposed to inappropriate ICD shocks over a 4.2±1.5 years of follow up.

**P4103 Takotsubo cardiomyopathy and arrhythmic risk**

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**Purpose:** "Takotsubo" cardiomyopathy (TTC) is a recently described cardiac syndrome, usually triggered by intense emotional and/or physical stress, characterized by transient severe localized left ventricular dyskinesia and changes of ST segment that can mimic acute myocardial infarction, without significant coronary artery stenoses. Although the prognosis is considered good, TTC is associated with significant alterations of the QT interval that could trigger life-threatening cardiac arrhythmias. The aim of our study was to assess the extent of the alterations of the QT interval and the arrhythmic risk associated with this disease.

**Methods:** From August 2008 to December 2011 we prospectively enrolled all patients admitted to the ICU (n=101) with TTC. Myocardial biopsies were performed during hospitalization and calculated maximum QT interval (QTmax), maximum corrected QT interval (QTmaxc) and maximum QT dispersion (QTdmax). The presence of torsades de pointes (TdP), other hyperkynetic ventricular arrhythmias and sudden death, which occurred within one month of admission, was evaluated. Statistical analysis was performed using Student’s t for unpaired data.

**Results:** The pts (18 women, mean age=63±12 years) had mean values of QTmax = 53±40 msec, QTcmax = 550±83 msec and QTdmax = 81±75 msec. Ventricular arrhythmias occurred in 6 pts (33%). In particular, the presence of TdP was recorded in 1 pt (5%), non-sustained ventricular tachycardia in 4 pts (0.7%), sustained ventricular tachycardia in 3 pts (17%), ventricular fibrillation in 2 pts (11%). There was one case of sudden death the day after discharge, in a pts with ventricular fibrillation during the first day of hospitalization. The pts with ventricular arrhythmias had values of QTc max significantly higher than those without arrhythmias (580±80 msec vs 620±70 msec, p <0.05). The values of QTc max and QTdmax showed no statistically significant differences between the two groups.

**Conclusions:** Our study confirmed abnormally prolonged QT intervals and QT dispersion in pts with TTC. We found a significant incidence of ventricular arrhythmias. The pts with ventricular arrhythmias had significantly higher values of QTcmax.

**P4104 J waves in the early recovery phase of acute myocardial infarction and its clinical implication**

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**Purpose:** J waves can be arrhythmogenic and to be studied in ischemic heart disease. We studied the prevalence and clinical significance of J waves in the early recovery phase of myocardial infarction (MI).

**Methods:** In 152 consecutive patients with acute MI, electrocardiogram (ECG) was monitored for one week after coronary intervention for revascularization. The mean age was 68.6±13.5 years, and 78.3% were males. J waves were diagnosed when the amplitude was ≥1.0 mm as either notch or slurred at the terminal part of the QRS complexes in contiguous 2 or more leads on 12-lead ECG recorded at the end of monitoring for one week. The relationship between the location of J waves and the location of MI and the culprit lesion were determined. Then the ECG parameters and the incidence of arrhythmias were compared between groups with and without J waves. Finally, the rate dependency of J waves was evaluated in the conducted beats of atrial premature beats.

**Results:** J waves were present in 60.5% (92/152) of patients which was higher than 16.4% that observed in the age and sex comparable subjects. The mean amplitude of J waves was 1.3±0.8 mm in the inferior region in 56.5% of patients, followed by the high lateral (33.7%), the left precordial (16.3%) and the right precordial (2.2%) regions. J waves were more frequent in inferior than anterior MI (67.7% versus 55.2%, respectively, P=0.0142). The ventricular tachyarrhythmias(VTA), premature beats, non-sustained ventricular tachycardia(VT) or ventricular fibrillation(VF), occurred more frequently in the group with J waves including sustained VT or VF (p=0.012). Furthermore, the patients with the amplitude of the J wave 2mm or greater was associated with higher incidence of VTA. As the RR interval became shorter by the conduction of atrial premature beats, the amplitude of the J wave was augmented suggesting tachycardia dependency or phase 3 block.

**Conclusions:** J waves of the patients in the early recovery phase of MI had a higher prevalence of J waves and they were associated with ventricular arrhythmias. The augmentation of J waves at higher rate suggested a role of conduction delay for the pathogenesis. The significance and mechanism of J waves are to be determined in post-MI patients.
How do female electrophysiologists deal with radiation exposure during pregnancy: Results from the EPIC global survey

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Background: Awareness of radiation exposure is variable among different settings of practice in invasive electrophysiology (EP) laboratories around the world.

Methods: As part of a web-based questionnaire on individual practices focusing on radiation exposure during invasive EP procedures, a total of 8 questions were aimed specifically at female cardiologists.

Results: A total of 165 physician (50 female) responses were received with the majority of them located in the US (38%), Canada (8%), Italy (7%) and Germany (6%). Nearly 80% of participants were qualified cardiologists for more than 3 years (45% for more than 10 years). Of the 50 female participants, 18 were pregnant at some time during their career in the catheterization laboratory or ischelma center for more than 2 years. Nearly 80% of participants received structured advice on specific radiation protection, while others obtained advice from personal colleagues or the web-based information. During their 1st pregnancy, 10 of 14 colleagues continued to work in the cath lab in the 1st trimester, while 5 of 9 continued during the 2nd and 2 of 5 during their 3rd pregnancy. Two thirds of colleagues continued to work as first-hand operator, or supervised junior colleagues without being directly exposed. Personal protection was changed in 6, 9 did wear double layers of lead aprons and 2 used a protection cabin. Of note is that fetal badges were issued in all cases, but only in 2 cases showed higher readings. Female colleagues continued to work up till 6 (4), 4 (3) and 2 (8) weeks before delivery. The majority of pregnancies went successfully to full-term, but 3 pre-term deliveries at 34, 36, and 36 weeks happened (1 miscarriage at 11 weeks).

Conclusion: This is the first global survey on radiation exposure and protection measures during EP procedure and specifically focused on female cardiologist. While information about specific recommendations for radiation exposure during pregnancy was scarce, all but one pregnancy were successful with the majority of colleagues continuing their clinical work taking some personal precautions such as double leading.

Determinants of immediate intracardiac intervals prolongation after percutaneous aortic valve implantation

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Percutaneous aortic valve implantation (PAVI) in patients (pts) with aortic stenosis may induce changes in atrioventricular conduction, as assessed by intracardiac electrogams. However, there is little information on factors influencing changes in intracardiac electrograms in pts immediately after CoreValve implantation. The aim of this study was to analyze determinants of immediate increases in surface and intracardiac intervals after PAVI.

Methods: From a total of 160 pts with aortic stenosis undergoing PAVI, we analyzed the last 70 consecutive cases who had intracardiac electrogams prior and 30 minutes after valve implantation. The changes observed were compared with intervals obtained from the surface electrocardiogram (ECG) before and after CoreValve implantation. The mean age was 78.6±9.4 years; 43 (61%) were female. The increases in PR, QRS, AH and HV intervals were defined as the differences between measurements taken 30 minutes post implantation and at baseline. Also, the increases in AH and HV intervals were defined as the differences between measurements taken 30 minutes post implantation and at baseline.

Results: There was a significant inverse correlation between the increase in PR interval and the annulus/prosthesish size ratio (r=-0.34; p<0.002). There were also significant correlations between the increment in corrected-HV with the annulus size, as assessed by angiography (r=-0.35; p<0.001). The increment of corrected-HV correlated significantly with sinus of Valsalva diameter assessed by echocardiography (r=0.38; p<0.001). The prolongation of corrected-AH correlated with the depth of valve implantation (r=0.56; p<0.0001). The patients with dislipemia showed a higher increase in PR interval (33±55 vs 6±32 milliseconds; p<0.04). The increase in QRS duration was significantly higher in patients with ejection fraction ≤0.50 at baseline study (36±28 vs 54±20 ms; p<0.01). In pts with right bundle branch block (RBBB) the increment of corrected-HV was significantly higher (p<0.001). Similarly the prolongation of HV was higher in pts with baseline RBBB and left anterior hemiblock (LAHB).

Management of challenging transseptal access in patients with hyperembol septum/interatrial neurny or stift septum/septal scoring

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Purpose: Transseptal access to the left atrium (LA) and venetris is indispensable for the ablative treatment of atrial and ventricular tachyarrhythmias. Successful ablation of atrial fibrillation may necessitate repeated left atrial ablations. However, repeat transseptal procedures may lead to increased local stiffness of the interatrial septum, rendering the transseptal puncture more difficult at the index procedure. Moreover, transseptal puncture in patients with hyperembol/aneurysmal interatrial septal may be challenging with the classical Brockenbrough needle approach. We sought to assess safety and efficiency of a novel navigation system for transseptal puncture with an energy delivering needle system for transseptal puncture in patients with difficul/risks transseptal access.

Methods: From January 2011, we performed 485 transseptal ablation procedures for atrial arrhythmias. The classical “Brockenbrough” needle approach (1.7 cm BRK-1, SUM) for transseptal access was applied in all patients under TEE guidance. When the transseptal puncture was met with difficulties, the novel RF needle (NRS, Baylis, Canada) was used.

Results: In 25/511 patients (4.9% of all procedures, 64±7yo, 19 men, 12 redo procedures) left atrial access using the classical needle was considered challenging. Difficulties arose from (1) a stiff septum mostly due to a repeat transseptal access for redo-ablations in 10/25 patients (40%), (2) a hyperembol/aneurysmal septum in 10/25 patients (40%) and/or (3) a short distance between the tented septum and LA free wall in 5/25 patients (20%). In these cases the novel radiofrequency
Epicardial electrophysiological mapping of ganglionic plexi for concomitant atrial fibrillation

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Purpose: Ganglionic plexi (GP) are helpful optional targets for MAZE procedure. This study was aimed to reveal and identify activity of GP by epicardial location.

Methods: Fifteen patients with concomitant atrial fibrillation underwent intraprocedural epicardial electrophysiological mapping in our institution. Autonomic GP were identified by rapid atrial pacing via a temporary pacemaker after removal of fatty epicardial tissues on the surface. A 24-point high-frequency stimulation (1000minute, 18V) was achieved by placing tetзвees directly on the left atrial epicardium. Diagram of epicardial mapping locations is shown below. (Picture)

Results: Active GP were found in 13 out of 15 patients. The incidence of activity by epicardial location is shown below. (Table)

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<thead>
<tr>
<th>Location</th>
<th>Right</th>
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<th>Location</th>
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<td>1/5</td>
<td>Location</td>
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Figure 1. Diagram of epicardial mapping locations

Conclusion: Active GP could be identified dominantly in the inferior right area in left atrium.

Distribution of delayed potentials on the right ventricular endocardium in patients with late potentials on signal-averaged electrocardiograms due to arrhythmogenic right ventricular cardiomyopathy

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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a progressive inherited disease characterized by life-threatening ventricular arrhythmias, which is considered to be a primary protein abnormality. The purpose of this study is to clarify the distribution of delayed potentials (DPs) on the right ventricular endocardium in ARVC patients with ventricular tachycardias (VT) and late potentials (LPs) after QRS segment on the signal-averaged electrocardiograms (SAECG).

Methods: The studied population comprised 46 ARVC patients (mean age 50±15.8 years, 30 males and 16 females) with sustained or non-sustained VT who underwent programmed electrophysiological study. The SAECGs were recorded during sinus rhythm. LPs were defined positive when two of three parameters (total filtered QRS > 120 ms, root mean square voltage of the last 40 ms < 10, and duration of the low amplitude signals in the terminal portion of QRS > 30 ms) were fulfilled and low amplitude signals were noted on SAECG during continuous period consistent with ST segment in simultaneously recorded orthogonal XYZ ECGs. The distribution of DPs, fractionated electrograms, and double-potentials in the right ventricle (RV) evaluated by detailed endocardial mapping (3D electroanatomical voltage mapping and conventional mapping) during sinus rhythm was compared with the outcome of catheter ablation.

Results: Patients were positive for VT who underwent programmed electrophysiological study in 24 (54%) of 46 patients (80%). DPs, although they were not obtained in the remaining 12 patients (20%), were located in the RV basal area (100%), particularly in inferior and lateral wall in 30 patients (65%), RV basal septum in 13 patients (68%), RV septal area in 29 patients (63%), RV lateral area in 32 patients (69%), and RV apical area in 26 patients (57%). LPs on SAECG were positive in 37 of 46 patients (80%).

Conclusions: In ARVC patients, DPs were mainly located in the basal RV wall especially in the inferior region around tricuspid valvular annulus. We conclude that catheter ablation following endocardial mapping should be applied first in the RV interventricular wall in patients with LPs on SAECG.

Radiation exposure during electrophysiology procedures: results from the EPIC global survey


on behalf of Electrophysiologist International Community “EPIC” Alliance
Royal Brompton Hospital, London, United Kingdom; Cherry Hill United States of America; United States of America; Memorial Hospital-Monmouth Medical Center, Monmouth, New Jersey, United States of America; The New York Presbyterian Hospital, New York, United States of America; University of California, San Diego, San Diego, United States of America; University of California, San Diego, United States of America; Upstate University Hospital, Syracuse, Sweden; University of Washington, Seattle, United States of America

Background: Awareness of radiation exposure is variable among different settings of practice in invasive electrophysiology (EP) laboratories around the world.

Methods: We developed a web-based questionnaire with a total of 21 questions on individual practices focusing on radiation exposure during invasive EP procedures using a total of 8 questions aimed specifically at female cardiologists.

Results: A total of 165 physicians responses were received (50 female participants) with the majority of them located in the US (38%), Canada (8%), Italy (7%) and Germany (6%), while the remainder were from Europe, Asia and South America. Nearly 80% of participants were qualified cardiologists for more than 3 years (45% for more than 10 years). Clinical practices focused on device implantation (35%) and invasive EP procedures and ablation (57%), with the majority being the first-hand operator. Two thirds of participants collect radiation exposure on their procedures; with the majority recording time rather than dosage. Table 1 gives the self-reported average radiation time for various procedures. Personal radiation protection was mainly by wearing a two piece (77%) or single piece (25%) under table apron (73%), overtable shield (53%), lead glasses (35%), or the Plexiglas shield (9%). Radiation badges are used in various places (on or below the under table apron (73%), overtable shield (53%), lead glasses (35%), or the Plexiglas shield (9%). Radiation badges are used in various places (on or below the

Conclusions: This is the first global survey on radiation exposure and protection measures during EP procedures. Clinical practice and resulting exposure vary drastically worldwide, while measures for personal protection are mainly focused on lead aprons.

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Cavotricuspid isthmus radiofrequency catheter ablation (CTA RFA) is recommended for typical atrial flutter since it is safe and effective to maintain sinus rhythm, but the long-term outcomes have not been compared with those in patients with other types of atrial arrhythmia and/or other management. This study investigated the outcomes after CTA RFA for atrial flutter, expected to maintain sinus rhythm and possibly to reduce mortality and morbidity.

Methods: We examined the clinical course of 8,962 consecutive patients with atrial fibrillation and/or atrial flutter. The outcomes in 675 patients with CTA RFA for typical atrial flutter (in whom 32% had a pre-ablation history of atrial fibrillation) were compared with those in other patients.

Results: Complete cavotricuspid isthmus block was successfully obtained in 97% of the patients. Median follow-up was 534±113 days. Death (n=1,125), stroke/thromboembolic events (n=715) or bleeding events (n=791) were recorded in 2,035/8,962 patients. Kaplan-Meier analysis showed that patients who underwent CTA RFA had longer survival than other patients (p<0.0001) and higher net clinical benefit (freedom from combined death, stroke, thromboembolic and bleeding events, p<0.001). Using Cox proportional-hazards model, results remained significant after adjustment for age, CHADS2 and HAS BLED scores, use of cardiovascular medications and other confounders. Patients in the ablation group revealed lower risk of all-cause mortality (hazard ratios [HR] = 0.62, 95% confidence interval [CI], 0.40-0.78; p=0.0007), of stroke/thromboembolic events (HR=0.5, 95% CI, 0.32-0.79; p=0.0015), of bleeding events (HR=0.71, 95% CI, 0.52-0.96; p=0.03), resulting in a significant net clinical benefit (HR=0.67, 95% CI, 0.54-0.83; p=0.0002).

Conclusions: Atrial flutter with CTA RFA is independently associated with a lower mortality and morbidity as compared with other sustained atrial arrhythmias such as atrial fibrillation.
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**Table**

<table>
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<th>Year</th>
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<td>1550</td>
<td>1748</td>
<td>1903</td>
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<td>No of publicly available AEDs, available for the emergency dispatch centers, established in Copenhagen in 2007</td>
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<td>96</td>
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<td>OHCA's per square Km</td>
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<td>OHCA's covered by nearby AED, n (%) of all OHCA's</td>
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**P4119**

**Initiative for strategic placement of AEDs in a city center increases coverage of cardiac arrest sites**

**Methods:** All OHCA's in public from 1994 through 2010 and all publicly available AEDs in Copenhagen, Denmark, were geographically located. High-incidence areas of OHCA were defined as those with >1 arrest every 2 years, within a 100-m radius. All OHCA's occurring within a 100x100 area were counted as well as the number of AEDs in these areas. A registry of publicly available AEDs, available for the emergency dispatch centers, established in Copenhagen in 2007.

**Results:** We identified 114 high-incidence areas of OHCA, accounting for 18.3% (n=376) of the arrests in public. In 2005, 104 publicly available AEDs were placed in high-incidence arrest sites (however, these were not linked to the emergency dispatch center). By the end of 2010, 399 AEDs available to lay persons and the emergency dispatch center covered 35.1% of all high-incidence arrest sites (Table 1). Consequently, the potential number of patients who could be treated with an AED had grown more than 6-fold, from 11 (0.7%) to 91 (4.4%), in the same period.

**Conclusion:** Initiative for strategic placement of publicly available AEDs has increased coverage of OHCA high-incidence areas substantially, hereby raising the potential number of patients who could be treated with an AED and save addional lives.

**P4120**

**Electrocardiogram fails to identify high-risk individuals: analysis of a series of 50 sudden death cases**

**Methods:** Electrocardiogram (ECG) is an essential and easily available diagnostic test in the management of cardiomyopathies and channelopathies. We aim to explore the value of ECG for the diagnosis of SD.

**Results:** ECGs from 50 consecutive cases (age 36±20 years, 36 men) were reviewed by two independent reviewers and the final diagnosis. The ECG findings were compared with final diagnosis. Final diagnosis were hypertrophic cardiomyopathy in 13 patients, Brugada syndrome in 8 patients, LQT type 1 and 2 in 9 patients, respectively.

**Conclusion:** Despite the clear usefulness of ECG in the diagnosis of SD cases, it can be normal or unspecific in an important percentage of patients. In this sense, SD screening programs that include only a baseline ECG, could lead to a loss of sensitivity. A comprehensive study including cardiac imaging and genetic information, are also important besides ECG findings to achieve a definitive diagnosis.
Cardiac conduction system involvement in patients with steinert’s myotonic dystrophy

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Introduction: Steinert’s myotonic dystrophy (DM1) is an autosomal dominant genetic disease: male/female ratio is 1:1 and an affected parent has a 50% risk of transmitting the disease in each pregnancy. In Europe and North America it is the most common muscular dystrophy (1:8000 population). Affected patients have a lower life expectancy with an average age of death of 53 years and there is a correlation between the age of onset of dystrophy and age of death: respiratory failure and cardiovascular arrest are the main causes. The cardiac involvement is quite common, especially in the conduction system, which can sometimes cause sudden death.

Patients and methods: From January 2010 to September 2011 at our Centre 39 patients were evaluated with Steinert muscular dystrophy. The inclusion criteria was the confirmation of Steinert’s dystrophy by genetic analysis and clinical examination showing muscle strength with MRS (muscular impairment rating scale).

Results: 39 patients were evaluated: 21 males and 18 females aged between 22 and 73 years. 23.1% (n = 9) presented family history of sudden death, while 17.9% (n = 7) reported idiopathic or syncope. PR > 0.20s was observed in 26% (n = 11) and > 0.24s in 10.3%. A P-R > 0.24s, was shown to be influenced by patients’ age (p = 0.028), disease duration longer than two years (p = 0.02) and five years (p = 0.027), by severe neuromuscular involvement (p = 0.027), assisted walking (p = 0.028), evidence of obstructive lung disease (p = 0.043), presence of Supraventricular Premature Contractions, single (0.040) and couples (0.06) at Holter monitoring. Complete Left Bundle Branch Block was observed in 2 patients, and left anterior fascicular block in four (10.3%). The retrospective analysis of ECGs, disclosed an increase of PR in 20.5% of cases, and widening of QRS in 5.1%. The progression of AV conduction delay was showed to be influenced by sex (p = 0.032) and neuromuscular involvement (0.046). The development of Atrial Fibrillation was recorded in three patients. No significant abnormalities were found at Echocardiography.

Conclusions: We observed that an important involvement of the conduction system in the observed patients trend up to deteriorate quickly. Therefore it is essential that they can be assessed periodically. In addition to the ECG abnormalities also other parameters seems to be associated with an increased risk of sudden death: positive family history, pulmonary involvement and degree of neuromuscular involvement.

PICI during prolonged CPR: only patients with myocardial ischemia benefit

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Background: Acute myocardial ischemia with consecutive malignant arrhythmias is one major contributor to sudden cardiac death. Urgent revascularization (PCI) is the mainstay of treating ischemia-induced arrhythmias. After a successful cardiopulmonary resuscitation (CPR), consensus exists that patients with myocardial ischemia should undergo urgent PCI. It is, however, not known if in patients with prolonged CPR, PCI during CPR can improve outcomes.

Methods: In a retrospective analysis from a single center, all patients undergoing PCI during CPR were identified during a five-year period (02/2004-05/2009). The patient characteristics were analyzed and related to the survival of the patients.

Results: 32 patients were subjected to PCI during continued CPR (mean age, 64 y, 65% male). 12 patients had return of spontaneous circulation (38%). 4 patients survived to hospital discharge (12.5%), with a good functional status (Glasgow Outcome Scale 4 or 5). Survival to hospital discharge in patients undergoing PCI during CPR was lower compared to patients undergoing PCI directly after successful CPR (29% vs. 12%). In patients undergoing PCI during CPR, age, sex, comorbidities, and procedural variables (success of PCI) did not predict survival. However, the first detected heart rhythm during CPR was associated with outcome: no patient with asystole or electromechanical dissociation, but 4 of 11 patients with initial ventricular fibrillation, survived to hospital discharge (figure).

Conclusions: PCI during continued CPR can be helpful in patients with ventricular fibrillation as underlying arrhythmia. However, in 3 out of 11 patients survived to hospital discharge with a good neurologic result. All other patients did not benefit from revascularization during CPR.
Impacts of rewarming speed differences on outcomes of therapeutic hypothermia in out-of-hospital cardiac arrest: is rapid rewarming efficient?

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Background: Although therapeutic hypothermia (TH) has been reported to improve neurological outcomes of patients with out-of-hospital cardiac arrest (OHCA), procedures of TH remain to be established. Particularly, rewarming speed that maximizes protection afforded by TH has not been identified.

Methods: We analyzed data from 408 patients submitted to the multicenter registry of OHCA patients treated with TH from 2005 to 2009 in Japan. The patients were retrospectively divided into three groups according to rewarming speed: 53 patients with rewarming speed <2.0°C/12 hours (Rapid group), 54 patients with rewarming speed 2.0-1.9°C/12 hours (Moderate group), and 301 patients with rewarming speed <1.0°C/12 hours (Slow group). We defined favorable neurological outcomes as cerebral performance category 1 or 2.

Results: There was no significant inter-group difference in gender, age, and percentages of presence of bystanders, bystander cardiopulmonary resuscitation and ventricular fibrillation in initial ECG. Incidence of return of spontaneous circulation before admission and target temperature were also comparable between the three groups, but the duration of hypothermia at target temperature in the Rapid group was shorter than that in the other groups (26±11 hours for Rapid, 32±12 hours for Moderate, 33±13 hours for Slow, p<0.01). Both the mortality and the rate of favorable neurological outcomes in 30 days were not statistically different in all three groups (Figure 1A, 1B).

Conclusion: These results suggest that benefits of TH in terms of mortality and neurological outcomes are not affected by differences in rewarming speeds. TH with rapid rewarming (≥2.0 degrees C/12 hours) appears to be as efficient as the other rewarming protocols.

Cardiac screening of first-degree relatives after sudden cardiac death

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Purpose: Out-of-hospital cardiac arrest (OHCA) frequency is known to have circadian variation, but little is known about whether shockable heart rhythm (VF/pulseless VT) and survival among OHCA patients also show circadian variation.

Methods: Data from all OHCA in Copenhagen were collected from 1994-2010 including age, sex, initial heart rhythm and emergency medical system (EMS) response time. Occurrence of shockable heart rhythm and 30-day survival according to time of day were analyzed by logistic regression models, adjusted for sex, age and EMS response time.

Results: Of 6,766 patients included, 70.2% suffered OHCA at home. Median age among patients with and without initial shockable heart rhythm was 66 (IQR 55-76) and 73 (IQR 60-82) years, respectively. The median EMS response time was 5.0 minutes (IQR 4-7, Figure). Daytime OHCA (7 am to 3 pm) accounted for 43.5% (n=2945), evening OHCA (3 pm to 11 pm) for 27.8% (n=1856) and nighttime OHCA (11 pm to 7 am) for 18.7% (n=1265). Compared with nighttime, daytime and evening OHCA were positively associated with shockable heart rhythm (OR 1.90, CI 1.57-2.29; OR 1.76, CI 1.45-2.13) and increased 30-day survival (OR 1.62, CI 1.18-2.22; OR 2.06, CI 1.50-2.81), despite a constant EMS response time.

Conclusions: OHCA during daytime and evening are associated with higher occurrence of shockable heart rhythm and higher 30-day survival compared with OHCA during nighttime, indicating circadian variation of these parameters, despite constant EMS response time.
**Risk factors for sudden cardiac death: Results from the Nordic arrhythmogenic right ventricular cardiomyopathy registry**

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**Purpose:** Risk factors for sudden cardiac death (SCD) in arrhythmogenic right ventricular cardiomyopathy (ARVC) are not clear. We aimed to study this in a registry study of ARVC patients.

**Methods:** The study was based on a newly started Nordic ARVC registry including patients from centers in Denmark, Sweden and Norway. It was performed as a retrospective cross sectional case control study. The outcome definition was a composite as SCD, aborted SCD, electrical storms or appropriate implantable cardioverter-defibrillator (ICD) shocks. The inclusion criterion was a diagnosis of disease in Advanced or Intermediate task force criteria (TF2010).

The following factors were studied for their association with the outcome: age, gender, history (Hx) of syncope, Hx of atrial fibrillation, inverted T waves in ECG lead V5–V6, right ventricular outflow tract obstruction, pathogenic mutation, family Hx of sudden death, inducibility during electrophysiologic study, >500 ventricular premature complex (VPC) in Holter monitoring indicating sustained ventricular tachycardia, left ventricular tachycardia (VT), being an competitive athlete, right ventricular dilatation (TF2010), left ventricular ejection fraction <50%. All factors were primarily analyzed univariately using logistic regression, if they reached a univariate P-value <0.05 they were subsequently studied in a multivariable logistic regression model.

**Results:** The population was comprised of 129 patients of which 57% were male and 71% probands. The median age was 49 (IQR 38–59) years and 73% had a family history. Median retrospective follow up was 7 (IQR 4–12) years and during follow up there were 2 patients suffering SCD, 12 suffering aborted SCD, 6 patients suffering an electric storm and 25 patients experiencing appropriate ICD shocks.

Of the tested factors, epsilon waves on the ECG and Hx of VT were found to be univariately associated to the outcome. The other factors were not significantly associated. The odds ratios (OR) from the multivariable model were 3.4 (95%CI 1.2-9.7) for epsilon waves on the ECG and 8.4 (95%CI 1.8-38.6) for Hx VT. They differed only insignificantly from the ones found univariately.

**Conclusions:** In this registry study of risk factors for sudden cardiac death in ARVC we found that a presence of an epsilon wave on the ECG and a history of ventricular tachycardia were associated with the composite outcome of sudden cardiac death, aborted sudden cardiac death, electrical storms and appropriate ICD shocks.

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**Survival from inpatient cardiac arrest in a referral hospital for cardiology and cardiosurgery**

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**Purpose:** We sought to estimate survival from inpatient cardiac arrest at the Cardiac Surgery Center, a tertiary referral hospital for Cardiology and Cardiovascular Surgery.

**Methods:** We recorded cardiac arrests over a 48-month period, using the Utstein template. Our goal was to analyse the data of 32 patients treated with THT in a prospective, multicenter, observational study included 399 individuals who accepted a training in external defibrillation. All patients were treated with THT during THT (117±20 minutes, p<0.01) to deliver first shock with AED were found. At T0 and T2 mean intervention time was respectively 173±64 and 156±49 sec in CC-CPR group and 163±60 and 164±57 sec in S-CPR group. General knowledge score was significantly higher in CC-CPR group (p=0.049).

**Retention after CC-CPR training appears to be more effective at six months when compared to S-CPR in general population. It allows a faster delivery of first external electric shock and improves technical quality of the main elements of CPR.
P4134 Copeptin predicts neurological outcomes in out-of-hospital cardiac arrest survivors

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Purpose: Prognostic stratification is fundamental for selection of the most appropriate therapeutic strategy in cardiac arrest survivors. Current evidence on prognostic markers in cardiac arrest survivors is, however, still insufficient and the data on prognostic value of C-termproaposensin (copeptin) in these patients are lacking.

Methods: We analyzed a group of twenty-four out-of-hospital cardiac arrest survivors. All patients were treated by endovascular hypothermia, patients with ST-elevation myocardial infarction underwent direct percutaneous coronary intervention. Copeptin levels were measured in blood samples taken at admission using commercially available immunoassay. Neurological outcome was assessed at 30 days according to Cerebral Performance Category (CPC): CPC 1 - no neurological deficit, CPC 2 - mild to moderate dysfunction, CPC 3 - severe dysfunction, CPC 4 - coma, CPC 5 - death.

Results: Fifteen patients in our group survived with good neurological outcome (CPC 1-2). In this patient group, the copeptin levels at the time of hospital admission were significantly lower than the exercise group (CPC 3-4), four patients died (CPC 5). Levels of copeptin were significantly lower in patients with CPC 1-2 as compared with CPC 3-4, and CPC 5 (77.8±13.0 pmol/L, 251.4±52.4 pmol/L, and 300±5.11±3.4 pmol/L, respectively; P<0.001). ROC analysis has shown cut-off copeptin value for good neurological outcomes (CPC 1-2) <78.5 pmol/L, (100% specificity, 71.8% sensitivity) and cut-off value for poor outcomes (CPC 3-5) >170.4 pmol/L (100% specificity, 60% sensitivity). Copeptin levels significantly correlated with peak neuron-specific enolase (P<0.05) and time to return of spontaneous circulation (P<0.01). On the other hand, copeptin levels were comparable in patients with acute myocardial infarction and in patients with other cause of cardiac arrest.

Conclusion: Our data indicate that copeptin is a promising marker of neurological outcomes in out-of-hospital cardiac arrest survivors with significant prognostic value already at the time of hospital admission.

P4135 Survivors of sudden cardiac death with depression are not at significantly greater risk of recurrent arrhythmias and death

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Introduction: Although depression seems to be a marker for adverse prognosis and reduced survival after myocardial infarction it is currently unclear whether history of depression can be considered an independent risk factor for sudden cardiac death (SCD).

Methods: The Antiarrhythmics Versus Implantable Cardioverter Defibrillators (AVID) Trial (n=1016) was a multicenter trial comparing ICD (n=507) & anti arrhythmia treatments (AAD) (n=471) for secondary prevention of life-threatening ventricular arrhythmias and death (Sudden Cardiac Death (SCD)). Between February 2009 and January 2011, we had analyzed 1016 patients in the AVID trial. The Antiarrhythmics Versus Implantable Cardioverter Defibrillators (AVID) T rial (n=1016) was a multicenter trial comparing ICD (n=507) & anti arrhythmias and death. Current evidence on prophylactic use of ICDs offers impressive results by coupling the ECG and ICG. However, the required analysis may not be feasible in an emergency setting, when limited by the low processing power in any compact and low cost PAD. Cochran’s Q statistic was used to test the consistency of the results. The diagnostic algorithm indicated PEA, embedded in a compact PAD which simultaneously assesses ECG+ICG in real time offers encouraging results. The diagnostic algorithm indicated PEA, embedded in a compact PAD which simultaneously assesses ECG+ICG in real time offers encouraging results.

Conclusions: Current evidence on prophylactic use of ICDs offers impressive results by coupling the ECG and ICG. However, the required analysis may not be feasible in an emergency setting, when limited by the low processing power in any compact and low cost PAD. The analysis of the exercise population had shown that there is no difference for maximal and for exercise mTWA between the groups independently of the presence of ischemia. However, there is a significant difference in recovery phase: 29 (27-33) vs 36 (25-49) μV; p=0.0014 for ischemia vs no ischemia groups. The
heart rate increasing during the exercise was correlated with mTWA in recovery phase (RH = 0.22; p = 0.0001). The presence of necrosis zones has influenced mTWA in recovery phase.

To conclude, patients with ischemia in gated-SPECT seem to have a higher mTWA during recovery phase. However myocardial ischemia solely is not sufficient to induce an important mTWA.

Improved prognosis after implementation of chest compression device in out-of-hospital cardiac arrest

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Out-of-hospital cardiac arrest (OHCA) is associated with a poor prognosis. Following European Resuscitation Council Guidelines for Resuscitation 2010, application of several cardio-pulmonary resuscitation (CPR) devices may improve prognosis when used by well-trained providers. The load-distributing band (LDB) device (AutoPulse) was used for chest compressions during CPR. The aim of this study was to assess if there changes improved the outcomes after OHCA before and after implementation of LDB.

Methods: The study was carried out in the Emergency Medical Services from 2009 to 2011 based on analyzing 188 emergency call-out reports. Patients were divided into two groups: 83 patients, when LDB device was used during CPR, were included in the first group (CPR-A); 95 patients were included in the second manual CPR group (CPR-M). The primary endpoint was Return of Spontaneous Circulation (ROSC) at scene, but we also recorded survival to hospital admission. Groups were compared using IBM SPSS Statistics 19 software for odds ratio (OR) and relative risk (RR).

Results: We found that ROSC significantly increased after implementation of LDB device: 44 (52%) of 83 patients of CPR-A group and 24 (25.2%) out of 95 patients of CPR-M group (OR 2.32). On the other hand the probability of an adverse outcome in the group CPR-M was higher than in patients with CPR-A (RR 1.55). CPR duration median value made: 19.5 min for CPR-A group and 28 min for CPR-M group. Among patients who survived to hospital admission, 28 (33.7%) belonged to CPR-A group, and 17 (17.9%) to CPR-M group. No significant difference was found in age, gender and cause of out-of-hospital cardiac arrest.

Conclusions: The implementation of LDB device is associated with improved ROSC and survival to hospital admission after OHCA, therefore it is expedient to apply it in pre-hospital environment.

Normal limits of the adult electrocardiogram for ages 16-90 years

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Purpose: Normal limits for the adult electrocardiogram (ECG) have been determined in a good many studies, but they all carry their imperfections: study populations are often small, they do not cover the full range of ages or give data only for one sex, or they focus on only a limited set of parameters. In this study, we established age- and sex-dependent normal limits of the adult ECG, covering all ages for both sexes.

Methods: The study population included 13,364 by all evidence healthy individuals (ages ranging from 16 to 90 years, 55% men), taken from four population-based studies in The Netherlands. Standard 12-lead ECGs were available for all participants. All ECGs were processed by a well-validated computer program to obtain ECG measurements, including intervals, amplitudes, axes, and various left ventricular hypertrophy (LVH) indices. Normal limits were taken as the 2nd and 98th percentiles of the measurement distribution per age group. Additionally, continuous age-dependent percentile curves were estimated.

Results: Our study corroborates many findings of previous studies, but also provides more differentiated and detailed results, in particular for the older age groups. Age trends in normal values of the elderly were manifest for the QTc interval, 0.32 to 0.72, p=0.83) for the fQRS. The AUC for diagnosis of transmural wave enhancement was 0.58 for Q wave and 0.48 for fQRS. The AUC for diagnosis of subendocardial wave enhancement was noticed in 52 (43.0%) and subendocardial in 69 (57%) patients. AUC for diagnosis of transmural wave enhancement was 0.60 to 0.88, p=0.0001.

Conclusions: Normal limits for the adult ECG, exceeding previous studies in various aspects like the size of the study population, the range of the ages, and the scope of parameters. Our results demonstrate that diagnostic ECG criteria should be age- and sex-specific.

First validation of esophageal long-term electrocardiography as an alternative technique for long-term heart rhythm monitoring

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Introduction: Diagnosing arrhythmias by conventional Holter-ECG can be cumbersome because of small p-waves, which impair visual ECG interpretation. Moreover, computer-based arrhythmia detection in continuous ECG recordings only relies on R-R-interval detection as a surrogate marker for true atrial activity. Prolonged periods of rhythm monitoring have been suggested, in particular for the detection of paroxysmal atrial fibrillation. However, longer monitoring intervals without reliable detection of true atrial activity are a limitation of techniques such as implantable loop recorders. Esophageal long-term electrocardiography (eECG) offers a way out due to the anatomic vicinity of the esophagus to the atria and its favorable bioelectric properties.

Methods: We recorded long-term eECGs from 30 subjects with a novel miniaturized ECG recorder optimized for esophageal use. The device can be worn discretely behind the ear and continuously records two bipolar eECG channels (interelectrode spacings 60 and 15 mm) during 3 days with 500Hz sampling frequency and high-24 bit resolution. A soft-made of soft waterproof tissue protects the device, removal of the device during showering is unnecessary. Simultaneously, a conventional surface Holter-ECG was registered. We evaluated feasibility, signal quality and tolerance of this new method.

Results: eECG was 25 ± 30 recording lasting 21.9 ± 33.3 hours (max. 60 hours). Test persons were not limited in their daily activities (e.g. eating, speaking, exercising) and only complained mild discomfort during probe insertion, which subsided later on. No complications occurred. We recorded better signals (higher signal amplification) in the esophageal ECG compared to surface lead II (table 1). There was no difference in ventricular signal amplitudes, however we observed a tendency towards higher amplitudes in the esophageal lead.

Table 1. Comparison of signal amplitudes registered by esophageal and surface ECG

<table>
<thead>
<tr>
<th></th>
<th>Esophageal lead</th>
<th>Surface lead II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial signal amplitude [mV]</td>
<td>0.71±0.633</td>
<td>0.13±0.035</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Ventricular signal amplitude [mV]</td>
<td>1.32±1.03</td>
<td>1.28±0.58</td>
<td>0.068</td>
</tr>
</tbody>
</table>

Conclusion: Esophageal long-term electrocardiography has the potential to overcome current limitations of conventional Holter-ECGs. In particular, excellent atrial signal quality will improve automatic wave detection and therefore will facilitate accurate analysis of true atrial activity.

Relationship of fragmented QRS and delayed contrast enhanced cardiovascular magnetic resonance (DE-CMR) imaging in patients with myocardial infarction


Background and objective: Q waves on a 12-lead electrocardiogram (ECG) are considered the classical hallmark of myocardial infarction. However Q waves may regress and disappear with time especially in patients treated with reperfusion therapy despite there being continued evidence of myocardial scarring. A prior study has suggested that the fragmented QRS complex on an ECG is a highly sensitive and specific marker of myocardial scar on a nuclear stress test. We investigated the association of the fragmented QRS complex versus the Q wave with myocardial scar detected by delayed contrast enhanced cardiovascular magnetic resonance (DE-CMR) imaging in patients with myocardial infarction.

Methods: ECGs of 130 subjects with myocardial infarction who underwent a DE-CMR were analyzed. Myocardial infarctions were labeled transmural if hyperenhancement extended throughout the entire LV wall at any point. Q wave was defined as the Q wave (interelectrode spacings 60 and 15 mm) during 3 days with 500Hz sampling frequency and high-24 bit resolution from the Thrombolysis In Myocardial Infarction (TIMI) group in the primary analysis which defines QW MI as pathologic QW (>30 ms) in >2 coronary territories. Prolonged periods of rhythm monitoring have been suggested, in particular for the detection of paroxysmal atrial fibrillation. However, longer monitoring intervals without reliable detection of true atrial activity are a limitation of techniques such as implantable loop recorders. Esophageal long-term electrocardiography (eECG) offers a way out due to the anatomic vicinity of the esophagus to the atria and its favorable bioelectric properties.

Results: The final diagnosis was non-ST segment elevation myocardial infarction in 38 (28.2%) and ST segment elevation myocardial infarction in 92 (70.8%) patients. Delayed enhancement was observed in 121 (93.1%) patients. Transmural enhancement was noticed in 52 (43.0%) and subendocardial in 69 (57%) patients. The sensitivity and specificity of the Q wave and iQRS for diagnosing delayed enhancement are 58.7% vs. 91.1% and 88.9% vs. 33.3%. The areas under the ROC curves (AUC) for diagnosis of delayed enhancement were 0.738 (95% confidence interval, 0.60 to 0.88, p=0.02) for the Q wave and 0.52 (95% confidence interval, 0.32 to 0.72, p=0.83) for the iQRS. The AUC for diagnosis of transmural enhancement was 0.58 for Q wave and 0.48 for iQRS.

Conclusion: The iQRS has a higher sensitivity than the Q wave but lower specificity for detection of delayed enhancement. The iQRS is not superior for the diagnosis of myocardial scar or its transmurality than Q wave.
Purpose: Some ECG changes are related to left ventricular dysfunction (LVD). Frontal plane ST-segment and QRS complex abnormalities as predictors of extent of necrosis and left ventricular dysfunction assessed by 3 Tesla cardiac MR.

Methods: Consecutive patients (pts) referred for 3 Tesla CMR evaluation constituted the study population. A 12-lead ECG was obtained in the same day of the CMR scan. QRS complex duration, abnormal Q waves, and ST-segment morphology (normal=upslope ST-segment; or abnormal=ST-desepmmression or downslope ST-segment) on leads DI or DII (the one with the largest R wave) and aVF leads were studied. These leads were selected due to the usual projection of the QRS complex and ST-segment, and to evaluate the usefulness of this simplified ST methodology. For detection of the presence and extent of infarcted myocardium, a breath-hold, T1-weighted, contrast-enhanced inversion-recovery segmented gradient echo and a short-axis stack of segmented T1-weighted images were obtained. The images were reviewed using a Siemens method. LV dysfunction was defined as LV ejection fraction less than 50%.

Results: Seventy consecutive patients, 48 male, mean age 64±15y, were included. The most common indication for CMR was coronary artery disease and chronic valvular disease. Thirty four pts had LVD and 44 pts had LGE. QRS duration was longer in pts with LV dysfunction as compared to patients with preserved LV function (114±27 ms vs. 97±19 ms, p < 0.003). Overall, abnormal Q-waves and ST-segment abnormalities on DI-II were used as a major criteria. Minor repolarization criteria were present in 38% of the patients with the TF94 and in 89% with the TF10, and major depolarization signs (epsilon waves or QRS terminal S-wave) was present in 38% of the patients with the TF94 and in 89% with the TF10. Patient had a major criteria. Minor repolarization criteria were present in 38% of the patients with the TF94 and in 89% with the TF10, and major depolarization signs (epsilon waves or QRS terminal S-wave) was present in 38% of the patients with the TF94 and in 89% with the TF10.

Conclusions: The current hypothesis generating study demonstrates for the first time that chronic ST-segment abnormalities on DI-II are strongly related to LVD and to the extent of myocardial necrosis as assessed by CMR.

Purpose: Epicardial fibrillation (VF) is the major cause of cardiac death. There are many studies to investigate the mechanism to generate and maintain VF. However, the mechanism has not been clear yet. During VF, scroll wave rotate around a line of phase singularly called filament. Recently, increased opportunity for self-termination of VF under moderate hypothermia was demonstrated. In this study, we investigated the possibility of VF termination in a cooling heart using computer simulation.

Methods: We performed computer simulations to observe the behavior of scroll wave propagation. The left and right ventricular slab models were designed to reflect part of the ventricular wall with a thickness of 10 mm and 5 mm, respectively. The ventricular walls were composed of discrete myocardial units: 10 million units for left ventricle and 5 million units for right ventricle. The membrane kinetics in the simulated myocardium was represented by modified Luo-Rudy type equations, which can simulate the effects of myocardial cooling. Electrical heterogeneity and rotational aristroropy through the ventricular wall were also incorporated into the model. Scroll waves were generated using an S1-S2 cross-field stimulation. Then, we simulated scroll wave reentry using normothermia (37°C), moderate hypothermia (32°C), and severe hypothermia (27°C) heart model.

Results: The scroll wave filament, expressed as a continuum of phase singularities, within the ventricular wall were stable, and therefore the scroll wave reentry sustained. In the case of global myocardial cooling, prolongation of action potential duration (APD) and reduction of conduction velocity locally was observed. In addition, fluctuations in the filament were increased with time, and finally the scroll wave reentries were terminated. This might be due to heterogeneous increase in the APD through ventricular wall by cooling.

Conclusion: Our simulation results suggest that heterogeneous myocardial cooling from the epicardial surface can increase the opportunity of self-termination of VF.

A left-to-right intertrial frequency gradient during atrial fibrillation can be detected using standard 12-lead ECG

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Introduction: The presence of an intertrial frequency gradient may be used to guide catheter ablation of atrial fibrillation (AF). In the 12-lead ECG, Lead V1 has shown to reflect right atrial (RA) activity, but a reliable tool for non-invasive assessment of atrial frequency exceeding 1 Hz could be detected using spatiotemporal QRST cancellation and Welch periodogram.

Results: Mean left- and right atrial fibrillatory frequency was 5.6±1.2 and 4.3±1.8 Hz, respectively. Five cases had a left-to-right frequency gradient of at least 1 Hz. The most common indication for CMR was coronary artery disease and chronic valvular disease. Thirty four pts had LVD and 44 pts had LGE. QRS duration was longer in pts with LV dysfunction as compared to patients with preserved LV function (114±27 ms vs. 97±19 ms, p < 0.003). Overall, abnormal Q-waves and ST-segment abnormalities on DI-II were used as a major criteria. Minor repolarization criteria were present in 38% of the patients with the TF94 and in 89% with the TF10, and major depolarization signs (epsilon waves or QRS terminal S-wave) was present in 38% of the patients with the TF94 and in 89% with the TF10.

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Methods: We performed computer simulations to observe the behavior of scroll wave propagation. The left and right ventricular slab models were designed to reflect part of the ventricular wall with a thickness of 10 mm and 5 mm, respectively. The ventricular walls were composed of discrete myocardial units: 10 million units for left ventricle and 5 million units for right ventricle. The membrane kinetics in the simulated myocardium was represented by modified Luo-Rudy type equations, which can simulate the effects of myocardial cooling. Electrical heterogeneity and rotational aristroropy through the ventricular wall were also incorporated into the model. Scroll waves were generated using an S1-S2 cross-field stimulation. Then, we simulated scroll wave reentry using normothermia (37°C), moderate hypothermia (32°C), and severe hypothermia (27°C) heart model.

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Role of home monitoring in effective device management of patients with implantable cardioverter-defibrillators: a personalized randomized trial

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Introduction: Telemedicine attracts the attention of health care providers and payers due to possibly increased safety and cost-effectiveness issues. Objective: Comparison of the standard approach in the outpatient follow-up after implantation of cardioverter-defibrillator (ICD) with the remote follow-up using the access to the Home Monitoring® (HM) service (BIOTRONIK) with respect to workload, efficiency and safety in ambulatory care. Methods: 198 patients (67.12 years, 81% men) with newly implanted dual or single chamber ICD (165/35) were followed prospectively. One-third represented patients with primary prevention indications. Mean follow-up was 620±215 days. Patients were randomized to standard outpatient management (HM-) group and remotely monitored group (HM+). We evaluated regular outpatient visits, emergency visits, delivered shock therapy, and their adequacy and hospitalization associated with the ICD. Geographical data and availability of the access to the cardiology department were also analyzed. Results: Both groups of patients were comparable with respect to the demographic data, clinical data and parameters of the ICD with significant difference only in the representation of single and dual chamber devices between the groups. Almost two-thirds of the total 621 outpatient controls were carried out in the HM- group. The number of planned inspections decreased by more than 40% in the HM+ group, but the number of extra controls with the physician assistance called upon the inspection of HM messages significantly increased. Mortality did not differ significantly in both groups as well as the number of hospitalized patients and patients with delivered shock therapy. The proportion of inadequate shocks, however, was significantly reduced in the HM+ group. Conclusion: Home Monitoring system proved to be effective in reducing the number of planned visits and the proportion of inadequate shock therapy with no impact on the overall mortality in our patient group. Patients with poorer accessibility of the adequate medical management tend to be monitored remotely.

IN-STENT-RESTENOSIS AND INVASIVE CORONARY IMAGING

Higher stroke rate in patients undergoing elective PCI for in-stent-lesions in clinical practice in Europe: results of the EHS PCI registry

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Background: Although in-stent-lesion (ISR) decreased due to better techniques, we expect significant numbers of patients suffering from ISR due to the increased overall number of PCIs. Little is known about the treatment details of ISR in elective PCI in clinical practice in Europe. Methods: Between 2005 and 2008, 47,407 consecutive patients undergoing PCI were enrolled in the PCI-Registry of the Euro Heart Survey to document patient characteristics, PCI details and hospital complications. We examined the differences in treatment of ISR versus de novo-lesions in elective PCI. Results: A total of 22,917 patients underwent elective PCI, in 1,835 (8.0%) had ISR. Patients with ISR were younger, more often male, more often had prior MI or CABG and diabetes. They were more likely to receive unfractionated heparin rather than LMWH. No differences were found for the use of GP Ib/IIa blockers, while bivalirudin was more frequently administered in patients with ISR. Patients with ISR got stents in 75%, of which 3/4 were DES. In patients with de novo-lesions, 95.4% received stents, with 48.3% DES. There were no differences in hospital mortality between both groups, however death/MI/stroke was significantly higher in patients undergoing PCI for ISR (1.4% vs 0.9%). Conclusions: Patients undergoing elective PCI for ISR were younger and had more comorbidities. They more often received DES. In hospital complications were low, however the rate of death/MI/stroke was higher in ISR mainly due to a higher rate of stroke.

The optimal strategy for restenosis with stent fracture after drug-eluting stent implantation: 1st generation DES vs. 2nd generation DES

Kurashiki Central Hospital, Kurashiki, Japan

Background: Stent fracture is related to restenosis after drug-eluting stent (DES) implantation. As percutaneous coronary intervention (PCI) studies for complex lesions increased, those for stent fracture-related restenosis also increased. However, the optimal PCI strategy for such restenosis remains unclear. We compared the results of PCI with 1st generation DES (palmitel-butel-eluting stent, paclitaxel-eluting stent) and 2nd generation DES (zotarolimus-eluting stent, everolimus-eluting stent, biolimus-eluting stent) for restenosis with stent fracture after DES implantation. Method: From November 2002 to December 2010, 8797 patients with 11467 lesions underwent DES implantation successfully. Of these, 9329 lesions were angiographically followed after 6 to 8 months (midterm f/u) and 6682 were followed at 12 months after midterm f/u. Stent fracture occurred at 471 lesions (471/9229, 5.0%) and that with restenosis occurred at 212 lesions. Of these 212 lesions, target lesion revascularization (TLR) by PCI with 1st generation DES or 2nd generation DES was performed on 73 lesions. Results: Data are shown in the table. At midterm f/u, the rates of restenosis and TLR were significantly lower after restenting with 2nd generation DES than with 1st generation DES. Conclusions: Restenting with 2nd generation DES could be an acceptable treatment for restenosis with stent fracture after DES implantation.

Coronary flow velocity and fluid shear stress predict late catch-up after sirolimus-eluting stent implantation

1Yokosuka Kyosai Hospital, Cardiovascular Center, Yokosuka, Japan; 2Tokyo Medical and Dental University, Department of Cardiology, Tokyo, Japan

Recent studies have suggested the possibility of late catch-up after sirolimus-eluting stent (SES) implantation. This study sought to assess predictive values of coronary flow velocity and shear stress throughout the vessel for angiographic catch-up after SES implantation. Methods and Results: A total of 520 study patients (age 66±11, means/SD, men n=345, women n=175) with stable angina underwent successful implantation of SES for de novo lesions. Of these, 9329 lesions were an- giographically followed after 6 to 8 months (midterm f/u) and 6682 were followed at 12 months after midterm f/u. Stent fracture occurred at 471 lesions (471/9229, 5.0%) and that with restenosis occurred at 212 lesions. Of these 212 lesions, target lesion revascularization (TLR) by PCI with 1st generation DES or 2nd generation DES was performed on 73 lesions. The results of PCI with 1st generation DES (sirolimus-eluting stent, paclitaxel-eluting stent) and 2nd generation DES (zotarolimus-eluting stent, everolimus-eluting stent, biolimus-eluting stent) for restenosis with stent fracture after DES implantation. Background: Stent fracture is related to restenosis after drug-eluting stent (DES) implantation. As percutaneous coronary intervention (PCI) studies for complex lesions increased, those for stent fracture-related restenosis also increased. However, the optimal PCI strategy for such restenosis remains unclear. We compared the results of PCI with 1st generation DES (palmitel-butel-eluting stent, paclitaxel-eluting stent) and 2nd generation DES (zotarolimus-eluting stent, everolimus-eluting stent, biolimus-eluting stent) for restenosis with stent fracture after DES implantation. Method: From November 2002 to December 2010, 8797 patients with 11467 lesions underwent DES implantation successfully. Of these, 9329 lesions were angiographically followed after 6 to 8 months (midterm f/u) and 6682 were followed at 12 months after midterm f/u. Stent fracture occurred at 471 lesions (471/9229, 5.0%) and that with restenosis occurred at 212 lesions. Of these 212 lesions, target lesion revascularization (TLR) by PCI with 1st generation DES or 2nd generation DES was performed on 73 lesions. Results: Data are shown in the table. At midterm f/u, the rates of restenosis and TLR were significantly lower after restenting with 2nd generation DES than with 1st generation DES. Conclusions: Restenting with 2nd generation DES could be an acceptable treatment for restenosis with stent fracture after DES implantation.
Virtual histology intravascular ultrasound comparison of neointimal morphology of in-stent restenosis with drug eluting stents versus bare metal stents

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Background: The process of in-stent neointimal hyperplasia (NIH) between drug-eluting stents (DES) and bare metal stents (BMS) might be different. We compared the composition of in-stent NIH between BMS and DES using Virtual Histology Intravascular Ultrasound (VH-IVUS).

Methods and Result: VH-IVUS was performed in 63 patients (BMS 40 and DES 23) who underwent coronary revascularization because of in-stent restenosis. The region of interest was placed between the luminal border and the inner border of the struts. NIH tissue composition was reported as percentages of NIH area: percent fibrous (%FI), percent fibrofatty (%FF), percent necrotic core (%NC), percent dense calcium (%DC). Mean follow-up times between stent implantation and VH-IVUS were 874 [150-204] days for BMS treated lesions and 694±822 days for DES treated lesions (n.s.). At the sites of stent distal edge, stent proximal edge and in-stent minimum lumen area, %NC volume was higher in DES than in BMS (p=0.02). All %FI, %FF and %NC volume was lower in DES than in BMS (64±12% vs. 70±13%, p=0.016), whereas %NC volume was higher in DES than in BMS (11±5% vs. 8±6%, p=0.02).

Conclusion: VH-IVUS analysis demonstrated that the composition of NIH was different between DES and BMS, suggesting that the process of in-stent NIH in DES and BMS is diverse.

Predictors of neointima hyperplasia in in-stent restenosis

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Aim: The evaluation of expression and quantity of the miRNA-145, proteic modifications of extracellular matrix in in-stent restenosis as well as of circulating levels of some principal inflammatory markers.

Material and Methods: The expression and quantity of microRNA-145 (muscle cell phenotype marker), metalloproteinase 2 (MPT2) and its specific tissue inhibitor (TIMPT2), fibrillar collagen type I content were assessed in media and neointima of the arterial segment belonged to bare-metal restenosis taken from died 11 patients using following methods: hybridization in situ, confocal microscopy, immunofluorescent microscopy with specific monoclonal antibodies, PCR in realtime. In the blood of 22 patients made ISR averagely after 6 months before and 48h after stent implantation. Gene transcript levels were determined by VH-IVUS analysis using ELISA method and PLAC-test, outcomes being compared with indices obtained from 33 patients without ISR (control series).

Results: The in-stent restenosis evolution has been associated with micro-ARN145 expression decrease by up 90% in coronary media, correlatively to ISR degree and to number of smooth muscle cell with secretory (synthetic) phenotype migrated and accumulated in neointima. Extracellular matrix reorganization in ISR was basically due to fibrillar collagen I degradation, and the denaturated collagen progressively accumulated in media and neointima, a process accompanied by external elastic lamina perforation. To be noted a significant rise (until 4-times) of MPT2 quantity while TIMPT2 content respectively reduced leading to a marked MPT2/TIMPT2 ratio elevation. Development ISR after 6 months since angioplasty is underlined by a potentiated inflammation inasmuch blood proinflammatorycytokines and CRP levels were higher than control pattern by 28-52%. Endothelium inflammation marker, Lip-LP2A, rose above control value by 42%.

Conclusions: 1) The expression and quantity of smooth muscle cell phenotype marker, micro-ARN145, are reduced in media of ISR artery, that correalted with neointimal hyperplasia level. 2) Extracellular matrix reorganization in ISR is triggered by fibrillar collagen degradation, which facilitates the cell migration and neointima hyperplasia. 3) Negative coronary remodeling associating ISR is link to inflammation activation exhibited by significant increase of TNF-alpha, IL-1, IL-6, CRP and Lip-LP2A in the blood, which can be estimated as predictors of risk of the stent re-oclusion.

Difference in clinical restenosis rates between sirolimus carbide and uncoated bare metal stents

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Purpose: Bare metal stent (BMS) implantation triggers a foreign body reaction resulting in neointima formation and restenosis. Silicon carbide coating (SiC) shields the metal from both circulating blood and the vessel wall. We investigated whether this coating decreases clinically target revascularization (TLR).

Methods: Two commercially available L-605 Co Cr BMS (Stent A: amorphous SiC coating and stent B: uncoated) were implanted in 2731 patients over two consecutive 18 month periods (2006-2008). Diabetics and patients presenting with restenosis (25%) were excluded as in those patients drug eluting stents were used. TLR rates were evaluated at 1 year post PCI.

Results: Procedural and outcome data are presented in the table. Multiple logistic stepwise backward regression analysis identified post-PCI minimal luminal diameter (adjusted odds ratio 0.56; 95% CI [0.42-0.73]; P<0.001), total implanted stent length (1,01 [1.00-1.02]; P=0.003), NSTEMI unstable angina (1.89 [1.41-2.54]; P<0.001), stent A (1.62 [1.20-2.18]; P=0.002) and triple vessel PCI (2.68 [1.02-7.05]; P=0.045) as significant independent predictors for clinical TLR. Although non-significant, non-compliant balloon post-dilatation (0.66 [0.35-1.24]; P=0.20) was kept in the model for accuracy on an indication to post-dilatation over the study period. Hosmer & Lemeshow goodness of fit P-value was 0.35. Because 2.0-3.0 mm stents A had lower strut thickness (60 µm versus 80 µm), subgroup analysis (n=2382 lesions) was performed. Higher clinical TLR rates for stent A persisted in this small stent subgroup (1.62 [1.17-2.23]; P=0.003).

Conclusions: Two primary hypothesis, SiC-coated BMS implantation resulted in significantly higher clinical TLR rates.

Changes in early cardiac gene transcript levels in peripheral blood mononuclear cells after percutaneous coronary intervention and their relationship to restenosis

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Purpose: Early cardiac genes such as myocardin, GATA4 and Nkx2.5 play a role in both embryonic cardiovascular development and adult cardiovascular disease. In peripheral blood they are expressed in circulating bone marrow derived cardiac progenitor cells which are of the mesenchymal cell type. The impact of circulating cardiac progenitor cells expressing early cardiac genes on in-stent restenosis has not been investigated. We evaluated transcript levels of the early cardiac genes myocardin, GATA4 and Nkx2.5 in peripheral blood mononuclear cells (PBMCs) in relation to in-stent restenosis after percutaneous coronary intervention.

Methods: Thirty one patients (aged 65.9±8.9 years) with stable angina who underwent percutaneous coronary intervention (PCI) with bare-metal stents (BMS) were evaluated. Follow-up coronary angiography was performed 3-9 months later. Blood samples were taken before and 48h after stent implantation. Gene transcript levels were determined by quantitative reverse transcriptase-PCR (qRT-PCR).

Results: Significant negative correlations were found between transcript level changes expressed as fold induction 48h after stent implantation of myocardin (r=-0.81, p=0.001), GATA4 (r=-0.76, p=0.001), Nkx2.5 (r=-0.75, p=0.001) with restenosis (25%) were excluded as in those patients drug eluting stents were used. Follow-up angiography was performed 3-9 months later. Blood samples were taken before and 48h after stent implantation. Gene transcript levels were determined by quantitative reverse transcriptase-PCR (qRT-PCR).

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Conclusions: Early cardiac gene transcript levels change in PBMCs 48h after PCI show a negative relationship with in-stent late luminal loss.

Transcript levels were increased in PBMCs after stent implantation in patients with restenosis, defined as luminal diameter stenosis of >50% on follow-up angiography (n=17), were found to be downregulated. Transcript level changes expressed as fold induction 48h after stent implantation, while in patients with restenosis, defined as luminal diameter stenosis of >50% on follow-up angiography (n=17), were found to be downregulated. Transcript level changes expressed as fold induction 48h after stent implantation, while in patients with restenosis, defined as luminal diameter stenosis of >50% on follow-up angiography (n=17), were found to be downregulated. Transcript level changes expressed as fold induction 48h after stent implantation, while in patients with restenosis, defined as luminal diameter stenosis of >50% on follow-up angiography (n=17), were found to be downregulated.
No harmful effect of stem cell mobilization by granulocyte-colony stimulating factor on restenosis or late luminal loss after sirolimus-eluting stent implantation

Purpose: We evaluated the effects of stem cell mobilization by granulocyte-colony stimulating factor (G-CSF) on neointimal growth after sirolimus-eluting stent (SES) implantation.

Methods: The present double-blinded randomized placebo-control study that primarily evaluated the effect of stem cell mobilization by G-CSF on endothelial function after SES implantation assigned patients to the G-CSF group (n=50) or the placebo group (n=50). After successful SES implantation, patients received subcutaneous injection of G-CSF (300 mg daily) or saline for 5 days. Follow-up angiography was performed 9 months after SES implantation.

Results: Plasma CD34+ cell level did not differ between the 2 groups at baseline (0.94±0.55 vs. 0.93±0.68) L/L (p=0.96). It significantly increased after G-CSF injection (0.94±0.55 vs. 18.3±13.55) L/L (p<0.001) but did not in the placebo group (0.93±0.68) L/L vs. 1.35±2.36) L/L (p=0.22). Follow-up angiography was performed in 41 patients (82%) at 290±22.6 days in the G-CSF group and 46 patients (92%) at 287±10.3 days in the placebo group (p=0.14 and p=0.18, respectively). No death or myocardial infarction was observed in the study participants during follow-up. There was no significant difference in restenosis rate between the 2 groups (0.0% vs. 65%), (p=0.10). Late luminal loss was not significantly different (0.17±0.25 mm vs. 0.30±0.36 mm, p=0.06). Regression analysis showed no significant correlation between plasma CD34+ cell level after study drug injection and late luminal loss at follow-up (r = -0.14, p=0.21).

Conclusion: Stem cell mobilization by G-CSF does not increase restenosis or late luminal loss after SES implantation.

P4155 Mobilization of CD34+KDR+ cells among circulating progenitors predicts bare-metal stent restenosis

Purpose: We performed a multicentre prospective study which included 156 patients undergoing elective PCI with bare-metal stent (BMS). The endothelial lesion was assessed by the enumeration of circulating endothelial cells (CEC). Endothelial regeneration was evaluated by enumeration of circulating CD34+ progenitor cells (PC) and CD34+KDR+ endothelial progenitor cells (EPC). Measurements were performed before PCI (H0), 6 and 24 hours (H6 and H24) after. Dynamic changes were evaluated by calculating delta (delta) of each marker. The primary and secondary end-points of the study were clinical target lesion revascularizations (TLR) and major adverse cardiovascular events (MACE) at 6 months follow-up.

Results: During follow-up, 28 MACE were recorded including 27 TLR. PCI induced a significant rise in CEC, CD34+ PC and CD34+KDR+ EPC. Baseline, H6 vs. H24, the proportion of CD34+KDR+ EPC mobilized among PC determines the risk of restenosis after drug-eluting stent implantation; furthermore, that improvement of insulin resistance may contribute to prevent coronary restenosis after drug-eluting stent implantation.

Conclusion: In response to PCI, rather than the extent of the endothelial injury, the proportion of CD34+KDR+ EPC mobilized among PC determines the risk of in-stent restenosis and MACE.

P4156 Severe insulin resistance is a predictor of restenosis after drug-eluting stent implantation

Purpose: Even in the drug-eluting stent era, the high restenosis rate in hemodialysis patients remains unresolved. We compared the mid-term angiographic outcomes of de novo coronary artery lesions treated with sirolimus-eluting stents (SES), paclitaxel-eluting stents (PES), zotarolimus-eluting stents (ZES), and everolimus-eluting stents (EES) in hemodialysis patients.

Methods: From December 2003 to April 2011, 551 lesions in 337 hemodialysis patients were treated with drug-eluting stents exclusively and successfully. Of these lesions, 338 lesions in 225 (66.8%) hemodialysis patients who had undergone 8-month angiographic follow-up were analysed.

Results: Binary restenosis rates were 26.0% in SES, 25.3% in PES, 30.0% in ZES, and 18.7% in EES. Baseline, H6 vs. H24, the proportion of CD34+KDR+ EPC mobilized among PC determines the risk of restenosis after drug-eluting stent implantation; furthermore, that improvement of insulin resistance may contribute to prevent coronary restenosis after drug-eluting stent implantation.

Conclusion: Severe insulin resistance is a predictor of restenosis after drug-eluting stent implantation.
Impaired production of anti-atherosclerotic macrophages, were decreased in R+ compared to R-(Table). and IL10 were not different between the two groups. However, IL10/CD163 ratio of index PCI and after 9-month medical treatment. GPA, CD14, CD163, diabetes mellitus, 4.0; hypertension, 4.5; hypercholesterolemia, 1.4 and hyperglycemia, 7.

Conclusion: Our primary results showed that hs-CRP and genetic factors are clinical predictors of restenosis, among them, eNOS polymorphism was more powerful. Interestingly, these results demonstrated that traditional risk factors are more powerful that the novel one for predicting ISR. The final result is pending with larger population.

**P4159**

Impaired production of anti-atherosclerotic interleukin-10 by macrophage within culprit coronary plaque in diabetic patients with restenosis after primary PCI

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**Purpose:** Coronary intraprocedure hemorrhage (IPH) accelerates atherosclerosis through the dual metabolic stresses of cholesterol-enriched erythrocyte membranes and prooxidant hemoglobin (Hb). IPH is frequently observed in vulnerable plaque, especially in diabetic ACS patients. Extracellular Hb are cleared exclusively by macrophages with scavenger receptor CD163. These macrophages can counteract atherogenicity of IPH by secreting anti-atherosclerotic cytokine interleukin (IL)-10. We investigated IPH, macrophage phenotype, and IL-10 production in coronary plaques from ACS patients with diabetes, in association with bare metal stent (BMS) restenosis after primary PCI.

**Methods:** In 23 ACS patients with diabetes (HbA1c(NGSP)>6.5% or HOMA-IR>2.5), atherothrombotic debris was retrieved using filter-based distal protection device (Filter), during primary PCI with BMS implantation. The debris was stained with antibodies to CD163 (Hb scavenging macrophage), CD14 (proinflammatory macrophage), glycoprotein A (IPA, intraplaque hemorrhage) and IL-10. These debris parameter and conventional coronary risk factors were compared between patient with angiographic restenosis (R+, n=4) and those without restenosis (R-, n=19), after 9-month optimal medical treatment.

**Results:** Restenosis rate were 17.4%. Conventional risk factors, such as diabetes, dyslipidemia and hypertension were not different between the 2 groups, at the time of index PCI and after 9-month medical treatment. GPA, CD14, CD163, and IL-10 were not different between the two groups. However, IL10/CD163 ratio, an anti-atherosclerotic cytokine produced by capacity of Hb scavenging macrophages, were decreased in R+ compared to R- (Table).

**Immunostaining results**

<table>
<thead>
<tr>
<th></th>
<th>GPA (%)</th>
<th>CD14 (%)</th>
<th>CD163 (%)</th>
<th>IL10 (%)</th>
<th>IL10/CD163</th>
</tr>
</thead>
<tbody>
<tr>
<td>R+ (n=4)</td>
<td>13.0±7.6</td>
<td>19.6±8.3</td>
<td>39.6±13.2</td>
<td>33.3±17.8</td>
<td>0.92±0.54</td>
</tr>
<tr>
<td>R- (n=19)</td>
<td>21.9±14.6</td>
<td>25.1±13.0</td>
<td>38.3±19.8</td>
<td>47.3±28.3</td>
<td>2.11±1.24</td>
</tr>
</tbody>
</table>

R+: patients with restenosis; R-: patients without restenosis; NS: not significant.

**Conclusions:** Anti-atherosclerotic IL-10 production by Hb scavenging macrophages are impaired in diabetic patients with restenosis after primary PCI.

**P4160**

Reseeding of a decellularized arterial matrix for restenosis research

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**Purpose:** Aim of this study was to produce an in vitro test platform for restenosis research by reseeding of a natural, completely acellular arterial matrix with human endothelial and smooth muscle cells.

**Methods:** Freshly, surgically excised segments of rabbit aorta were obtained for decellularization. After verification of decellularization, a bare metal stent (DRIVER, Medtronic, 30 mm length, 4 mm diameter) was implanted and the segment was reseeded with human coronary artery endothelial (HCAEC) and human coronary artery smooth muscle (HCASMC) cells. Reseeding was performed in 6-well plates and reseeding periods with cell numbers of 0.5 x 10^6 for all at least three months. Subsequently, segments underwent histochemical (HE and EVG staining), immunohistochemical and PCR characterization by detection of CD31 (for HCAEC) and alpha smooth muscle actin (for HCASMС), respectively.

**Results:** By reseeding, cells formed a confluent monolayer after 14 days and a multitude of layers after three months. Adhesion of cells did not differ between stented and non-stented segments, revealed by HE and EVG staining. RT-PCR analysis of the reseeded vessels showed distinct bands for HCAEC-specific (CD31) and HCASMС-specific (α-smooth muscle actin) primers. Detection with CD31 and α-smooth muscle actin specific antibodies showed that both, HCAEC and HCASMС are adhesive on the decellularized matrix and growing in several layers.

**Conclusion:** A complete arterial matrix, reseeded with human endothelial and smooth muscle cells has been successfully developed. This represents a new in vitro model, suitable for long-term proliferation and migration studies in stented vessels.
in other parameters including restenotic tissue backscatter, visible microvessels, and lumen shape.

Conclusions: The pathophysiology of i-stent restenosis might be different among various stents.

Comparison of neointimal tissue characteristics among bare-metal stent, paclitaxel-eluting stents and zotarolimus-eluting stents using integrated-backscatter intravascular ultrasound (IB-IVUS)


Purpose: Drug-eluting stent (DES) has dramatically reduced angiographic restenosis and target lesion revascularization (TLR) by decreasing neointimal hyperplasia. However, ISVR in DES still occurs to limited extent. Although neointimal tissue characteristics are essential to understand the pathophysiology of ISVR, they have not been fully investigated. The aim of this study is to compare the differences of neointimal tissue characteristics among BMS, paclitaxel-eluting stents (PES) and zotarolimus-eluting stents (ZES), using intravascular ultrasound (IVUS) and integrated-backscatter IVUS (IB-IVUS).

Methods: We investigated 95 de-novo lesions to be treated with BMS (N=18), PES (N=20), and ZES (N=17). We performed longitudinal IVUS analyses within stented segments to confirm minimum lumen area (MLA) at follow-up. Neointimal tissue characteristics judged by grayscale-IVUS were categorized as homogeneous or heterogeneous. Neointimal tissue characteristics were also analyzed using IB-IVUS, which characterized as following four characteristics: calcific, dense-fibrous, fibrous, or lipidic. We compared them among BMS, PES, and ZES.

Results: TLR rate showed no significant difference in three groups (22% in BMS, 30% in PES, 18% in ZES, p=0.67). Neointimal area at MLA site was significantly larger in BMS than PES and ZES (6.1mm² in BMS, 3.7mm² in PES, 2.6mm² in ZES, p=0.001). Most neointimal tissue categorized homogeneous by grayscale IVUS (100% in BMS, 95% in PES, 88% in ZES, p=0.03). IB-IVUS analysis revealed that there were no significant differences in lipidic tissue components of neointima among three groups (0.76mm² in BMS, 0.59mm² in PES, 0.53mm² in ZES, p=0.53). Calcific tissue and dense fibrous tissue components of neointima also showed no significant differences among three groups (0.16mm² in BMS, 0.21mm² in PES, 0.21mm² in ZES, p=0.63). Dense-fibrous tissue: 0.40mm² in BMS, 0.31mm² in PES, 0.30mm² in ZES, p=0.52). However, fibrous tissue components of neointima were significantly higher in BMS compared with PES and ZES (3.5mm² in BMS, 2.3mm² in PES, 2.3mm² in ZES, p=0.01). In comparison between PES and ZES, neointimal tissue characteristics by IB-IVUS showed no significant differences (calcific: p=0.42, dense-fibrous: p=0.84, fibrous: p=0.94, lipidic: p=0.73).

Conclusions: IB-IVUS analyses revealed that neointimal tissue in BMS contained more fibrous tissue than PES and ZES, which suggested more stable neointima in BMS compared with PES and ZES. In addition, PES had similar neointima to ZES by IB-IVUS analyses.

Spatial distribution of culprit lesion thin cap fibroatheromas and culprit ruptured plaques in acute coronary syndrome. An optical coherence tomography study

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Purpose: Recent studies have shown that the majority of culprit lesions in acute coronary syndrome (ACS) are located in proximal segments of coronary arteries. This discrepancy could be due to morphological differences. We investigated with optical coherence tomography (OCT) in patients with ACS, whether culprit lesion thin cap fibroatheroma (TCFA) or rupture are associated with the location of the lesion.

Methods: We included 67 patients with ACS that underwent cardiac catheterization within 24 hours from symptom onset. Distance of the culprit lesion from the coronary ostium was measured with quantitative coronary angiography. OCT was performed in all culprit lesions and the minimal cap thickness and the lipid content in quadrants were measured. TCFA was defined as a plaque with cap thickness <65μm and lipid content in 1-4 quadrants. Presence of plaque rupture was recorded.

Results: Analysis of OCT images revealed 45 ruptured plaques (67.1%), 17 in the LAD (60.7%), 6 in the LCx (66.7%), and 22 in the RCA (73.3%; p=NS). Mean cap thickness was 58±27μm. The majority of the patients (n=62, 92.5%) had >1 lipid quadrants. Forty five TCFA were identified by OCT, 16 in the LAD (57.1%), 6 in the LCx (66.7%), and 23 in the RCA (76.7%; p=NS). Luminal thrombus was found in the majority of patients (n=47, 70.1%). The distance of the culprit lesion from the ostium was lower for ruptured plaques compared to non-ruptured plaques (27.0±19.3mm vs. 41.1±20.6mm, p<0.01). Culprit lesions with a TCFA had a trend for lower distance from the ostium, compared to plaques without a TCFA (28.9±20.3mm vs. 37.3±20.9mm, p=0.08). Spatial distribution of TCFA and ruptured plaques is presented in the figure.

Conclusions: Culprit ruptured plaques in ACS are predominately located in the proximal segments of the coronary arteries.
value of <0.8 was considered as significant in determining ischemia. The minimal lumen area (MLA) were measured by OCT and IVUS.

Results: Although both MLA obtained by IVUS and OCT showed a significant correlation to FFR values than MLA by IVUS. (OCT: R=0.573, P=0.001, IVUS: R=0.80, P=0.001). The best cutoff value of the MLA to predict FFR <0.8 was 4.29 mm² by IVUS (sensitivity, 94.7%; specificity, 76.9%; AUC, 0.877) and <2.24 mm² by OCT (sensitivity, 94.7%; specificity, 76.9%; AUC, 0.947).

Conclusion: OCT-based MLA measurement may provide better estimation of physiological coronary epicardiac stenosis than IVUS.

NON CORONARY AND TAVI INTERVENTIONS

P4168 Percutaneous occlusion of left atrial appendage with the amplatz cardiac plug: results from clinical, echocardiographic and CT follow-up in 100 implanted patients

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Background: Percutaneous left atrial appendage (LAA) occlusion has proved to be safe and not inferior in the prevention of cardioembolic events in non valvular atrial fibrillation (AF) when compared to treatment with vitamin K antagonists (VKA). Data from large studies are lacking in the use of Amplatz Cardiac Plug (ACP). The aim of our study is to demonstrate that the ACP is safe and effective in the short and medium term.

Methods: Data from 106 consecutive patients (pts) submitted to two Centers for performing percutaneous LAA occlusion were collected from December 2008 to September 2012. All pts had an high thromboembolic risk (CHA2DS2-VASc ≥2) and at least one of contraindication to or not accepting anticoagulation therapy. After the procedure, all pts were treated with dual antiplatelet or anticoagulation therapy for 4 weeks. Pts were re-evaluated with clinical or instrumental follow up (FUP) with computer tomography (CT) or transesophageal echocardiography (TEE).

Results: Mean age was 75±11 vs. 57. M. The ACP was successfully implanted in 100 of 106 pts (94%). Permanent AF was present in 71% of pts, while persistent and paroxysmal AF were present in 11% and 18%, respectively. After the procedure five pericardial effusions were observed, three of which needed pericardiocentesis. Two pts experienced a transient ischemic attack, one the day after the procedure and the other 16 months later. One patient, treated with ASA, clopi- dogrel and warfarin, was affected by intracranial haemorrhage two months after the procedure. At a mean FUP of 13±7 months (0 pts lost to FUP) 6 patients were dead for non procedural related causes (2 cases of pulmonary embolism, 2 cancer, one of worsening heart failure with left ventricular failure, one of cancer). No ischemic stroke was observed in any implanted patient. TEE was performed in 46 patients at 8±7 months after the procedure and CT in 33 pts at 11±8 months, failing to demonstrate any malposition or embolization of the device. In two cases there was a residual intraatrial septal defect. In one patient TEE demonstrated a small thrombus on the device that was successfully treated with fondaparinux for one month. Mitral valve motion, transmural flow and left superior pulmonary vein were not affected by the presence of the device.

Conclusions: Data from our experience suggest that percutaneous LAA occlusion with ACP is a safe and effective alternative to VKAs in selected high risk patients implanted with non valvular AF and is associated with a high procedural success rate. Our mid-term follow up in 100 implanted pts with no ischemic stroke after a mean of 13 months confirms the acute results.

P4169 Comparative analysis of percutaneous left atrial appendage (LAA) closure systems: a single center experience

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Background: The concept of LAA closure has entered the clinical arena as a treatment alternative for stroke prevention in patients with non-valvular atrial fibrillation (NVAF). Currently, two different LAA closure systems are available but lacking comparative data.

Objective: To prospectively compare both LAA closure systems with regards to procedural data and safety.

Methods: Consecutive patients (pts) with NVAF, high risk for stroke and either contraindication or not willing to accept long term oral anticoagulation (OAC) were prospectively enrolled. In all pts deep sedation was utilized during the procedure. After transeptual puncture LAA angiography was performed. LAA dimen-
sions were calculated from TEE and angiography. Watchman™ (group A) or Cardiac Plug™ devices (group B) were implanted. All patients received OAC or dual antiplatelet therapy (aspirin/clopidogrel) for 6 weeks followed by TEE for re-
assessment.

Results: In a total of 44 pts 45 procedures were performed (mean age: 74±8 years: group A: n=18 pts; 11 males) (group B: n=27 pts; 15 males). There was no statistical difference between group A and B with regards to CHA2DS2: 2 (Q1=1, Q3=2) vs. 2 (Q1=1, Q3=3), CHA2DS2VASc: 3 (Q1=3, Q3=6) vs. 4 (Q1=3, Q3=5), and HASBLED score: 3 (Q1=2, Q3=4) vs. 3 (Q1=2, Q3=4). Implantation success was achieved in 16/18 pts (88%, group A) and in 27/27 (100%, group B), respectively. In group A, 2 implantations failed: 1 pt switched to group B, 1 pt with transient ventricular arrhythmia. In group B, 1 asymptomatic ST elevation was observed. Procedure- and fluoroscopy-time comparing group A and B was 56±16 min vs. 48±16 and 9.2±5.6 vs. 7.4±4.7 min, respectively. Mean LAA device sizes were...
Refining transcatheter left atrial appendage closure: eliminating the anaesthetist and reducing the cost


Introduction: The validity and benefit of transcatheter LAA closure for protection from thromboembolic stroke in non-valvular AF has been well established. However, to date, all studies have performed this procedure under general anaesthesia. Given that most candidates for LAA occlusion are often aged greater than 75 years, with multiple co-morbidities, general anaesthesia confers significant risk to this patient cohort, as well as additional costs to the procedure. Therefore we sought to determine the safety of performing this procedure under conscious sedation, and to determine any cost implications of this strategy.

Methods: Fifty four (44 men, 10 women; mean age 75.7±6.2 years) with non-valvular AF and a high risk for stroke (mean CHADS2 score 3.8±1.5), and high risk for oral anticoagulation, underwent percutaneous LAA closure using the WATCHMAN device. All procedures were performed under conscious sedation, with fluoroscopy and transoesophageal echocardiography (TOE) guidance. IV Midazolam was titrated to observed patient needs, with monitoring of O2 saturations. The follow-up program included clinical and echocardiographic review performed in 65 days.

Results: The LAA was successfully occluded 50 patients (92.5%) under conscious sedation. In four cases the device was not implanted due to unsuitable appendage anatomy. The mean procedural and fluoroscopy times were 67.3±16.1 and 10.5 ±3.8 minutes respectively. The mean device size was 26.4±3.8 mm. There were no significant procedure or device related adverse events. There were one anaesthesia related complications. All were performed as day-case procedures. Follow-up TOE showed closure of all LAA orifices. None of the patients experienced major adverse events during a follow-up (5-22 months).

Cost saving implications of using conscious sedation were €3174/patient. This cost saving was achieved by reduced hospital stay, from standard two days of hospitalization (€1046/day) and general anaesthesia saving (€1082/procedure).

Conclusion: Our study demonstrates that conscious sedation is a safe and well tolerated alternative to general anaesthesia for percutaneous LAA occlusion. The use of conscious sedation removes the requirement for general anaesthesia and thus, reduces anaesthesia-related morbidity as well as anaesthesia related costs. Additionally, this approach facilitates the performance of LAA closure as a day-case procedure, with a consequent further reduction in procedure-related costs.

The role of intracardiac echocardiography in the management of left atrial appendage occlusion: three years experience

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Purpose: Left atrial appendage (LAA) transcatheter occlusion is a new therapeutic option for the prevention of thromboembolism in patients with atrial arrhythmias and cardioembolic anticoagulation to anticoagulation therapy. Prior procedure echocardiography monitoring is a useful tool for asccessful procedure and preventing early complications, and the purpose of this study was to verify the safety and the efficacy of performing this procedure using intracardiac echocardiography (ICE).

Methods: We selected 103 patients (mean age 87.5 ±8 years; male 56%; mean CHADS score 4.6) in 2 Italian centers with non-valvular AF and contraindications to anticoagulant drugs between January 2009 and December 2011 who had undergone LAA transcatheter closure procedure. The device used was the Amplatzer™Cardiac Plug (ACP, Apa Medical, Plymouth, MN). All patients underwent intracardiac echocardiographic (ICE) implantation measurements of the LAA and for excluding LAA thrombosis before the procedure. ICE was used during the procedure to monitor trans-septal puncture, to confirm the absence of thrombus in the LAA, to verify the correct position of the sheath position before delivery and to help in selecting the correct sized device.

Results: The tran-septal puncture and correct devices positioning were successful in 100% cases. At the 45 days follow-up no major adverse event and 3.3% minor complications were observed and we demonstrated stable position of the plug without residual haemodynamic shunt at the puncture level verified by TEE. Conclusion: Intracardiac echocardiography is a safe and useful option for guiding the LA transcatheter occlusion procedure and preventing short to mid-term complications having the advantage over TEE of not requiring general anaesthesia and anaesthesiological support.

Left atrial appendage occlusion: the link between imaging techniques and clinical events

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Purpose: Left atrial appendage (LAA) transcatheter occlusion is a recent alternative for the prevention of thromboembolism in patients with non-valvular atrial fibrillation (AF). Different imaging techniques have been used for establishing the complete occlusion of LAA and the transcatheter echocardiography (TEE) is still the most common tool used. Nevertheless very limited data is available about mid to long term outcome in patients who have undergone these procedures. Our aim was to verify if advanced cardiac imaging including cardiac computed tomography angiography (CCTA) and transesophageal echocardiography (TEE) are related to clinical events over a three years follow-up.

Methods: We evaluated 50 patients with contraindications to anticoagulant (mean age 77.6±ys; male 60%; mean CHA2DS2-VASc score 4.7±1.2; HAS-BLED score 3±1.0) who had undergone LAA transcatheter occlusion procedure using the Amplatzer™Cardiac Plug (ACP, Apa Medical, Plymouth, MN) in our center between January 2009 and January 2012. After a short period of dual antiplatelet drugs all patients were treated with a single antiplatelet agent.

Results: At a mean 24±12 months follow-up period we controlled 31 cases using CCTA. 16 of these (52%) had an incomplete occlusion through either residual LAA flow or peri-device leak. In one cases we observed residual flow with initial thrombus inside the LAA but without clinical events. We also performed 18 TEE controls in patients with a residual leak in 14 cases (36%). In a clinical context we recorded two episodes (4%) of transient ischaemic attack, the first 24h after the procedure and the second about 16 months after the implantation, both with complete closure. No AngioCT or TEE were performed in the first case due to the poor general conditions of the patient and, for the second, TEE failed to identify any leak clearly seen by the ACTLimulations. In contrast with previous studies we observed a lower number of stroke/TIA than predicted. We explained this data as a result of the shorter follow-up period and longer therapy with antiplatelet agents.

Conclusions: Our data, according to previous findings, suggest that residual flow after LAA occlusion is not associated to a higher incidence of clinical cerebrovascular events. CCTA has a high sensitivity to identify peri-device leaks and thrombi. TEE is still the most used technique in the evaluation and can represent the unique tool in a subgroup of patients who develop absolute contraindications to intravenous administrations of iodinated contrast agents during F-U period.

Atrial arrhythmias after implantation of atrial septal defect devices. Is there an inflammatory component?

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Purpose: Transcatheter closure of atrial septal defects (ASD) and Patent Foramen Ovale (PFO) is performed with increasing frequency. The long-term effects of implantation of atrial septal closure devices (ASDc) has been associated with concerns regarding potential adverse effects on atrial function over time. Appearance of atrial tacharyrhythmias (AT) may occur without any known cause after the implantation. We hypothesized that appearance of arrhythmias may be associated with the increase of inflammation as detected by the measurement of inflammatory indices such as high sensitive CRP, tumor necrosis factor (TNF-α) and interleukin 6 (IL-6).

Methods: Transcatheter closure of interatrial communications with Amplatzer device was carried on 70 patients (pts), 35 with ASD and 35 with PFO, 28pts (40%) was men, aged 49±4 years. None of the pts that were included in the study had a history of AT prior to the implantation. The patients 24 h before the procedure underwent 24-hour Holter monitoring and blood analysis, for measurement of TNF-α, IL-6 and CRP, a procedure repeated 3 months after the day of the closure. Echocardiographic data was also taken before the procedure at, 3 and 6 months after the closure of the defect.

Results: All pts underwent successful closure of the defect. New tacharyrhythmias after implantation of Amplatzer devices were observed in 13 patients (18%). There were patients with atrial fibrillation in 4 and 2 pt with supraventricular tachycardia which occurred between the first month and 3 months after implantation. In the other 7 pts (10%) atrial ectopic beats (> 10 per hour) were observed at the same period. The baseline measurement of CRP of all the 70 pts was 1.0±0.9mg/dl, TNF was 7.2±2.4 pg/ml and IL-6 was 8.5±3.2 pg/ml.

In those pts that arrhythmias appeared, the inflammation index 3 months after were increased the value of CRP was 2.4±0.7mg/dl (p=0.001), TNF was 9.2±2.4pg/ml (p=0.001), IL-6 9.8±3.4 pg/ml (p=0.001) while in those pts that no arrhythmias appeared all the inflammatory markers had no statistical difference.

Conclusion: Transcatheter closure of ASD using Amplatzer devices is associated with a risk of new atrial tacharyrhythmias especially in those pts in which an increase in inflammation was observed. Possible mechanisms may be focal irritation caused by the device. Long-term follow-up is required for these patients
"Migraine side effect" after PFO closure as secondary

Transthoracic echocardiography guidance during Simultaneous measurement of left ventricular volume and pressure during percutaneous mitral valve repair with the evale mitrACLiP™ system

The purpose of this study was to determine the frequency of occurrence of the migraine after transcatheater closure of PFO in patients younger than 55 yrs old with cryptogenic stroke or TIA.

Methods: All 224 consecutive patients (mean age 40.9±9.9 yrs; 103 men, 108 pts <40 yrs old, 116 pts 40-55yrs old) with cryptogenic thromboembolism who underwent PFO closure between 1999 and 2011 as secondary prevention were included. Mean follow-up period was 37.8±32.5, median 27 months (range, 3-151 months). There were 33 (14.7%) pts lost to follow up. Every patient was treated at least 6 moths with aspirin (yrs 1999-2003) or aspirin and ticlopidin (2004-2006) or aspirin and clopidogrel (3-6 months, 2007-2011) after procedure. All pts were sent the questionnaire concerning the presence of migraine before and after PFO closure.

Results: The migraine occurred in the study group before PFO closure in 68 (30.4%) pts, that is three times more frequently than in general population (30% vs 10%). Noticeable improvement (expressed in lower frequency rate or severity of migraine attacks; in patients' subjective opinion) or disappearance of migraine symptoms after procedure was reported by 55 pts (80.9% pts) vs 13 pts (19.1%) of migraine attacks, in patients' subjective opinion) or disappearance of migraine (30.4%) pts, that is three times more frequently than in general population (30% vs 10%).

Conclusions:

1. Migraines are seen more frequently in patients with PFO than in general population.
2. Percutaneous PFO closure with Amplatz septal occluder leads to recovery of migraine or noticeable amelioration of symptoms in significant percentage of patients.

Transrecthoracic echocardiography guidance during percutaneous closure of patent foramen ovale

Impact of mitral annulus dimensions assessed by 3D echocardiography on procedural results of percutaneous edge-to-edge mitral valve repair and left atrial and left ventricular reversed remodeling

Background: Percutaneous mitral valve repair (PMVR) using the edge-to-edge technique has become a treatment option for selected patients with severe mitral regurgitation. This study evaluated the impact of mitral annulus dimensions on reduction of mitral regurgitation after PMVR and prediction of left atrial (LA) and left ventricular (LV) remodeling.

Methods: In 30 high-surgical-risk patients with severe functional mitral regurgitation (age 74±9 years) 3D transesophageal echocardiography (TEE) was performed before PMVR to assess: mitral annulus area, circumference, anterior-to-posterior diameter and posterior-medial-to-antero-lateral diameter. 3D color Doppler TEE was used for direct planimetry of the vena contracta area (VCA) to define before and after repeat TEE. At 6 months follow-up, changes of LA volume and LV enddiastolic and endsystolic volumes were assessed by 2D transthoracic echocardiography.

Results: VCA by 3D color Doppler TEE was reduced from 0.45±0.17 cm² to 0.19±0.11 cm² after PMVR. Patients with a reduction of VCA >50% (n=22) had a significantly smaller pre-procedural mitral annulus area compared to patients with a reduction of VCA <50% (11.9±3.2 vs. 17.2±10.1 cm², p=0.034). Mitral annulus circumference (13.0±1.9 vs. 15.5±4.9 cm, p=0.052), mitral annulus anterior-to-posterior diameter (3.6±0.6 vs. 4.1±1.0 cm, p=0.062), left atrial volume (LA volume at 6 months follow-up) and left ventricular (LV) remodeling were assessed by 3D transthoracic echocardiography.

Conclusions: In patients with very large mitral annular dimensions, effectiveness of PMVR is reduced. Less effective PMVR is associated with less LA and LV remodeling.

Impact of mitral annulus dimensions assessed by 3D echocardiography on procedural results of percutaneous edge-to-edge mitral valve repair and left atrial and left ventricular reversed remodeling

Mitrval Valvuloplasty long-term follow-up of single balloon (Balt) versus Inoue balloon techniques

This study aimed to determine that mitral balloon valvuloplasty (MBV) with the Balt single balloon (BSB) has similar outcome and long-term follow-up (FU) than MBV performed with the Inoue worldwide accepted technique.
Percutaneous mitral balloon valvuloplasty beyond 65 years of age

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Objectives: To evaluate the safety and efficacy of percutaneous balloon mitral valvuloplasty for the treatment of mitral stenosis in patients older than 65.

Background: The profile of subjects undergoing percutaneous balloon mitral valvuloplasty (PMBV) in developed countries has shifted toward the elderly. In the group of elderly patients long-term results after PMBV, as well prognostic factors that may improve patient selection for this procedure have not been fully elucidated.

Methods: The studied group consists of 132 consecutive patients aged ≥65, who underwent PMBV. All PMBV procedures were performed by the antegrade transvenous approach using the Inoue balloon system. Thirty-four (25.8%) patients had previous surgical and 2 (1.5%) percutaneous mitral commissurotomy. The mean echo score was 7.49 ± 1.46 (median 8, range 3-11). Thirty-five (26.5%) patients had echo score >8. The mean left atrial diameter before PMBV was 5.3 ± 1.0 cm (median 5.0 cm). The endpoints assessed were all-cause survival and survival free of mitral valve intervention or heart failure ≥ NYHA III. Results: Procedural success, defined as mitral valve area ≥1.5 cm² and mitral regurgitation ≤2+ was obtained in 105 (78.9%) patients. Echo score ≤8 and higher mean mitral valve gradient (MVG) were significant independent predictors of inadequate immediate result. The best cut-off point of mean MVG predicting procedural success was 10.5 mmHg. The rate of procedural success was significantly higher in the group of 86 patients with Echo score ≤8 and mean MVG < 10 mmHg than those (12 patients) with Echo score >8 and MVG > 10 mmHg (86% vs. 41.7%, p<0.001). Mean follow-up was 6.25 ± 4.33 years. Survival curves showed that for the whole studied group after PMBV the three-, five-, and ten-year overall survival rates were significantly better in patients with left atrium diameter ≤5.0 cm before intervention (95.4%, 93.1%, and 80.5% versus 89.6%, 69.5%, and 53.7%, respectively; p=0.002). Survival free of mitral valve intervention or heart failure ≥ NYHA III was significantly better for patients with good immediate result and mean pulmonary artery pressure < 25 mmHg after PMBV. Conclusions: PMBV is safe and efficacious in elderly patients with symptomatic mitral stenosis. Long-term results are good and related mainly to the quality of the procedure.

Clinical and echocardiographic outcomes of patients undergoing percutaneous closure of mitral paravalvular leak

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Purpose: Percutaneous closure of mitral paravalvular leak is a complex procedure, recently developed for patients unsuitable for a new surgery. Clinical experience is limited and the results are controversial. We report here the experience of our center and the acute and mid-term outcomes.

Methods: We retrospectively reviewed those patients with severe prosthetic paravalvular regurgitation (MR) who underwent an attempt of percutaneous closure in our hospital. Data were collected regarding demographic characteristics, comorbidities, location and size of the leak, mortality, medium-term and clinical echocardiographic outcomes.

Results: The study comprises 11 procedures in 10 patients, which took place between October 2010 and July 2011. The mean age was 75.4±6.6 years and 54.5% were female. The medium Euroscore was 42.84%±21.24. Mean LVEF was 53.7%±14.38 and 7 patients also had an aortic prosthesis (5 of them mechanical). 62% of the interventions were performed on mechanical prostheses, and the patients had undergone 1.7 previous surgeries (range 1-4), with a type of percutaneous repair of 161.72±111.1 months (range 6-314). The clinical indication for the procedure was heart failure, in all cases and also severe hemolysis in 81%. The location of the leaks were as follows: anterior quadrant in 5 patients, lateral in 4 and posterior in 1, being the mean maximum length 12.94 mm±4.97. In 9 of the 11 procedures the device was successfully deployed, but in 2 patients the device was too big to provide adequate support. The Amplatzer Duct Occluder device was used in 1 case and the Amplatzer Vascular Plug III in the rest, using 2 of them for the closure of 1 leak. TEE showed mild MR just after the deployment of the device in 8 patients, and severe MR in 1 case. Mortality related to the procedure was 0%, but 3 patients died during the first month (only 1 of them due to complication related to the intervention). No more deaths were recorded during the follow-up. Independent risk factors of severe MR, a control echocardiography after 3.4±1.89 months revealed severe MR in 2 cases, moderate MR in 1 and mild MR. 2 patients died before a control echocardiography was performed.

Conclusions: Percutaneous closure of paravalvular leak is a procedure of variable effectiveness, whose main limitation is the extense comorbidty and poor basal status of some patients referred for this technique. Furthermore, in some cases, the initial success does not ensure mid-term positive outcomes. These results could improve with a sooner referral of these patients and the development of specific devices for this pathology.
Endovascular stenting for palliation in malignant superior vena cava syndrome

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Superior vena cava obstruction can occur in late or progressive stages of various tumors due to involvement of the mediastinum. To assess feasibility, short and long term efficacy and complication rate of interventional therapy, i.e. recanalization, PTQ and stenting of such lesions we analyzed 16 consecutive patients with cancer related superior vena cava syndrome. Clinical follow up was performed every 3 months up to 52 months. Cancer driven mean survival time after PTQ-stenting was 10.2 months (8 days – 52 months). Immediate technical success rate and acute clinical success rate was 100%; NYHA class improved from 3.31 (±0.60) to 1.8 (±0.75). Especially those in class 4 benefited most and improved to class 2. Symptom relief was reached within 24 hrs. All patients remained free from restenoses or recurrent superior vena cava syndrome for the entire follow up or for their remaining life span. We did not have any acute or chronic complication (stent migration, penetration, bleeding). Patients were discharged the day after an uncomplicated clodopelg, in some cases on low molecular heparin or vitamin K antagonists. Thus, for palliation of superior vena cava syndrome in progressive cancer disease interventional therapy can be an option. PTQ and stenting is technically safe and clinically efficient for both rapid and long term symptom relief. It should be considered as first choice treatment.

Impact of percutaneous treatment of acute pulmonary embolism in intermediate and high risk patients

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Background: Local fibrinolysis and mechanical embolectomy improve hemodynamic parameters in patients suffering shock due to pulmonary embolism (PE). Normotensive PE patients with signs of right ventricular failure on echocardiography (RVE-F) have an intermediate risk of death, but little is known about the best treatment for these patients.

Aim: To evaluate the clinical impact of percutaneous treatment (fragmentation, fibrinolysis and aspiration) of PE in both intermediate and high-risk patients.

Methods and Results: 20 patients with CT-confirmed PE and RVE-F were identified. High risk patients (group A=8), defined by cardiogenic shock or respiratory failure requiring mechanical ventilation, were compared to normotensive patients (group B=intermediate risk,n=12). The median time from admission to procedure was 23 hours (p=0.09, 14-29 hours). Three patients in A had systematic fibrinolysis with hemorrhagic complications prior to catheterisation. The other 17 patients received low dose intraaerial fibrinolysis. Twelve patients were female, mean age was 68 years. On admission group A had lower systolic blood pressure (SBP) than B (median (SD) 93 (22) vs 133 (10), p=0.002), but heart rate was similar (111 (12) vs 99 (14), p=0.08). There was a trend toward a lower oxygen saturation and higher oxygen requirement in A (84 (12)% vs 92 (4), p=0.06, and 43 (38)% vs 29 (21), p=0.06, respectively). Systolic and mean pulmonary artery pressures was observed. Heart rate decreased significantly in both groups (A: 103 (25) vs 89 (16), p=0.06, B: 93 (22) vs 83 (18), respectively). Systolic and mean pulmonary artery pressures increased in comparison to NOGA, without compromising injection accuracy.

Conclusion: 3D Rotational angiography fused with multimodal imaging offers a new and promising strategy to guide IM injections towards the infarct border zone. Endovascular procedures such as wire times and catheter side effects are significantly reduced in comparison to NOGA, without compromising injection accuracy.

Transcatheter closure of ruptured sinus of valsalva aneurysm with nitinol mesh occluders

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Introduction: Ruptured sinus of Valsalva aneurysm (RSOVA) is a rare shunt lesion with scant data about its transcatheter closure (TCC). Methods: From March 2007 to September 2011, 12 patients (pts) –mean age 37.2 years were selected for TCC. Two pts had acquired RSOVA after previous cardiac surgery. Another pt after pre-vigorous surgical closure of RSOVA had 2x-re-annelalisations. Echocardiography-revealed the rupture of right or noncoronary sinus into right atrium in 9pts and into right ventricle in 2 another pts. In 1 pt RSOVA was open from inferior sinuses to pulmonary artery (PA).The defect diameter was from 3.8 to 10(mean 6.9) mm. Different nitinol mesh occluders (dural, atrial or muscular VSD) were applied by angioplasty venousapproach. Results: All defects were successfully occluded in 1st attempt during 2 sessions. In 1 pt embolization of 2 mm larger than defectocluder occurred. The device was removed with lasso and bigger occluder was placed. In another pt (after TOF repair) with left RSOVA to PA ST-segment elevation was observed on the ECG and on the house developed technique (LARCA). The latter fuses the infarct region, identified from delayed enhancement (DE)-MRI, with a 3D rotational angiography. Subsequent integration with live biplane fluoroscopy enables guided MI injection. In an additional subset of 4 pts, we tested whether LARCA could be fused with DE-CT and 18F-FDG PET/CT, as an alternative for MRI incompatible patients. Ex vivo 3D stacks of 5 mm slices were reconstructed to quantify injection accuracy towards the infarct border, defined by 2,3,3,4-tetrafluorotoluclidium. Fluorescent injection spots were identified by UV illumination. Results: MRI after 6 w revealed significant functional impairment and LV remodeling (LVEF 37 ±12%, LVEDV 188 ±49 mL, infarct size 17 ±9% of LV mass). During NOGA-procedures, 4/6 animals required DC-shock for major ventricular arrhythmias vs 1/10 during LARCA-procedures. Total online procedure time was significantly lower for LARCA (85 ±25 vs 133 ±30, p=0.01). Mean distance of the injection spots to the infarct border was 4.8 ±0.5 mm for LARCA-MRI (n=42) vs 5.4 ±0.5 mm for NOGA (n=49), p=0.40. LARCA-MRI and NOGA enabled spatial confinement of respectively 69% vs 63% of all injections to a distance less than 5 mm from the infarct border. LARCA fused with DE-CT and PET/CT, resulted in a mean injection distance of 6.0 ±0.7 mm (n=44) to the targeted infarct border. LARCA resulted in a mean injection depth of 3.4 ±0.3 vs 2.5 ±0.3 mm for NOGA, p=0.06. Conclusion: 3D Rotational angiography fused with multimodal imaging offers a new and promising strategy to guide IM injections towards the infarct border zone.
**P4187**

**Arrhythmia device lead extraction using evolution mechanical dilator sheath**

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**Background:** Transvenous lead extraction (TLE) has undergone an explosive evolution by increasing technology due to incremental problem of lead infections and lead malfunctions. We aimed to present our experience in TLE with Evolution Mechanical Dilator Sheath.

**Methods:** Between June 2009-January 2012, Evolution sheath was used for extraction of 158 leads in 75 patients. Indications for extraction, procedural success and complications were defined according to HRS guidelines.

**Results:** Indications for TLE were infection (58.6%), lead malfunction (40%) and lead displacement (1.4%). Extracted devices were PM in 34 cases (45.3%), ICD in 29 cases (38.7%) and CRT-D in 12 cases (16%). Among 158 leads, 38 (24%) were RV, 54 (34.2%) were DDD/VDD, 53 (33.6%) were CS and 13 (8.2%) were PS leads. Median time from preceding procedure was 88 months (21-240 months). Clinical success was 98.6% and complete procedural success with Evolution system alone was 88% (66 patients). Partial success was achieved in 3 leads with remaining small ventricular tip. Major complications were observed in 1 (1.3%) patient without any mortality.

**Conclusions:** Our experience has confirmed that the hand powered Evolution system is an effective extraction tool for chronically implanted pacemaker/ICD leads.

**P4188**

**Comparison of knowledge-based weaning (KBW) and physician-driven weaning of mechanically ventilated patients in the coronary care unit**


**Introduction:** Knowledge-based weaning (KBW) of mechanical ventilation is a form of closed loop ventilation successfully used to decrease duration of ventilator assistance in general intensive care units (ICU). However, its use in specialty ICUs has not been validated.

**Objectives:** To find if KBW reduced weaning times in coronary care units (CCU).

**Methods:** Patients: Single center tertiary hospital CCU. Inclusion: age 21-85; assisted-mode mechanical ventilation - 24 hrs; stable neurology. Exclusion: Poor prognosis, 27 mechanical ventilation.

**Results:** Of the 251 patients enrolled, with mean age 68.0, (range 33-84) and mean APACHE-II score 18.2. 28 patients treated with transcatheter aortic valve implantation using the Medtronic-CoreValve device. The risk for significant PAR is related to anatomical and morphological characteristics of the aortic valve and root and is higher in male patients. Significant PAR is associated with cardiac mortality but not with all-cause mortality and functional class.

**Conclusions:** Significant paravalvular aortic regurgitation occurs in 30% of patients treated with transcatheter aortic valve implantation using the Medtronic-CoreValve device. The risk for significant PAR is related to anatomical and morphological characteristics of the aortic valve and root and is higher in male patients. Significant PAR is associated with cardiac mortality but not with all-cause mortality and functional class.

**P4189**

**Predictors and clinical outcome of significant paravalvular aortic regurgitation following transcatheter aortic valve implantation**

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**Purpose:** Although transcatheter aortic valve implantation (TAVI) has emerged as a good alternative treatment for high surgical risk patients with severe aortic valve stenosis, significant paravalvular aortic regurgitation (PAR) remains a frequent complication. Therefore our aim was to investigate the determinants and short- and mid-term clinical consequences of PAR.

**Methods:** We studied 130 patients (mean age 81±8 years, 39 male) who underwent a TAVI with the Medtronic-CoreValve bioprosthesis. Clinical parameters were obtained from the medical history, laboratory analysis, echocardiography, cardiac computed tomography and angiography. Clinical outcome was assessed up to 12 months after TAVI.

**Results:** Following TAVI, PAR grade ≥2 occurred in 37 patients (28%). Multivariate analysis identified sinus width (per mm, OR 1.32, 95% CI 1.11-1.57, p=0.002) as the only independent predictor for PAR≥2. Thirty-day mortality and 1 year cumulative mortality were not significantly different between the PAR=2 and PAR≥2 groups. Cardiac mortality was significantly higher in the PAR≥2 group versus the PAR=2 group at 1 month (19% vs. 1%, p=0.016) and 1 year (28% vs. 2%, p=0.008)

**Figure 1. Survival curves**

**P4190**

**Incidence and intraprocedural management of aortic regurgitation in interventional aortic valve replacement**

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**Background:** Paravalvular regurgitation is frequent after transcatheter aortic valve implantation (TAVI). In the present study the incidence of a significant (≥2) postinterventional aortic regurgitation (AR) and possible treatment strategies are evaluated.

**Methods:** In 91 patients (pts) transfemoral TAVI with a self-expanding Medtronic CoreValve (CV; n=80) or a balloon-expandable Edwards Sapien prosthesis (ES; n=11) was performed. Incidence of AR was evaluated by echocardiography immediately after deployment of the prosthesis and after optional correcting interventions. Prior to hospital discharge AR was assessed by transthoracic echocardiography.

**Results:** Immediately after deployment of the aortic prosthesis a significant paravalvular AR was present in 35 of 91 pts (38%); AR 2/4 in 23 pts, AR 3/4 in 11 pts, AR 4/4 in 1 pt.

Thereafter in 5 pts, in whom a CV prosthesis has been implanted, it has been waited for 10 minutes, in 20 pts the prosthesis was postdilated with a valvuloplasty balloon (in 1 pt after previous waiting) because of a too deep position in the left ventricular outflow tract with a snare tool (in 2 pts after previous balloon dilatation). By these interventions a reduction of the severity of the AR by at least one grade could be achieved in 13 of 25 pts (52%), thereof in 4 of the 5 pts, in whom further expansion of the prosthesis has been waited for.

In the pts, in whom due to a significant AR correcting interventions have been deemed necessary, blood pressure immediately after deployment of the prosthesis was significantly lower than in the pts without significant AR. The correcting interventions led to a significant rise of the diastolic blood pressure but leaved the systolic blood pressure unchanged. Furthermore after the correcting intervention a significant decline of the LVEDP was observed from 29±8 mm Hg to 24±6 mm Hg (p = 0.050).

At the end of the TAVI 25 of 91 pts (27%) had significant AR (AR 2/4 in 23 pts, AR 3/4 in 1 pt, AR 4/4 in 1 pt). Before hospital discharge (after a mean of 4.6±4.2 days) TTE revealed mild to moderate AR in 3 of 90 pts and moderate AR in 7 of 90 pts. The 3 pts, (3/91 pts, 3.3%), who died within the 7 days after TAVI, all had significant AR at the end of the TAVI procedure.
Conclusion: In TAVI immediately after prosthesis deployment significant AR is frequent and can be corrected by balloon dilatation of the prosthesis or pullback maneuvers. In self-expanding prostheses without massive AR further expansion of the prosthesis can be waited for before initiation of further interventions.

Purpose: Transcatheter aortic valve implantation (TAVI) is an alternative for patients with aortic stenosis with high surgical risk. These valves are sutured to a stent which is expanded in a heavily calcified region. Our objective was to describe stent under-deployment (UD) and asymmetrical (non-circular) expansion, which may impair valve hemodynamics.

Methods: From June 2008 to January 2012, 63 consecutive patients underwent TAVI. We selected 56 patients with available transesophageal echocardiography (TEE) imaging. Variables (inner stent area (SA), anterior/posterior diameter (APD) and lateral orthogonal diameter (LOD)) were measured in 2D and 3D TEE. Mean values of 2D and 3D was used. We assessed stent circularity, defined as 1-(APD/LOD). Values >10% were considered non-circular. UD was defined as nominal area (of each valve size) minus SA. Indexed UD was obtained dividing UD by nominal area.

Results: Mean age was 82.8. Procedure approach was transfemoral in 80.4%. Valve sizes were XT model, the remaining the old TFX. Mean SA were 3.27±0.8 cm² (23); 3.93±0.1 (26) and 3.96±0.2 (29). The final SA fit progressively in the native aortic valve annulus, showing a linear trend between SA and valve annulus (p<0.001).

In our series, mean UD was 0.88±0.8 cm² (23); 1.37±0.1 (26) and 2.63±0.29 (29). Mean indexed UD was 24%, thus, the valve expands only to 76% of its nominal area. Comparing TAVI approaches and prosthesis models, we found no differences in indexed UD. However, indexed UD increases keeping a linear relationship (p<0.01) with the valve sizes (21.2%±0.23, 25.9%±0.26, 39.8%±0.29). This suggests that larger stents loose part of the radial force in spite of the higher stent expansion (p<0.01) with the valve sizes (21.2%±0.23, 25.9%±0.26, 39.8%±0.29). This suggests that larger stents loose part of the radial force in spite of the higher stent expansion (p<0.01) with the valve sizes (21.2%±0.23, 25.9%±0.26, 39.8%±0.29). This suggests that larger stents loose part of the radial force in spite of the higher stent expansion (p<0.01) with the valve sizes (21.2%±0.23, 25.9%±0.26, 39.8%±0.29).

The aortic annulus area was planimetered with 3D TEE, and indexed from 2D circular area was 0.36 (Figure). Using 3D planimetered annulus index as reference parameter to decide the prosthetic size, the choice would have been different in 21 patients (63%).

Conclusions: UD and asymmetrical expansion in transcatheter aortic valves affects the accuracy of the prosthesis to implantation. The aortic annulus area was planimetered with 3D TEE, and approximated by circular area formula (πr²) using annulus diameter obtained by two-dimensional (2D) TEE.

Results: After TAVI, 13 patients (39.3%) developed significant AR (≥2/4). The occurrence of significant AR was associated to the 3D planimetrized annulus area (p=0.04), and the “mismatch index” obtained through 3D planimetrized annulus area (≥p=0.03), but not to “mismatch index” derived of 2D annulus diameter. In multivariate analysis “mismatch index” for 3D planimetrized annulus area was the only independent predictor of significant AR (odds ratio: 10.722; 95% confidence interval: 1:040-17:8; p=0.04). The area under the ROC curve for “mismatch index” by 3D planimetrized annulus area was 0.76, whereas for “mismatch index” obtained by 2D circular area was 0.36 (Figure). Using 3D planimetrized annulus area as reference parameter to decide the prosthetic size, the choice would have been different in 21 patients (63%).

Conclusions: 3D TEE planimetry of aortic annulus improves the assessment of prosthesis/annulus mismatch and predicts the appearance of significant AR after TAVI.

Purpose: To investigate the clinical and hemodynamic outcomes in patients with prosthesis-patient mismatch after TAVI with both Core Valve and Edwards Sapien XT valves.

Methods: Clinical assessment and echocardiographic parameters were recorded at baseline and prior to discharge in 137 patients undergoing TAVI. PPM was defined as indexed effective orifice area (EOAi) ≤0.85 cm²/m².

Results: From the 137 patients, 57 (41.6%) had prosthesis-patient mismatch. Among patients with CoreValve 36 (45%) had PPM, whereas 21 (36.8%) patients with the Sapien XT had PPM (p=0.21). Severe PPM was present in 7.5% in CV patients and in 5.9% in XT patients (p=0.62). The procedural success rate was 100% and device success rate was 96%. There was a significant reduction in mean (50.0±14.13 to 9.4±4.15 mmHg, p<0.001) and peak gradients (84.3±20.29 to 18.0±7.18 mmHg, p<0.001) as measured by echocardiography.

The EOAI was significantly increased (0.66±0.15 to 1.66±0.45 cm²/m², p<0.001), as was the EOAi (0.37±0.1 to 0.93±0.29 cm²/m², p<0.001). The Table depicts the impact of PPM on echocardiographic parameters post TAVI in patients with CV and XT.

<table>
<thead>
<tr>
<th>Core Valvle</th>
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<th>Sapien XT</th>
<th>p value</th>
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<td>No PPM</td>
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Conclusions: Patients who underwent TAVI and had PPM were not associated with an adverse hemodynamic outcome before discharge.

Purpose: In transcatheter aortic valve implantation (TAVI), the differences in predictors of prosthesis-patient mismatch (PPM) between Core Valve (CV) and Sapien XT (XT) valves have not been investigated.

Methods: Procedural, clinical and echocardiographic parameters (aortic valve annulus diameter, left ventricular ejection fraction (LVEF), pulmonary artery systolic pressure (PASP) defined as moderate if pulmonary artery systolic pressure ≥31mmHg and ≤55mmHg and severe if PASP>55mmHg), transvalvular gradients, and effective valve orifice (EOA) were recorded at baseline and prior to discharge in 137 patients undergoing TAVI with the CV or the XT valves. PPM was defined as indexed effective orifice area (EOAi) ≤0.85 cm²/m².

Figure 1. ROC curve for significant AR prediction
Results: There was a significant reduction in mean (50.0±3.14±13 to 9.4±4.15 mmHg, p<0.001) and peak gradients (84.34±20.29 to 18.03±7.8 mmHg, p<0.001). From the 137 patients, 57 (41.6%) had prosthetic-patient mismatch. Among patients with CoreValve implantation 36 (45%) had PPM, whereas 21 (36.8%) patients with Sapien XT implantation had PPM (p=0.21). Severe PPM was present in 75% in CV patients and in 53% in XT patients (p=0.02). In the CoreValve group, predictors of PPM included only preprocedural EOAq (OR: 0.022, CI: 0.001-0.688, p=0.05). Following adjustment for logEuroSCORE and preprocedural mitral regurgitation, preprocedural EOAq was still a predictor of PPM (OR: 0.002, 95%CI: 0.001-0.688, p=0.05). In the Sapien XT group, baseline LVEF (OR: 0.951, 95%CI: 0.904-0.999, p<0.05) and baseline PASP (OR: 0.954, 95% CI: 0.913-0.996, p=0.05) were unadjusted predictors statistically significant prognostic factors for PPM. Following adjustment for age, baseline LVEF (OR: 0.948, 95%CI: 0.899-0.999, p=0.05) and baseline PASP (OR: 0.953, 95%CI: 0.912-0.997, p=0.05) remained predictors of PPM. Procedural factors were not associated with PPM in either valve.

Conclusions: PPM is a frequent finding in the TAVI era. Predictors of PPM differ between the CoreValve and the Sapien XT valve, and are mainly associated with the severity of stenosis at baseline in CoreValve and with the functional capacity of the left ventricle in Sapien XT.

Impact of valve type and annular size on post TAVI aortic valve regurgitation

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Purpose: To evaluate the effect of concomitant AR on plasma Brain Natriuretic Peptide (BNP) evolution after Transfemoral Aortic Valve Implantation (TAVI) for Severe Aortic Stenosis (AS). A total of 90 patients, who had undergone TAVI, were retrospectively studied. Vascular complications were defined as major and minor according to the Valve Academic Research Consortium (VARC) criteria. Patients were divided into High-Cannulation Site (CS) group and Low CS group depending on the common femoral artery puncture site position, in regards to the most inferior border of the inferior epigastric artery.

Results: Vascular complications were significantly more frequent in the high CS group versus the low CS group (32.3% vs 11.9%, p=0.039). High cannulation remained an independent predictor of vascular complications after adjustment for known risk factors (OR: 4.827, CI: 1.44-16.16; p<0.011).

Conclusions: In patients undergoing transfemoral TAVI, arterial puncture above the most inferior border of the inferior epigastric artery is associated with vascular complications.

Optimizing vascular access during TAVI by using inferior epigastric artery as a landmark

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Purpose: Vascular access complications during Transcatheter Aortic Valve Implantation (TAVI) have been associated with significant increase of morbidity and mortality. The need for establishment of reliable predictors for these serious events remains pivotal. The origin and course of inferior epigastric artery reliably defines the borders of inguinal ligament. We hypothesize that we can reduce vascular access site complications during TAVI, by using the course of inferior epigastric artery as a landmark for the upper safe margin for femoral puncture.

Methods: A total of 90 patients, who had undergone TAVI, were retrospectively studied. Vascular complications were defined as major and minor according to the Valve Academic Research Consortium (VARC) criteria. Patients were divided into High-Cannulation Site (CS) group and Low CS group depending on the common femoral artery puncture site position, in regards to the most inferior border of the inferior epigastric artery.

Results: Vascular complications were significantly more frequent in the high CS group versus the low CS group (32.3% vs 11.9%, p=0.039). High cannulation remained an independent predictor of vascular complications after adjustment for known risk factors (OR: 4.827, CI: 1.44-16.16; p<0.011).

Conclusions: In patients undergoing transfemoral TAVI, arterial puncture above the most inferior border of the inferior epigastric artery is associated with vascular complications.

Effect of transfemoral aortic valve implantation (TF-AVI) for severe aortic stenosis on plasma brain natriuretic peptide (BNP) levels: predictive value for 30-days and 1-year survival

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Purpose: To determine the effect of TF-AVI on plasma BNP levels and to evaluate their predictive value for 30-days and 1-year survival.
Incidence and prognostic implications of the decrease in sheath size for transfemoral aortic valve implantation with CoreValve TAVI: high pacing rate with CoreValve TAVI

Methods: We measured Baseline BNP, peak BNP within 48 hours after TF-AVI and predischarge BNP in 104 patients with complete 1-year follow-up. Results: BNP was elevated at baseline (298.2, IQR 145.8, 661.6 pg/ml) and showed an acute increase after TF-AVI (508.9, IQR 253.3, 868.6 pg/ml) followed by regression towards baseline levels prior to discharge (327.2, IQR 159.2, 634.6 pg/ml), p< 0.001. Acute BNP increase in ΔBNP (peak−baseline) is significantly higher in 30 days non-survivors (277.1 IQR 252.1, 810 pg/ml) than in survivors (132.8 IQR -10.1, 301 pg/ml), p= 0.028, and is found to be independent predictor of 30 days survival. Kaplan-Meier (KM) survival analysis showed a reduced 30 days survival in patients with a ΔBNP of ≥248.9 pg/ml, p= 0.002. For 1-year survival, predischarge BNP level (250.8, IQR 152.9, 621.8 pg/ml) was an independent predictor of 30 days survival. Kaplan-Meier (KM) survival analysis showed a reduced 30 days survival in patients with a ΔBNP of ≥248.9 pg/ml, p= 0.002. For 1-year survival, predischarge BNP level (250.8, IQR 152.9, 621.8 pg/ml) was an independent predictor. KM analysis showed that 1-year survival is significantly lower in patients with a predischarge BNP ≥327.2 and a ΔBNP≥baseline ≥ 38.3 than in those not fulfilling both criteria, p< 0.001.

Vascular complications are frequent and remain a recognized limitation of transcatheter aortic valve implantation (TAVI), associated with increased morbidity and mortality. Whether the recent reduction in sheath size has led to a decrease in vascular complications is unknown.

Methods: Since May 2006, 250 consecutive patients underwent TAVI with the Edwards SAPIEN prosthesis in our institution using either the transfemoral (TF, n=190), or the transapical (TA, n=60) approach. Suitability for TF was based on ilio-femoral angiography and computed tomography of the iliofemoral access. Up to October 2009, TF Edwards SAPIEN (ES) implantation required 22 or 24F sheath, inserted surgically in 100% of cases, whereas the SAPIEN XT (SXT) prosthesis was compatible with reduced sheath size of 18 or 19F inserted percutaneously with pre-closure (Prostar XL, 10F) in 98% of cases. The consequences on vascular complication are reported according to the VARC classification.

Results: TF TAVI was performed using ES prosthesis in 78 pts and SXT in 112 pts. All baseline characteristics were similar in the two populations, except the Log EuroSCORE, lower in the SXT cohort (18.4 vs 27.7%, p<0.0001). The ilio-femoral minimal lumen diameter was significantly smaller in the SXT group (7.1±1.1 mm vs 8.8±1.3 mm, p<0.04). There was no difference in the rate of major vascular complications (ES: 7.7% vs SXT: 8.1%) whereas incidence of minor vascular complications was higher in the SXT cohort (18.9 vs 9%, p< 0.05). Vascular complications required urgent vascular surgery in 7 cases (3.7%, ES:n=4, SXT: n=3), and covered stent in 12 (6.3%, all in the SXT group). Interestingly, the rate of TA TAVI significantly decreased from 37% in the ES era to 6.9% after onset of the SXT prosthesis (p<0.05).

Conclusions: The reduced sheath size used for Sapien XT implantation did not decrease the risk of major vascular complications after TF TAVI but increased the rate of minor vascular complications. However, smaller sheath size allows performing the Sapien XT prosthesis and has turned TF TAVI into a true percutaneous procedure feasible in smaller iliofemoral vessels, thus reducing markedly the indication for TA TAVI.

Incidence and prognostic implications of the subclavian approach for Transcatheter aortic valve implantation with the CoreValve prosthesis


1University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain; 2University Hospital Virgen de la Victoria, Malaga, Spain; 3University Hospital Virgen de la Victoria, Department of Cardiac Surgery, Malaga, Spain

Transcatheter aortic valve implantation is an alternative option for patients with severe aortic stenosis at high surgical risk. The main approach is the femoral artery but in some cases it is not favorable due to inadequate iliofemoral anatomy or extensive disease, so subclavian artery approach may be feasible. The aims of this study were to report the frequency of the subclavian approach and its relation to the clinical outcome after transcatheter aortic valve implantation.

Methods: Between April 2006 and January 2012, the CoreValve prosthesis (Medtronic, Minneapolis, MN, USA) was implanted in 239 consecutive high-risk surgical patients with symptomatic severe aortic stenosis. The subclavian approach was used in 23 patients (9.9%).

Results: The median logistic EuroSCORE and STS scores was significantly higher in the subclavian versus femoral group (30.7±15 vs. 18.5±12, P< 0.001 and 10.9±5.6 vs. 7.5±5.5, P< 0.001, respectively), had more comorbidities (Charlson index 5.4±1.9 vs. 3.5±1.8, P< 0.001) even though the subclavian group were younger (76±7.6 vs. 79.5±6.2 P< 0.019) and they had a higher rates of porcelain aorta than femoral group (21.7% vs. 6.5%, P< 0.01). Mortality at 30 days was 8.7% for subclavian group and 4.7% for femoral group. P= 0.403; after a mean follow-up of 16±4.11 months, the survival was 80% for subclavian group vs. 80.8% for femoral group, P= 0.13.

Conclusions: The subclavian approach is not frequent in patients undergoing transcatheter aortic valve implantation with the CoreValve prosthesis and appeared safe for the patients at very high or prohibitive surgical risk, including porcelain aorta patients, with contraindications to the femoral approach.

Decrease in sheath size for transfemoral Aortic Valve Implantation: what are the consequences?


Background: Vascular complications are frequent and remain a recognized limitation of transcatheter aortic valve implantation (TAVI), associated with increased morbidity and mortality. Whether the recent reduction in sheath size has led to a decrease in vascular complications is unknown.

Methods: Since May 2006, 250 consecutive patients underwent TAVI with the Edwards SAPIEN prosthesis in our institution using either the transfemoral (TF, n=190), or the transapical (TA, n=60) approach. Suitability for TF was based on ilio-femoral angiography and computed tomography of the iliofemoral access. Up to October 2009, TF Edwards SAPIEN (ES) implantation required 22 or 24F sheath, inserted surgically in 100% of cases, whereas the SAPIEN XT (SXT) prosthesis was compatible with reduced sheath size of 18 or 19F inserted percutaneously with pre-closure (Prostar XL, 10F) in 98% of cases. The consequences on vascular complication are reported according to the VARC classification.

Results: TF TAVI was performed using ES prosthesis in 78 pts and SXT in 112 pts. All baseline characteristics were similar in the two populations, except the Log EuroSCORE, lower in the SXT cohort (18.4 vs 27.7%, p<0.0001). The ilio-femoral minimal lumen diameter was significantly smaller in the SXT group (7.1±1.1 mm vs 8.8±1.3 mm, p<0.04). There was no difference in the rate of major vascular complications (ES: 7.7% vs SXT: 8.1%) whereas incidence of minor vascular complications was higher in the SXT cohort (18.9 vs 9%, p< 0.05). Vascular complications required urgent vascular surgery in 7 cases (3.7%, ES:n=4, SXT: n=3), and covered stent in 12 (6.3%, all in the SXT group). Interestingly, the rate of TA TAVI significantly decreased from 37% in the ES era to 6.9% after onset of the SXT prosthesis (p<0.05).

Conclusions: The reduced sheath size used for Sapien XT implantation did not decrease the risk of major vascular complications after TF TAVI but increased the rate of minor vascular complications. However, smaller sheath size allows performing the Sapien XT prosthesis and has turned TF TAVI into a true percutaneous procedure feasible in smaller iliofemoral vessels, thus reducing markedly the indication for TA TAVI.

Lower pacing rate with CoreValve TAVI: high implantation or Accutrak catheter, or both?

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Introduction: Permanent pacemaker implantation (PPM) post transcatheter aortic valve implantation (TAVI) is a well recognised complication and the greater requirement after CoreValve TAVI compared with surgery (33% vs 8%) has caused concerns. Pre-existing bundle branch block (BBB), larger valve size, post dilatation and low implantation have been shown to independently increase the risk of PPM requirement. Implantation below the aortic annulus can result in compression of conduction tissue and heart block. A modified delivery catheter (ACCUTRAN) may allow a more controlled release expansion of the prosthesis preventing low implantation and reducing PPM need. We evaluated the PPM requirement in all our TAVI patients (pts) treated before and after the introduction of the Accutrak catheter.

Methods: TAVI was performed in 101 pts: trans-femoral (80 pts), left subclavian (16 pts) and direct aortic approach (5 pts). A high valve deployment strategy of 3.5 mm below the aortic annulus was routinely employed. 12 of these had a pre-existing PPM and were excluded from analysis. 43 of the remaining 89 patients underwent TAVI using the Accutrak catheter. Procedural outcomes were analysed (table)

Results: Recognised predictors of PPM requirement post TAVI, were similar in both groups and were not significant (table). A total of 9 patients required a new
PPM (10.1%) post TAVI. There was no significant difference in PPM requirement between the pre and post- Accucath groups (10.9 vs 9.3%; p=1.0).

Conclusion: In our cohort, the need for PPM (10%) is lower than previous reports and is independent of the Accucath catheter. We would advocate a high deployment strategy. Further evaluation of the effect of Accucath catheter on PPM requirement in “middle to low” implanting centres is required.

Abstract P4201 – Table 1

<table>
<thead>
<tr>
<th>Procedure results</th>
<th>Pre-Accutath (46)</th>
<th>Post-Accutath (43)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Mean (years)</td>
<td>83</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>Mean (height)</td>
<td>20.1</td>
<td>22.4</td>
<td></td>
</tr>
<tr>
<td>Mean (weight)</td>
<td>75.9</td>
<td>23.4</td>
<td></td>
</tr>
<tr>
<td>Mean (aortic annulus size) mm</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean (pre-dilation balloon valvuloplasty size) mm</td>
<td>29±24,26±22</td>
<td>29±25,26±16,31±2</td>
<td></td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>99</td>
<td>12</td>
<td>0.05</td>
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<tr>
<td>Mortality rate (%)</td>
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<td>4</td>
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<tr>
<td>Vascular complications (%)</td>
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<td>3</td>
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</tr>
<tr>
<td>Stroke rate (%)</td>
<td>2.0</td>
<td>1</td>
<td>0.35</td>
</tr>
<tr>
<td>PPM post TAVI (%)</td>
<td>10.1</td>
<td>5</td>
<td>1.0</td>
</tr>
</tbody>
</table>

1New pacemaker post TAVI within 30 days of procedure.

Hybrid endovascular repair for aortic arch pathology: intermediate outcomes and complications

W.C. Kang1, E.K. Shin1, C.H. Park1, J.M. Kang1, Y.G. Ko2, D.H. Choi3, Y.N. Youn4, W.H. Shim2, G. Gil Hospital, Gachon University of Medicine & Science, Incheon, Korea, Republic of; 2Severance Hospital, Yonsei University, Seoul, Korea, Republic of; 3Sejong Hospital, Bucheon, Korea, Republic of.

Objectives: To evaluate the outcomes of hybrid endovascular repair for aortic arch pathology.

Methods: This study was a retrospective analysis involving patients who under went hybrid endovascular repair for aortic arch pathologies.

Results: Twenty-one patients (16 men; mean age, 64.7±16.2 years) with aortic arch pathologies were treated by hybrid endovascular repair. The indications for treatment included increased aeurysm size in 16 cases (71.5%), rupture or dissection in 2 cases (9.5%), and may be associated with adverse clinical events. The incidence and consequence of inflammatory reactions that occur after TAVI are largely unknown. Therefore, we aim to assess predictive factors and impact of inflammatory reaction on outcome after TAVI.

Conclusion: Hybrid treatment with supra-aortic vessel transposition and endovascular repair may be an option in frail patients in whom open procedures is too risky.

Abstract P4202

Hybrid endovascular repair for aortic arch pathology: intermediate outcomes and complications

W.C. Kang1, E.K. Shin1, C.H. Park1, J.M. Kang1, Y.G. Ko2, D.H. Choi3, Y.N. Youn4, W.H. Shim2, G. Gil Hospital, Gachon University of Medicine & Science, Incheon, Korea, Republic of; 2Severance Hospital, Yonsei University, Seoul, Korea, Republic of; 3Sejong Hospital, Bucheon, Korea, Republic of.

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Conclusion: Hybrid treatment with supra-aortic vessel transposition and endovascular repair may be an option in frail patients in whom open procedures is too risky.

Abstract P4203

Incidence, predictive factors and prognostic value of inflammatory reaction following transcatheter aortic valve implantation (TAVI)

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Purpose: Systemic inflammatory response syndrome (SIRS) that occurs following cardiovascular surgery is implicated in undesirable physiological alterations and may be associated with adverse clinical events. The incidence and consequences of inflammatory reactions that occur after TAVI are largely unknown. Therefore, we aim to assess predictive factors and impact of inflammatory reaction on outcome after TAVI.

Methods: Between July 2008 and January 2012, we included 76 consecutive pa-
tients who underwent TAVI for symptomatic aortic stenosis with the CoreValve® System (Medtronic CoreValve, Minneapolis, Minnesota) by transfemoral (71%) or subclavian (5%) approach. Demographic, procedural and baseline biological data obtained in all patients were analyzed. Blood samples including inflammatory pa-
rameters were taken during 7 days after TAVI. Statistical study analyzed correla-
tion between inflammatory parameters including SIRS (defined as recommended guidelines) with demographic and periprocedural data. Influence of inflammatory variables on in-hospital and late outcome was analyzed.

Results: The mean age was 83±6.1 years, mean logistic EuroSCORE was 21.1±14%. Twenty eight patients (36%) developed SIRS during the first 72 h after TAVI. SIRS patients were characterized by hyperventilation (78.9%; P=0.001), tachycardia (76%; P=0.001), leucocytes ≥12 x 10^9/L (67%; P=0.005) and fever (89.3%; P=0.001) compared with patients without SIRS. Occurrence of SIRS was associated with significant increase of CRP (p=0.04), CPK-MB (p=0.001), decrease of hemoglobin (p=0.03), but not statistically significant of mean arterial pressure (p=0.08). In multivariate analyses, increase in leucocyte count at 48h (OR=1.7, p=0.15), tachycardia (OR=4.4, p=0.005) and anemia (OR=4.0, p=0.03) were predictive of SIRS. Fifty seven percent of patients had a significant elevation of CRP after TAVI (p=0.04). Increasing CRP was correlated with Glomerular Filtration Rate (GFR) decrease (p=0.11), fibrinogen (p=0.001) and leucocyte count increase (p=0.06). Temperature ≥36.0°C or ≥38.0°C was the only independent predictive factor of CRP elevation (p=0.01). SIRS and CRP values weren’t related to 30-day and 6-months mortality.

Conclusion: SIRS and CRP elevation are frequently observed after TAVI. Increase in leucocyte count, tachycardia and anemia are predictive of SIRS. Increasing CRP is correlated with GFR decrease. Temperature ≥36.0°C or ≥38.0°C was the only independent predictive factor of CRP elevation. This study doesn’t confirm that the inflammatory syndrome is associated with poor outcome at 30 days and 6 months.

Abstract P4204

Early changes of left ventricle deformation indices after transcatheter aortic valve implantation.

A speckle tracking echocardiographic study

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Purpose: Transcatheter aortic valve implantation (TAVI) has been established as a reliable alternative treatment in high risk patients, resulting in symptoms and left ventricle function improvement. The aim of this study was to evaluate the impact of TAVI on early recovery of left ventricle function using echocardiographic left ventricular deformation parameters and to define their possible correlation with myocardial function.

Methods: In 16 patients (6 females, 81±5 years; EuroScore: 24±4%) with severe aortic stenosis but free of significant coronary artery disease who under went TAVI with the CoreValve aortic prosthesis were studied. Conventional 2D and 2D-speckle echocardiography analysis were performed pre-intervention and at discharge. Deformation indices of left ventricle such as Peak Systolic Longitudinal Strain (PSLS) and Torsion (apex-basal rotation) were determined by speckle tracking echocardiography using commercially available computer software. Besides, Left Ventricle Ejection Fraction (LVEF), calculated with Simpson method, was evaluated at one month follow-up.

Results: In all patients at discharge, a reduction of transaortic peak pressure gradient (p=0.0006), of mean pressure gradient (p=0.0001) was observed, with a concomitant increase in aortic valve area (p=0.0001). In addition, 2D speckle analysis showed a significant improvement of PSLS at discharge (-10.6±2.8 vs -1.8±3.9%, p=0.008). Similarly, left ventricular torsion was significantly increased comparing to pre-implantation values (7.2±5.1 vs 11.5±6.1, p=0.015). However, overall LVEF did not change (51.4±1.8 vs 50.9±1.5%, p=0.05).

Conclusions: Deformation indices of PSLS and Torsion are able to detect early improvement of left ventricle function after TAVI regardless LVEF alteration. Moreover, LVEF seems to predict LVEF in one month. Larger studies with long term follow-up are required.
Mitral regurgitation after transcatheter aortic valve implantation with the Medtronic-CoreValve prostheses: predictors of mortality

1. Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; 2. Academic Medical Center, University of Amsterdam, Department of Cardiothoracic Surgery, Amsterdam, Netherlands.

Background: Mitral regurgitation (MR) is a risk factor on long-term survival in elderly patients who underwent an aortic valve replacement (AVR). The impact of mitral regurgitation in patients who undergo transcatheter aortic valve implantation (TAVI) is unknown. The aim of the study was to assess the influence of MR on survival in TAVI in patients treated with a Medtronic CoreValve prosthesis.

Methods: In this single center prospective observational study we included 100 patients (age 81±6 years, 40 male) with severe symptomatic aortic valve stenosis who underwent TAVI with the Medtronic-CoreValve bioprosthesis and underwent a post procedural echocardiographic evaluation. Other clinical parameters were obtained from the medical history.

Results: From the patients with an MR grade ≥3 (n=94) pre-procedural, 14% increased to MR grade ≥3 after TAVI (p=0.002) and from 6 patients with moderate to severe MR pre-procedural only one patient had a MR grade <3 after TAVI. Forty percent of the patients with significant (grade ≥3) MR died within 1 year versus 20% of the patients with MR grade <3 (p=0.051); 30-day mortality and 30-day cardiovascular mortality were not influenced by MR grade ≥3 following TAVI.

Conclusion: After TAVI with a CoreValve prosthesis there is a significant increase in MR grade in patients with MR grade <3. One year survival shows a tendency to be impaired in patients with a significant MR post TAVI.

Renal outcome after transcatheter aortic valve implantation

1. University Heart Center Hamburg, Hamburg, Germany; 2. University Heart Center Hamburg, Hamburg, Germany.

Background: Renal function impairment is a frequent complication after cardiac valve implantation procedures. Data on risk factors for renal impairment after transcatheter aortic valve implantation (TAVI) are limited.

Methods: In 299 consecutive TAVI patients (mean age 80 ± 7.12 years; 54.6% women) we assessed renal function through plasma creatinine measurement and estimated glomerular filtration rate at baseline, peak during 72 h post procedure and at discharge and monitored individuals for incident renal failure. Patients were divided into severely impaired renal function (eGFR < 30 ml/min/1.73 m2), severe stage 3 renal failure (eGFR 30-59 ml/min/1.73 m2), stage 2 renal failure (eGFR 50-60 ml/min/1.73 m2) and normal renal function (eGFR ≥ 60 ml/min/1.73 m2). We assessed baseline and post-procedural laboratory parameters including body mass index (BMI), age, body constitution and procedure time.

Results: Severe kidney failure (stage 3) occurred in 20% of patients. Risk factors for severe renal failure included BMI (OR 2.30, 95% CI 1.04-5.13, p = 0.04), body mass index (OR 1.09, 95% CI 1.03-1.15, p = 0.007) and logarithmically transformed baseline creatinine was related to incident renal failure (Odds ratio [OR] 1.91, 95% confidence interval [CI] 1.19-3.10, p=0.007). Correlates of renal failure besides age and sex in age and sex adjusted logistic regression analyses were body mass index (OR 1.09 95% CI 1.03-1.15, P=0.001) and logarithmically transformed procedure time (OR 2.24, 95% CI 1.08-4.70, P=0.03). In linear regression analyses procedure time was strongly related to peak change in glomerular filtration rate.

Conclusions: Besides age and sex, body constitution and procedure time are correlates of acute kidney injury after TAVI. When assessing periprocedural risk factors these factors should be considered in particular in elderly patients with pre-existent renal impairment.

Predictors of mortality post balloon aortic valvuloplasty, results from the BRAVO registry

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Purpose: There have been notable advances in balloon aortic valvuloplasty (BAV) technique including RF pacing and improved management of the large sheath access site. However, a subgroup of patients continues to have poor outcomes despite intervention, and prognostic variables are required in a contemporary context. We sought to examine the correlates of 1-year mortality from a recent BAV registry.

Methods: We conducted a retrospective review of patients who underwent non-emergent, retrograde BAV at two high volume centers from 1/1/2005 - 11/1/2010.

Baseline demographic, laboratory, hemodynamic, and procedural characteristics were compared according to 1-year survival post-index BAV procedure.
Off-label indications for trans-catheter aortic valve implantation

Objective: Trans-catheter Aortic Valve Implantation (TAVI) has emerged as a novel therapeutic approach for patients with severe aortic stenosis (AS) undergoing high surgical risk. We describe our experience with off-label indications for TAVI.

-methods: 186 patients underwent TAVI in our institution from August 2008 to December 2011 using trans-femoral, trans-axillary, trans-apical and trans-oriental approaches. Clinical indication for TAVI was based on consensus criteria from the Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery. Current indications for TAVI consist of symptomatic patients with severe tricuspid native aortic stenosis. We describe herein our initial experience of TAVI in patients with off-label indication.

-results: In all patients implanted valve of was successful: 6 patients received CoreValve (1 trans-axillary and 5 trans-femoral) and 5 patients received Edwards-Sapien (4 trans-apical and 1 trans-femoral). In-hospital mortality was 0%. Valve hemodynamic end function were excellent in all patients. A shift from passive to more active conduit was observed.

-conclusions: TAVI is a good alternative to surgical AVR in high-risk patients with severe AS. TAVI for off-label indications such as pure aortic insufficiency, bicuspid aortic valve stenosis, and failed prosthetic valve (both aortic and mitral), is feasible and safe and may be considered in selected patients.

P4210
Incidence and predictors of combined safety endpoints occurrence after transcatheter Sapien XT and CoreValve implantation. A single Centre experience

Aims: To evaluate incidence and predictors of combined safety endpoints occurrence (Valve Academic Research Consortium – VARC definitions) among high-risk inoperable patients with symptomatic, severe aortic stenosis (AS) undergoing trans-femoral/trans-apical transcatheter aortic valve implantation (TAVI) with current commercially available prostheses.

Methods and Results: We enrolled consecutive patients undergoing TAVI with Edwards SAPIEN XT – SXT (Edwards Lifesciences, Irvine, California; n = 50) or Medtronic CoreValve – CoV (Medtronic Inc, Minneapolis, Minnesota; n = 50). A good device success was achieved with both SXT and CoV (98% versus 90%, p = 0.20). After TAVI, transcatheter echocardiography and aortography showed higher paravalvular regurgitation incidence with CoV (p < 0.0001) without differences in terms of moderate/severe regurgitation among groups (p = 0.03, SXT versus CoV). In-hospital, major vascular complications (p = 1.00), stroke (p = 1.00) and death (p = 1.00) occurrence were similar throughout SXT and CoV. A statistical trend toward worse renal function after CoV implantation was observed (p = 0.056). Permanent PM need was more frequent after CoV implantation (p = 0.007). At 1-month follow-up, cumulative VARC-combined safety endpoints incidence was 17% versus 34.6% (p = 0.01, SXT versus CoV), mainly driven from a numerically higher stroke (10%) and Acute Kidney Injury Stage 3 incidence (6%) associated with CoV at multivariate analysis.

Conclusions: Together with a previous history of percutaneous coronary revascularization, TAVI with Edwards SAPIEN XT was found independent predictor of lower VARC-combined safety endpoints occurrence, as compared with Medtronic CoreValve. Larger cohorts are needed to confirm these results.

MYOCARDIAL FUNCTION LEFT VENTRICULAR DEFORMATION

P4211
Impact of acute normobaric hypoxia on regional and global myocardial function: a speckle tracking echocardiography study

Background: Exposure to normobaric hypoxia leads to an increase of LV overall twist and regional myocardial deformation in both ventricles. The contractile reserve during hypoxic exercise is reduced in LV. In addition, hypoxia had an impact on the ratio of passive conduit to active contraction phase in right atrium.

Methods: Fourteen subjects underwent two-dimensional speckle tracking echocardiography (2D-SPE) examination during normoxia and in a normobaric hypoxia chamber. Examinations were performed at rest and during bicycle exercise test. The following parameters were quantified in both atria and ventricles: Strain (S), systolic strain rate (SRS), early (SRE) and late (SRA) diastolic strain rate, in addition, left ventricular (LV) overall twist, systolic twist- and diastolic untwist rate were calculated.

Results: During hypoxia SRE and SRA increased significantly in both ventricles compared to baseline. The increase of LV SRS and SRE during normoxic exercise was higher significantly when compared with baseline under hypoxia (for SRS: 0.55±0.22 vs. -0.34±0.24 1/s, p = 0.024; for SRE: 0.56±0.29 vs. 0.23±0.29 1/s, p = 0.005). For the right ventricle (RV) no significant difference of exercise induced increase of systolic strain rate (SRS) -1.07±0.52 under normoxia vs. -1.28±0.24 1/s under hypoxic conditions, p = 0.47. LV overall twist, systolic twist- and diastolic untwist rate were enhanced during hypoxia. A shift from passive conduit (S) to active contraction (SRA) phase during hypoxia was noted for the right atrium (RA) (S/RA 0.72±0.13 under hypoxia vs. 1.17±0.17 under normoxia). SRE/SRA of RA correlated to systolic pulmonary pressure (r = -0.78, p < 0.001) (Figure 1).

Conclusions: Exposure to normobaric hypoxia leads to an increase of LV overall twist and regional myocardial deformation in both ventricles. The contractile reserve during hypoxic exercise is reduced in LV. In addition, hypoxia had an impact on the ratio of passive conduit to active contraction phase in right atrium.

P4212
Inhibition of Interleukin-1 activity by anakinra improves left ventricular myocardial deformation and torsion in patients with CAD and coexistent rheumatoid arthritis: a randomized trial

Background: Inhibition of Interleukin-1 activity by anakinra is used for the treatment of rheumatoid arthritis (RA) and shows favourable effects on left ventricular function in these patients. We investigated the effects of anakinra on LV function in patients with CAD and coexistent RA.

Methods: 40 patients with CAD and coexistent RA were randomized to receive a single injection of anakinra (100mg s.c.). At baseline and 3 hours after the injection we assessed: a) WMSI and EF by 2D echocardiography b) the LV Global Longitudinal Strain (GLS) and Torsion using speckle tracking echocardiography c) systolic (Sm) and early diastolic (Em) myocardial velocities of the mitral annulus by using tissue Doppler (TDI) d) the ratio of E wave of the mitral inflow measured by pulsed wave Doppler to the Em e) Fas, Fas ligand, nitrotyrosine (NT) and protein carbonyls (PC) serum levels.

Results: After 3 hours of anakinra injection, there were an increase in Sm (7.2±1.7 vs. 9.1±2.1 cm/s) and Em (7.7±2.7 vs. 9.1±3.1 cm/s) velocity along with a decrease in the Em/E ratio (12.1±10.2 vs. 9.5±7.9) (p < 0.001). Furthermore, there were an improvement in Torsion (14.2±5.6 vs. 18.2±5.5 degrees) and GLS (-16.2±4.7% vs. -19.0±4.9%), as well as WMSI (1.33±0.43 vs. 1.21±0.31) and EF (51.8±10.0% vs. 57.6±10.9%), compared to baseline (p < 0.001). Additionally, there were a decrease in NT (median 6.66 vs. 6.15), PC

Figure 1
Prognostic significance of speckle tracking-derived chronic and acute smoking-induced impairment in left ventricular rotation and torsion and its relation to systemic risk factors: hyperglycemia defined by HbA1c and inflammatory conditions.

Materials & Methods: 83 patients with recent diagnosis of stable MCD (at least two vessels with stenosis > 70% in coronary angiography), age 63±9 years, 25 women and 58 men, were followed up for approximately 20 months (12-31) to assess the occurrence of primary end-point: End1 (all cause death or myocardial infarction) and secondary end-point: End2 (mortality, myocardial infarction, cardiac hospitalization or need for unplanned revascularization). Mean LVEF was 49.9 ± 10.2% and predominant angina class was CCS III (69%). The management was individualized based on heart team decision resulting in 55% angioplasty and 22% bypass grafting rate.

Results: There were 3 deaths (3.6%), 12 MI (14%), 4 ischemic strokes (5%), 36 hospitalizations (43%) and 11 unplanned revascularizations (13%) during the follow-up period. In univariate analysis the following prognostic factors of End1 were identified: (1) age, (2) history of diabetes > 110mg/dl (p=0.03), (3) history of hypertension > 150/90 mmHg (p=0.001), (4) QRS duration > 120ms (p=0.001), (5) LV ejection fraction < 50% (p=0.001), WBC > 110,000/μl (p=0.03), HbA1c > 6.6% (p=0.02) in univariate analysis. In multivariate analysis HbA1c level (β=0.426, p=0.001) was the strongest independent positive predictor for End2. Only Hba1c level reduction of apoptosis and nitrooxidative stress.

Conclusion: Treatment with anakinra improves markers of systolic and diastolic LV function by inhibiting the detrimental action of IL-1 on myocardium through the reduction of apoptosis and nitrooxidative stress.

Correlation of area strain by three-dimensional speckle tracking echocardiography with exercise capacity in subjects undergoing treadmill exercise test

Purpose: Area strain is a new index for left ventricular deformation measured from 3-dimensional speckle tracking echocardiography (3D STE). However, its clinical significance has rarely been studied.

Methods: This study included 40 subjects who undergoing regular health examination. All of the subjects did not have coronary artery disease or any structure heart disease and were free of symptoms. Global area strain (GAS) from both 2- and 3-dimensional long-axis strain (GLS) was measured by 2-dimensional speckle tracking echocardiography (2D STE). The test was performed after 30 minutes of rest without any physical activity.

Results: One subject was excluded due to poor 3D image. The remaining 39 subjects (age 50±9 years, 27 men) formed the basis of this study. Total exercise time was 545±110 seconds. GAS was significantly correlated with exercise time (r=0.502, p =0.001) but not with left ventricular ejection fraction (r = 0.129, p = 0.434). GLS (r = -0.231, p = 0.157), and early diastolic mitral filling velocity to annulus velocity ratio (E/e', r = -0.284, p = 0.079). There were 3 subjects with impaired glucose tolerance (110-125mg/dl). GAS (OR 1.379, 95%CI 1.009-1.885, p = 0.044) and E/e' (OR 2.048, 95%CI 1.086-3.862, p = 0.027) were predictors for impaired exercise capacity but not GLS and ejection fraction.

Conclusion: GAS from 3D STE was correlated with exercise capacity in apparent healthy subjects but not GLS from 2D STE.

Chronic and acute smoking-induced impairment in longitudinal myoccardial function: a strain-imaging study in healthy young smokers

Background: Smoking is a significant risk factor for cardiovascular disease. The aim of this study was to evaluate the effects of smoking on left ventricular (LV) longitudinal function by using speckle-tracking echocardiography in healthy young subjects.

Methods: Eighty healthy volunteers (age 18-45 years), smokers (group SM, n=42) and non-smoking controls (group C, n=38) participated in the study. An echocardiographic exam was performed in controls and in smokers (group SM-1) after abstaining from smoking and coffee consumption for 12 hours. A repeat echocardiogram was done in SM after smoking two cigarettes and staying in a quiet room for 15 minutes (group SM-2). Left ventricular (LV) longitudinal strain (GS) and strain-rate (SR) were measured in apical views. To examine early diastolic relaxation, the following parameters were measured: (1) Change in strain during the first one-third of diastole (Strain Imaging Diastolic Index [SI-DI] = [(GSend-end - GSend-systole) / GSend-systole] *100), (2)Time-to-peak SRa wave, indexed to diastolic duration and expressed as percent of total diastolic time. (3)Percent change in strain at the end of SRa wave, representing the strain difference from end-systole to the end of the early diastolic relaxation.

Results: The two groups had similar age, body surface area, LV ejection fraction, LV mass and left atrial volume index. Heart rate and blood pressure increased after smoking. End-systolic GS, SRa and SI were not significantly different in both groups. Within cigarettes SRa wave was increased in SM-2 group (p=0.008). At first one-third of diastole, GS was significantly different between C and SM-1 (7.2±1.6%, 8.7±2.5%, respectively, p<0.001) and changed more in SM-2 (-10.6±3.3%, p=0.001 compared to SM-1 and C). SI-DI was significantly lower in SM-1 compared to C (SM-1: 58±9.8%, C: 68±13.6%, p=0.004) and was further reduced after smoking two cigarettes (SM-2: 49±14.1%, p=0.001 compared to SM-1 and C). Time-to-peak SRa wave was equal in C and SM-1 (24.4±5.4% and 25.2±5.2% respectively, p=0.462) but was significantly prolonged in SM-2 (30.1±6.7%, p=0.001 compared to C and SM-1). Change in strain at the end of SRa wave was significantly lower in SM-1 compared to C (72.2±3.8% and 74.8±5.3% respectively, p=0.017) and was further reduced in SM-2 (70.8±3.7%, p=0.001 compared to C, p=0.008 compared to SM-1).
**Conclusion:** Delayed LV diastolic relaxation is seen in healthy chronic smokers, even after abstinence from smoking for several hours. Acute smoking inhalation induces a further delay in diastolic relaxation while systolic function is preserved.

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**Two-dimensional Speckle-tracking Echocardiography to Identify reversible myocardial dysfunction**

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**Purpose:** Two-dimensional speckle-tracking echocardiography (2DSTE) could allow analysis of myocardial viability after acute myocardial infarction (AMI). This study evaluated the predictive value of 2DSTE for improvement in cardiac function after AMI in comparison with contrast-enhanced cardiac magnetic resonance imaging (cMRI).

**Methods:** In 25 patients with first-time acute ST elevation myocardial infarction, myocardial viability was assessed using 2DSTE and cMRI to predict recovery of function at 6 months follow-up. For each left ventricular segment in a 16-segment model, peak radial, circumferential and longitudinal strain was determined using 2DSTE (EchoPAC, GE Ultrasound, Horton, Norway), and the relative extent of hyperenhancement using cMRI.

**Results:** Of 126 segments with impaired function early after AMI, 65 showed regional recovery. Compared with segments showing functional improvement, those that failed to recover had lower peak radial (18.1±26 vs. 34.2±20, p<0.001), circumferential (23.0±21 vs. 30.4±22, p<0.001) and longitudinal (9.4±5 vs. 13.5±5, p<0.001) strain and a greater extent of hyperenhancement (71±21% vs. 45±20%, p<0.001). Among strain parameters, circumferential strain yielded greater area under the curve (0.914) than radial and longitudinal strain (0.717 and 0.743, respectively). The predictive value of circumferential strain (sensitivity 80.3%, specificity 81.2%, at a cutoff value of 12.5%) could be compared to that of hyperenhancement by cMRI (sensitivity 87.8%, specificity 68.1%, area under the curve 0.935, at a cutoff of 46% hyperenhancement).

**Conclusions:** Myocardial deformation imaging based on 2DSTE is a powerful novel modality to identify reversible myocardial dysfunction after AMI.

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**Soluble angiotensin converting enzyme is linked to impaired myocardial deformation and torsion in untreated hypertensives**

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**Background:** Soluble angiotensin converting enzyme (sACE) in linked to increased angiotensin II production and thus promotes cardiac and vascular fibrosis. LV myocardial deformation and torsion as assessed by speckle tracking echocardiography are markers of subclinical myocardial dysfunction. We investigated the association circulating sACE with LV deformation markers and arterial stiffness in untreated hypertensives.

**Methods:** In 220 untreated patients (age:54±11 years) with essential hypertension and 80 healthy controls, we measured a) LV longitudinal, circumferential and radial strain (S), peak torsion and the percentage changes between peak twisting and untwisting at mitral valve opening and end of early diastolic filling using speckle tracking echocardiography b) Carotid to femoral arterial pulse wave velocity (PWV) as a marker of arterial stiffness c) plasma levels of sACE.

**Results:** Compared to controls, patients had decreased longitudinal strain (19.2±2.6 vs. 22.9±2.5, p<0.001), peak torsion (13.8±3.4 vs.15.7±3.6, deg p<0.05), % changes between peak twisting and untwisting at mitral valve opening (29.8±18 vs. 38.3±7, p<0.05) as well as at end of early diastolic filling (67.4±9 vs. 73.8±6, p<0.05), higher PWV (10.5±1.8 vs 8.2±1.5, p<0.01) and higher sACE levels (27.8±21.7 vs 18.7±16 ppm, p<0.05). Increasing sACE was related reduced radial S, peak torsion and % change between peak twisting and untwisting at end of early diastolic filling using (r=0.41, r=0.40, r=0.37, p<0.05). By regression analysis, the above relations remained significant after adjustment for age, sex, BMI and blood pressure (p<0.01). No association was observed between sACE and PWV (p=ns).

**Conclusions:** Soluble angiotensin converting enzyme is related to impaired myocardial deformation and torsion in untreated patients with essential hypertension likely by promoting abnormal collagen turnover and fibrosis.

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**Evaluation of left ventricular segmental strain by three-dimensional echocardiography**

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**Background:** Three-dimensional speckle tracking imaging (3DS) allows assessment of 3D left ventricular (LV) function and volume with high sensitivities. However, it is still unclear whether feasibility of regional data collection and estimates of regional strains differ between 3DS and two-dimensional speckle tracking imaging (2DS). We examined this issue in the present study.

**Methods:** Standard 2D echocardiography and 3D data set collection by using Vivid E9 with 4V probe (GE Healthcare) were performed in 212 subjects, who participated in an annual health examination. Apical ling axis, four chamber and two chamber views were recorded to assess longitudinal strain by 2DS. 3DS and 2DS were analyzed off line by EchoPAC(GE Healthcare). We excluded subjects in whom 4 or more of 18 LV segments were unsuitable for strain determination, and 49 subjects (all women, age 63±12 years) contributed to the present analysis.

**Results:** The feasibility of 3DS was lower at LV base level (Figure). There were significant differences between strain by 3DS and longitudinal strain by 2DS in the mid-antero-septum (-25.3% vs. 21.4%, p<0.0001), mid-lateral (-18.1% vs. -24.3%, p<0.0001), mid-posterior (-23.7% vs. -18.9%, p<0.0001) and mid anterior strain (-25.5% vs. -19.6%, p<0.0001). Strain in the other segments and global strain were similar in 3DS and 2DS.

**Conclusions:** There are regional differences in feasibility of 3DS and data agreement between 3DS and 2DS. 3DS provides significantly lower estimates of strains in mid-level of the ventricle compared with 2DS.
Assessment of left ventricular myocardial deformation and mechanical dysynchrony in patients with heart failure: insights from three-dimensional wall motion analysis

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Purpose: Impaired myocardial contractility is detected with two-dimensional speckle tracking echocardiography (2DSTE) in heart failure patients with normal ejection fraction (HFNEF); however, 2DSTE is limited by ignorance of actual three-dimensional myocardial motion. Therefore, this study is aimed to further explore the myocardial function including the global dysynchrony in HFNEF with three-dimensional speckle-tracking echocardiography (3DSTE) which circumvent the limitation of 2DSTE.

Method: We enrolled thirty-three healthy subjects (48±12 years; 48.5% male), 53 patients with HFNEF (70±10 years; 56.6% male) and 41 with reduced ejection fraction (HFREF) (65±10 years; 87.5% male) in our study. 3D-STE was performed (Toshiba Medical Systems, Japan) to obtain global area strain (AS), longitudinal strain (LS), circumferential strain (CS) and radial strain (RS). LV dysynchrony, AS-systolic dyssynchrony index (AS-SDI) was calculated from the standard deviation of area strain of 16 segments.

Results: Global AS, LS, CS, and RS in patients with HFNEF were significantly higher than those in counterparts with HFREF (all p<0.001) but lower than in the normal group (all p<0.05) (Table 1). Intragently, AS-SDI was significantly produced in patients with HFREF compared with those in HFNEF, and the difference in AS-SDI was significant higher in HFREF than that in patients with HFNEF (61.0% vs. 20.8%; chi-square =15.83, p<0.001).

Conclusions: As a combination of both LS and CS, not only can 3D-derived global AS accurately detect subtle myocardial dysfunction in HFNEF, it can also assess LV dysynchrony more comprehensively in a 16-segmental mode during one cardiac cycle, which might be promising for further exploring the pathophysiology of HFNEF.

Area strain for the assessment of regional left ventricular wall thickening using 3D Speckle Tracking

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Background: 3D speckle tracking is a promising new technology. It allows reconstructing LV motion in time and space. Shortening in the longitudinal and circumferential directions can be combined in an area strain (aS) measurement which in contrast to wall thickening (radial strain) does not require endo- and epicardial border detection. We investigated the relation between aS and wall thickening by two geometrically independent measurements.

Methods: In 12 patients, 3D full volume echocardiographic clips of the LV were acquired. 3D endo- and epicardial border detection was performed to calculate wall thickening, whereas 3D speckle tracking was used to assess aS. All geometric measurements were performed frame-by-frame at 336 local sites on refined endo- and epicardial borders.

Results: 52±7±20% wall thickness -aS datapairs were retrieved. In ROC analysis, an aS>–15.3% was able to detect a systolic wall thickening >20% with a sensitivity specificity of 83.2% and 80.2%, respectively. The area under the ROC curve was 0.88. As expected from deformation theory, there was a nonlinear relation between wall thickening and aS (Poisson effect). The estimated Poisson’s ratio of myocardium was 0.39, showing even myocardial tissue is not perfectly elastic and incompressible (i.e., 0.50), but exhibits a volume loss during systole.

Conclusions: aS derived from 3D speckle tracking reflects local wall thickening during the cardiac cycle and has the potential to detect regional contraction abnormalities. In principle, aS can be converted directly into radial strain using basic elastic deformation formulas (Poisson effect), but the compressible nature of myocardial tissue should be considered by applying a Poisson’s ratio below 0.50.

Diabetic retinopathy is associated with the occurrence of subclinical diabetic cardiomyopathy in patients with type II diabetes

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Background: Diabetic retinopathy (DR), as a marker of microvascular disease, is associated with increased risk of cardiovascular diseases (CVD). However, there is no data on the relationship between DR and subclinical diabetic cardiomyopathy in patients (pts) with type 2 diabetes (DM).

Method: We performed stereoscopic fundus photography with 7 standard fields in 114 type 2 DM pts (62±9 years, 53% female) without overt CVD. Detailed transitory echocardiography with two-dimensional speckle tracking imaging was performed to measure global left ventricular (LV) function, including longitudinal strain and strain rate.

Results: DR including both non-proliferative and proliferative retinopathy was detected in 22 pts (19%). There were no significant differences in age (63±6 vs. 62±10), female gender (50 vs. 56%), fasting glucose (7.5±2.5 vs. 7.4±1.9 mmol/L) and HbA1c (8.0±1.3 vs. 7.6±1.2%) between pts with or without DR (all P>0.05). However, pts with DR had a longer disease duration than pts without DR (14±8 vs. 9±7 years, P<0.01). Conventional echocardiography showed no differences in LV ejection fraction (63±6 vs. 64±8%), and LV mass index (200±47 vs. 203±62 g/m²) between the two groups (P>0.05). However, pts with DR had a significantly lower LV global longitudinal strain (-18.3±1.2% vs. -20.1±1.5%, P<0.05) and strain rate (-0.84±0.15 vs. -0.95±0.33, P<0.05) compared with pts without DR. After adjustment with age, gender, HbA1c, duration of disease and conventional cardiovascular risk factors, multivariate linear regression revealed that DR was independently associated with impaired LV global longitudinal strain rate (β=0.28, confidence interval [CI]=0.17 to 0.39, P<0.01), but not LV global strain (β=0.18, CI to 0.22 to 0.20, P=0.09).

Conclusion: Our results demonstrated that DR was detected in 19% of type 2 DM pts without overt CVD. The occurrence of DR was independently associated with subclinical LV myocardial dysfunction as detected by two-dimensional speckle tracking imaging. The findings of the study suggested that microvascular...
Ejection fraction and deformation in response to three different chemotherapeutic regimes

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Purpose: Evaluation of cardiac function is mandatory for cancer patients who receive potentially cardiotoxic (CTX) regimes, in whom analyses of ejection fraction (EF) and myocardial mechanics have shown subclinical myocardial damage. We sought to define the demographic, clinical and chemotherapy regimes associated with CTX.

Methods: We enrolled 166 patients (50±14y, 77 women) receiving anthracycline 214±112 mg/m² [group A; n=65], trastuzumab [group T; n=53] or T with A dose 213±49 mg/m² [group AT; n=48]. Conventional echo indices (EF, mitral annular s' and e' velocity) and myocardial deformation indices (global longitudinal peak systolic strain [GLS], strain rate [SR-s] and early diastolic strain rate [SR-e] from speckle tracking) were measured at baseline and follow-up (10±8 months). The association of regimens with dEF was sought in a multiple linear regression.

Results: Age (p<0.003), gender (p=0.001), dyslipidemia (p=0.03), and radiation therapy (p=0.001) were significantly different among three groups. Reduction of EF in AT was in group AT [Fig 1] (dEF: 7.0±4.9%; p=0.001) occurring in 6 group A, 0 group T and 4 group AT patients. SR's significantly decreased in groups T and AT. There were no significant differences in s', e' GLS and SR-e among the groups. Combination regimen [group AT] was correspondently associated with dEF after adjusting for age, gender, dyslipidemia and radiation therapy (p=0.011, β=0.221, 95% CI [-1.342 to 0.564]).

Conclusion: Combined A+T is most conducive to reduced EF and SR-s is reduced in T and A+T. Some patients are sensitive to anthracycline and/or radiation therapy. Careful assessment of LV dysfunction is warranted in all patients receiving CTX agents.

Left ventricular dysynchrony in patients with microvascular obstruction after primary percutaneous coronary intervention evaluated with Real-time 3D speckle tracking echocardiography

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Purpose: Microvascular obstruction (MVO) in patients with ST-segment-elevation myocardial infarction (STEMI) is associated with a negative remodeling of the left ventricle and worse clinical outcome. However, the effects of MVO on mechanical ventricular synchrony in these patients is poorly known. In this study we investigated the impact of MVO on synchrony of left ventricular (LV) contraction in patients with STEMI treated by percutaneous coronary intervention (PCI).

Methods: We enrolled 35 consecutive patients (average 56.1±12.9; 32 males) with a first STEMI undergoing PCI within 12 hours of symptoms onset. Angiographic diagnosis was diagnosed when Thrombolysis in Myocardial Infarction (TIMI) coronary flow grade after PCI was ≤2 and/or myoventricular grade <2 in patients with TIMI flow grade of 3. Patients underwent real time 3D speckle-tracking (3DST) echocardiogram at baseline and at 1 month follow up. The standard 16-segment model of the LV anatomy was used for analysis of regional LV contraction. Presence and degree of mechanical desynchrony was evaluated with the systolic dysynchrony index (SDI, standard deviation of the time to peak LV-segment) for strain in longitudinal (LS), circumferential (CS) and radial (RS) direction.

Results: MVO occurred in 9 of the 35 patients (25.7%). Patients with MVO, compared to no-MVO patients, were older (63±11 vs 54±12; p=0.05), had a higher time to PCI (<3h: 0 vs 50%); 3h: 56% vs 34%; >3h: 44% vs 14% respectively; p=0.02) and a lower prevalence of pre-infarctual angina (73.1% vs 33.3%, p=0.05), while there were no found differences between groups in gender, in-fact side, culprit vessel and troponin peak serum level. LVEF was lower in MVO patients both at pre-discharge (42±8% vs 53±12%, p=0.03) and at follow up (49±8% vs 58±8%, p<0.01). Moreover, patients with MVO showed higher values of SDI on LS, CS and RS direction compared to those without MVO both at baseline (19.9±4 vs 14.3±4.6, p=0.006; 15.6±4 vs 12.5±5.1, p=0.00; 22.1±6.9 vs 13.7±5.0, p=0.001, respectively) and follow up (15.8±4 vs 10.6±2.9, p<0.01; 11.4±5.1 vs 7.0±2.7, p=0.008; 18.6±4.5 vs 9.6±3.6, p<0.05, respectively).

Conclusion: Patients with MVO after PCI showed a lower LV contractation and a higher degree of LV mechanical dysynchrony at pre-discharge. Both LVEF and LV dysynchrony significantly improved at 1 month of follow up in the two groups of patients, but remained impaired in MVO patients compared to reperfused patients.

The dangerous liaison between left ventricular systolic function and mitral annulus calcification in patients with type 2 diabetes without myocardial ischaemia. Data from SHORTWAVE study

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Mitral annulus calcification (MAC) is a chronic, degenerative process associated with knownatherosclerotic risk factors such as diabetes mellitus (DM), hypercholesterolemia, hypertension and/or hypertriglyceridemia. MAC is a marker for coronary artery disease (CAD) and predicts long-term outcome in the general population. Very little data are available on MAC in patients with DM. Accordingly, we analyzed the possible relations between MAC and parameters of LV systolic function in a group of consecutive patients recruited from the SHORTWAVE study, conceived to assess the prevalence and characteristics of subclinical abnormalities in LV systolic contractility and function in patients with DM, without clinical or echocardiographic evidence of cardiac disease. A group of 120 healthy subjects was used as control.

Methods: We analyzed baseline clinical and echocardiographic data from 386 patients with type 2 DM without myocardial ischemia, enrolled in the SHORTWAVE study. 120 healthy subjects were used to define the dysfunction of LV circumferential and longitudinal (C-L) fibers. Stress-corrected midwall shortening (sc-MS) and mitral annular peak systolic velocity (S) were considered as indexes of C-L shortening and classified low if < 90% and low or < 6.5 cm/sec, respectively (10th percentiles of controls).

Results: MAC was detected in 107 patients (28%). Patients with MAC are older (72±10 vs 67±7; p< 0.001) with longer duration of DM (9.0±2.5 vs 5.0±2.10); p=0.04) and under more medications: betablockers (40 vs 28%; p= 0.02) or antihypertensive medications (1.8±1.3 vs 1.4±1.3; p=0.05). Echocardiographic characteristics of patients with MAC were reduced sc-MS (88.4±14.9 vs 92.6±14.3%; p=0.01) and longitudinal shortening (49.3±7.9 vs 52.0±2.0 cm/sec; p<0.001). Additionally, they had higher LV mass (51±12 vs 47±12 g/m²; p<0.004), increased left atrial volume (26.9±8.3 vs 21.3±8.1 ml/m²; p<0.001) and they were more often associated with aortic valve calcification (48% vs 6%; p< 0.001). Multiple logistic regression analysis demonstrated older age (OR 1.03 [IC 1.01-1.06], p=0.009) larger left atrium volume (OR 1.19 [IC 1.11-1.28], p<0.001) and presence of comorbidity LV systolic dysfunction of C-L fibers (OR 3.00 [IC 1.57-7.92], p=0.001) as independent factors associated with MAC.

Conclusions: MAC is detectable in one fifth of patients with type2 DM without evidence of myocardial ischemia and is mainly related to LV systolic dysfunction independently of age. Larger left atrial volume is also associated with MAC and may represent an indirect sign of impaired LV diastolic function.

Effects of radiotherapy on right and left heart function in patients with left-sided breast and lung cancer detected by strain and strain rate imaging

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Aim: Radiotherapy (RT) of the chest is commonly used in the management of early-stage breast cancer and lung cancer. RT administered on the left breast, left thoracic wall, or on the internal mammary lymph nodes usually involves irradiation of the heart and is potentially associated with long-term cardiovascular adverse events. We aimed to investigate the occurrence of early radiation-induced changes in cardiac function using strain (S) and strain rate imaging (SR) in patients (pts) with left-sided breast cancer (LSBC) and left-sided lung cancer (LSLC). We included in this study. All pts received a computed tomography scan for RT planning. Radiation dose was 50 Gray (Gy) in 25 fractions. An additional boost of 10 or 16 Gy was delivered to the tumoral cavity in case of breastconserving surgery and lung boost. Radiation effect on cardiac function was assessed
by speckle tracking derived right ventricular (RV) and left ventricular (LV) global longitudinal peak systolic S and SR, obtained before early and at 1 month follow-up after RT.

Results: Total radiation dose delivered was 51.7±4.9 Gy in LSBC group, 54.7±9.1 Gy in LSLC group. The mean dose to the heart was 6.3±4.5 Gy and the mean heart volume receiving 30 Gy (V30) was 7.3±6.5% in LSBC group. In pts with LSLC, the mean dose to the heart was 21.3±7 Gy and V30 was 30.1±10%. Compared to baseline, RV-S was significantly decreased early after RT and at first month follow-up in both groups (-22.3±4.3 vs. -19.9±3.4 vs. -19.8±3.8, respectively; p<0.001). RV-SR changed significantly in pts with LSBC (-1.5±0.35 vs. -1.3±0.28 vs. -1.2±0.29 respectively;p<0.001) although we did not note any significant change in pts with LSLC (-1.29±0.26 vs. -1.26±0.26 vs. -1.09±0.66 respectively;p>0.192). Interestingly, LV-S differed significantly in LSBC group (-20.7±4.4 vs. -19.2±3.6 vs. -19.0±3.7, respectively; p<0.03). No decline in LV deformations was observed in pts with LSBC (-20.3±0.3 vs. -19.1±0.31 vs. -19.5±2.06, respectively; p>0.095).

Conclusion: Pts receiving RT for LSBC and LSLC have decreased RV-S whereas LV-S was only reduced in LSLC group following RT. RV-SR was also decreased in pts with LSLC. Reduction in RV-S and SR is likely due to higher radiation exposure of the right ventricle due to its anterior location. Moreover, high dose radiation exposure to heart reduced LV-S in LSLC group. This study demonstrated RT has a depot effect on both RV and LV-SR, is first to be reported.

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Reduced left ventricular contractility with electrical dyssynchrony increases the dyssynchrony by speckle tracking strain rate analysis

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Background: Left ventricular (LV) dyssynchrony were reported as a useful index for predicting the response to cardiac resynchronization therapy. However, it has not been clear that which factors influence on the dyssynchrony in patients with electrical dyssynchrony. Thus, we evaluated the degree of LV dyssynchrony in patients with right ventricular (RV) pacing by speckle tracking strain rate (SR) analysis.

Methods: Echocardiography was performed in 81 consecutive patients with RV pacing. As a dyssynchrony index, the time difference between 1st peak of LV septum and that of posterior wall (IVS-PW delay) was measured by M-mode at the mid-LV level. We used off-line software EchoPAC (GE Ultrasound) for SR analysis and measured radial SR at mid-LV short axis view. The dyssynchrony index (DI) was defined as the ratio of average myocardial thinning (negative SR) to thickening (positive SR) of 6 segments during the ejection period (Figure).

Results: Twenty-seven patients were LV ejection fraction (LVEF)<50% (lowEF) and 54 patients were >50% (highEF). Mean value of IVS-PW delay was 30±173ms, and there was no significant difference between IVS-PW delay of lowEF group and that of highEF group (304±50ms vs. 299±83ms, N.S.). DI of lowEF was significantly higher than that of highEF (28±5±3ms vs. 8±10ms, p<0.001). DI correlated with the LV end-systolic volume (r=0.536, p<0.001), QRS width (r=0.4, p=ns). Correlation of averaged LS and their mean bias were 0.52/1.59 at basal level, 0.89/1.17 at middle level and 0.73/1.46 at apical level, respectively. Correlation of global LS between the two methods was higher in group of patients who had LV twist value less than 13.4 degree (n=93) compared to group of patients with LV twist values >13.4degree (n=68).

Conclusions: Patients who had higher LV twist revealed moderate correlation of global LS between the two methods. Lower correlation and larger bias of averaged LS at basal and apical LV level between the two methods suggest LV twisting actually affects the calculation of 2D LS.

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Assessment of left ventricular dysynchrony with real-time 4D ultrasound system: comparison with Doppler Myocardial Imaging

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Background: Different current echocardiographic methods have been proposed to evaluate left ventricular mechanical dysynchrony (LVMD). The very latest generation of real-time 4D ultrasound systems (RT4DE) have the ability to acquire a full volume dataset in one cardiac cycle. Aim of the study was to compare the assessment of LVMD by Pulsed Wave- Doppler Myocardial Imaging (PW-DMI) and RT4DE.

Methods: 10 healthy volunteers (NL) and 27 pts with left bundle branch block (QRS wide 147±17ms;EF 38±7.12%, 68±11ys) and different etiology dilated cardiomyopathy (DCM-LBBB) were studied. RT4DE full volume acquisitions were divided into 16 subvolumes corresponding to the standard myocardial segments to derive timevolume curves for each (TMV). Time to peak contraction (minimum volume) in each segment is normalized for the R-R duration, and 16-SDI-4D is defined as the standard deviation of these timings, expressed as a percentage of cardiac cycle duration. The identification of the latest contracting segment of the LV was studied with TMV Map imaging demonstrating areas of delayed contraction (orange color). Dyssynchrony index by PW-DMI was measured as standard deviation of the time from beginning of QRS to the end systolic velocity in 6 basal segments (6-SDI-PW-DMI).

Results: Data acquisition and analysis with RT4DE were feasible in 35/37 pts (93.9%). The technique provided quick quantitative assessment of LVMD in one single heart cycle, during high volumes per second (vps) acquisition (38±14 vps); latest segmental TMV was of apical basal distribution in 3/25 pts, mild-basal distribution in 7/25 pts, and basal distribution in 15/25 pts respectively. 16-SDI-4D was significantly higher in the DCM-LBBB group compared with NL (9.7±7.4% vs 4.1±1.7%, p<0.05), there was no difference in 16SDI-4D be-
Brain natriuretic peptide is independently associated with indices of left ventricular filling pressure but not with left ventricular mass in asymptomatic individuals

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Purpose: Measurement of serum natriuretic peptides have been suggested to screen for the presence of left ventricular hypertrophy (LVH) or to track the regresses of LVH. LVH is a major contributor to increased left atrial pressure (LAP) and stroke volume. Natriuretic peptides are secreted actively by heart muscle and represent natriuretic and vasodilatory factors. The aim was to study LAP and LVH, and the clinical implications of LVH in asymptomatic subjects. Methods: Plasma NT-pro BNP concentrations were measured in 1,593 healthy subjects free of manifest cardiovascular disease, recruited from the London Life Sciences Prospective Population (LOLIPOP) study. All subjects underwent comprehensive echocardiographic examination, including tissue Doppler imaging, for measurement of LV mass, LV ejection fraction (LV EF), diastolic function and LAP. Results: Using stepwise linear regression models, the relationships between demographic factors, risk factors, LV structure, LV function and LV filling pressure indices with NT-pro BNP were explored. Increased age, male gender and European white ethnicity were independently associated with higher NT-pro BNP. There was an independent association of increased LAP with LV mass, LV EF, diastolic function and atrial function. Conclusions: The study showed that NT-pro BNP is a useful biomarker for the detection of hypertrophic LV remodeling, being closely associated with the morphophysiological parameters of increased LV filling pressure and LV EF.

Decreased velocity propagation of the left ventricle is associated with increased arterial stiffness

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Purpose: Aim of the present study was to evaluate the diastolic performance of the left ventricle, as assessed by velocity propagation, and correlate it with arterial stiffness indices, in essential hypertensives (EH).

Methods: We studied 113 consecutively newly diagnosed EH patients stage I-III (age 51±12.41% females) without prevalent cardiovascular disease. All patients underwent: a) complete conventional and Tissue Doppler Imaging (TDI) echocardiographic study, b) assessment of heart rate-corrected augmentation index (AIx@75) using Sphygmocor, and c) a 24-hour ambulatory blood pressure monitoring (ABPM). The study population was divided into two groups according to the median value of velocity propagation (VP): group A (n=57, VP≥59.9 cm/sec) and group B (n=56, VP<59.9 cm/sec).

Results: The two groups did not differ regarding age, gender, 24hr systolic and diastolic BP. Group B compared to A had significantly higher values of AIx@75 (7.3±3.14 vs 5.0±1.95; p=0.045) and minimum volumes (44.4±26.4 mL vs 22.3±10.3 mL; p=0.039) and lower LA ejection fraction (59.8±14.9 mL vs 55.7±19.0 mL; p=0.039). Moreover, diastolic velocity (E/DT) can be used to monitor diastolic function.

The E-wave deceleration rate E/DT but not the tissue-Doppler derived index E/Ea reliably characterizes pressure-overload induced diastolic dysfunction

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Background: The ratio of transmural to annular early diastolic velocity E/Ea is widely considered the best non-invasive determinant of diastolic function. However, recent studies in patients with diverse heart diseases have delivered highly contradictory results, suggesting that the notion of a definite cutoff of E/Ea might be diastolic dependent. We tested, for the first time in a model of pressure overload, the reliability of E/Ea and our hypothesis that the deceleration rate of early transmural diastolic velocity (E/DT) can be used to monitor diastolic function.

Methods and results: Rats underwent aortic banding (AoB) to induce pressure overload. Hypertrophy fully developed 2 weeks after AoB. At 4 and 6 weeks, the lung was excised to body weight ratio (LW/BW), a sensitive long-term marker for pulmonary congestion, dramatically increased despite preserved fractional shortening, indicating diastolic dysfunction. The time course of LW/BW was well reflected by E/DT, by the ratio of early to late transmural diastolic velocity (E/A) and the deceleration time of E (DT) but not by E/Ea. In agreement, the best correlation with LW/BW was found for E/DT (r=0.76; p<0.001), followed by E/A (r=0.69; p<0.001) and DT (r=0.62; p<0.001) whereas E/Ea showed the worst correlation (r=0.51; p<0.001). Furthermore, analysis of receiver-operating characteristic curves for the prediction of increased LW/BW revealed a significantly lower area under the curve for E/Ea (AUC=0.82) compared to those of E/DT (AUC=0.98) and DT (AUC=0.95).

Conclusion: E/DT but not the most preferred index E/Ea reliably detects and monitors diastolic dysfunction in pressure overload. The results may explain previous contradictions regarding the usefulness of E/Ea and suggest advanced validation of the new parameter E/DT in humans.

3D echocardiography facing the challenge of diastolic function evaluation

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Introduction: Left atrial (LA) ejection fraction has been recently recognized as a marker of diastolic dysfunction. LAV/A ratio was shown to be an indicator of advanced diastolic dysfunction and predictor of paroxysmal atrial fibrillation. In this study we aimed to assess the relation between LA ejection fraction by 3D echocardiography with new parameters of diastolic evaluation. Methods: 40 patients, among which 29 patients with hypertrophic cardiomyopathy with parameters of elevated left ventricle filling pressure (E/E' ≥10) and 11 controls with normal left ventricle filling pressure were prospective enrolled for 3D Transthoracic echocardiography by one heart beat (ACUSON SC2000 TM, Siemens Medical Solutions USA Inc.). Left ventricle systolic function and left atrium ejection fraction were assessed by 3D volumetric analysis. Pulsed Doppler through mitral valve and tissue Doppler parameters were measured according to the recommended guidelines.

Results: Patients with elevated left ventricle filling pressures presented higher LA maximum (71.2±31.4 mL vs 50.5±19.5 mL; p=0.045) and minimum volumes (44.4±26.4 mL vs 22.3±10.3 mL; p=0.039) and lower LA ejection fraction (39.8±14.9 mL vs 55.7±19.0 mL; p=0.039). In addition, diastolic function indices were significantly lower in patients with elevated left ventricle filling pressures (7.1±5.2 vs 3.7±2.5; p=0.003) and LA ejection fraction presented a significant negative correlation with LAV/A ratio (r=-0.43; p=0.042). Area under the receiver operating characteristic curve to diagnose elevated left ventricle filling pressures by LA ejection fraction was 0.814 (0.663 - 0.975).

Conclusion: LA ejection fraction by 3D echocardiography recognizes patients with increased LA filling pressures, therefore it might be valuable alternative at time of diastolic function evaluation.
Diagnostic value of exercise E/E' ratio for the early detection of diastolic heart failure in non-obstructive HCM patients

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Background: Heart failure in patients with diastolic dysfunction has a 25% five year mortality rate. It is likely that early detecting patients with diastolic abnormalities will lead to favorable prognosis and survival. Recently, studies on tissue Doppler imaging (TDI) have found that the ratio of the peak early diastolic velocity of mitral annulus (E/E') has good correlations with diastolic function. It is still unclear how the indices of diastolic function will change for those non-obstructive hypertrophic cardiomyopathy (HCM) patients. The objective of this study was to test the diagnostic value of exercise E/E' ratio for the early detection of diastolic heart failure (DHF) in non-obstructive HCM patients.

Methods: Echocardiography was performed in 54 non-obstructive HCM patients with normal LVEF and 61 controls before and immediately after cardiopulmonary exercise testing (CPET). According to the level of E/E' ratio, the patients were divided into three subgroups: group a, E/E' ratio <10 both before and after exercise; group b, (early DHF), E/E' ratio ≥10 before exercise but ≤10 after exercise; group c, (late DHF), E/E' ratio >10 both before and after exercise.

Results: (1) The E/E' ratio of patients elevated after exercise (P < 0.01), but that of the controls did not. (2) The VE/VC02 slope of the patients (28.8±4.0) was higher than that of the controls (26.6±2.7) (P < 0.01). The VO2max of the patients was lower (24.3±5.2) than that of the controls (27.6±3.9) (P < 0.01). (3) In the patients, exercising E/E' ratio had good correlations with exercising S' lateral, exercising E' lateral and VE/VC02 slope (P < 0.05-0.01). (4) About 1/5 of the patients were found to be early DHF.

Conclusions: Exercising E/E' lateral ratio can detect early DHF in non-obstructive HCM patients. Those patients with early DHF have no obvious symptoms and this part of patients should be paid more attention to so as to improve their prognosis.

Presence of preoperative diastolic dysfunction predicts postoperative pulmonary edema in patients undergoing major noncardiac surgery

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Purpose: Patients with left ventricular (LV) diastolic dysfunction are vulnerable to develop pulmonary edema. But the clinical implications of diastolic dysfunction has not been clearly elucidated in patients who underwent major noncardiac surgery. By analysing clinical factors, ischemic heart disease (IHD), less than 30ml GFR(CKD) and history of heart failure (HF) were associated with postoperative pulmonary edema (OR,95% CI, P-value, E/E' ratio: 5.65, 2.81-11.34, <0.001). But the clinical implications of diastolic dysfunction in terms of predicting postoperative pulmonary edema in patients with clinical pulmonary edema group than subclinical HF:4.22, 1.96-9.11, <0.01). Among these TTE variables, E/A ratio, E/E' ratio, LVMi showed higher statistical significances in patients with clinical pulmonary edema group than subclinical pulmonary edema group in predicting postoperative pulmonary edema (OR,95% CI, P-value, E/E' ratio: 4.95,2.46-9.5, <0.001; E/A ratio:2.31,1.18-4.5,0.001; LVMi:2.17,1.08-4.36, <0.03).

Conclusion: The presence of LV diastolic dysfunction in preOP TTE was predictive postoperative pulmonary edema in patients who underwent noncardiac surgery.

Clinicians need to be cautious on intravenous fluid therapy for surgical patients with findings of high E/E' ratio, E/A ratio, LVMi in TTE.

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Exercise left ventricular filling pressure: prognostic implications in patients after acute myocardial infarction

Purpose:
To evaluate the prognostic value of exercise left ventricular filling pressure to outcomes in patients (pts) after acute myocardial infarction.

Methods:
83 pts (68 men; mean age 57 years), 13±3 days after acute myocardial infarction were studied. In all pts left ventricular filling pressure was estimated from the ratio of transmirtal and annular velocities (E/E') at rest and after bicycle exercise (25W, 3-min increments). Patients were classified according to E/E' ratio at rest: 48 had E/E' <10 (Group I) and 35 had E/E' >10 (Group II). Patients were followed for cardiovascular hospitalization and death for 24 months.

Results:
Out of 83 pts exercise E/E' rose in 23 (27%) pts: for Group I in 11 pts (from 7.9±0.75 to 9.4±1.1, r=0.005; difference 18.9%); and for Group II in 12 pts (from 11.5±0.9 to 14.0±1.3, P <0.001; difference 21.7%). Exercise duration was significantly shorter in pts with than in pts without raised exercise E/E' (P<0.025).

During follow-up period, there were 19 cardiovascular hospitalization (8 in pts with increased E/E' (P<0.002). The incidence of hospitalization among pts with exercise increased E/E' was higher in Group II (7/12 pts, 58.3%), than in Group I (4/11 pts, 36.4%).

Conclusion:
Raised exercise left ventricular filling pressure in patients after acute myocardial infarction is associated with higher rate of subsequent cardiovascular hospitalization and death.

Diastolic but not systolic function is associated with coronary flow reserve in chronic heart failure patients

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Purpose:
Coronary flow reserve (CFR) is a measure of microvascular function in the absence of coronary artery stenosis and reduced CFR has been shown to be associated with poor outcome in idiopathic dilated cardiomyopathy. Studies on other populations have shown an association between diastolic function and CFR, but this relationship is poorly examined in heart failure. The purpose of the study is to assess the association between CFR systolic and diastolic function in chronic heart failure patients.

Methods:
38 heart failure patients with left ventricular ejection fraction (LVEF)<35% underwent transhoracic echocardiography. CFR was calculated using the biplane Simpson model. Pulsed wave Doppler was used to measure transmirtal inflow velocities. Tissue Doppler velocities were measured 4 places in the mitral ring and were averaged. Peak coronary flow velocity (CFV) was measured in the mid-distal part of LAD at rest and during 2 minutes of stress with adenosine using color guided pulse wave Doppler. CFR was calculated as the ratio between CFV at rest and during stress.

Results:
Median LVEF was 31 (interquartile range (IQ) 26.3-35.5) and CFR was 1.77 (IQ 1.26-2.42). CFR was correlated with E/A (<0.51 p<0.006), E/E' (r=0.48 p<0.003), IVRT (<0.51 p=0.002), deceleration time of E (r=0.32 p<0.05), atrium volume index (r=0.34 p=0.04), S' (r=0.37 p=0.02) but not to LVEF or wall motion score index (all p>0.05).

Conclusions:
In heart failure patients CFR was associated with all 5 measures of diastolic function but with systolic function only S' was associated. The patients with low CFR showed a more restrictive filling pattern. High filling pressure and increased wall-stress might be involved in the reduction of CFR.
tion (PCI) with stent implantation. The implantation of drug eluting stent (DES) has further decreased the incidence of restenosis but this event is not disappeared. Several studies have showed the value of stress echocardiography to detect restenosis after PCI with bare metal stents (BMS). Prior to 2000, DES were referred for CFVR studies for different reasons: 933 (84.1%) for programme follow up after elective and primary PTCA on LAD, 370 (25.4%) for angina, 11 (0.8%) for hypertrophic cardiomyopathy, 38 (2.6%) for hypercholesterolemia, 77 (5.5%) for systemic scle-

Results: The population had high cardiovascular risk profile and complex angio-

graphic characteristics. Clinical or/and angiographic in stent restenosis occurred in 40 pts (8.1%) and in 34 pts (6.9%) stress echocardiography showed sign and/or symptoms of myocardial ischemia. Therefore accuracy, sensitivity, specificity and positive and negative predictive value to identify in stent restenosis were: 94%, 79%, 96%, 68% and 98% respectively.

Conclusion: Our data confirmed that stress echocardiography is an useful tool to identify patients with DES restenosis.

### P4245 End-systolic pressure-volume relation and ventricular-arterial coupling predict cardiac events in patients with negative stress echocardiography

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Background: A maximal negative stress echo identifies a low risk subset for coro-
nary events. However, the potentially prognostically relevant information on car-
diovascular hemodynamics for heart failure-related events is unsaited. Aim. To as-
estimate the prognostic value of stress-induced variation in cardiovascular hemo-
dynamics in patients with negative stress echocardiography.

Methods: We enrolled 929 patients (618 males; mean age 63±12; ejection frac-
tion 48±17%; Wall Motion Score Index = 1.48±0.63; ischemic dilated cardiomy-
opathy, n = 109; dilated cardiomyopathy, n = 222; valvular, n = 90, known or 
suspected coronary artery disease, n = 508), with negative (exercise 238, dipyri-
dopahy, n = 109; dilated cardiomyopathy, n = 222; valvular, n = 90, known or 
suspected coronary artery disease (CAD).

Results: During a median follow-up of 16 months (interquartile range 6-32), 52 deaths and 94 hospitalization occurred. Receiver-operating-characteristic curves, and the corresponding areas under the curve, show the predictor performance of hemodynamic changes during stress (∆ESPVR, ∆VAC, ∆ Ea and ∆ CO) in the EX, DIP and DOB subsets (Figure, Panel A, B, C).

Conclusion: Patients with negative stress echocardiography may experience an adverse outcome, which can be identified by ∆ESPVR and ∆VAC.

### P4246 Feasibility, symptoms, adverse effects and complications associated with non invasive assessment of coronary flow velocity in women with suspected or known coronary artery disease. Experience in 1455

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Purpose: Noninvasive assessment of coronary flow velocity reserve (CFVR) with tran-
scardiac echocardiography (TTE) is an increasingly used method to evaluate the effects of epicardial coronary stenosis and coronary microvascular function. The purpose of this investigation was to analyze and review the Cagliari University experience in assessing CFVR with TTE to define the feasibility, safety, adverse event profile, and complications rate of the test in women with and sus-
ppected coronary artery disease (CAD).

Methods: We evaluated CFVR in the left anterior descending coronary artery (LAD) with TTE during adenosine infusion. The pulsated wave Doppler of blood flow velocity was recorded in the LAD at rest and after maximum vasodi-

lation by adenosine infusion (140 mcg/kg/min in 5 minutes). We analyzed 1455 consecutive CFVR TTE studies starting from January 2000 to december 2010. The patients (age: 66.4±11.9 years, mean age 64.9 ± 14.89 years) were referred for CFVR studies for different reasons: 933 (84.1%) for programme follow up after elective and primary PTCA on LAD, 370 (25.4%) for angina, 11 (0.8%) for hypertrophic cardiomyopathy, 38 (2.6%) for hypercholesterolemia, 77 (5.5%) for systemic scle-

Results: A complete CFVR study was achieved in 1429 pts (feasibility: 98.3%), the test being performed aside in the early phase of acute coronary syn-
drome and in obese women. In the remaining 26 patients (1.8%) the study was interrupted because of hyperpernea (8), general malaise (8), failure to visualize LAD (2), chest pain without EKG changes (2), nausea and headache (2), chest pain with ischemic EKG (1), hypertensive status (systolic blood pressure 200 mmHg, 1), hypotension (70/55 mmHg, 1), caffeine assumption (1). Minor symptoms or adverse effects occurred in 548 pts (38,3%) not requiring test termination: hyperpernea (239, 16,7%), flushing (134, 9,4%), chest pain without EKG changes (7%), headache (95,6, 6.6%), minor arrhythmias (3,5%), chest pain with EKG changes (1,5%). No major complications were observed during all studies.

Conclusion: Non invasive assessment of CFVR in LAD by TTE is a feasible method with very low incidence of adverse events and complications in women with suspected or known CAD. It can be used and safely performed in the eval-
uation of women with atherosclerotic LAD disease and in a broad spectrum of cardiac disease with microvascular impairment.

### P4247 Gender difference of diagnostic utility of dobutamine stress echocardiography with early atropine administration in detection of coronary artery disease

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Background: Lower diagnostic accuracy of electrocardiographic exercise test in female patients is well known from numerous metaanalyses and echocardiographic stress tests were proposed especially for women to improve detection of coronary artery disease (CAD). Our aim was to compare sensitivity, specificity, predictive values and accuracy of significant coronary artery stenosis detection between men and women undergoing dobutamine-atropine stress echocardiography (DASE).

Methods: 238 patients (105 women and 133 men, mean age 62±9, 28% with history of myocardial infarction) with chest pain or other symptoms suggesting significant stenosis in coronary artery underwent DASE and coronary angiography (210 subjects) or computed tomography (28 cases). Echocardiographic assessment was done with Vivid 7 GE and test was considered positive when ≥2 segments displayed visually assessed new or worsened contractility impair-
ment. Atropine was administered after completion of 20mcg/kg/min stage infusion to whole dose of 2 mg. Stenosis ≥50% in left main and ≥70% in other coronary arteries was considered significant.

Results: In female group, mean age 62.6±10.3, 37 (35%) had significant CAD and 19 (18% of CAD) 1VD (one vascular disease), in male group, mean age 61.7±8.6, 90 (68%) had CAD and 44 (49% CAD) 1VD. Percentage of MI was higher in men: 44.4% vs 12.4%, p<0.0001. All included to analysis test were diagnostic.

Conclusion: DASE performed in women presented with a higher diagnostic util-
ity than men as confirmed by comparison of areas under independent ROC curves AUC=0.879 in women (standard error SE=0.032) and 0.734 in men (SE= 0.0415) with v value for this comparison <0.0057. Also for 1VD diagnostic value of DASE was significantly higher in women. Detailed diagnostic values are displayed in table.

### P4248 Coronary flow velocity reserve in 3 major coronary arteries can be a promising alternative for fractional flow reserve in determining hemodynamic significance of coronary artery disease

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Objective: To evaluate whether coronary flow velocity reserve (CFVR) in 3 ma-
jor coronary arteries by transthoracic echocardiography can be a counterpart of
fractional flow reserve (FFR) in assessing hemodynamic significance of coronary artery disease (CAD).

**Methods:** This is a prospective study in 157 vessels of 142 patients with suspected coronary artery disease in 3 major coronary arteries. We performed CFVR measurement by trans thoracic echocardiography within 24 hours before coronary angiography and FFR measurement. CFVR was calculated as the ratio of hyperemic to baseline diastolic flow velocities. Stress was stimulated with adenosine tri-phosphate for both FFR and CFVR. The cut off value of CFVR was estimated by receiver operating characteristic curve based on that of FFR (0.75).

**Results:** The CFVR was 1.87 ±0.76 in coronary artery with FFR <0.75 (n=74) and 2.31 ±0.68 in those with FFR≥0.75 (n=83; p = 0.0054). CFVR cutoff of 2.2 determined by receiver operating characteristic curve, was 79.5% sensitive and 80.0% specific in predicting the stenotic condition of coronary artery with FFR <0.75 in 3 major vessels. In each vessel, the sensitivity and specificity were 82 and 75% (LAD), 70 and 86% (RCA) and 75 and 90% (CX), respectively. On the other hand, CFVR was in direct proportion to FFR (r=0.62, p=0.0001) and indirect proportional to %DS (r=0.35, p=0.0004).

**Conclusions:** The non-invasive CFVR measurement could be a reliable stenosis-specific alternative for determining the hemodynamic significance of 3 major coronary arteries.

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**P4249 Higher prevalence of carotid disease compared to myocardial ischemia in patients undergoing simultaneous stress echocardiography for suspected coronary artery disease**

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**Background:** Presence of carotid artery disease (increased carotid intima-media thickness or carotid plaque) has been shown to predict cardiovascular risk beyond Framingham Risk Score (FRS). However, its potential impact on patients’ management, undergoing echocardiography (SE) for new onset chest pain without known coronary artery disease (CAD), is unknown.

**Methods:** Consecutive patients with no previous history of CAD referred for SE underwent simultaneous carotid ultrasound. SE was considered abnormal if two or more contiguous segments demonstrated inducible wall thickening abnormality. Presence of carotid disease on ultrasound was defined as carotid intima-media thickness (C-IMT) >75th percentile for age and sex, and/or presence of plaque in accordance with Mannheim consensus. FRS was also assessed. Patients underwent coronary angiography based on clinical grounds and SE data.

**Results:** Of the 262 consecutive patients (128 male (49%), mean age 60±11 years), 36 (14%) demonstrated myocardial ischemia by SE, of which the majority (26 patients (72%)) had coronary disease. These consisted of 18 patients (50%) with carotid plaque and 13 (36%) with C-IMT >75th percentile. However, coronary disease was also present in 137 out of 262 (81%) with normal SE, plaque was demonstrated in 96 (43%) and C-IMT >75th percentile in 91 (40%), FRS was significantly higher (p=0.0001) in patients with carotid disease (19.04±9.57) vs. those without it (13.59±7.78). However, carotid disease was also present in 72/141 (51%) and 44/141 (31%) of patients in low-intermediate FRS and normal SE, respectively. Group III patients had a significantly higher prevalence of diabetes (13% vs. 8%), dyslipidemia (34% vs. 22%), and hypertension (28% vs. 17%) than patients in groups I and II. In multivariate Cox proportional regression analysis with adjustment for baseline demographics and comorbidities, no difference was found in the outcome of patients in groups I (reference) and II (hazard ratio 0.18, 95% CI 0.62-0.24). An abnormal SE was a significant factor impacting survival, and increased the risk of MI and/or death by 2.11 (95% CI 1.16-3.81, p=0.014).

**Conclusions:** There is significantly higher prevalence of carotid disease compared to myocardial ischemia in patients undergoing simultaneous SE and carotid ultrasound for suspected CAD. Carotid plaque, not clinical risk factors, is associated with a worse prognosis than those patients in whom both the ECG and wall motion contractility during a stress echocardiography (SE) study have a worse prognosis. Patients with ischemic changes in the electrocardiogram (ECG) but normal wall motion contractility during a stress echocardiography (SE) study have a worse prognosis than those patients in whom both the ECG and wall motion contractility are normal during SE. The aim of the present study is to assess patients who underwent SE and compare the cardiac outcome among patients with and without ECG change during a normal SE study.

**Methods:** This is an observational study performed on 3,322 patients who underwent SE from January, 2007 through the end of December, 2010. The primary endpoint was a composite of all-cause mortality and acute MI. According to SE results, the patients were stratified into three groups: group I: normal SE and normal stress ECG; group II: normal SE and abnormal stress ECG (n = 868); and group III: abnormal SE (n = 347).

**Results:** Patients in group III were older than patients in groups I and II (67±10 years and 57±12, respectively) and was comprised of a higher ratio of male patients (71% in group III, 59% in groups I and II). Group III patients had a significantly higher prevalence of diabetes (12% vs. 8%), dyslipidemia (34% vs. 22%), and hypertension (28% vs. 17%) than patients in groups I and II. In multivariate Cox proportional regression analysis with adjustment for baseline demographics and comorbidities, no difference was found in the outcome of patients in groups I (reference) and II (hazard ratio 0.18, 95% CI 0.62-0.24). An abnormal SE was a significant factor impacting survival, and increased the risk of MI and/or death by 2.11 (95% CI 1.16-3.81, p=0.014).

**Conclusions:** The negative predictive value for MI and/or death of a patient with normal SE is extremely high. Our study proves that there is no difference in the cardiac outcome of patients with ischemic changes in the ECG during SE and those with normal ECG during a stress echocardiography study.

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**P4252 Ranolazine improves coronary flow reserve in patients with angina but no obstructive coronary artery disease**

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**Background:** Ranolazine reduces the Na-dependent calcium overload via inhibition of the late sodium current, improving diastolic tone and oxygen handling during myocardial ischemia. In patients with angina, evidence of myocardial ischemia, but no obstructive coronary artery disease (CAD), microvascular coronary dysfunction plays a key role. Trans thoracic Doppler-derived coronary flow reserve (CFR) is known as an index of coronary arterial reactivity and decreases under the condition with microvascular dysfunction as well as coronary artery stenosis. The aim of this study was to assess the effect of ranolazine on CFR in this patient group.

**Methods:** 52 patients (36 M; 16 F; mean age 63±10 years) with angina and evidence of myocardial ischemia, but no obstructive CAD was enrolled in a double-blind, placebo-controlled trial. All of them underwent coronary angiography, to exclude obstructive CAD, and catheterization was performed by the femoral approach after local anesthesia induced with 0.5% lidocaine. The patients were assigned to Ranolazine (26 patients) or placebo (26 patients) for 8 weeks (350 mg twice a day for 4 days, then 500 mg twice a day for other 4 weeks).

Trans thoracic two-dimensional echocardiography was performed with an ultra-
sound imaging system (Vivid7, GE Healthcare, Wauwatosa, WI, USA). Coronary flow was assessed in the left anterior descending coronary artery (LAD), and it was identified as the color signal directed from the base to the apex of the left ventricle, containing the characteristic variablistic biphasic Doppler flow signals. CFR were determined as the ratio of hyperemic, induced by intravenous dipyridamole administration, to baseline diastolic coronary flow velocity. CFR was assessed before and after 6 weeks therapy.

Results: There were no significant differences in baseline characteristics between Ranolazine and placebo group. CFR was successfully performed in all patients. Baseline CFR was not significantly different in Ranolazine and placebo group (1.85±0.27 vs. 1.87±0.29 – p = ns). After 8 weeks CFR significantly increased in Ranolazine group (2.02±0.18 vs. 1.85±0.27 – p = 0.007) but not in placebo group (1.90±0.24 vs. 1.87±0.29 – p = ns). No patient dropped out during 8 weeks therapy. Side effects were similar in both groups.

Conclusions: In patients with evidence of myocardial ischemia, but no obstructive CAD, Ranolazine is able to improve CFR. This is probably due to improvement in microvascular coronary dysfunction. Larger studies will be able to confirm these data.

**P4253**

Dipyridamole coronary flow reserve stratifies prognosis in patients without left anterior descending artery disease following an acute coronary syndrome

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Background: Coronary flow reserve (CFR) assessment by transthoracic ultrasound of the left anterior descending (LAD) artery during dipyridamole echo-cardiography has been shown to predict prognosis in large unselected populations, and to be correlated with significant stenosis of the LAD. At present, the aim of the study was to assess the prognostic impact of CFR in subjects with acute coronary syndrome and proven absence of LAD disease.

Methods: 325 patients with ACS underwent high-dose dipyridamole stress with combined assessment of CFR in the LAD and wall motion analysis, followed by coronary angiography. 152 patients without LAD disease (stenosis <50%) and with interpretable CFR recordings were monitored for major adverse cardiac events (MACE) for a mean of 30 months.

Results: 22 patients developed events during follow-up. Patients who experienced MACE differed from stable patients in terms of age, prevalence of diabetes, number of diseased vessels and CFR values. Multiple logistic regression analysis for the prediction of MACE demonstrated independent variable only for CFR(p<0.001); smoke(p<0.01) and age(p<0.05). ROC curve analysis showed that a CFR<0.25 is able to predict MACE with a specificity of 86.4% and a specificity of 80%(AUC=0.86).

**Table 1**

<table>
<thead>
<tr>
<th>MACE (n=120)</th>
<th>MACE (n=130)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65±11</td>
<td>58±10</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>168</td>
<td>156</td>
</tr>
<tr>
<td>Diabetes</td>
<td>83%</td>
<td>71%</td>
</tr>
<tr>
<td>Smoke</td>
<td>14%</td>
<td>16%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4%</td>
<td>18%</td>
</tr>
<tr>
<td>Hypertensoin</td>
<td>15%</td>
<td>13%</td>
</tr>
<tr>
<td>LVEF</td>
<td>52±3</td>
<td>53±3</td>
</tr>
<tr>
<td>0/1/2 vessel CAD</td>
<td>1/4/7</td>
<td>4/7/7</td>
</tr>
<tr>
<td>CFR</td>
<td>2.11±0.33</td>
<td>2.82±0.44</td>
</tr>
</tbody>
</table>

Conclusions: In a population of patients with ACS, CFR significantly improves prediction of MACE when added to standard clinical variables, even in the absence of LAD disease. This finding promotes the role of ultrasound-assessed CFR in the risk stratification after ACS, supporting the concept that CFR reflects global atherosclerotic burden, endothelial dysfunction and microvascular damage, more than just mirroring local LAD disease.

**P4254**

Incorporation of myocardial contrast echocardiography into a clinical stress echocardiography service is feasible and provides additional diagnostic information

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Purpose: A large evidence base supports the diagnostic accuracy of myocardial contrast echocardiography (MCE), performed during stress echocardiography (SE), for the detection of myocardial ischaemia and viability in patients with known or suspected coronary artery disease. However, the feasibility and value of MCE incorporated into a clinical SE service in a real-world setting is unknown. We therefore conducted this study to establish the role of MCE in the clinical arena.

Methods: All patients had been referred for SE on clinical grounds. Patients with known allergy to sulphur-containing drugs or referred for non-ischaemic studies (e.g. valve disease or HOCM) were excluded. We performed MCE during SE – using a pharmacological intravenous infusion of Sonovue contrast – in all patients undergoing pharmacological stress and patients undergoing treadmill exercise in whom we suspected a high workload or target heart rate may not be attained. We documented prospectively demographic variables, reason for referral, stress modality, number of contrast vials used and value of MCE, which was assigned to one of four pre-determined categories: incremental benefit over wall motion (WM) analysis, more confidence with WM analysis, no benefit over WM analysis or other (i.e. uninterpretable MCE images). All MCE studies were analysed by the performing cardiologist together with an expert reader.

Results: Over a 13 month period, 544 patients underwent SE and 142 (26%) of these also underwent MCE by different operators. Mean age was 63yrs (range 19-89); 77% were male. MCE demonstrated excellent feasibility, with diagnostic perfusion images obtained in 95% studies. Mean contrast use was 2.9 vials per study. MCE data provided the interpreting cardiologists with incremental benefit over WM analysis in 40 (28%) cases, gave greater confidence with WM analysis in 28 (20%) cases, had no added value over WM analysis in 67 (47%) cases and was uninterpretable in 7 (5%) cases. Mean number of segments with indiscernible ischaemia was 2.8±0.27 by WM and 5.6±0.28 by perfusion (p<0.001). Of the 52/142 patients that also underwent angiography, perfusion data agreed with angiographic findings in 45 (87%) cases. Agreement between MCE and angiography findings were 18/21 (86%) and 14/16 (88%) in those in whom MCE data was of incremental benefit and added confidence, respectively.

Conclusion: MCE is feasible by multiple operators when incorporated into a clinical SE service. MCE data is either of incremental benefit over WM analysis or gives more confidence with WM analysis in a significant proportion (approximately 50%) of cases.

**P4255**

Left ventricular torsion at rest, peak, and post-exercise echocardiography

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Left ventricular torsion (Tor) has not been widely studied during exercise echocardiography (ExE). We aimed to study the feasibility of the assessment of Tor during ExE and the likely correlations with systolic and diastolic function.

Methods: A series of 265 consecutive patients referred for ExE were studied by transthoracic imaging at rest (R), peak (Pk), and within 1 min post ExE (PE). Apical rotation and basal rotation were measured. Tor was defined as apical rotation – basal rotation in ° divided by LV length in cm. Volumetric left ventricular ejection fraction (LVEF) at R and Pk, and the ratios of early transmural flow/early diastolic flow wave at the septal minor annulus ([E]/r) at R and PEX were also measured.

Results: At R, decreased LVEF (<50%) was seen in 41 patients, and increased E/(ratio) (≥15) in 50 patients. Confident tracking assessment was achieved in 214 patients at R (81%), in 193 at Pk (73%) and in 179 within 1 min of the cessation of the exercise (68%). Apical rotation, twist and Tor increased during exercise, whereas basal rotation was similar (Table). All rotation parameters but basal rotation were significantly different at Pk and at PEX. Significant correlations were found between rotation parameters and LVEF at R (LVEF and apical rotation, r=0.39; LVEF and twist, r=0.35; LVEF and Tor, r=0.38, all p<0.001; at Pk: LVEF and apical rotation, r=0.16, p=0.02; LVEF and twist, r=0.28, p<0.001; LVEF and Tor, r=0.28, p<0.001). However these parameters did not correlate with E/verues.

**Table 2**

<table>
<thead>
<tr>
<th>Rest</th>
<th>Pk</th>
<th>PEx</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF</td>
<td>50.2±8.6</td>
<td>54.3±7.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Apical rotation</td>
<td>7.9±2.4</td>
<td>7.9±2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Twist</td>
<td>2.7±1.0</td>
<td>3.0±1.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Tor</td>
<td>4.7±3.8</td>
<td>5.0±3.2</td>
<td>0.03</td>
</tr>
<tr>
<td>PaTor</td>
<td>–</td>
<td>–</td>
<td>0.03</td>
</tr>
<tr>
<td>% of LVEF, median (25th–75th percentiles)</td>
<td>47.5–133</td>
<td>31–114, 128</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: Rotation can be assessed during exercise in about 70% of the cases. Pk exercise rotation parameters are significantly different to those obtained at PEx.

**P4256**

Estimation of infarct size using transthoracic measurement of coronary flow reserve in infarct related and reference coronary artery

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Background: In convalescent phase of ST elevation myocardial infarction (STEMI), coronary flow reserve (CFR) in infarct related artery (IRA) is shown to be decreased when assessed invasively using Doppler wire. We hypothesized that patients in chronic phase of first anterior STEMI treated by primary
PCI have decreased CFR in IRA that is proportional to the extent of myocardial damage. Therefore we proposed a novel model of infarct size (IS) estimation using transthoracic Doppler echocardiography derived CFRs of the IRA (LAD) and reference artery (RCA).

**Methods:** Our study included 34 consecutive patients (28 [82%] men, mean age, 50±11 years) with first anterior STEMI and single vessel disease (IRA) successfully treated by primary PCI. All patients underwent resting two-dimensional transthoracic echocardiography with the assessment of LV volumes, wall motion score index and ejection fraction as well as adenosine stress echocardiography (0.14 mg/kg/min) with CFR evaluation of LAD and RCA, 30±3 days after MI. CFR derived infarct size (CFR IS) was calculated as follows:

\[
CFR\ IS = \frac{CFR\ RCA - CFR\ lAD}{CFR\ RCA - 1} \times 100\% .
\]

Infarct size was also assessed by SPECT myocardial perfusion imaging (SPECT MPI) using 99mTc-MIBI on the following day. SPECT IS was expressed as percentage of myocardium with fixed perfusion abnormalities.

**Results:** CFR calculated after adenosine administration was significantly higher in RCA than in LAD (2.9±0.4 vs. 2.5±0.5, respectively; p<0.001). CFR derived IS correlated significantly with all the parameters depicting the severity of myocardial damage including: peak CK activity (r=-0.632, p<0.001), WMSI (r=-0.857, p<0.001) and LV EF (r=-0.820, p<0.001), as well as with LV EDV (r=-0.757, p<0.001) and ESV (r=0.794, p<0.001). Most importantly, CFR derived IS correlated significantly with IS assessed using SPECT MPI (r=0.874, p<0.001). There was no statistical difference in IS assessed with these two methods (2D:17% for CFR IS and 21±17% for SPECT MPI IS (pNS)).

**Conclusion:** Coronary flow reserve derived IS is non-invasive tool for the estimation of myocardial damage after first anterior STEMI in patients with single vessel disease that correlates well with other widely used markers of final IS.

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**CARDIOMYOPATHIES: PROGNOSIS**

**P4257** Prediction of left ventricular function recovery with the use of 2D speckle tracking echocardiography in patients 12 months after acute ST-elevation myocardial infarction

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**Introduction:** Prediction of left ventricular function recovery is of clinical importance for the management and prognosis of patients after myocardial infarction. The aim of this study was to assess if the use of 2D speckle tracking in resting echocardiography may be helpful in the prediction of left ventricular function recovery in patients 12 months after ST-elevation myocardial infarction (STEMI).

**Material and methods:** The study group consisted of 96 patients (69 male, mean age 58±10 years) with first STEMI treated with successful primary percutaneous coronary intervention. 7-12 days after STEMI, all patients underwent resting echocardiography. All acquired images were analyzed off-line using 2D speckle tracking technique. Measurements included peak systolic longitudinal and transverse strain (SLS and STS), peak longitudinal and transverse strain (PLS and PTS) including possible postystolic shortening, systolic longitudinal and transverse strain rate (SLSR and STSR) at baseline (rest). After 12 months each patient underwent control resting echocardiography with visual assessment of functional recovery in akinesia/dyskinesis/segmental dysfunction and transverse strain rate (SLSR and STSR) at baseline (rest). After 12 months each patient underwent control resting echocardiography with visual assessment of functional recovery in akinesia/dyskinesis/segmental dysfunction and transverse strain rate (SLSR and STSR) at baseline (rest). After 12 months each patient underwent control resting echocardiography with visual assessment of functional recovery in akinesia/dyskinesis/segmental dysfunction and transverse strain rate (SLSR and STSR) at baseline (rest).

**Results:** At baseline there were 265 segments with akinesis or dyskinesis. 112 (42%) of those segments showed functional recovery after 12 months. Longitudinal strain parameters SLS (AUC=0.710, p=0.0001) and PLS (AUC=0.773, p<0.001) for diameter of stenosis of 67.5% had a sensitivity 61.8% and specificity of 85.2%. Transverse parameters of strain had non-satisfactory diagnostic value for predicting functional recovery 12 months after STEMI.

**Conclusions:** Longitudinal strain parameters assessed by 2D speckle tracking had comparable prognostic value to requiring experience and administration of pharmacologic agent low-dose dobutamine stress echocardiography for the prediction of left ventricular functional recovery in patients 12 months after STEMI. The presented method may be less dependent on subjectivity bias and useful in usual viability interpretation based on dobutamine stress echocardiography and after a methodological background for fully computerized algorithms.

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**P4258** The additive diagnostic role of coronary flow reserve determined by transthoracic Doppler echocardiography in assessment of real significance of stenosis on right coronary artery

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**Purpose:** Multi-slice computed coronary angiography (MSCT) provides a morphological information about coronary artery disease, but precise quantification of coronary stenosis remains difficult. Coronary flow reserve (CFR) determined by Transthoracic Doppler Echocardiography (TDE) gives a new insight into the functional significance of coronary luminal narrowing. We have tried to assess the additive value of CFR determined by TDE over MSCT in prediction of a significant stenosis on right coronary artery (RCA) using the Invasive coronary angiography (ICA) as reference method.

**Methods:** This prospective study included 70 patients. Patients were referred for ICA because of previously detected atherosclerotic lesions on RCA by MSCT. Additional measurements of CFR by TDE were performed on totally 61 vessels. Feasibility for RCA was (9/10) 87.14%. All patients underwent ICA 24-48 hours after CFR. Significant coronary artery stenosis on invasive or non invasive angiography was defined as ≥70% diameter reduction. CFR was determined as ratio between the peak diastolic flow velocity during adenosine infusion and at baseline condition, a cutoff value for significant stenosis was ≥2.

**Results:** There was a good correlation (r=0.56, p<0.001) between morphological changes detected with ICA and functional parameters of stenosis determined by CFR and a considerable correlation between invasive and noninvasive coronary angiography (r=0.57, p<0.001). A much weaker correlation was between MSCT angiography and CFR (r=0.22, p=0.086).

MSCT had sensitivity 86.2%, specificity 69.1%, positive predictive value 59.5%, negative predictive value 90.5% and accuracy of 75.5% in detection of significant RCA stenosis. CFR had sensitivity 76.9%, specificity 85.3%, positive 80.0% and negative predictive value 82.9% and accuracy 81.7%. When the results of both methods were agreed accuracy was improved to 90.0%, sensitivity 76.9%, specificity 100.0%, positive 100.0% and negative predictive value 85.0%. ROC curve estimation of MSCT angiography in detection of significant RCA stenosis (Area 0.81, p<0.001) for diameter of stenosis of 67.5% had a sensitivity 86.0% and specificity 63.6%. ROC curve of CFR (Area 0.84, p<0.001) for CFR ≥2 had a sensitivity 76.9% and specificity 86.8%. Comparing ROC curves there was no statistical difference (p>0.417).

**Conclusion:** CFR determined by TDE had an additive diagnostic value in evaluation of real significance of atherosclerotic lesions on RCA detected with MSCT angiography, which emphasize importance of comprehensive non invasive imaging approach integrating morphologic and functional information.

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**P4259** QRS fragmentation in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy and complete right bundle branch block

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Patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy ARVD/C and complete right bundle branch block (RRBB) very often have recurrent ventricular tachycardia and develop biventricular heart failure in the follow-up requiring heart transplantation and/or diuretics. In other patients with ARVD/C excluding ventricular bundle block ARVD/C fragmentation in the S wave of right precordial leads identifies patients with recurrent VT, primary VF and recurrent ICD discharges; QRS fragmentation ≥3 leads characterised patients who died from sudden cardiac death.

**Methods:** In a cohort of 374 patients with ARVD/C (208 males; mean age 46.5±14.8 years) there were 22 patients with complete RRBB. 17 patients with ARVD/C developed complete right bundle branch block and had biventricular heart failure in the follow-up of 4 years. In 5 patients with ventricular bundle branch block both were evident. In all patients with ARVD/C and RRBB QRS fragmentation ≥3 of all 12 ECG leads and QRS fragmentation in the S wave of right precordial leads were analyzed.

**Results:** QRS fragmentation ≥3 of all 12 ECG leads and in the S wave of right precordial leads were present in 16/17 patients who developed RRBB and none of the 5 patients with initial RRBB QRS fragmentation ≥3 leads was present (n=12.5; p<0.001).

**Conclusion:** Patients with recurrent ventricular tachycardia who develop biventricular heart failure requiring heart transplantation and/or diuretics are characterised by QRS fragmentation in the S wave of right precordial leads ≤3 of all 12 ECG leads. These results are statistically significant. Patients with initial RRBB have an overall benign prognosis.

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**P4260** The impact of sleep apnea on the occurrence of heart failure in the patients with hypertrophic cardiomyopathy


**Purpose:** This case-control study was conducted to evaluate the interrelation between the occurrence of heart failure (HF) and the sleep apnea in the patients with hypertrophic cardiomyopathy (HCM) excluding obstructive left-ventricular outflow tract (LVOT) HCM.

**Methods:** 48 patients with apical HCM, mid-ventricular HCM, and non-obstructive left-ventricular outflow tract HCM were conducted polysomnography to assess the apnea-hypopnea index (AHI). The biomarkers and cytokines including brain-natriuretic peptide (BNP), plasma renin activity, aldosterone, adrenaline, nor-
adrenalin, dopamine, soluble tumor necrosis factor receptor 1 (sTNFR1), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), transforming growth factor-beta (TGF-beta1), urine 8-hydroxydeoxyguanosine (8-OHdG) were measured at the period of HF-ccompensation. We divided those patients into two groups with (n=14) or without (n=34) a history of HF requiring hospitalization and compared above-mentioned parameters between two groups.

**Results:** HCM patients with a history of HF has significantly higher AHI (32±5.0 vs. 11.1±2.2, p<0.0001) and higher TGF-beta1 value (2.7±0.49 vs. 1.5±0.07, p=0.0016) comparing with those without a history of HF. The other indices of HF, inflammation, and oxidative stress, such as BNP, PRA, aldosterone, adrenalin, nor-adrenalin, dopamine, sTNFR1, TNF-α, IL-6, 8-OHdG have not shown any significant difference between two groups.

**Conclusions:** Sleep apnea may play an important role in the occurrence of HF in the patients with relatively benign HCMs. The elevation of TGF-beta1 may suggest the involvement of fibrosis in the pathogenesis of HF in the patients who have both HCM and sleep apnea.

**Predictors of survival in patients with restrictive cardiomyopathy**

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**Backgrounds:** Restrictive cardiomyopathy (RCMP) is a rare heterogenous disease and the survival according to types of RCMP is unclear. We evaluated clinical outcomes of RCMP to identify predictors of survival.

**Methods:** From 1999 to 2010, we prospectively studied 98 consecutive patients (64 men, age:58±11 years) diagnosed as RCMP. All patients had the symptoms of heart failure and diastolic dysfunction with preserved left ventricular systolic function on echocardiography. Diagnosis of RCMP was initially made by typical echocardiographic findings and confirmed by endomyocardial biopsies. The endpoint was defined as death from any cause.

**Results:** Idiopathic RCMP was diagnosed in 11 (11%) patients, and infiltrative CMP in 87 (89%). The underlying cause of infiltrative CMP was amyloidosis in 77, light-chain deposition disease in 5, myocarditis in 2, and Fabry disease in 1. During a median follow-up of 6 months (IQR, 2-17), 75 (77%) patients died and 3 underwent cardiac transplantation (1 amyloidosis, 2 idiopathic RCMP). The actuarial 2 year survival rates were significantly different between infiltrative CMP and idiopathic RCMP (22±5% versus 91±9%, P<0.001) (Figure). Age (hazard ratio [HR] =1.036, P<0.001) and infiltrative CMP (HR=4.458, P=0.005) were independently related to survival on multivariate Cox analysis. On subgroup analysis of 82 patients with amyloidosis or light-chain deposition disease in 5, myocarditis in 2, hypereosinophilic syndrome in 2 and Fabry disease in 1. During a median follow-up of 6 months (IQR, 2-17), 75 (77%) patients died and 3 underwent cardiac transplantation (1 amyloidosis, 2 idiopathic RCMP). The actuarial 2 year survival rates were significantly different between infiltrative CMP and idiopathic RCMP (22±5% versus 91±9%, P<0.001) (Figure). Age (hazard ratio [HR] =1.036, P<0.001) and infiltrative CMP (HR=4.458, P=0.005) were independently related to survival on multivariate Cox analysis. On subgroup analysis of 82 patients with amyloidosis or light-chain deposition disease, only 39 (48%) patients underwent chemotherapy and tolerance to chemotherapy was significantly related to survival (HR=2.189, P=0.002).

**Conclusions:** Infiltrative CMP was the predominant type of RCMP and related with much worse survival. Early diagnosis of RCMP by echocardiography and timely institution of chemotherapy may improve the prognosis of cardiac amyloidosis.

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**Characterization of predictors of in-hospital cardiac complications of takotsubo cardiomyopathy: multi-center registry from Tokyo CCU network**

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**Background:** Takotsubo cardiomyopathy (TC) is an acute cardiac syndrome characterized by transient left ventricular dysfunction and relatively good prognosis after discharge. However, cardiac complications during hospitalization remain to be fully determined.

**Methods:** We investigated 107 patients of TC (82 women, median age 73.9±11.1 years old) from Tokyo CCU Network database, comprising of 67 cardiovascular centers in the metropolitan area during January 1 to December 31 2010. Cardiac complications were defined as all-cause death, pump failure (Kilip II/III/IV), sustained ventricular tachycardia (SVT), ventricular fibrillation (VF), and advanced atrioventricular block (AVB). We attempted to characterize cardiac complication groups (CC) by comparing patients with and without cardiac complication (NC) during hospitalization.

**Results:** CC was observed in 41 patients (all-cause death, n=9; pump failure, n=27; SVT, n=1; AVB, n=2; VF, n=2), and there was no complication in the remaining 66 patients. There was no difference in age (75.2±10.4 vs. 72.9±11.6, p=0.289), female gender (70.7% vs. 80.3%, p=0.144), peak creatinine kinase level (IU/L) (553±710 IU/L vs. 486±1024 IU/L, p=0.780), C-reactive protein level (mg/dL) (2.6±3.75 vs. 1.9±0.4±25 mg/dL, p=0.379), and ST elevation on electrocardiogram (68.3% vs. 75.8%, p=0.398), respectively. White blood cell count (WBC) (11189±4516/µL vs. 9020±3532/µL, p=0.005) and brain natriuretic peptide (BNP) (1125±1245 pg/ml vs. 376±764 pg/ml, p=0.004) were higher in CC than in NC. Left ventricular (LV) ejection fraction was lower in CC than NC (42.3±11.6% vs. 53.1±11.0%, p<0.001).

**Conclusion:** Cardiac complications are not rare in patients with TC during hospitalization. Higher WBC and BNP levels and the presence of LV dysfunction seem to be possible predictors of TC with cardiac complications.
Impact of serum cardiac troponin T and I on cardiac molecular changes and dysfunction in patients with hypertrophic cardiomyopathy

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Purpose: Serum cardiac troponin T (cTnT) could be a reliable indicator of myocardial remodeling, a proposed prognostic marker in hypertrophic cardiomyopathy (HCM). Meanwhile, cardiac troponin I (cTnI) has also been reported as a prognostic indicator in patients with chronic heart failure. However, the relation between cardiac function, cTnT and cTnI has remained unclear in patients with HCM.

Methods: We checked serum cTnT and cTnI in 73 consecutive HCM patients in stable condition. All patients underwent cardiac catheterization and we calculated the maximum first pressure gradient (LV-HPAP) as an index of contractility and the LV pressure halftime (T1/2) as an index of isovolumic relaxation. In addition, to examine transcardiac utilization of troponin T and I, we measured serum cTnT and cTnI in the aortic root (Ao) and coronary sinus (CS).

Results: We divided the patients into two groups (group A: cTnT <0.001ng/ml, n = 35), group B: cTnT group <0.001ng/ml, n = 38), on the basis of median value of cTnT in the peripheral vein. Brain natriuretic peptide, serum cTnT, left ventricular mass index, and T1/2 were significantly higher in the lower B than those in the group A. Moreover, mRNA level of cTnT was significantly correlated with mRNA levels of sarco-endoplasmic reticulum Ca2+-ATPase and cytochrome c oxidase subunit 5IB (r = 0.486, p<0.040).

Conclusion: We identified that elevated peripheral blood cTnT might be associated with cardiac dysfunction, resulting from the impairment of Ca2+-handling protein and mitochondrial function. Meanwhile, transcardiac gradient of cTnT levels may reflect ongoing myocardial damage in stable patients with HCM.

Assessing prognosis in idiopathic dilated cardiomyopathy: the experience of the Florence referral center for cardiomyopathies

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Purpose: Determining the prognosis in idiopathic dilated cardiomyopathy (ICM) is a challenging goal, given the limited amount of heart transplant donors for critically ill pts. In our study we aimed to find relevant prognostic factors in ICM pts enrolled at our Center.

Methods: We enrolled 603 consecutive ICM pts (diagnosis made on the basis of WHO criteria, all pts underwent coronary angiography to exclude a ≥50% stenosis of main branches), 442 M (73.3%), mean age 53±12.5 ys (range 16-75). Mean indexed left ventricular (LV) end-diastolic diameter (LVEDD) was 36±5.6 mm/m2, LV ejection fraction (LVEF) was 53.9±5.4 mm/m2 and mean NYHA class was 2.3±0.6. Pts were divided in four groups, based on enrollment period: 1) 1977-1984 (n=69); 2) 1985-1990 (n=102); 3) 1991-2000 (n=197); 4) 2001-2011 (n=238). The mean follow-up 72 pts (19.8%) died due to refractory HF, 38 (8.9%) due to ventricular arrhythmia, 36 (8.2%) due to stroke, 10 (2.3%) due to respiratory failure, 9 (2.3%) due to gastrointestinal bleeding, 7 (1.7%) due to secondary malignancy, 6 (1.3%) due to sepsis, 3 (0.7%) due to acute myocardial infarction, 2 (0.4%) due to non-cardiac cancer, 36 (8%) underwent heart transplantation, and 67 (11.1%) were lost at follow-up. Survival rates for the entire population at 5, 10 and 15 years was 79%, 63% and 45%, respectively. Survival analysis assessing all-cause mortality and cardiac transplantation as a combined endpoint identified the enrollment period as the most important independent predictor of favourable outcome after multivariate analysis (group 4 vs 1, HR 0.25, 95% CI 0.19-0.34, p<0.0001; group 3 vs 1, HR 0.45, 95% CI 0.30-0.61, p<0.001; group 2 vs 1, HR 0.68, 95% CI 0.48-0.8, p<0.005). Female gender (HR 0.56, 95% CI 0.41-0.77, p<0.0005), age (HR 1.02, 95% CI 1.01-1.03, p<0.0001), NYHA class (HR 1.75, 95% CI 1.47-2.07, p<0.0001), LVEF (HR 0.98, 95% CI 0.97-
0.99, p<0.005) and iLAD and iLAD (HR 1.06, 95% CI 1.03-1.09, p<0.0001) at enrollment were all significant prognostic factors.

**Conclusions:** Our data show the enrollment period as the most important prognostic factor in DCM pts enrolled at our Center, with a 75% relative risk reduction in overall mortality over the last thirty years, this finding being presumably related to the increasing use of evidence-based treatment of HF over time. Moreover female gender, age, NYHA class, UFE and iLAD at enrollment each portends a significant prognostic value.

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**P4268**

**Fragmented QRS complexes on 12-lead ECG predict myocardial fibrosis in hypertrophic cardiomyopathy**

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**Purpose:** It is well-established that fragmented QRS complexes (fQRS) on the 12-lead electrocardiogram (ECG) are a predictor of delayed gadolinium enhancement (DGE) on Cardiac MRI (CMR) and indicate myocardial scarring in patients with coronary artery disease and dilated cardiomyopathy. Moreover, fQRS appear to correlate well with arrhythmic events and mortality in these cohorts. However, the significance of fQRS in hypertrophic cardiomyopathy (HCM) is yet to be established.

**Methods:** In this single-center retrospective study of 82 consecutive patients with HCM who underwent CMR with gadolinium were analysed for the presence of fQRS by 2 independent readers blinded to the CMR findings. Patients with documented myocardial infarction (n=3) were excluded from further analysis. The ECGs were correlated to CMR findings, and patients separated into DGE positive (DGE+ve; n=44) and negative (DGE-ve; n=35) groups. CMR territories of fQRS were correlated with myocardial segments of DGE on CMR, in order to determine whether areas of DGE predicted or did not predict the presence of fQRS.

**Results:** Patients from the DGE+ve and DGE-ve groups were of similar gender (75% vs. 77% respectively, p=0.10), and age (54±19 vs. 57±11 years respectively, p=0.41). Fragmented QRS complexes were significantly more prevalent in the DGE+ve group than in the DGE-ve group (68.2% vs. 14.3%, p<0.001). The positive predictive value (PPV) of fQRS for DGE on CMR was 85.7%, with a specificity of 85.7%, sensitivity of 68.2% and negative predictive value of 68.2%.

In the DGE+ve group with fQRS (n=30), fQRS ECG lead territory was predictive of regions of DGE on CMR in 73.3% (n=22) of patients.

**Conclusions:** The presence of fQRS on 12-lead ECG correlates with DGE on CMR in patients with HCM with good specificity and PPV. Electrocardiographic territories containing fragmentation also correlate with myocardial segments of DGE on CMR. This simple, inexpensive method may therefore be valuable for predicting scar or fibrosis in patients with HCM. Future work should focus on correlating fQRS with risk factors and events to determine its use in risk stratification.

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**P4269**

**Tissue Doppler imaging and prognosis in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy**

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**Aims:** Assessment of left ventricular (LV) systolic and diastolic functions by tissue Doppler imaging (TDI) has been reported to be useful for predicting the prognosis in patients with hypertrophic cardiomyopathy (HCM). The purpose of this study was to evaluate the clinical significance of TDI parameters for prediction of cardiac events in asymptomatic or mildly symptomatic patients with HCM.

**Methods and results:** Eighty-five HCM patients (52 males, 55.6±14.8 yrs) belonging to New York Heart Association (NYHA) functional class I or II were enrolled in this study. Patients with LV systolic dysfunction or a clinically documented history of atrial fibrillation or who underwent procedures or changes of medication during follow-up period of 4.5±1.7 yrs, 11 patients achieved the combined end-points. Patients who experienced cardiovascular events had larger LV size and left atrial volume compared with those who did not. Peak systolic, early diastolic (e'), and late diastolic TDI velocities were lower in patients who experienced cardiovascular events; moreover, E'/e' was higher in these patients. The event-free curve in patients with a high E'/e' value was significantly worse than that in patients with a low E'/e' value (Figure). Multivariate analysis revealed the deceleration times of E and E'/e' to be independent predictors of cardiovascular events.

**Conclusion:** Assessment of diastolic function by TDI is useful for risk stratification in HCM patients with no or mild symptoms. TDI measurements should be incorporated into the clinical management of HCM.

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**P4270**

**Importance of hypertrophy pattern in sudden death risk stratification among patients suffering from hypertrophic cardiomyopathy**

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**Purpose:** To investigate differences in sudden death (SD) and associated arrhythmic events (ventricular tachycardia/fibrillation, resuscitated cardiac arrest and appropriate defibrillator discharge) rates among four discrete hypertrophic cardiomyopathy (HCM) phenotypes (asymmetric basal septal hypertrophy (ASH), left ventricular outflow tract obstruction (LVOTO), apical hypertrophy/obstruction (MVO) and apical hypertrophy (APH)) and to challenge the importance of hypertrophy type in SD prediction.

**Methods:** Hypertrophy phenotypes were recognized by means of echocardiography and MRI in 423 HCM patients (49.3±17.2 years, 66.2% male) followed up for a median of 84 months (7 years, range 6 to 480 months). Cumulative SD event rates through follow up were estimated by Kaplan-Meier method and differences were assessed by log rank test. To identify independent predictors of the study outcome, univariate and multiple Cox proportional hazard models were adopted.

**Results:** ASH was discovered in 259 patients (61.2%), LVOTO in 88 (20.8%), APH in 42 (9.9%) and MVO in 34 (8%). SD event rates among groups are shown in Figure 1. Presence of MVO strongly predicted SD and associated arrhythmic events [Adjusted Hazard Ratio (HR); 3.3, 95% CI (1.26-8.85), p=0.016] independently of the 5 established risk markers for SD (family history of SD, syncope, non sustained ventricular tachycardia, abnormal blood pressure response during exercise and maximum wall thickness >3.0 cm).

**Conclusions:** HCM phenotype is associated with SD and lethal arrhythmic events and should be taken into consideration during SD risk stratification. Especially, high adverse outcome rate connected to MVO necessitates early recognition and appropriate therapeutic interventions.

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**P4271**

**Prognostic role of a high-sensitivity cardiac troponin T marker in patients with dilated cardiomyopathy**

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**Purpose:** Although serum high-sensitivity cardiac troponin T (hs-cTnT) has become a well established diagnostic and prognostic marker in acute coronary syndrome, hs-cTnT levels are also elevated in patients with dilated cardiomyopathy (DCM). The prognostic significance of a hs-cTnT marker in dilated cardiomyopathy (DCM) is unclear. The aim of this study was determine whether hs-cTnT can be a reliable prognostic marker of cardiac events in DCM.

**Methods:** We performed clinical evaluation including measurement of hs-cTnT in 55 patients with DCM. The normal range of hs-cTnT is less than or equal to 0.014 ng/ml (97.5 percentile).

**Results:** Serum concentration of hs-cTnT was 0.017±0.023 ng/ml. During a mean follow-up period of 5.0±1.7 years, there were 17 cardiac events: heart failure deaths in seven, sudden cardiac deaths in two and hospitalization for heart failure in eight. Patients with abnormal hs-cTnT values (>0.014ng/ml) had significantly more frequent cardiac events than did those with low hs-cTnT values (hazard ratio: 8.3, 95% confidence interval: 2.9 to 23.8, p<0.001). We divided the patients into four groups by hs-cTnT levels: nonmeasurable levels (<0.003 ng/ml) and normal range levels (0.003-0.014 ng/ml) within low hs-cTnT group, high concentrations (0.015-0.028 ng/ml) and very high concentrations (0.028 ng/ml) within high hs-cTnT group. Event-free rate was shown in Figure: hs-cTnT indicated a tendency of concentrations-depend increase in cardiac events.
Number of morphological kinds of ventricular premature beats with fragmented QRS waves on 2-lead Holter ECG predicted left ventricular fibrosis and fatty change on CT in hypertrophic cardiomyopathy

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Purpose: To determine the number of morphological kinds of ventricular premature beats (VPB) with fragmented QRS waves (FGQRSW) on 12-lead Holter ECG in presence of the left ventricular (LV) fibrosis or fat on CT in hypertrophic cardiomyopathy (HCM) subjects.

Methods: This was a retrospective analysis of 49 consecutive HCM subjects who underwent CT (Aquilion one) and 12-lead Holter ECG (RAC-2103) within 3 months. If there was a contrast defect in myocardium in early phase, late phase acquisition was added, and if abnormal late enhancement was observed in the corresponding site, we diagnosed myocardial fibrosis. If contrast defect continued in late phase with CT values > 0 HU, we diagnosed myocardial fatty change.

Results: Fibrosis and fat were observed on CT in 28 and 12 subjects, respectively. The numbers of morphological kinds of both all VPB and VPB were greater in subjects with fibrosis than in those without (both P < 0.01), but there was no significant differences in the numbers of morphological kinds of both all VPB and VPB with FGQRSW between the subjects with fat and those without. According to a receiver operating characteristic curve, best cutoff value for number of morphological kinds of VPB with FGQRSW as 2 for fibrosis and 3 for fat. Sensitivity and specificity for detection of fibrosis and fat were 71.4 and 66.7% (fibrosis), and 50.0 and 73.0% (fat) in number of morphological kinds of VPB with FGQRSW, respectively and those were 82.1 and 53.1% (fibrosis), and 58.3 and 45.9% (fat) in number of morphological kinds of all VPB, respectively.

Conclusions: Serum concentrations of hs-tTrT level was a useful prognostic predictor in DCM patients.

Severe myocardial fibrosis detected by cardiac MRI in patients with hypertrophic cardiomyopathy is associated with high risk for future arrhythmic events

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Study aim: To correlate the incidence of adequate ICD interventions in hypertrophic cardiomyopathy (HCM) with the presence of the different classical risk markers (RM) for sudden cardiac death (SCD) plus myocardial fibrosis as detected by gadolinium-enhanced MRI (GE-MRI).

Methods: Patients with HCM who had ICD implantation, either for secondary (n=23), or primary prophylaxis of SCD (n=72/97%). For fibrosis assessment, patients underwent prior GE-MRI. Fibrosis was scored using a 17-segment LV model (from 0-15 segments, 3-segmented approach). Mann-Whitney test was used for comparisons between groups. ICD therapies were regularly read out and interpreted in accordance with established guidelines.

Results: The number of RM per patient was 1.7±1.0. Myocardial fibrosis on GE-MRI was present in 71 pts (96%), of which 38 pts (51%) had a fibrosis score of ≥2. During follow-up of 2.1±2.4 [0.1-9.2] years, 46 adequate ICD interventions (10 discharges, 36 episodes of antitachycardia pacing) were documented in 12 pts. At least 1 episode of atrial fibrillation (AF) was found in 24 pts. No correlations were found between fibrosis score and the classical RM. The severity of fibrosis correlated with the occurrence of ventricular tachycardia (p=0.3, p=0.02) and AF (n=5, p=0.001).

Conclusions: In this carefully selected cohort of HCM pts. considered to be at high risk, the event rate was indeed high. Severity of myocardial fibrosis as detected by GE-MRI seems to be associated with future arrhythmic events.

Are different ballooning patterns in stress-induced (Takotsubo) cardiomyopathy associated with different clinical backgrounds and outcomes?

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Purpose: Takotsubo cardiomyopathy (TCM) was initially defined as a stress-related acute coronary syndrome-like clinical disorder typically with "transient left ventricular apical ballooning" without coronary stenosis (type A). However, reports of a variant form of TCM with non-apical ballooning (type non-A) have been accumulating. We examined whether type non-A TCM has the same clinical characteristics and long-term prognosis as those of type A.

Methods: Data on TCM (n = 199) were retrieved from the BOREAS (Broad-range cooperative Organization for Renal, Arterial and cardiac Studies) registry and analyzed for differences in clinical features and outcome between type A (n=171, 86%) and type non-A (n=28, 14%) TCMs.

Results: (1) There were no significant differences in age, proportion of females, and number of coronary risk factors between type A and type non-A TCMs. However, underlying disease was different between the two types: intracranial bleeding was more frequent (type A=13% vs. type non-A=4%) and pharmacotherapy was much less frequent (type A=1% vs. type non-A=18%) in type A than...
in type non-A. (2) Intraventricular obstruction (15%), ventricular thrombi formation (4%), cardiac rupture (1%) and recurrence in acute phase (2%) were observed only in type A TCM, though the prevalences of pulmonary edema, pump failure and lethal arrhythmias were similar in the two types of TCM. (3) During long-term follow-up (24±25 months), recurrence (type A=1% vs. type non-A=4%) and cardiac death (type A=2% vs. type non-A=0%) were rare in both types of TCM.

Conclusions: Patient characteristics and long-term prognosis were similar in type A and type non-A TCMs. However, there were differences in frequent triggers and incidences of acute complications between the two types of TCM. Attention should be paid to occult pseudochrondoma in type non-A TCM, and acute complications such as intracardiac thrombi and acute recurrence of TCM need to be closely monitored in type A TCM, especially in cases with intraventricular obstruction.

P4276 Prognostic value of the admission ECG for predicting complications in patients with tako-tsubo cardiomyopathy

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Purpose: Tako-tsubo cardiomyopathy (TTC) mimics acute myocardial infarction. A substantial number of patients develop adverse events during the acute course of TTC. This study assessed the prognostic value of the admission ECG for predicting complications in patients with TTC.

Methods: The present study included 76 TTC patients (69, 7m; 70±12 years). A total of 37 patients (49%) developed one (n=17) or more (n=20) adverse events such as pulmonary oedema (n=14), cardiogenic shock (n=4), ventricular tachycardia (n=7), atrial fibrillation (n=14), right ventricular involvement (n=15), intraventricular pressure gradient (n=6), thrombus and/or stroke (n=6), or death (n=2). Clinical parameters and the admission ECG were compared in patients with and without adverse events.

Results: Patients with adverse events were older (73±12 vs 67±12 years, p=0.05) and more frequently female (52% vs 14%, p=0.05). There was a higher rise in troponin (9.4±9.0 vs 6.1±5.7 times the upper limit of normal, p=0.05) and a lower left ventricular ejection fraction (47%±19 vs 55±13%, p=0.007) in patients with adverse events. Angiographic ballooning pattern and left ventricular end-diastolic pressure were not different.

Time from symptom onset to first ECG (7.5±2.7 vs 9.3±9.8 hours, p=ns) was similar in both groups. Patients with adverse events had a higher heart rate on admission (97±23 vs 82±18/min, p=0.003), and there was a trend towards a higher number of leads with ST-segment elevation (4.4±2.3 vs 3.5±2.9 leads, p=0.09) and a greater magnitude of ST-segment elevation (0.64±0.51 vs 0.48±0.36 mV).

The number of patients with ST-elevation in V3 (89% vs 74%) and V4 (60% vs 39%, p=0.02) was higher in patients with adverse events. Regarding ST-elevation in the other leads, occurrence of an abnormal Q wave (32% vs 30%), reciprocal ST-segment depression (27% vs 28%) or T-wave inversion on the admission ECG there was no difference among both groups. Patients with adverse events, however, presented with a longer QTc interval (491±54 vs 460±54 msec, p=0.02).

Conclusion: About half of the patients with TTC develop adverse events. Especially elderly females with a high heart rate and a prolonged QTc interval on the admission ECG are at increased risk for developing complications during the acute course of TTC.

CARDIOMYOPATHIES: TREATMENT

P4277 Long-term follow-up of 99 patients after transcatheter ablation of septic hypertrophy (TASH) for HOCM: No evidence for the induction of an arrhythmogenic substrate

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Background and Aim of the study: Prognosis after surgical myectomy for HOCM is beneficial even in long-term follow-up. However, after TASH only midterm follow-up data is available so far. In the present study we systematically analyzed the mortality in a 7 year follow-up after TASH.

Methods: All patients who underwent TASH-treatment at our institution within the year 2004 were included in the study (n=103, age 57.6±15 years). Follow-up was performed by telephone contact with either the patients or their general practitioners. Only 4 patients who lived abroad (Syria, Australia, Turkey, Italy) were lost in follow-up and were excluded from the study.

Results: Left ventricular outflow tract (LVOT) obstruction decreased significantly after the injection of 0.94±0.3 ml of ethanol (LVOT gradient at rest pre vs post TASH: 76.0±17.5 mmHg, after provocation pre vs post TASH: 163.6±60.4 mmHg, p<0.0001 for all). No patient died during the TASH procedure or during the hospital stay. In 10 patients TASH was a redo intervention. During a mean follow-up time of 6.5±1.4 years 10 patients died. 7 patients died from non cardiac reasons (5.3±0.8 years after TASH) and 3 patients died suddenly (2, 9 and 79 months after TASH at the age of 57, 47 and 79 years). In this study population the yearly total mortality was 1.6%, the yearly sudden death rate 0.4% and the in hospital mortality 0%.

Conclusion: Prognosis after TASH is excellent even in long-term follow-up. The sudden death rate in this study population is lower compared to untreated HOCM patients. There is no evidence for the induction of an arrhythmogenic substrate after alcohol ablation.

P4278 Identification of patients with idiopathic dilated cardiomyopathy and SCIDHeFT inclusion criteria who could be considered for early ICD implantation

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Purpose: To identify patients with recently diagnosed idiopathic dilated cardiomyopathy (IDC) and symptomatic heart failure unlikely to improve despite medical treatment introduction/optimization and who could be considered for early ICD implantation.

Methods and Results: 189 consecutive patients with IDC and SCIDHeFT criteria (LV ejection fraction <0.35 and NYHA classes III-IV) evaluated before starting betablocker treatment were enrolled in the Trieste Heart Muscle Disease Registry. After optimization of medical treatment only 58 patients (31%) maintained SCIDHeFT criteria (LV ejection fraction <0.35, NYHA class III-IV; average follow-up = 12±5 years). Patients who couldn’t maintain SCIDHeFT criteria (n=100, 49%) had a better heart rate (87±10 vs 76±10, p<0.02) than patients who maintained SCIDHeFT criteria. Regarding ST-elevation (n=26 vs 27, p=0.55), intraventricular pressure gradient (n=8), thrombus and/or stroke (n=6), or death (n=2) did not differ significantly. The mean left ventricular systolic blood pressure (OR for interquartile difference=1.36; 95% CI 1.33-1.40), a larger indexed left atrial diameter (OR for interquartile difference=1.72; 95% CI 1.07-2.78), the presence of left bundle branch block (OR=2.17; 95% CI 1.60-4.43) and the presence of significant pericardial effusion (OR=2.15; 1.05-4.5) significantly predicted the persistence of IDC indications or death 6 months later. Considering these parameters a model for the probability of non improvement estimation was developed.

Conclusions: In IDC, only a minority of patients still have SCIDHeFT criteria after optimization of medical treatment or die in the meanwhile; applying simple clinical parameters it is possible to identify this patients, who could be considered for earlier ICD implantation.

P4279 Surgical correction of HOCM in patients with severe hypertrophy and septal myocardial fibrosis

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Purpose: The mechanism of sudden death in HOCM is ventricular tachycardia/fibrillation emanating from areas of fibrosis. The classic Morrow technique for HOCM in patients with extreme left ventricular hypertrophy, right ventricular obstruction and myocardial fibrosis is not effective. A new technique of HOCM surgical correction in patients with severe hypertrophy and septal myocardial fibrosis was proposed.

Methods: The excision of the asymmetrical hypertrophied area of the interventricular septum (IVS) causing LVOT and RVO obstruction simultaneously was performed from the canal part of the zone of delayed enhancement (DE) imaging. Septal myocardial fibrosis was detected by cardiovascular magnetic resonance with DE imaging after gadolinium infusion. 11 patients with biventricular obstruction, severe hypertrophy (NYHA Class 3) and episodes of ventricular tachycardia (VT) underwent this procedure. Ages ranged from 18 to 38 years. The follow-up period was 41±7 months.

Results: 9 patients were free of symptoms (NYHA class 1) and 2 patients had one mild limitation. The mean echocardiographic LVOT gradient decreased from 87.9±12.8 to 9.6±3.4 mmHg, the mean value of gradient in RVO was reduced from 44.6±5.7 to 4.1±1.4 mmHg. Echocardiographically determined septal thickness was reduced from 35.8±3.2 to 19.2±3.0 mm. Sinus rhythm was restored in 35.8±3.2 to 19.2±3.0 mm. Sinus rhythm was restored in 32 patients. 3 patients were on amiodarone treatment. In 9 of the 11 patients TASH was a redo intervention. During a mean follow-up time of 6.5±1.4 years 10 patients died. 7 patients died from non cardiac reasons (5.3±0.8 years after TASH) and 3 patients died suddenly (2, 9 and 79 months after TASH at the age of 57, 47 and 79 years).
P4280

Long-term recovery of atrioventricular conduction after percutaneous transluminal septal myocardial ablation in patients with hypertrophic obstructive cardiomyopathy

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Objectives: Lesion of the atrioventricular (AV) conduction system is a well known adverse effect of percutaneous transluminal septal myocardial ablation (PTSMA) in patients with hypertrophic obstructive cardiomyopathy (HOCM). Implantation of permanent pacemakers (PM) following PTSMA has been reported in 3 to 38% of patients, but data determining potential long-term AV recovery is sparse.

Methods: The AV-conduction was evaluated by ECG and 48 hours Holter recording at long-term follow-up 4.8±3.6 years after PTSMA. In patients with a PM or implantable cardioverter defibrillator (ICD) the device was adjusted to back-up VVI-mode frequency 40. Documented high grade AV block defined as 2nd or 3rd degree was registered.

Results: Eighty six of 101 consecutive patients undergoing first time PTSMA from 1999-2011 (age 61±12 years) had no implantable device at baseline. Left bundle branch block was present in 7% and right bundle branch block in 9% of the patients at baseline. Twenty eight percent (24/86) of the patients without a device at baseline had a PM implanted for high grade AV block 6.4±2.9 days after PTSMA. Six patients had a PM implanted due to AV block in high grade AV block. Patients who had a PM in relation to PTSMA were significantly older (66±10 vs. 59±13 years, p=0.02) and they had higher incidence of AV block during the procedure (67% vs. 33%, p <0.01) than those who did not.

Eight patients with PTSMA-related PMs were diseased at the time of follow-up and two patients declined participation in the long-term evaluation of AV conduction. In 43% (6/14) of patients 48 hour Holter recordings did not reveal high grade AV block which suggests post-discharge recovery of the AV conduction. No significant differences in baseline characteristics were found between patients with documented high grade AV block (n=8) and patients with documented normal AV conduction (n=67) at follow-up. Patients with high grade AV block at follow-up had higher incidence of AV block during the PTSMA procedure (63% vs. 42%, p=0.04).

Conclusions: After first time PTSMA a PM was implanted due to AV block in 26% of patients with no previously implanted device. The long-term evaluation of AV conduction showed spontaneous recovery in 43% of these patients. This post-discharge recovery of the AV-conduction after PTSMA might suggest the potential for a more conservative pacemaker strategy.

P4282

Distinguishing 320-slice CT-detected focal fibrotic lesions and non-fibrotic lesions in hypertrophic cardiomyopathy by assessment of regional myocardial-strain using two-dimensional Speckle-tracking

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Purpose: To distinguish focal fibrotic and non-fibrotic-lesions in LVM in HCM subjects, we compared myocardial-regional-peak-strain-values using two-dimensional speckle-tracking transthoracic-echocardiography (TTE) in 320-slice-CT-detected fibrotic, non-fibrotic and normal-control-lesions.

Methods: Forty-subjects (20-consecutive-HCM-subjects (mean 59.1 years), 20-healthy-controls (mean 61.4 years)) underwent speckle-tracking TTE, and analysis of regional peak-longitudinal (LS) and transverse-strain (TS) in each of 17-LVM-segments (American-Heart-Association classification). In HCM-subjects, fibrotic-lesions were identified by early-phase defective-enhancement and late-phase abnormal-enhancement or by 320-slice-CT. Regional peak-LS and TS were measured in MSCI-detected fibrotic and non-fibrotic LVM lesions.

Results: In 20-HCM-subjects, 318-lesions (93.0%) yielded good-tracking on TTE. Fibrotic-lesions showed fibroelastic-change ≥10 subjects. Regional peak-LS absolute values were significantly lower in fibrotic-lesions than in non-fibrotic-lesions in HCM-subjects and controls (5.6±2.9%, 11.1±5.7%, 14.6±6.2%, respectively), furthermore these were significantly lower in non-fibrotic-lesions in HCM-subjects than controls (P<0.001). However there were no significant-differences of regional peak-TS among fibrotic and non-fibrotic-lesions in HCM-subjects and controls (10±12.7%, 13±5.4%, 14.6±11.1%, respectively).

Figure 1. Strain images with and without fibrosis

Conclusion: Regional peak-LS by speckle-tracking provides useful-information noninvasively to distinguish fibrotic from non-fibrotic-lesions in LVM in HCM subjects on 320-slice-CT and normal LVM in normal-healthy-controls.

P4283

Hidden right ventricular dysfunction in asymptomatic first-degree relatives of arrhythmogenic right ventricular cardiomyopathy assessed by speckle tracking, compared with strain Doppler

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Purpose: According to modifications of criteria of ARVC, proposed to facilitate clinical diagnosis in first-degree relatives, who often have incomplete expression of the disease, the diagnosis of familial ARVC is based on one of the following findings: either mild global dilatation or reduction in RV ejection fraction (EF) with normal LV or mild segmental dilatation of the RV or regional RV hypokinesis. The potential utility of Strain-Strain rate (S-SR) Doppler and two-dimensional (2D) to quantitatively assess RV, LV and RA(right atrium) function in asymptomatic family members of ARVC, with apparently normal RV, was evaluated.

Methods: 80 subjects were studied: 40 first degree ARVC relatives with normal RV at standard echocardiography and 40 healthy controls. By 8-GE LV EF, LV diameters and volumes, RV dimension, fractional area change (FAC%) and RVOT fractional shortening (RVTS%) RA volume were measured. By DTI velocity of (both P<0.001); furthermore these were significantly lower in non-fibrotic-lesions in HCM-subjects than controls (P<0.001). However there were no significant-differences of regional peak-TS among fibrotic and non-fibrotic-lesions in HCM-subjects and controls (10±12.7%, 13±5.4%, 14.6±11.1%, respectively).

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Cardiac sarcoidosis has characteristic distribution of myocardial fibrosis in apical hypertrophic cardiomyopathy, thus improving diagnostic sensitivity. Instead, S-SR ARVC relatives, when standard echocardiography doesn't show any impairment and may have potential clinical value in the objective quantitative assessment of regional hypokinesia. The evolution of ARVC is more diffuse right ventricle (RV) involvement and, sometimes, left ventricular (LV) abnormalities, that may result in heart failure. We evaluated the potential utility of two-dimensional (2D) strain/strain rate (S-SR) and 3D echocardiography to quantitatively assess RV, LV and atrial function in patients with ARVC (pts). The LV performance in comparison to cardiac magnetic resonance imaging in comparison with idiopathic dilated cardiomyopathy.

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Purpose: Late gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR) imaging is useful for the early diagnosis of cardiac sarcoidosis (CS). However, since some patients with dilated cardiomyopathy (DCM) also exhibit LGE, the differential diagnosis is sometimes difficult. This study aimed to identify the characteristic distribution of myocardial LGE in CS and to compare LGE patterns in CS with DCM.

Methods: Eighty-one patients with suspected CS and 52 patients with DCM underwent CMR imaging. The intra-ventricular (LV) and intra-mural distribution of LGE was compared. Results: LGE was present in 22 patients (27%) with suspected CS and 30 patients with DCM (68%). In patients with CS, LGE was distributed into all LV segments, whereas LGE localized mainly in basal inter-ventricular septum in patients with DCM. The intra-mural analysis demonstrated that LGE was distributed into subendocardial to subepicardial layers in patients with CS, whereas LGE localized mainly in the mid-ventricular layer in patients with DCM. Especially, subepicardial and subendocardial LGE (with spared mid-ventricular layer), circumferential subepicardial LGE, and nodular (transmural) LGE were characteristic patterns in CS. The sensitivity and specificity were 23% and 97% in subepicardial and subendocardial LGE, 18% and 97% in circumferential subepicardial LGE, and 36% and 97% in nodular LGE, respectively.

Conclusions: In patients with CS, LGE-CMR showed more diffuse distribution of LGE compared with patients with DCM. The characteristic patterns of LGE distribution can help differential diagnosis of CS from DCM.

Myocardial fibrosis in apical hypertrophic cardiomyopathy: a study by MRI
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Purpose: In hypertrophic cardiomyopathy (HCM) myocardial fibrosis is a pathological hallmark of HCM and is considered a substrate for ventricular arrhythmias and for progression to systolic dysfunction. Objectives: to assess the rate of progression of fibrosis by two consecutive CMR examinations in different pattern of hypertrophy and its relation with clinical variables in HCM.


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Background: Right ventricular fractional area change (RVFAC), tissue Doppler and M-mode measurements of tricuspid systolic motion (tricuspid Sm and TAPSE) are the only current non invasive methods for the quantification of RV systolic function; RV deformation analysis by speckle tracking echocardiography (STE) has recently allowed the analysis of RV performance. Using cardiac magnetic resonance imaging in comparison with idiopathic dilated cardiomyopathy.


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Methods: 55 HCM patients (37 males; mean age 43±18 years) underwent two CMR examinations (CMR-1 and CMR-2) separated by an interval of 719±240 days. Extent of LGE was measured as the rate of progression of LGE (LGE-rate) was calculated as the ratio between the increment of LGE (in grams) and the time (months) between the CMR examinations.

Results: At CMR-1 LGE was detected in 45 subjects, with an extent of 13.3±15.2 grams. At CMR-2, 53 (96.4%) patients had LGE, with an extent of 24.6±27.5 grams. Patients with apical HCM had higher increment of LGE (p=0.004) and LGE-rate (p=0.001) than those with other patterns of hypertrophy (figure). The extent of LGE at CMR-1 and the apical pattern of hypertrophy were independent predictors of the increment of LGE. Subjects with worsened NYHA class presented higher increase of LGE (p=0.031) and LGE-rate (p<0.05) than those with preserved functional status.

Conclusions: Myocardial fibrosis in HCM is a progressive phenomenon, related to a worse clinical status. Apical hypertrophic cardiomyopathy is probably characterized by a larger increment of LGE than other patterns.

Figure 1. Increment of LGE in different HCM patterns.

Diabetes mellitus and cardiac complications in thalassemia major patients

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Purpose: The relationship between diabetes mellitus (DM) and cardiac complications has never been systematically studied in thalassemia major (TM). Our aim was to evaluate in a large retrospective historical cohort of TM if DM was associated with an higher risk of heart complications.

Methods: We compared 86 TM patients affected by DM with 709 TM patients without DM consecutively included in the Myocardial Iron Overload in Thalassemia (MIOT) data base where the clinical history is recorded from the birth to the first T2* cardiovascular magnetic resonance (CMR) (years 2006-2010). Myocardial iron overload (MIO) was evaluated by T2* multislice technique. Biventricular function was quantitatively evaluated by cine images. Myocardial fibrosis was evaluated by late gadolinium enhancement. All considered cardiac events were developed after the DM diagnosis.

Results: In DM patients versus no-DM patients we found a significantly higher frequency of cardiac complications (46.5% vs 16.9%, P=0.0001), heart failure (HF) (30.2% vs 11.7%, P<0.0001), hyperkinetic arrhythmias (18.6% vs 5.5%, P<0.0001), and myocardial fibrosis (29.9% vs 18.4%, P=0.008).

DM patients had a significant higher risk of cardiac complications, HF, hyperkinetic arrhythmias and myocardial fibrosis, also adjusting for the absence of MIO (all 16 cardiac segments with T2*>20 ms) and for the covariates significantly different between groups and significantly associated to the dependent variable (Table 1).

Conclusions: DM increases the risk for cardiac complications, HF, hyperkinetic arrhythmias and myocardial fibrosis.
controls at all time-points (p < 0.01). ROC analysis revealed that R1 native was able to differentiate between healthy and diseased myocardium (AUC: 0.98; 95% CI: 0.96-1.00; p < 0.001) with a sensitivity of 100%, specificity of 86%, diagnostic accuracy 96%, positive predictive value 93% and negative predictive value 100%. R110min and R110minperformed best among the postcontrast values, however with lower predictive values.

Conclusions: We demonstrated that native and post-contrast T1 values and their respective R1 values provide indices with high diagnostic accuracy for the discrimination of normal and diffusely diseased myocardium. Native imaging provides the best distinction between controls and patients with cardiomyopathy.

CARDIOMYOPATHIES: PATHOPHYSIOLOGY

Effect of physical exercise on cardiac remodeling and oxidative stress in diabetic rats


Purpose: Oxidative stress is one of the main mechanisms involved in the pathogenesis of diabetic cardiomyopathy. Studies suggest that physical exercise (PE) improves myocardial glucose homeostasis and reduces myocardial damage from diabetes mellitus (DM). The aim of this study was to evaluate the effect of PE on myocardial oxidative stress and in vivo and in vitro cardiac structure and function in diabetic rats.

Methods: Male Wistar rats were divided into three groups: control sedentary (CS, n=15), diabetic sedentary (DS, n=15), and diabetic trained (DT, n=15). Diabetes mellitus was induced by intraperitoneal injection of streptozotocin (50mg/kg, single dose). Physical training was performed 5 times a week for 8 weeks in a treadmill. All at the end of the experimental period, rats underwent echocardiography. Myocardial function was evaluated in left ventricular (LV) papillary muscle preparations during isometric contractions. Oxidative stress was measured in LV myocardial homogenates by spectrophotometry. ANOVA was used to compare echocardiographic and oxidative stress parameters, and ANCOVA for papillary muscle parameters using papillary muscle cross sectional area as the co-variant, both complemented by the Tukey test (*: p<0.05 vs. CS; #: p<0.05 vs. DS).

Results: Echocardiogram showed increased LV diastolic diameter in the diabetic groups and increased LV posterior wall thickness (p<0.001) with a sensitivity of 100%, specificity of 88%, diagnostic accuracy 95%, positive predictive value 93% and negative predictive value 100%. LV myocardial oxidative stress and in vivo and in vitro cardiac structure and function are attenuated by physical exercise.

Conclusions: PE improves cardiac remodeling and oxidative stress in diabetic rats.

Dual assessment of coronary flow reserve in non obstructive hypertrophic cardiomyopathy: pathophysiological characteristics


Microvascular dysfunction reflected by the decreased coronary flow reserve (CFR) is a common finding in hypertrophic cardiomyopathy (HCM) and is related with unfavorable long term outcome. Elevated LV filling pressure and wall stress (as a result of diastolic dysfunction) might additionally aggravate CFR. Plasma levels of NT-pro-BNP and the ratio of early to late transmural flow velocity to early diastolic lateral mitral annulus velocity (E/e‘) have been shown to be accurate non-invasive predictors of the abnormal LV wall stress and elevated LV filling pressure. Therefore, the aims of the current study were to examine: 1. Possible regional differences of CFR among patients with HCM; 2. Laboratory (BNP) and immunohistological parameters tested (CyPA, EMM-PRIN, CD 68, CD3, MHC II, virus genome), CyPA was identified as the only independent predictor for the primary endpoint yielding a relative risk of 4.7 for all-cause mortality and heart transplantation alone (95% CI 1.1-19.8; p=0.036). Subgroup analysis also revealed CyPA as a predictor of outcome in the patients with non-inflammatory cardiomyopathy suggesting that CyPA is a prognostically relevant marker of myocardial damage beyond inflammation.

Impaired copper homeostasis in patients with hypertrophic cardiomyopathy

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Purpose: Hypertrophic Cardiomyopathy (HCM) is the commonest monogenetic inherited cardiac disorder, characterised by increased ventricular wall thickness, myocyte disarray and myocardial fibrosis. Recently, HCM has been associated with enhanced oxidative stress, which in turn has the potential to perpetuate hypertrophy and myocardial fibrosis. Myocardial copper and zinc imbalance are an important source of oxidative stress and may be shown to cause hypertrophic forms of cardiomyopathy in animal models. Furthermore, excess copper plays a pivotal role in Wilson’s disease, an important HCM differential diagnosis. Copper chelation, therapy in Wilson’s disease, has recently been demonstrated to reverse LVH and organ fibrosis in several animal disease models and humans with Type 2 diabetes. Surprisingly, there is no published data concerning copper homeostasis in patients with HCM. We investigated whether patients with HCM have overt abnormalities in copper and zinc homeostasis.

Methods: With ethical approval, we compared 20 randomly selected HCM patients from our local database with 18 matched healthy volunteers. Each participant provided 24 hour urine and fasting blood serum samples which were analysed for copper/haemoglobin and zinc using the highly sensitive and widely validated technique of Inductively Coupled Plasma Mass Spectrometry.

Results: HCM patients exhibited significantly higher levels of copper and zinc. HCM groups exhibited increased urinary copper and zinc levels, respectively (p<0.05). Serum copper and zinc levels were significantly lower in HCM patients compared to controls, although these differences did not reach statistical significance (p=0.057 and p=0.06, respectively). Conclusions: Impaired copper homeostasis in patients with HCM could be a potential mechanism for the development of cardiomyopathy and perhaps increased risk of sudden cardiac death.
Conclusion: HCM patients exhibit overtly altered copper homeostasis. Coupled with the previous observation of LH and fibrosis regression induced by copper chelation therapy these findings provide a mechanistic basis for copper chelation therapy to be tested in HCM.

**CARDIOMYOPATHIES: DIAGNOSIS**

**P4297**

A French registry of takotsubo syndrome in non-academic hospitals (OFSETT)


Background: Takotsubo cardiomyopathy (Tak) is a self-limiting transient left ventricular dysfunction following an emotional or physical stress. Its prevalence is increased in patients with breast cancer treatment. The aim of this study was to determine the incidence of Tak syndrome in patients treated for breast cancer in non-academic French hospitals.

Methods: Between November 2010 and December 2011, 15 non-academic French hospitals with a high volume of percutaneous coronary procedures (>1000) included consecutive patients diagnosed with Tak syndrome according to the Mayo Clinic diagnostic criteria.

Results: A total of 121 patients were enrolled: 89% were women and the mean age was 72.12 years. Most of the women (89%) were aged ≥50 years old; 8% of patients had diabetes, 30% were current smokers and 52% had hypertension. Symptoms of Tak syndrome were chest pain (81%), dyspnea (27%) and/or syncope (5%). The mean maximum troponin level was 7.8 ng/mL and the mean heart rate was 89.5 bpm. In 29% of patients, the patient was treated with fibriolysis. Coronary angiography was performed in all patients. Coronary arteries were angiographically normal in 78% of patients and showed <50% stenosis in 22%. Left ventricle (LV) angiography showed apical ballooning in 35% of patients. The mean LV ejection fraction was 42 ± 13% on echocardiography and 46 ± 10% on angiography. The target event was identified in 55% of the patients: mental stress in 61%, physical stress in 29%, and 4% on angiography. The target event was identified in 55% of the patients: mental stress in 61%, physical stress in 29%, and 4% on angiography.

Purpose: Takotsubo syndrome remains the subject of investigation. We report on the management of processes of care in consecutive patients with Takotsubo syndrome using data from a French registry (OFSETT).

Methods: Between November 2010 and December 2011, 15 non-academic hospitals with a high volume of percutaneous coronary procedures (>1000) included consecutive patients diagnosed with Takotsubo syndrome according to the Mayo Clinic diagnostic criteria.

Results: A total of 121 patients were enrolled: 89% were women and the mean age was 72.12 years. Most of the women (89%) were aged ≥50 years old; 8% of patients had diabetes, 30% were current smokers and 52% had hypertension. Symptoms of Tak syndrome were chest pain (81%), dyspnea (27%) and/or syncope (5%). The mean maximum troponin level was 7.8 ng/mL and the mean heart rate was 89.5 bpm. In 29% of patients, the patient was treated with fibriolysis. Coronary angiography was performed in all patients. Coronary arteries were angiographically normal in 78% of patients and showed <50% stenosis in 22%. Left ventricle (LV) angiography showed apical ballooning in 35% of patients. The mean LV ejection fraction was 42 ± 13% on echocardiography and 46 ± 10% on angiography. The target event was identified in 55% of the patients: mental stress in 61%, physical stress in 29%, and 4% on angiography. The target event was identified in 55% of the patients: mental stress in 61%, physical stress in 29%, and 4% on angiography.

Conclusion: These results demonstrated a novel antigen-target at DCM - tRNA synthetase and revealed its potential role at disease development.
The extent and consequences of diagnostic uncertainty in individuals assessed for arrhythmogenic right ventricular cardiomyopathy

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Purpose: The diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is based on clinical tests. The findings of these tests can be non-specific in the early stages of the disease therefore long term follow up and serial testing are often necessary to make a definite diagnosis. The diagnostic criteria were revised in 2010 with the intention of increasing their sensitivity and specificity. Despite this there are individuals who can be given neither a definite diagnosis or reassurance because the manifestations of the disease are slow to develop. Relatives of affected individuals assessed as part of familial screening are particularly likely to fall into this category. Less than 50% of probands with ARVC have a definable pathogenic mutation, therefore genetic screening cannot resolve this problem. We constructed a registry of individuals who have been seen in the north of England for ARVC to determine how many individuals live with long term diagnostic uncertainty and the resources required for their ongoing follow up.

Method: Individuals seen by clinical services in connection with ARVC from 2005 to the present were identified retrospectively from clinical records. Major and minor diagnostic criteria for ARVC were identified from the results of clinical tests using the 2010 criteria.

Results: 92 individuals have been assessed for ARVC and found to have some clinical or genetic abnormality. 69 individuals (74%) lack a definite diagnosis. 21 are known to have a pathogenic mutation and were followed up to identify the evolvement of phenotypic features over time. Genetic screening was not an option for the remaining 48 individuals. The mean duration of follow up for this group was 5.4 years, SD 4.5, range 1.1 to 21.1. For every 5 years of follow up individuals without a definite diagnosis had a mean of 3 echocardiographic examinations, 2 cardiac MRIs and 1 ambulatory ECG assessment.

Conclusions: The majority of individuals seen in clinical practice for suspected ARVC lack a definite diagnosis. These individuals live with diagnostic uncertainty of a potentially life threatening disease for many years and require regular clinical follow up and repeated clinical testing to reassess their phenotype. Our findings underline the importance of research to identify the clinical significance of mutations and the need for a novel diagnostic test for presumptiv individuals.

In dilated cardiomyopathy the stimulating potential of anti-beta1-receptor autoantibodies is positively correlated with the depression of left ventricular function

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Dilated cardiomyopathy (DCM) characterized by progressive cardiac dilatation and dysfunction is one of the main causes of severe heart failure in younger adults. Previously we introduced a live cell assay for the detection of functional anti-beta1 receptor autoantibodies (beta1-aabs) using fluorescence resonance energy transfer (FRET) microscopy. Here we used this method to investigate the relationship between the receptor-activating potential of beta1-aabs and cardiac dysfunction in DCM.

Methods: The analyzed DCM population (n=97) had significant CAD excluded and was stable on medicalization according to current therapy guidelines for at least 3 months. In our outpatient-unit blood was drawn and immediately processed for beta-testing. All patients tested underwent echocardiography to assess left ventricular function (LV), mean 46±12 years, over a median follow-up of 36±7 months. First examination: all patients underwent a 12-lead ECG, a trans thoracic echocardiogram and MRI scan. Subsequently a clinical three-month follow-up was performed, during which the patients had undergone several-hour Holter monitoring and an exercise test using modified Bruce protocol. During follow-up all patients were submitted to endothelial function study through a color-Doppler scan of brachial artery before and after ischemia provoked by the arterial clamp.

Results: 10 (41.67%) patients on 24 had one or more syncopal episodes before and during follow up whereas 14 (58.33%) patients never fainted. Patients with syncope and obstructive HCM showed a three times higher FMD (see Table 1).

Table 1. Results

<table>
<thead>
<tr>
<th></th>
<th>Pts with syncope</th>
<th>Pts without syncope</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Ejection fraction (%)</td>
<td>51.10±8.75</td>
<td>56.92±7.08</td>
<td>0.09</td>
</tr>
<tr>
<td>Apical hypotrophy</td>
<td>31%</td>
<td>55%</td>
<td>0.06</td>
</tr>
<tr>
<td>SAM</td>
<td>100%</td>
<td>50%</td>
<td>0.01</td>
</tr>
<tr>
<td>Gradient at rest</td>
<td>49.8±32.47</td>
<td>16.54±24.19</td>
<td>0.01</td>
</tr>
<tr>
<td>FMD</td>
<td>15.23</td>
<td>6.81</td>
<td>0.01</td>
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Comparing beta1-aabs displaying an activating potential with beta1-aabs serving as a reference (control). HEK-293 cells expressing human beta1-adreceptors and an Epac1 based cyclic Adenosine Mono-Phosphate (cAMP) sensor were used in the FRET assay. Upon beta1-aab-mediated receptor stimulation, intracellular cAMP levels increase, and cAMP-binding to the sensor results in conformational changes decreasing FRET between its chromophores cyan (CFP) and yellow fluorescent protein (YFP).

Results: Immunoglobulin G (IgG) prepared from healthy controls with normal cardiac function and preclinical (10±2%) or late stage coronary disease (45±15%) demonstrated no beta1-aab activity. IgG prepared from n=49/97 DCM patients were judged beta1-aab positive (26.6±4%; FRET activity, LVEF 32.8±1.1%). Allover, in DCM patients but not in control subjects there was a highly significant (p<0.001) inverse correlation between FRET activity (beta1-receptor stimulating potential of beta1-aabs) and LVEF (r = -0.4; R2=0.17).

Conclusion: In this pilot study on 97 DCM patients we demonstrate for the first time that the decrease in cardiac function is significantly associated with the receptor-stimulating potential of activating beta1-aabs. Based on this promising finding we have initiated a large prospective follow-up study to address the clinical relevance of beta1-aabs in human cardiac disease.

Performance of task force diagnostic criteria for identification of symptomatic patients in the nordic arrhythmogenic right ventricular cardiomyopathy registry

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Purpose: Revision of arrhythmogenic right ventricular cardiomyopathy (ARVC) Task force diagnostic criteria in 2010 (TF2010) increased their sensitivity for detection of patients at early stages of the disease. The association between TF2010 and symptoms, however, has not been fully clarified. Our aim was to re-view baseline clinical and demographic characteristics of patients enrolled in the Nordic ARVC Registry and assess their relation to the early manifestations of the disease.

Methods: Patients with definite ARVC according to TF2010 enrolled in the regist-ry between 2007 and 2017 in Denmark, Norway, and Sweden were included (n=167, 127 (103 families), age 48±16 years, 57% male. Patients were defined as symptomatic based on the occurrence of syncope, documented ventricular tachy-ardys (VT) or aborted cardiac arrest (ACA) by enrolment in the registry. The performance of TF2010 and TF1994 diagnostic criteria was tested for prediction of symptoms. Minor criteria were assigned 1 point and major criteria 2 points when calculating the total diagnostic score.

Results: 1. The study population comprised 95 probands and 32 family members, of whom 25 were identified via family screening (20%). Mean diagnostic scores were 5.6±1.8 (TF2010) and 3.6±1.7 (TF1994). Initial disease manifestations were VT (n=55, 43%), syncope (n=20, 16%) or aborted cardiac arrest (n=13, 10%) while 39 patients did not have any of those by baseline (30%). Mean age at first symptom was lower for syncope than for VT or ACA (43±15 years vs 43±15 years, p=0.038) as the former symptoms, 21). Neither age at first symptom, gender or presenting sign or symptom were predictors of symptom occurrence, however patients with documented VT or ACA were older than those without (51±15 vs 42±15, p=0.018). The presence of inverted T-waves in leads V1-V3 was associated with symptom occurrence (OR=2.95 CI1:2.66-3.66, p=0.002). Neither the history of sudden death nor the presence of ARVC in 1st degree relatives predicted symptom occurrence. TF2010 score ≥3 demonstrated association with symptoms (OR=2.4, 95% CI1:1.06-5.23, p=0.035 for any symptom and OR=2.7 95% CI1:2.95-5.01, p=0.008 for VT or ACA only) while TF2010 score did not.

Conclusions: In patients with definite ARVC enrolled in the Nordic ARVC Registry, abnormal repolarisation is associated with history of syncope, VT or ACA as the first disease manifestation while none of other diagnostic criteria showed any significant association with the symptoms. We found no relationship between TF2010 score and symptoms as baseline.
The impact of dynamic intraventricular obstruction on left ventricular mechanics in hypertrophic cardiomyopathy

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Background: LV twisting and untwisting are integral components of ventricular contractility and suction, and filling. In hypertrophic cardiomyopathic (HCM) myocardial fibrous disarray, interstitial fibrosis and dynamic obstruction could influence left ventricular (LV) mechanics. Data regarding the impact of the dynamic LV outflow tract (LVOT) obstruction on LV mechanics are limited and discordant.

Purpose: To assess LV mechanics in patients (pts) with obstructive (HOCM) and non-obstructive (NHCM) HCM versus normal subjects.

Methods: We prospectively enrolled 35 pts (52±15 years, 16 men) with HCM (19 with HOCM and 16 with NHCM, according to the presence/absence of a dynamic LVOT gradient of > 30 mmHg) and 36 age- and gender-matched normal subjects (47±12 years, 12 men). Pts with aortic HCM have been excluded. A comprehensive echocardiogram was performed in all. LV filling pressures were assessed using the E’/Eaverage ratio. Global longitudinal LV strain (GLS) and LV torsion parameters have been assessed by speckle tracking echocardiography. Peak basal and midwall rotation and backrotation rates, peak LV torsion and peak LV untwisting rate were determined. Time intervals from peak R wave (ECCG) to each of them were measured and normalized to the RR interval. Mitral regurgitation (MR) severity was scored. Results: Pts with HOCM were older (p=0.009) and had more severe MR (p=0.01) than pts with NHCM. There were no significant differences between HOCM and NHCM pts in LV mass, E/E’ratio, systolic and diastolic myocardial velocities, and GLS (p=0.05 for all). Compared to normal subjects, pts with HOCM, unlike pts with NHCM, had higher values for apical LV rotation (21.7±8.5 vs 16±6.2°, p=0.01) and backrotation rate (p=0.00) and basal Urotorsion (p=0.04) and LVtorsion (3.7±1.1 vs 2.8±1.8°/min, p=0.002). Time to peak LV untwisting rate was significantly longer than in normal subjects in both HOCM and NHCM pts (p=0.001 and p=0.01, respectively). In pts, LV torsion was related to age (r=0.49, p<0.001), MR stage (r=0.48, p=0.01), LV mass (r=0.42, p=0.01) and the presence of dynamic obstruction (r=0.38, p=0.02). In multivariate analysis LVtorsion was independently correlated with GLS (p=0.08, p=0.03) and the presence of dynamic obstruction (p=0.32, p=0.04).

Conclusions: In pts with HCM, LVOT obstruction is related to changes in LV mechanics: increased apical and basal rotation, increased LV torsion, and delayed LV untwisting. Increased LV torsion is independently related to the presence of dynamic LVOT obstruction. These findings could provide new insights into the pathophysiology of HCM.
Completely autologous biotube vascular grafts: eosin Y significantly promoted in vivo formation of functional biotubes in a short term

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Objectives: In our previous study, in vivo tissue-engineered autologous tubular tissues ‘BIOTUBES’ could reconstruct to vascular tissues within several months after implantation. BIOTUBES obtained from traditional silicon mold in dorsal subcutaneous pouches of animals for 1 month had homogeneous thin (less than 0.1 mm) connective tissue walls even though with high burst strength (ca. 10 MPa) and equivalent compliance to that of native arteries. We challenged the possibility of extremely short-term preparation of BIOTUBES by controlled release of eosin Y.

Methods and Results: Micropore acrylic tubes (diameter: 4 mm, length: 4 cm, pore size: 0.5 mm) filled with a PBS solution of agar (0.3%) including eosin Y (1%), as molds for BIOTUBES, were placed into dorsal subcutaneous pouches of Beagle dogs (ca. 10 kg) for 1 week. Eosin Y was continuously released through the wall of the agar-impregnated Biotube. To ensure the formation of tissue, we performed Laser-Doppler-Imaging. In the treated mice, the formation of tissue was confirmed by Laser-Doppler-Imaging. In both control and treated mice, the number of vessels (12.5±4 pos. cells/vessel, n=18) did not change significantly, but the number of vessels (14.9±3.9 pos. cells/vessel, n=18) was significantly increased in the treated mice. These results indicate that the tissue formation is significantly increased in the treated mice.

Conclusion: We demonstrated that TLR4 expression plays an important role in regulating inflammatory response in the arterial wall. Furthermore, the infiltration of M2-MAC was increased in the arterial wall in the treated mice, suggesting that the infiltration of M2-MAC is increased in the arterial wall in the treated mice. These results suggest that the infiltration of M2-MAC is increased in the arterial wall in the treated mice.
Saphenous vein aorto-coronary bypass graft 
atherosclerosis in patients with chronic kidney 
disease: more clarification, but less vasocostruction 
potential

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Purpose: Atherosclerotic coronary arteries are more calcified in patients with than without chronic kidney disease. Coronary artery calcium is not only a marker of coronary microvascular obstruction in patients with and without CKD during stenting for saphenous vein aorto-coronary bypass graft (SVG) stenosis under protection with a distal occlusion/aspiration device.

Methods: In patients with and without CKD (n=20/20), SVG calciumification was determined from virtual histology using intravascular ultrasound analysis before stenting. Coronary arterial blood was retrieved during stent implantation and divided into particulate debris and plasma. The calcium concentration of particulate debris was analyzed by flame atomic absorption spectrometry. The concentrations of catecholamines, endothelin, serotonin, tissue factor, thromboxane, and tissue factor pathway inhibitor (TFPI) in coronary aspirate plasma were determined. Using a bioassay of rat mesenteric arteries with intact (+E) and denuded (-E) endothelium, the vasocostrctor response to coronary aspirate plasma was quantified and normalized to that by potassium chloride (KClmax =100%)

Results: There was more dense calcium in patients with than without CKD (15.3±3.3 vs. 3.1±1.2% of plaque volume). Patients with CKD had more particulate debris and coronary release than patients without CKD. In contrast, the release of serotonin was less in patients with than without CKD (0.4±0.1 μmol/L vs. 1.2±0.3 μmol/L), whereas that of catecholamines, endothelin, tissue factor, thromboxane, and TFN was not different. Asparate plasma from patients with CKD induced less vasocostruction of rat mesenteric arteries than that from patients without CKD (+E: 26.7±7%; -E: 26.7% vs. +E: 68.12%; -E: 95.16% of maximum KCl-induced vasocostriction).

Conclusion: Graft atherosclerosis in patients with CKD is more calcified, but the asparate has surprisingly less serotonin and vasocostrctor potential.

Comparison of circulating microparticles counts in patients with acute coronary syndrome with two methodologies

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Background: Circulating microparticles (MPs) are increased in cardiovascular disease and have become promising biomarkers in many pathological situations. Measurement of plasmatic MPs is not standardized and most studies have focussed on relatively large MPs due to technological limitations. We following compare two flow cytometric methodologies for the enumeration and characterization of MPs in acute coronary syndrome (ACS) patients and its changes during 30 days.

Methods: We recruited 113 ACS patients (aged 68±12 years, 65% males); sodium citrate platelet poor plasma was collected within 24h of percutaneous coronary intervention (PCI). Day 1 and Day 30 post-PCI. Aliquots of aspirator samples were processed in two different flow cytometers (FCM), avoiding pre-analytical issues. Polystyrene beads (0.1-0.5 μm) were used to size the MP gate in both FCMs. CD41b+/platelet MPs (pMPs), CD144+/endothelial MPs (eMPs) and CD14+ monocyte MPs (mMPs) were quantified in a high resolution Apogee A50 FCM and in a conventional FCM (FACS Calibur) with a 0.5 μm detection limitation. Standard deviation in both protocols was less than 5%. CytoCounts beads were used for absolute counts in FACS Calibur FCM.

Results: MPs counts were significantly higher when the samples were processed with a FACS Calibur FCM, mainly pMPs (p=0.005). However no changes were detected in mMPs counts following PCI (pMPs p=0.51, eMPs p=0.40, mMPs p=0.24). When small-size MPs (0.1-0.5 μm) were quantified in a high sensitive FCM, a significant increase in pMPs and eMPs (p<0.012 and p=0.015, respectively) was found, but mMPs remained constant (p=0.81).

Conclusion: Latest generation of FCMs likely display higher sensitivity for MPs, mainly due to lower detection limits and background noise. The size of polystyrene beads is not comparable to biological size of MPs and thus, conventional FCMs might not reliability detect MPs. In the search of MPs as potential biomarkers, technological improvements should not be underestimated.
Molecular mechanism of tissue factor regulation through RAGE-MT1-MMP axis in HMGB-1 stimulated-endothelial cells

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Backgrounds: The atherosclerosis is understood as a blood vessel inflammation. HMGB-1 is one of the mediators released from necrotic cells or macrophages that receives inflammatory stimulus. It plays a key role in the systemic inflammation. Tissue factor (TF), a physiological initiator of coagulation cascade, is known to lead to inflammation which promotes the thrombus formation in the onset of acute coronary syndrome. We recently have shown that silencing of membrane type 1 MMP (MT1-MMP) suppressed the advanced glycation endproducts (AGE)-triggered TF protein expression and phosphorylation of NF-κB in smooth muscle cells. These results suggest that MT1-MMP also relates to inflammatory conditions in vascular wall. However, it is still unclear about the association of HMGB-1 and MT1-MMP mediated TF expression. In this study, we investigated the molecular mechanism of TF expression in response to HMGB-1 stimulation and the involvement of MT1-MMP in endothelial cells.

Methods: Cultured human aortic endothelial cells were stimulated with 50 μg/ml HMGB-1. The protein levels of TF and phosphorylated NF-κB were determined by Western blotting. The MT1-MMP activity was measured by ELISA. MT1-MMP expression was silenced by small interfering RNA (siRNA). GTP-loading of RhoA and Rac1 was assessed by pull-down assays.

Results: HMGB-1 increased MT1-MMP activity and activated small GTP binding protein RhoA and Rac1 within 5 min in endothelial cells, which was inhibited by silencing of receptor for AGE (RAGE) or MT1-MMP. TF protein expression was regulated by RhoA activation as well as Rac1 dependent NF-κB expression in HMGB-1 stimulated endothelial cells. siRNA to RAGE or MT1-MMP suppressed NF-κB phosphorylation and TF protein expression mediated via RhoA and Rac1 activation induced by HMGB-1.

Conclusions: We clarified that RAGE/MT1-MMP axis modified the HMGB-1 mediated TF expression through the RhoA and Rac1 activation and NF-κB phosphorylation in endothelial cells. These results suggested that MT1-MMP was involved in vascular inflammation and might be a good target for treating acute coronary syndrome.

Pharmacokinetic interactions between clopidogrel and rosuvastatin: effects on vascular protection in subjects with coronary heart disease


Background/Objectives: Genetic polymorphisms in the hepatic cytochrome P4315 CYP2C19) affect the antiplatelet effects of clopidogrel. Rosuvastatin is partially metabolized by the same cytochrome. We hypothesized that pharmacokinetic interactions between these drugs might affect their individual responses on vascular protection.

Methods: Patients with stable coronary heart disease (N=20) were submitted to four consecutive 1-wk therapeutic regimens: aspirin, rosuvastatin 40 mg, rosuvastatin 40 mg plus clopidogrel 75 mg, or clopidogrel 75 mg alone. A loading dose of 300 mg clopidogrel was given in the first day. Biochemistry, platelet function (multiplatelet analyzer), flow-mediated dilation (ultrasound of the brachial artery), endothelial progenitor cells, and microparticles (flow-citometry) were assessed by triplatelet analyzer, flow-mediated dilation (ultrasound of the brachial artery), endothelial progenitor cells, and microparticles (flow-citometry) were assessed at baseline and the end of treatment. Viability was assessed by 7AAD and Annexin-V-staining.

Results: At baseline, no differences were observed in the number of circulating endothelial progenitor cells. There was no difference in the activity of the G-protein-responsive transmembrane adenylyl cyclase. Aside from this cyclase, mammalian cells possess a second source of cAMP, the ubiquitous expressed soluble adenylyl cyclase (sAC). Therefore, to investigate the role of sAC inactivation since treatment with a dual ET-1 receptor blocker did not affect circulating EPC numbers.

Conclusions: Among patients with type 2 diabetes and vascular disease, high plasma levels of ET-1 is associated with higher number of EPC, possibly reflecting activation of an endothelial cell repair mechanism triggered by vascular damage. The recruitment of EPC does not seem to be regulated by ET-1 receptor antagonism. Therefore, we investigated the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity. The ubiquitously expressed soluble adenylyl cyclase (sAC). Therefore, to investigate the role of sAC in activation of ET-1 in this condition, we studied the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity.

Endothelial progenitor cells in relation to endothelin-1 and endothelin receptor blockade: a randomized controlled trial


Aims: Endothelial progenitor cells (EPC) represent an endogenous repair mechanism involving endothelialization and neangiogenesis. Patients with both diabetes and vascular disease associated with endothelial dysfunction have low numbers of circulating EPC. The endothelin-derived peptide, endothelin-1 (ET-1), is increased in patients with diabetes and vascular complications, and the ET B receptor has been suggested to contribute to endothelial dysfunction in this condition. Therefore, we investigated the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity. Therefore, we investigated the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity.

Methods: In this double blind study patients with type 2 diabetes mellitus and microalbuminuria were randomized to treatment with the dual ETA/ETB receptor antagonist bosentan (125 mg bid, n=17) or placebo (n=19) for four weeks. Different EPC subpopulations were enumerated by flow cytometry using triple staining (CD34, CD133, Kinase domain receptor, KDR) at baseline and at the end of treatment. Viability was assessed by 7AAD and Annexin-V-staining.

Results: Baseline ET-1 levels correlated significantly with C-reactive protein levels. Patients with ET-1 levels above the median value had higher levels of CD34+CD133+ and CD34+KDR+ EPC (Table 1). There was no difference in markers of EPC apoptosis or circulating markers of endothelial damage between patients with ET-1 levels below or above the median. Four weeks treatment with bosentan did not change EPC levels.

Table 1

<table>
<thead>
<tr>
<th>Patients with ET-1 below median</th>
<th>Patients with ET-1 above median</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62±4 vs 66</td>
<td>4.5±5.3 vs 6.6</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>91±16 vs 16</td>
<td>101±16 vs 16</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>139±25 vs 25</td>
<td>159±24 vs 24</td>
</tr>
<tr>
<td>CD34+CD133+ EPC (cells/μl)</td>
<td>5.3±2.3 vs 2.3</td>
<td>8.6±6.6 vs 6.6</td>
</tr>
<tr>
<td>CD34+KDR+ EPC (cells/μl)</td>
<td>0.9±0.7 vs 0.7</td>
<td>1.9±1.6 vs 1.6</td>
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</tbody>
</table>

Conclusion: Among patients with type 2 diabetes and vascular disease, high plasma levels of ET-1 is associated with higher number of EPC, possibly reflecting activation of an endothelial cell repair mechanism triggered by vascular damage. Therefore, we investigated the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity.

Soluble adenylyl cyclase controls oxidative stress-induced apoptosis of smooth muscle cells

S. Kumar, A. Appukuttan, H.P. Reusch, Y. Ladilov. Ruhr-University Bochum, Dept. of Clinical Pharmacology, Bochum, Germany.

Apoptosis of vascular smooth muscle cells (VSMC) in advanced atherosclerotic plaques is an important cause of plaque instability and may result in plaque rupture followed by thrombosis and sudden death. Within several pro-apoptotic factors, enhanced reactive oxygen species generation has been suggested as a cause for VSMC death and plaque instability. However, the precise mechanism of oxidative stress-induced VSMC apoptosis is still poorly understood. NOS signaling pathway and endothelin receptor blockade: a randomized controlled trial. Therefore, we investigated the relation between EPC and plasma ET-1 and the results of dual ET-1 receptor antagonism as a sequent of CAMP activity.

Results: Baseline ET-1 levels correlated significantly with C-reactive protein levels. Patients with ET-1 levels above the median value had higher levels of CD34+CD133+ and CD34+KDR+ EPC (Table 1). There was no difference in markers of EPC apoptosis or circulating markers of endothelial damage between patients with ET-1 levels below or above the median. Four weeks treatment with bosentan did not change EPC levels.

Table 1

<table>
<thead>
<tr>
<th>Patients with ET-1 below median</th>
<th>Patients with ET-1 above median</th>
<th>p-value</th>
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<tbody>
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<td>Age (years)</td>
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The p110alpha subunit of PI 3-kinase is crucially involved in neointima formation by mediating smooth muscle cell proliferation, migration and survival.

**The p110alpha subunit of PI 3-kinase is crucially involved in neointima formation by mediating smooth muscle cell proliferation, migration and survival.**

J. Jesus1, M. Vanlier1, E. Berghausen2, E. Caglayan3, H. Ten Freyhaus1, O. Leppaenjen1, Z. Zhao3, S. Rosenkranz4, J. Herz4, S. Rosiek1, E. Caglayan1, H. Ten Freyhaus1.

1Cologne University Hospital - Heart Center, Clinic III for Internal Medicine, Cologne, Germany; 2Uppsala University, Uppsala, Sweden; 3Harvard Medical School, Boston, United States of America.

The proliferation, migration and survival of vascular smooth muscle cells (SMCs) are essential for the neointima formation following balloon angioplasty. In this context, growth factors such as platelet-derived growth factor (PDGF) that activate receptor tyrosine kinases (RTKs) play a key role. RTKs play a significant role, RTK-activated signaling processes are largely mediated by activation of phosphatidylinositol 3-kinase (PI3K). Previously, we were able to demonstrate that in vitro inhibition of the catalytic PI3K isoform p110alpha completely abrogated growth factor mediated proliferation of SMCs. With the help of SMC-specific p110alpha deficient mice (p110alpha ko) we analysed in vivo the relevance of p110alpha in restenosis formation following balloon angioplasty. The extent of neointima formation was quantified 4 weeks following balloon angioplasty of carotid arteries in wild-type (WT), p110alpha ko and in heterogeneous animals. In addition, we isolated aortic SMCs from these mice and analysed growth factor-mediated cellular proliferation, migration and apoptosis using BrdU incorporation assay (proliferation), modified Boyden-chamber (chemotaxis) and nucleosome ELISA (apoptosis).

PDGF-BB (30 ng/mL) induced proliferation (x-fold increase compared to nonstimulated SMCs) in WT SMCs (1.3 ± 0.07; n = 3) and heterozygous SMCs (1.2 ± 0.18) and heterozygous LDLR−/−/smLRP1−/− double knockout increased the percentage of TUNEL-positive cells by 3.1 ± 0.3% versus 3.6% (n=4) whereas PDGF had only poor effects on H2O2 induced apoptosis of heterozygous SMCs (3.36 ± 0.7%, P ≤ 0.05, n = 6, respectively). These data suggest that the p110alpha subunit of PI3K is crucial for growth factor-mediated proliferation, migration and survival of SMCs in restenosis following balloon angioplasty. Therefore, p110alpha represents a promising therapeutic target.

**The p110alpha subunit of PI 3-kinase is crucially involved in neointima formation by mediating smooth muscle cell proliferation, migration and survival.**

K. Stark1, M.L. Von Bruel1, A. Steinhardt1, S. Chandraprakash1, M. Lorenz1, R. Coletti2, S. Pfleider2, D. Mascher1, B. Engelmann1, S. Massberg1, W.H. Zimmermann3, J. Herz4, S. Rosenkranz4, 1German Heart Center, Munich, Germany; 2Ludwig-Maximilians University, Institute of Clinical Chemistry, Munich, Germany.

Objectives: Neutrophils have been primarily implicated in host defence, but it is increasingly recognised, that they also contribute to coagulation. One mechanism how they could do that is exposure of Neutrophil extracellular traps (NET). These extracellular DNA structures have been found in deep venous thrombosis (DVT), but how they participate in thrombus formation in vivo is unclear. In this study we wanted to assess the dynamics of NET formation in vivo and their impact on DVT development in a murine flow reduction model of the inferior vena cava (IVC).

Methods: Thrombosis was induced in C57BL6 mice by placing a narrowing figure around the IVC, resulting in a reduction of blood flow velocity (n=16). NET formation in vivo was visualized by intravital 2-photon microscopy. Thrombogenesis and NET formation were quantified in GFP−/−, Dnase and heparin treated animals (n=7 each). The ability of NETs to bind and activate factor XII was assessed in vitro.

Results: Neutrophils were recruited very early after initiation of flow reduction in the IVC, supported by platelets. NET formation in the IVC, triggered by platelets, could be detected in vivo as early as 3h after flow reduction. We found that NETs were binding platelets, tissue factor, and fibrinogen, demonstrating a concentration of procoagulatory and prothrombotic factors on their surface. This is highlighted by the fact that coinoculation of activated platelets and neutrophils resulted in significant FXII activation. Inhibition of NETs by an antibody directed against the H2A−H2B-DNA complex significantly attenuated FXII activation. The functional impact of NETs for DVT formation is indicated by the finding that disruption of NETs by DNase treatment resulted not only in a reduced number of NETs, but also in a markedly reduced thrombus weight compared to control. Surprisingly, injection of heparin resulted in a diminished number of NETs inside the IVC, which could add to its antithrombotic effect (n=3).

Conclusion: Here we show that neutrophils contribute to DVT by NET formation, which is triggered by adherent platelets. This provides a platform for platelet adhesion and concentration of procoagulatory factors on their surface, linking inflammation and thrombosis at the cellular level. Thus, disruption of NETs could be an interesting new therapeutic approach for prophylaxis and treatment of DVT.

**Neutrophils contribute to DVT formation by forming procoagulant and prothrombotic neutrophil extracellular traps.**

S. Montoro-Garcia1, E. Shantsila1, L. Tapp1, B.J. Wrigley1, F. Marin1, G.Y.H. Lip2, 1University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; 2University Hospital Virgen de la Arrixaca, Murcia, Spain.

Background: Recent data suggest that circulating microparticles (MPs) contribute to inflammation, coagulation and vascular repair. The dynamics of MPs counts following S-Elevation myocardial infarction (STEMI) and their relation to levels/activity of fibrinolytic factors are unknown. We studied trends on MP levels and relationship to the fibrinolytic status in STEMI patients.

Methods: Citrated platelet poor plasma was obtained from 48 STEMI patients and 40 “control” patients with stable CAD. In STEMI, study parameters were measured within 24h of primary percutaneous coronary intervention (PCI) (day1) and days 3, 7 and 30 after admission. Small (0.1-0.5 μm) apoptotic annexin V-binding MPs (AnV-MPs), CD42b+ platelet MPs (pMPs), CD144+ endothelial MPs (eMPs) and CD141− monocyte MPs (mMPs) were quantified using a high resolution Apoese A50 flow cytometer. Fibrinolytic factors (type-11 factor [fPA] and urokinase-type plasminogen activator, plasminogen activator inhibitor-1 anti- gen/activity and thrombin activable fibrinogen inhibitor [TAFI]) were analysed by ELISA.

Results: Small-size AnV-MPs and eMPs were significantly reduced at admission with STEMI (Table). There was a significant increase in small size-AnV-MPs, eMPs and pMPs (p<0.001, p<0.007 and p<0.028, respectively).
Leptin is expressed in human carotid atherosclerotic plaques and plays an active role in plaque stability via its effects on human vascular smooth muscle cells phenotype.

**Purpose:** Leptin is assumed to contribute to the pathogenesis of atherosclerosis, through interaction with its receptor OBR on vascular cells. However, no quantitative data on its expression in human plaques has been reported so far and its impact on plaque vulnerability remains unclear. In the present study, we investigated this link in patients with carotid artery disease and hypothesized that leptin could play an active role in this process via its effects on human vascular smooth muscle cells (VSMCs), which promotes redox signaling.

**Methods:** Carotid plaque specimens were collected from 60 patients undergoing carotid endarterectomy. Each sample was evaluated by ELISA and q-PCR for leptin, OBR, and VSMCs. Collagen, macrophages, cell proliferation (Ki67), and Western blot for ERK signaling pathway were performed on carotid plaque specimens.

**Results:** Leptin was positively correlated with plaque macrophage content (moderate correlation) and plaque redox signaling (moderate correlation) in carotid plaques. The activation of the ERK signaling pathway was found to be significantly associated with plaque size (p=0.014, r=0.681) and plaque stability (p=0.001, r=0.652) in carotid plaques. Furthermore, ERK activation in leptin-stimulated VSMCs was found to be significantly correlated with plaque size (p=0.001, r=0.652) and plaque stability (p=0.001, r=0.652) in carotid plaques.

**Conclusions:** Leptin induces signals of endothelial replenishment in vivo and in vitro. The Annexin I/Phosphatidylserine receptor signaling pathway was a crucial mechanism for Endothelial Microparticle uptake by target cells.

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**Endothelial Microparticles (EMP) are taken up in an Annexin I/PSR-dependent pathway by target cells and promote endothelial regeneration.**

**Purpose:** Endothelial Microparticles (EMP) are released by endothelial cells and play a role in endothelial regeneration. Annexin I/PSR is widely expressed on the surface of endothelial cells and has been shown to mediate the uptake of EMP by target cells.

**Methods:** EMP were isolated from human plasma and incubated with Annexin I/PSR positive target cells, such as HAEC and early EPC. Uptake of EMP by target cells was assessed using Annexin V-FITC and Annexin V-PE staining.

**Results:** Endothelial Microparticles (EMP) were taken up by target cells in a Annexin I/PSR-dependent manner. The uptake of EMP by target cells was significantly increased in the presence of Annexin I/PSR.

**Conclusions:** Endothelial Microparticles (EMP) are taken up in an Annexin I/PSR-dependent pathway by target cells and promote endothelial regeneration.
Recently, perivascular adipose tissue (VAT) has been shown to play a crucial role in the development of atherosclerosis; however, the effects of AT1 on VAT properties and their functional relevance in atherogenesis remain undefined.

Methods: In the present study, we investigated the functional properties of VAT in mice, comparing AT1 knockout (AT1−/−) and wild-type (AT1+/+) mice. VAT from AT1−/− and AT1+/+ mice was isolated and cultured under hypoxic conditions. The expression levels of adipocyte differentiation marker genes (PPARα, FABP4, c/EBPα) were measured using qRT-PCR. The results were analyzed using one-way ANOVA followed by Tukey’s post-hoc test.

Results: The expression levels of adipocyte differentiation marker genes (PPARα, FABP4, and c/EBPα) were significantly reduced in AT1−/− adipose tissue compared to AT1+/+ adipose tissue. The reduction was found to be dose-dependent, and the effect was observed at a concentration of 100 nM of AT1 receptor agonist.

Conclusions: Our findings demonstrate that AT1 regulates the expression levels of late-stage adipocyte differentiation marker genes in VAT, suggesting that AT1-mediated modulation of perivascular adipocyte differentiation could be a novel therapeutic target for the prevention of atherosclerosis.
Hypoxia reoxygenation-induced endothelial barrier failure: Role of RhoA, Rac1, and MLCK

M. Aslam1, S. Rohrbach1, K.-D. Schüller1, D. Sedding2, C. Hamm2, T. Noll3, D. Guenduez1. 1Institute of Physiology, Justus Liebig University, Giessen, Germany; 2University Hospital Giessen and Marburg, Medical Clinic I, Cardiology and Angiology, Giessen, Germany; 3Dresden University of Technology, Institute for Physiology, Dresden, Germany

Background: Loss of endothelial barrier function leading to oedema formation during hypoxiareoxygenation presents major impediment for the recovery of the organ. This loss of barrier function is mainly due to loss of cell-cell adhesions and endothelial contractile activation. Several signaling pathways including RhoA/Rock or Ca+2/PKC are activated during reoxygenization which could mediate barrier failure, but the precise role of these pathways is still elusive. The aim of the present study was to analyse the role of these signaling pathways in reoxygenation-induced barrier failure.

Methods: In cultured porcine aortic endothelial cells, the effect of hypoxia (30 min, PO2=5 mmHg; pH 6.4) and reoxygenation (45 min, PO2=140 mm Hg; pH 7.4) was analyzed on endothelial permeability (albumin flux), contractile activation (MLC phosphorylation), Ca+2, PKC, RhoA, Rac1 (pul down assay), and cell-cell adhesions (contactinicoherence). BAFTA (10 μM), BIM (100 μM), C3Transferase (1 μg/ml), and Y27632 (10 μM) were used to inhibit Ca+2, PKC, RhoA, and Rock signalling, respectively.

Results: Reoxygenation lead to 150±7.3% increase in permeability, 2.5-fold MLC phosphorylation, and 2.5-fold Rac1 activation, but had no effect on Ca and RhoA activation. Contactinicoherence was lost by 20%, RhoA/Rock inhibitors caused a robust rise in cytosolic Ca+2-concentration, PKC activation, loss of cortical actin and VE-cadherin from cell-cell adhesions. Pharmacological inhibition of RhoA, Rock, Ca+2 or PKC with specific inhibitors exacerbated reoxygenation-induced barrier failure and abrogated the resealing of adhesion junctions. On the other hand inhibition of cAMP/Epac signalling by a cAMP analogue (100 μM), blocked reoxygenation-induced actin cytoskeleton derangement and hyperpermeability and enhanced endothelial cell resealing. However, it had no effect on RhoA or MLC. Inhibition of MLC kinase (ML-7 10 μM) along with Epac activation had an additive effect. The results were confirmed using isolated perfused rat hearts.

Conclusions: The quantifiable features of plaque components’ distribution and heterogeneity provided by the proposed system could provide further insight in the assessment of vulnerable plaques. Especially features of necrotic core and calcification in relation to lumen border may by significant determinants of plaque vulnerability and plaque-stein interaction. In this respect these new computed data might be useful for the detection of the vulnerable plaque as well as for the evaluation of stent deployment and selection.

The paraoxonase 55 L/M polymorphism influences the onset of acute coronary syndrome but not stable angina

S. Gomes1, A. Pereira1, A.C. Sousa1, B. Silva1, S. Freitas1, G. Guerra1, A. Brehm2, J.J. Araujo1, M. Mendonça1, R. Palma1, D. Reis1. 1Hospital Funchal, Funchal, Portugal; 2University of Lisbon, Faculty of Medical Sciences, Lisbon, Portugal

The paraoxonase 1 (PON1) is an antioxidant enzyme synthesized by liver. It has two known polymorphisms: 192 Q/R and 55 L/M. Multiple studies, including ours, has associated these polymorphisms with coronary artery disease (CAD) risk. In CAD coexists changes in the vessel wall with emphasis on atherogenesis, clinically expressed by stable angina (SA), and acute thrombotic changes, expressed by acute coronary syndrome (ACS). However, the mechanism by which these variants influence the CAD susceptibility is still unknown.

Objective: The aim of this study was to evaluate whether PON1 polymorphisms influence the onset of ACS or SA.

Methods: Two case-control studies were performed. The first one included 1665 individuals, 728 with CAD and hospitalized with ACS (mean age 53±3.7 years, 79.3% male) and 937 controls without CAD (mean age 52±6.8 years, 78.8% male). The second one included a total of 1099 individuals: 208 consecutive patients with SA and significant CAD confirmed by coronary angiography (mean age 56±6.8 years, 71.3% male) and 800 controls without CAD (mean age 55±6±5.8 years, 72.9% male). In both studies, cases and controls were matched by gender and age. PON1 variants were analyzed using specific primers. The equilibrium Hardy-Weinberg was investigated and a bivariate analysis (tables 3x2), with and without gender, was performed in order to determine the CAD risk. A p-value <0.05 was considered statistically significant.

Results: PON 55 MM genotype showed an increased risk for ACS, with an OR of 3.16 (95% CI 1.38-7.02) but not for SA (OR=0.82, 95% CI 0.43-1.60). PON 192 Q/R was not significantly associated either with the ACS or with SA.

Conclusions: This study supports the concept that PON 55 MM is an initiator factor of ACS. Not leading to stable angina but to ACS, this polymorphism may be particularly deleterious and may be involved in thrombotic and nongenetic mechanism. The patients carrying this genotype should be approached with particular care in terms of primary prevention, possibly through antiplatelet or anticoagulant drugs.

Uric acid levels are associated with asymmetric dimethylarginine, L-arginine and arterial stiffness in essential hypertensive patients

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Purpose: Elevated uric acid (UA) levels are associated with enhanced cardiovascular risk, while arterial stiffening. L-arginine and asymmetric dimethylarginine (ADMA) contribute to diffuse vascular dysfunction. In this study, we investigated the relationships between UA levels, L-arginine, ADMA and arterial stiffness in essential hypertensives.

Methods: A biometric computational analysis based on backtracking program- ming was performed, with emphasis given on the low computational cost and processing time. Single and sequences of VH-IVUS images were analyzed. For each image analysis 29 parameters were computed. Results: The basic plaque characteristics (lumen, vessel areas, percent of stenosis, area and percent of each plaque component), the following param- eters related with the spatial distribution and the homogeneity of plaque com- ponents were computed: a) the percent of lumen border that is surrounded by each component, b) the number of different segments and the area of the largest solid segment of each component adjoining to the lumen border, and c) the number of different segments and the area of the largest single segment of each component within the plaque area. A sequence of VH-IVUS images that is recorded during catheter pullback along the coronary vessel is then analyzed in order to automatically classify the examined plaques as thin cap fibroatheroma, the most common type of vulnerable plaque. The classification is made accord- ing to standard criteria: a) The percent of the necrotic core area is ≥10%, b) the necrotic core covers more than 1/3 of the lumen border and c) the two previous conditions are met for at least three serial frames of the images sequence. The total number of sequential and non-sequential frames that meet the criteria (a) and (b) are also determined.

Conclusions: The quantifiable features of plaque components’ distribution and heterogeneity provided by the proposed system could provide further insight in the assessment of vulnerable plaques. Especially features of necrotic core and calcification in relation to lumen border may by significant determinants of plaque vulnerability and plaque-stein interaction. In this respect these new computed data might be useful for the detection of the vulnerable plaque as well as for the evaluation of stent deployment and selection.

Angiotensin II induces early mechanical heterogeneity along the abdominal aorta, preceding murine aneurysm formation

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Background: Abdominal aortic aneurysm (AAA) pathogenesis involves a broad spectrum of inflammation, cellular proliferation and extracellular matrix alteration. However, little is known about the initiation of aneurysm formation. In specific animal models, localized chemical damage to the aortic wall is used to trigger a focal vascular demarcation, eventually resulting in AAA. In contrast, suprarenal AAA can readily be induced in apoE−/− mice by systemic Angiotensin II (AngII) infusion without any focal vascular manipulation. This study was designed to test the hypothesis that systemic AngII infusion induces focal mechanical alterations (i.e. heterogeneous strain along the abdominal aorta) that may initiate AAA for-
Materials and methods: AngII (1000ng/kg/min) or saline (control) was infused via osmotic pump in 10-week-old apoE−/− male mice (C57Bl/6J background). At baseline and after 2 days of treatment, systolic (SD) and diastolic (DD) diameters of suprarenal (SR) and infrarenal (IR) aortic segments were measured using M-mode ultrasonography, and strain was calculated as (SD-DD)/DD. Strain ratio along the abdominal aorta was calculated as SR-strain/IR-strain. Gene expression of AngII type 1b receptor (Agtr1b), known to mediate the mechanosensitive vasodilatory response to AngII, was measured in SR and IR regions via qRT-PCR.

Results: AngII infusion for 2 days induced both a significant increase in SR-strain as well as a decrease in IR-strain, resulting in a significant strain heterogeneity (SR/IR strain-ratio: 2.5±0.8 vs. 1.2±0.3 at day 0; p<0.001). Saline infusion altered none of these parameters. While elevated SR-strain per se failed to demonstrate a correlation to SR diameter changes after 2 days, we found that SR/IR-strain ratio was positively correlated to early SR aortic diameter increase (R=0.53; p<0.05). Overt atheroma formation was only detectable after 4 days of AngII infusion, at the earliest. As a possible mechanism for these strain differences, Agtr1b expression was found to be ~40-fold higher in IR aorta than in the SR aorta at baseline.

Conclusion: AngII infusion rapidly induces heterogeneous strain (SR−IR) along the abdominal aorta, preceding aneurysm formation. These strain differences may be due to initial heterogeneous AngII Agtr1b density, and they correlate statistically with the strain heterogeneity of an intact strain-prone SR region. These data suggest a mechanism for the early translation from systemic AngII infusion into a focal vascular response (AAAs induction), and highlight vascular mechanical heterogeneity as a possible prerequisite of AAA formation.

Phenotypic characterization of leukocytes at the culprit lesion site in acute coronary syndrome patients

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Background: ST-elevation acute coronary syndrome (STE-ACS) is the leading cause of cardiac death. Mechanical mismatch of coronary plaque rupture are poorly understood. In contrast to common knowledge implicating monocytes and T-cells in the pathogenesis of acute coronary vascular syndromes, we hypothesize that circulating inflammatory cells mediate plaque rupture and thrombotic occlusion. The goal of this study was to phenotype inflammatory cells at the site of plaque rupture and to determine their effector functions.

Methods: STE-ACS patients who underwent primary percutaneous coronary intervention at the General Hospital were consented (n=70). Culprit site blood was aspirated with a thrombectomy catheter and particulate thrombus material was separated. In parallel, blood was sampled from the femoral arterial sheath. Flow cytometry was employed to determine cell types accumulating at the plaque rupture site. These results were complemented by ELISA, cell culture and immunofluorescence assays.

Results: The vast majority of inflammatory cells at the culprit lesion site are neutrophils. Coronary neutrophils produce neutrophil extracellular traps, release large amounts of MPO and are apoptosis-resistant. CD4CD28null T cells are increased with low content of Perforin and Granzyme B. Plaque-site monocytes display a CD14lowCD16high phenotype that is found in aggregation with platelets. These results were complemented by ELISA, cell culture and immunofluorescence assays.

Conclusion: The selective enrichment of inflammatory cell subsets at the culprit lesion site suggests a disease-specific inflammatory process, suggesting an outside-in mechanism of acute atherosclerotic vascular obstruction.

Circulating apoptotic endothelial cells and apoptotic endothelial microparticles independently predict the presence of cardiac allograft vasculopathy

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Objectives: Maintenance of endothelial homeostasis may prevent the development of cardiac allograft vasculopathy (CAV). We investigated whether biomarkers related to endothelial injury and endothelial repair discriminate between CAV negative and CAV positive heart transplant recipients.

Background: CAV is the most important determinant of cardiac allograft survival and a major cause of death after heart transplantation.

Methods: Two patients undergoing coronary angiography between 5 and 15 years after heart transplantation were recruited in this study. Flow cytometry was applied to quantify endothelial progenitor cells (EPCs), circulating endothelial cells (CECs), and endothelial microparticles. Cell culture was used for quantification of circulating EPC number and hematopoietic progenitor cell (HPC) number and for analysis of EPC function.

Results: EPC number and EPC function did not differ between CAV negative and CAV positive patients. In univariable models, age, creatinine, steroid dose, granulocyte colony-forming units, apoptotic ECs, and apoptotic endothelial microparticles discriminated between CAV positive and CAV negative patients. The logistic regression model containing apoptotic ECs and apoptotic endothelial microparticles provided high diagnostic differences between CAV positive and CAV negative patients (C statistic 0.812; 95% CI 0.692-0.932).

Conclusions: The high discriminative ability of apoptotic ECs and apoptotic endothelial microparticles is a solid foundation for the development of clinical prediction models of CAV.
VASCULAR REMODELLING

Wnt4 contributes to intimal thickening by promoting VSMC proliferation via up-regulation of RCAN1

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Purpose: We investigated whether Wnt4-induced VSMC proliferation utilizes nuclear transcription factor activity of T-cells (NFAT) as a downstream effector as well as β-catenin. Vascular smooth muscle cell (VSMC) proliferation causes intimal thickening observed in early atherosclerosis and restenosis. Previously demonstrated that Wnt4/β-catenin signaling stimulates VSMC proliferation in vitro via cyclin D1 up-regulation and promotes intimal thickening. Although the “canonical” Wnt/β-catenin pathway plays a vital role in the promotion of Wnt4-driven VSMC proliferation, Wnts can also signal independently of β-catenin, amongst others via a calcium-related pathway involving NFAT. Here we assessed the role of NFATc1 (the predominant isoform in VSMCs) and the induction of known NFAT-responsive genes in Wnt4-induced VSMC proliferation and intimal thickening.

Methods: VSMCs were cultured and in some cases subjected to siRNA; extracted mRNA was analysed by Q-PCR while protein was assessed by Western blotting and/or immunocytochemistry. Mouse cardiac arteries were ligated to induce intimal thickening and lesions were analysed by immunohistochemistry.

Results: Addition of recombinant Wnt4 protein in vitro induced a significant increase in the percentage of VSMCs with nuclear NFATc1 within 4h (by 2.43±0.63 fold, p<0.05, n=3), directly demonstrating the activation of Wnt/Calcineurin (WNT/Ca2+) pathway by Wnt4. Recombinant Wnt4 protein treatment for 6h in vitro significantly upregulated the mRNA levels of two previously identified NFAT-responsive genes, regulator of calcineurin 1 (RCAN1) and cyclooxygenase 2 (COX2) as well as Cyclin D1, by 1.54±0.28, 1.39±0.24 and 1.35±0.15 fold respectively (p<0.05, n=3).

Treatment with NFAT inhibitor (11β-IVGT) for 24h in vitro significantly retarded Wnt4-induced VSMC proliferation from 46.5±3% to 30.7±7% (p<0.05). Wnt4 protein knockdown (by 89±15%) of NFATc1 in vitro resulted in a significant reduction of both Cyclin D1 and RCAN1 mRNA by 21±7% and 21±7% respectively (p<0.05, n=3). Finally, we observed elevated NFATc1 protein levels while RCAN1 protein was significantly increased in ligated mouse cardiac arteries when compared to unligated control arteries (161±16.1 vs. 26±7.3 fluorescent pixels per area unit respectively, n=4).

Conclusions: Wnt4 is an important contributor to intimal thickening by playing a key role in the stimulation of VSMC proliferation via activation of both “canonical” β-catenin and “non-canonical” NFAT downstream pathways. We show here for the first time that RCAN1, a downstream target of NFAT, is up-regulated by Wnt4 signalling and may be a key modulator of intimal thickening.

A non-polymeric cigitazone-eluting stent inhibits neointimal proliferation stronger than sirolimus-eluting stents: an experimental study using optical coherence tomography in rabbit iliacal arteries

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Background: Drug-eluting stents (DES) are currently the best choice to reduce restenosis after coronary stenting. Optical coherence tomography (OCT) is a high-resolution intravascular imaging technique that precisely quantify neointimal proliferation and endothelial strut coverage.

Objective: We investigated the antiproliferative effect of a peroxisome proliferator-activated receptor-gamma agonist as a novel stent coating.

Methods: Bare metal stents Yukon Choice 2.5/12 mm with microporous surface (BMS) were polymer-free coated with either sirolimus (SES) or cigitazone (CES) at 225 mcg/cm. Sixteen New Zealand White rabbits fed with western diet underwent implantation of different stents in both iliacal arteries via the carotid artery. The animals were equally divided into 2 groups: BMS vs. SES and BMS vs. CES. Stents were imaged in vivo using OCT at 28 days in 4 animals and after 90 days in the remaining 12 animals. OCT assessment of stent coverage was performed by classifying all visible struts and computing % of well- and malapposed struts, with and without endothelialization. Additionally, an algorithm of quantification of neointimal growth was implemented (Figure) and applied to different stent segments and adjacent vessel areas.

Results: All struts were well apposed without significant differences in endothelialization between BMS, SES and CES. Relative proliferation area (S_PA%), calculated as neointimal area within a stent segment in relation to the stent area was significantly smaller in CES, but not in SES as compared to BMS (Figure).

Conclusions: The novel polymer-free cigitazone-coated stent proved significant anti-restenotic efficacy without delaying endothelialization in this rabbit model and therefore merits attention as a promising stent development.

Functional inhibition of microRNA-92a increases endothelial regeneration and reduce neointimal formation after vascular injury by targeting kruppel-like factor-4

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Purpose: One of the mechanisms responsible of late stent thrombosis after Drug Eluting Stent (DES) implantation is that endothelial recovery is inhibited by the antiproliferative approach, which, although intended to prevent smooth muscle cells (SMCs) proliferation, also may have inhibited proliferation of endothelial cells (ECs). Recently, one of the key breakthroughs for the study of gene expression regulation has been the discovery of microRNAs. MicroRNAs are small non-coding RNAs of 20-22 nucleotides that regulate, at post-transcriptional level, gene expression. Therefore, the aim of the present study was to evaluate the role of microRNA-92a on ECs and VSMCs proliferation and migration in vitro as well as after balloon injury or arterial stenting in vivo.

Methods: ECs and VSMCs proliferation and migration were measured by BrdU incorporation and wound healing assays. In the in vivo protocol, balloon injury or stenting of the carotid artery were produced in male Wistar rats. Moreover, inhibition of microRNA-92a expression was assessed in vivo by systemic administration of antagoniR-92a. Immunohistochemical staining for von Willebrand factor (vWF) and planimetric analysis after in vivo injections of Evans Blue dye were employed to analyze the process of re-endothelialization. Fixed carotid arteries were stained with hematoxylin/eosin 14 days after balloon injury to assess neointimal formation.

Results: MiR-92a was highly expressed in ECs but to a much lower extent in VSMCs. Importantly, BrdU incorporation and wound healing assay provide evidence that functional inhibition of miR-92a resulted in an increased proliferation and migration of ECs but not of VSMCs in vitro. Immunoblotting analysis revealed an increased phosphorylation of eNOS in ECs as a consequence of miR-92a inhibition. Therefore, functional inhibition of miR-92a stimulated nitric oxide (NO) production in ECs. Using reporter luciferase assay, we identified specific targets of miR-92a: KLF4, key regulator of endothelial homeostasis, and MKK4, component of MAPK pathway. Finally, in vivo administration of antagoniR-92a increased re-endothelialization in injured carotid arteries and reduced neointimal formation after balloon-injury or arterial stenting.

Conclusions: These data provide the first evidence that inhibition of miR-92a may represent a novel strategy to improve endothelial regeneration and reduce restenosis after vascular injury. This new approach could be useful to design new stents aimed to increase the reendothelialization and eventually to reduce the occurrence of stent thrombosis.

The PI 3-kinase isofrom p110alpha promotes vascular remodelling in pulmonary arterial hypertension

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Purpose: Vascular remodelling is a major characteristic of pulmonary hypertension. The vessel wall especially of the small pulmonary vessels thickens triggered by an abnormal proliferation and migration of vascular smooth muscle cells (VSMC). In vitro assays demonstrated that the PI3-kinase isoform p110 alpha is crucial for growth factor induced SMC proliferation and migration. However the role of the PI3-kinase (PI3K) p110 isoform p110 alpha for vascular remodelling in pulmonary hypertension is poorly understood. We assessed the function of p110 alpha for...
vascular remodelling in the hypoxia induced mouse model of pulmonary hypertension.

Methods: We generated a smooth muscle specific p110 alpha deficient mouse and subjected it to chronic hypoxia to induce pulmonary hypertension. Right ventricle (RV) systolic pressure was determined via invasive measurement using a millar pressure catheter. RV hypertrophy was assessed as ratio RV weight to LV + septum weight. Aortic remodelling was quantified and demonstrated as medial wall thickness and degree of vascular muscularization.

Results: RV systolic pressure in consequence to hypoxia was decreased in the p110 alpha deficient mice compared to wild-type littermates. Consistently, hypoxia induced RV hypertrophy was significantly reduced in hearts of p110 alpha deficient mice in comparison to wild-type hearts. Medial wall thickness of vessel with a diameter less than 50μm was significantly narrowed in lungs of SM-specific p110 alpha KO mice. Morphometric analysis of the small pulmonary vessels (diameter < 50μm) also revealed a smaller fraction of fully and partially muscularized vessels in hypoxia treated p110 alpha deficient mice in comparison to hypoxia treated wild-type mice.

Conclusion: These results indicate that the PI3K isomor p110 alpha is crucial for vascular remodelling in hypoxia induced pulmonary hypertension. A SM-specific loss of p110 alpha prevented vascular remodelling and would therefore represent a promising therapeutic approach.

P4345 Valsartan inhibits aortic remodeling by blocking transforming growth factor-beta 1-Smads pathway in diabetic rats

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Objective: Angiotension II (Ang II) and transforming growth factor β1 (TGFβ1) are closely involved in the pathogenesis of diabetic complications. We aimed to determine whether an aberrant thrombospondin 1 (TSP1)–mediated TGFβ1 signaling pathway specifically affects vascular fibrosis in diabetic rats and whether valsartan, an Ang II subtype 1 receptor blocker, has an anti-fibrotic effect.

Methods: Age-matched male Wistar rats (200-240 g) were randomly divided into 3 groups: control (n=8), diabetes (n=16) and valsartan (30 mg/kg/day) (n=16). Type 2 diabetes mellitus (T2DM) was induced by a high-calorie diet and streptozotocin injection. Morphological and biomechanical properties of the thoracic aorta were assessed by echocardiography and cardiac catheterization. Masson staining was used for histological evaluation of collagen. The expression of components in the TSP1–mediated TGFβ1-Smads signaling pathway was analyzed by immunohistochemistry and real-time quantitative RT-PCR.

Results: Expression of p110 was increased in diabetic aortas, and diabetic aortas showed reduced desmoplasia and compliance, with excess collagen deposition. Components in the TSP1–mediated TGFβ1-Smads signaling pathway were analyzed by immunohistochemistry and real-time quantitative RT-PCR.

Conclusions: We show for the first time that increased HA metabolism and elevated CD44 levels are associated with the enlargement of human abdominal aortic aneurysm by increased MMP-9 activity.

P4344 Hyaluronic acid metabolism is increased in human abdominal aortic aneurysm

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Background: Hyaluronic acid (HA) is expressed in atherosclerotic lesions, but its exact role in abdominal aortic aneurysm remains unknown. As degradation of hyaluronic acid by hyaluronidase into low molecular weight hyaluronic acid (LMW-HA) is associated with inflammation and matrix metalloproteinase (MMP)-9 activity, we hypothesized that hyaluronic acid metabolism is increased in abdominal aortic aneurysm, especially the area between almost normal margin and maximum diameter. Those area were characterized by high number of macrophage, MMP-9 activity, and destruction of elastin.

Methods: Five specimens were obtained as a whole abdominal aortic tissue (from proximal margin to distal margin). A whole sample was categorized into three zones; zones of (1) margin, (2) middle, and (3) maximum diameter (Figure A). Then, whole tissue were cut into around one inch of pieces, and character-
A novel adipocytokine, CTRP9 attenuates vascular smooth muscle cell proliferation and neointimal formation after vascular injury

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Background: C1q/TNF-related protein (CTRP) 9 is a novel adipocytokine that has beneficial effects on glucose metabolism and endothelial function. However, the role of CTRP9 in vascular remodeling is unknown. Here, we investigated the effect of CTRP9 on vascular smooth muscle cell (VSMC) proliferation and neointimal hyperplasia in a restenosis model.

Methods and Results: An adenovirus expressing CTRP9 (Ad-CTRP9) or β-galactosidase as a control was injected into the jugular vein of wild-type (WT) mice 3 d after vascular injury. Left femoral arteries of mice were injured by a 0.015 inch stainless-steel wire inserted from the lumen. Administration of Ad-CTRP9 increased CTRP7 levels by a factor of 5.1 ± 0.9 at day 5 after injection compared with control. At 21 days after vascular injury, delivery of Ad-CTRP9 significantly attenuated intimal hyperplasia compared with that of control (p < 0.01, n = 8). Ad-CTRP9 also decreased the number of bromodeoxyuridine (EdU) positive proliferating cells in the neointima at day 7 after vascular injury versus control. In cultured VSMCs, recombinant CTRP9 protein attenuated DNA synthesis by downregulating genes expressed in proliferating cells, such as PDGF and heparin-binding epidermal growth factor (EGF)-like growth factor (HB-EGF) as assessed by BrdU incorporation. Furthermore, treatment of VSMCs with CTRP9 significantly inhibited PDGF-induced phosphorylation of ERK.

Conclusion: CTRP9 reduces VSMC growth and prevents neointimal thickening after vascular injury in vivo, suggesting that the therapeutic approaches to endothelial cells during vascular remodeling.

β-NGF secretion from VSMCs. Extracellular β-NGF secretion. In addition, we found increased mRNA and protein expression of β-NGF by the proprotein convertase furin (FUR1) in carotid artery and qRT-PCR showed that both NGF and furin gene expression is significantly inhibited PDGF-induced phosphorylation of ERK.

MicroRNA-146a and its role in endothelial cells during vascular remodeling processes

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Background: MicroRNAs (miRNAs) are a new class of small noncoding RNA molecules, comprising key regulators for major cellular events including proliferation, differentiation and apoptosis. Targeting miRNAs that influence the behavior of cells of the human vasculature like endothelial cells may offer an interesting approach for the prevention or treatment of vascular proliferative diseases.

Methods/Results: Using miRNA microarray expression analysis, we screened for regulated miRNAs during neointima formation. Restenosis was induced by dilation of the femoral artery, and miRNA was isolated 10 and 21 days after injury. About 59% of all known miRNAs was found to be aberrantly regulated after 10 days what was even enhanced to 88% after 21 days. Noticeably, miR-146a appeared to be one of the most regulated miRNAs during restenosis. Analysis on isolated cells of the human vasculature like monocytes/macrophages, smooth muscle cells and endothelial cells showed a strong expression of miR-146a, especially in endothelial cells. In vitro, the upregulation of miR-146a could be attributed to the inflammatory stimulus IL-1β. To further assess the functional role of miR-146a, endothelial cells were transfected with the precursor form of miR-146a that led to an attenuated migration, sprout formation and vessel network formation. On the other hand, using 2-O methylated RNA (m2C) for co-translation of miR-146a as inhibitor, sprout formation, tube structure formation and cell migration were significantly enhanced. In the following, computational miRNA target prediction, the ‘TargetScan database’, was used to find potential target genes for miR-146a. Quantitative Real-Time-RT-PCR tests were performed after overexpression of miR-146a. The transcripts for TRAF6 and IRAK1, two key adapter molecules in TLR- and IL-1 receptor signaling cascades, were significantly downregulated and hence represent molecular targets for miR-146a. Further in vitro analysis showed that miR-146a induction seems to be mediated by NF-κB. In complementing in vivo experiments, inhibition of miR-146a following dilation of the femoral artery was performed. The data of Evans’ Blue-dye staining showed significantly enhanced neointimal thickening after 10 and 21 days. Noticeably, miR-146a in restenosis development, we identified miR-146a likely involved in the disease development and progression and could further assess the importance of miR-146a. Thus, these observations add substantially to our understanding of the molecular mechanisms involved in miRNA function.

Furin-dependent maturation of proNGF induces migration of vascular smooth muscle cells by TrkA-mediated recruitment of paxillin to focal adhesion sites

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Background: Vascular smooth muscle cell (VSMC) migration is a key feature of vascular restenosis. Recently, it was shown that the nerve growth factor (NGF) and its high-affinity receptor, the neurotrophic tyrosine kinase receptor type 1 (TrkA), are expressed in restenotic lesions. However, the underlying mechanism and functional relevance is poorly understood. NGF is synthesized as a proprotein and is released from cells acting as an autocrine signaling molecule. Here, we studied the effect of platelet-derived growth factor (PDGF-BB) on transforming growth factor beta-1 (TGF-β1), both highly expressed in restenotic lesions, on furin-dependent proNGF maturation and evaluated the impact of furin on VSMC migration.

Methods and results: First, qRT-PCR and western blot analysis showed that PDGF-BB and TGF-β1 synergistically enhance NGF gene expression and proNGF expression. Inhibiting proNGF expression and furin activity using a dominant negative form of TGF-β1, both highly expressed in restenotic lesions, on furin-dependent proNGF maturation and evaluated the impact of furin on VSMC migration.

Conclusion: CTRP9 reduces VSMC growth and prevents neointimal thickening after vascular injury in vivo, suggesting that the therapeutic approaches to endothelial cells during vascular remodeling.
Ablation of PDGF receptor signaling reduces neo-intima formation after balloon angioplasty and does not affect the proliferation and migration of endothelial cells

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Despite the introduction of new techniques such as drug-eluting stents, restenosis and stent thrombosis following angioplasty remain serious clinical problems. To prevent neo-intima formation and the development of stent thrombosis after balloon angioplasty and stent implantation, it is essential to reduce the accumulation of vascular smooth muscle cells (SMC) on the one hand and to ensure the re-endothelialization as far as possible on the other hand. The proliferation and migration of SMCs and endothelial cells (ECs) are mainly induced by receptor tyrosine kinases which are activated by growth factors.

Previously, we could demonstrate that the mutation of central binding domains of the platelet-derived growth factor receptor (PDGFR) in a mouse model causes a significant reduction of neo-intima formation after balloon angioplasty. The influence of an inhibition of PDGFR on endothelial cells is not known.

In this study, we analysed the effects of two PDGFR inhibitors (imatinib and Nilotinib) on proliferation and migration of human coronary artery SMCs (hcSMCs) and human coronary ECs (hcECs). For this purpose, the cells were stimulated with PDGF (30 ng/ml) or VEGF (50 ng/ml) and various concentrations of imatinib or nilotinib were tested. The cellular proliferation was determined by Brdu incorporation assay and chemotaxis using a modified Boyden chamber. Protein expression and activation were investigated by Western blot analyses.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SSc (n=60)</th>
<th>Controls (n=21)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PW (mm)</td>
<td>9.7±3.9</td>
<td>8.76±2.01</td>
<td>0.29</td>
</tr>
<tr>
<td>Endothelin-1 (pg/ml)</td>
<td>1.86±1.37</td>
<td>1.28±0.67</td>
<td>0.006</td>
</tr>
<tr>
<td>TIMP-1 (ng/ml)</td>
<td>204.63±63.05</td>
<td>182.8±28.83</td>
<td>0.12</td>
</tr>
<tr>
<td>ADMA (umol/l)</td>
<td>0.59±0.34</td>
<td>0.46±0.08</td>
<td>0.01</td>
</tr>
</tbody>
</table>

PW, pulse wave velocity; TIMP-1, tissue inhibitor of matrix metalloproteinase; ADMA, asymmetric dimethylarginine.

Conclusions: SSC patients found to have higher ADMA and ET-1 serum level. ET-1 and TIMP-1 positive correlation and positive correlations between ET-1 and TIMP-1 with PWV suggest that both endothelial dysfunction and matrix remodeling are associated in the pathogenesis of large arteries in systemic sclerosis.
Changes of vascular walls in different levels of arterial system in patients with stable coronary artery disease and type 2 diabetes mellitus

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Aim: To assess the relationship between large arterial wall remodelling and changes in microcirculation in small resistance arteries and capillaries in patients with stable coronary artery disease (CAD).

Patient and methods: In patients with CAD (n=25; male; 10; mean age: 62.7±6.1; BMI: 30.7±4.4) and 25 healthy participants (male: 11; mean age: 57.3±7.9; BMI: 26.3±4.1) digital photoplethysmography and nail fold videocapillaroscopy at resting baseline, during venous occlusion were performed. We evaluated a remodeling of large artery arterial stiffness (Si), augmentation index (AIx75) and structural changes of microcirculation in small resistance arteries (reflection index (RI)) and capillaries (maximal capillary densities (CD max), coefficient of capillary remodelling (Kv/dv) diameter of venous capillary part/diameter of arterial part of capillary).

Results: Measurement of remodeling of large vessels Aix75 was significantly higher in CAD patients than in healthy controls (20.4±19.1% vs. 12.3±11.1%; p<0.05). There was no different Si and RI in groups (SI CAD: 7.14±m/s ±1.7 vs. 7.26±1.88 m/s; p=0.7) (RI Control: 42.4±19.1% vs. 51.7±34.5%; p=0.3). While RI was above normal in both groups (norm=30%). CD max in CAD group was significantly lower than in control (49.7±6.9ap/cm² vs. 58.6±12.9cap/mm²; p<0.005). There was no significant difference of Kv/dv between two groups (CAD vs. Control: 1.13±0.18 vs. 1.09±0.25; p=0.6). Aix75 was significantly correlated with RI (r=0.43; p<0.05). No correlation between Aix75 with CD max (r=0.17; p=0.05). RI with CD max (r=-0.07; p<0.05) was observed.

Conclusions: In CAD patients presents both remodeling of large vessels and structural changes of microcirculation in small resistance arteries and capillaries. Structural changes of small resistance artery may be associated with large artery remodeling, while capillary changes do not. High level of measure of small resistance arterial changes in control group may be associated with the traditional risk factor of cardiovascular in the group.

Echocardiographic epicardial fat thickness is associated with arterial stiffness

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Purpose: Epicardial adipose tissue represents visceral adiposity and early detection of visceral adiposity could be helpful for assessing subclinical target organ damage. Although previous studies have reported the relationship between epicardial fat thickness (EFT) and carotid intima-media thickness, there is no report regarding the relationship between EFT and arterial stiffness. The present study was performed to evaluate the association between epicardial fat thickness and arterial stiffness.

Methods: We consecutively enrolled 655 subjects (445 men, 55.9 years), who underwent echocardiography and brachial-ankle pulse wave velocity (baPWV) with ankle-brachial index greater than 0.95. Echocardiographic EFT was measured from parasternal long-axis and short-axis views on the free wall of the right ventricle at the end of diastole. The subjects were divided into four quartiles according to EFT (≤3.49 mm, 3.41-4.95 mm, ≤4.96 mm, and >4.96 mm in quartile I, II, III, and IV, respectively). Subjects were also classified into two groups according to baPWV: group I (324 subjects), baPWV >1366cm/sec; and group II (331 subjects), baPWV ≤1366cm/sec.

Results: The EFT in group II were significantly higher than those in group I (4.2mm versus 3.7 mm, p<0.001). There were significant differences in baPWV value among the four quartiles of the EFT (quartile I, 1327±148.8 cm/sec; quartile II, 1371±215.0 cm/sec; quartile III, 1434±228.3 cm/sec; quartile IV, 1507±233.1 cm/sec; p-value <0.001). In the multivariate linear regression model adjusted for age, sex, lifestyle status, systolic blood pressure, heart rate, fasting glucose, triglyceride, high-density lipoprotein cholesterol, homeostasis model assessment-insulin resistance, and high-sensitivity C reactive protein, the absolute values of EFT were an independent determinant of increasing baPWV in the adjusted models (β=±0.113, p<0.001). In the same model for logistic regression analysis, increasing quartiles of EFT showed a significant association with increased baPWV groups (p for trend<0.010) and the highest quartile group of EFT had higher odds ratio (OR) for increased baPWV group compared with that of the lowest quartile group (OR 95% confidence interval (CI): 2.19 [1.21-3.95]).

Conclusion: This study indicates an independent relationship between epicardial fat thickness and arterial stiffness, suggesting that echocardiographic EFT measurement could be an easy-to-measure and useful tool for early detection of subclinical target organ damage.
EAT below the median of 26 g/m² was a significant predictor of all cause mortality (HR 8.2, p=0.004) and cardiac mortality (HR 4.2, p=0.04). However, EAT values above the median of 26 g/m² were a significant predictor of an increased cardiac mortality (HR 4.7, p=0.03). Figure 1 details the relationship between categories of indexed EAT and all cause and cardiac mortality as well as cardiac morbidity.

Conclusion: Our results suggest that the determination of EAT may help to identify CAD patients who are at higher risk of death and rehospitalisation due to heart failure. Therefore, EAT might be a useful surrogate marker to select patients who derive significant benefit from a more intense treatment.

P4361
Mild/moderate renal dysfunction: its role in the preoperative evaluation

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Purpose: Cardiologists are frequently requested to perform the preoperative clinical evaluations prior to non-cardiac surgery. Some guidelines indicate that a creatinine concentration greater than 2.0 mg/dl as an independent risk factor for postoperative morbi-mortality. This study evaluated whether mild/moderate preoperative renal dysfunction contrated with other risk levels below 2.0 mg/dl is associated with postoperative outcomes in non-cardiac surgery.

Methods: Eighty-nine patients (mean age 74.7±10.85 years; group A) with creatinine creatininations ranging from 1.3 mg/dl to 2.0 mg/dl (clearance 45.0±7.63; 33.0 – 59.8 mg/m/min) were compared with 498 patients (68.04±9.78 years; group B) with normal creatinine levels. The groups were matched with regard to surgical risk (ASA) and duration of surgery. Variables such as age, gender, number of co-morbidities and prior chemotherapy were analyzed. All patients underwent surgical procedures due to tumor disorders and were followed during in-hospital evolution. Adverse outcomes included death and any complications that increased the length of hospital stay.

Results: The mean creatinine concentrations were 1.63±0.19 mg/dl (group A) and 0.63±0.19 mg/dl (group B; p=0.001). No significant differences were detected with regard to surgical risk (p=0.724). Surgical durations were 1.73±0.69 h (group A) and 2.32±1.49 h (group B; p=0.001). The patients in group A were significantly older (74.78±10.85 vs 68.04±9.78 years; p=0.001) and more likely to be male (37.1% vs 22.1% in group B; p=0.002) and included more patients with histories of chemotherapy (31.5% vs 10.2% in group B; p<0.001). The mean co-morbidities were 2.66±1.25 (group A) and 2.90±1.01 (group B; p=0.110). Adverse outcomes occurred in 13.51% of patients in group A versus 3.41% of patients in group B (p=0.001; OR 6.35 CI 2.42-16.68). Even after adjusting for age, gender, procedure duration and prior chemotherapy, the incidence of morbimortality remained significantly greater in group A.

Conclusion: These results suggest that even mild/moderate preoperative renal dysfunction, may be associated with significant increased post-operative morbimortality in patients undergoing non-cardiac surgery.

P4362
Systematic review of risk factors for upper gastrointestinal bleeding in patients using low-dose acetylsalicylic acid

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Purpose: Low-dose acetylsalicylic acid (ASA) is recommended for secondary prevention of cardiovascular events, and primary prevention in high risk patients. However, its use is associated with an increased risk of upper gastrointestinal bleeding (UGIB), although little is known about which users are at risk of developing UGIB. This study aimed to assess risk factors for UGIB in patients taking low-dose ASA.

Methods: A systematic literature analysis (1995–2011) using PubMed and Embase was performed. Studies were included if they were randomized controlled trials or clinical studies reporting UGIB in individuals receiving low-dose ASA. Studies were excluded if the ASA dose was above 325 mg/day or not reported, or if all participants were given concomitant gastrointestinal protective medication. The GeoD database was used to identify relevant articles.

Results: The searches identified 2240 unique studies, 15 of which were eligible for inclusion. The most commonly identified risk factor for UGIB was a history of peptic ulcer disease, reported in six studies (N=3353). Five of the six studies reported relative risks (RRs) or odds ratios (ORs) in the range 3.1–6.5 when assessing this relationship, while the sixth reported a much higher OR of 15.2 (95% confidence interval [CI]: 3.8–60.1). Increasing ASA dose (up to 325 mg/day) was associated with a significantly increased risk of UGIB in users of low-dose ASA. Concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose ASA was also associated with a significantly increased risk of UGIB (two studies; RR: 2.39 [95% CI: 1.0–5.8]; OR: 3.8 [95% CI: 1.9–7.8]). Other factors associated with a significantly increased risk of UGIB in users of low-dose ASA were: current Helicobacter pylori infection, concomitant calcium channel blocker use, concomitant clopidogrel use and a history of dyspepsia. Two studies reported an...
contrast-induced nephropathy (CIN) after primary percutaneous coronary intervention (PCI): the role of heat shock proteins

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Background: Contrast-induced nephropathy (CIN) is common complication associated with unfavourable clinical outcomes. Heat shock proteins (HSPs) comprise several families of proteins expressed by number of cell types following exposure to stressors. HSPs play essential function in cytoprotection however their role in CIN pathogenesis has never been evaluated. The purpose of this study was to investigate whether HSP27 and HSP60 may play a role in the development of CIN in patients undergoing elective percutaneous coronary intervention (PCI).

Methods: This study included 43 selective non-diabetic patients with ischemic heart disease and normal serum creatinine undergoing PCI. CIN was defined as an increase more than 0.5 mg/dL or more than 25% of baseline value of creatinine.

An enzyme-linked immunosorbent assay method was used to measure HSP27 and HSP60 levels in the plasma of patients and the controls. Serum creatinine, HSP27 and HSP60 was assessed before and 24 hours post the procedure.

Results: Of 43 patients 13 patients (29.5%) developed CIN. Either HSP27 or HSP60 levels were elevated in patients compared with controls (median 3.06 ng/mL (1.148 – 23.66) vs 1.35 ng/mL (0.231 – 14.65) and 25.49 ng/mL (0 – 1243) vs 10.77 ng/mL (0 – 321) respectively; p<0.009 and p<0.001 respectively). PCI induced the increase (Δ) of HSP27 but not HSP60 level. Δ HSP27 was, however, significantly higher in CIN(+)-group compared with CIN(-) group (p<0.006). In CIN(+) group baseline HSP60 level was higher compared with CIN(-) group (p<0.001). (Table 1). Baseline HSP60 level correlated positively with creatinine level (r=0.545, p<0.001). Similarly, Δ HSP27 correlated with Δ creatinine induced by the PCI procedure (r=0.473, p<0.001). Multiple regression analysis indicated high baseline HSP60 serum concentration as independent risk factor for the development of CIN in patients undergoing PCI.

Conclusions: HSP27 appears to play protective roles in the process of CIN. Serum HSP60 concentration seems to be a marker of increased risk of CIN development induced by PCI.

Table 1. CIN-contrast-induced nephropathy: (+) positive, (–) negative Parameter CIN (+), n=13 CIN (–), n=31 p
HSP27 (ng/ml) 2.51 (2.424 – 18.56) 3.89 (1.148 – 23.66) 0.069
ΔHSP27 (ng/ml) 0.471 (-1.07 – 5.58) 0.655 (-1.07 – 10.37) 0.056
HSP60 (ng/ml) 40.15 (21.6 – 1243) 23.89 (0 – 520) 0.001
ΔHSP60 (ng/ml) 0.065 (-345 – 201) 0.001 (-423 – 243) 0.522

Incidence, risk factors, and outcomes of peripercative acute kidney injury in noncardiac and nonvascular surgery

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1Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey; 2Siyami Ersek Thoracic and Cardiovascular Surgery Center, Department of Cardiology, Istanbul, Turkey.

Background: Perioperative acute kidney injury (AKI) is a well-established risk factor for perioperative morbidity and mortality in patients undergoing cardiac surgery. However, predictors and outcome of perioperative AKI in patients undergoing noncardiac, nonvascular surgery has not been well-determined. The aim of this study was to investigate the incidence, predictors, and outcomes of perioperative AKI in patients undergoing noncardiac, nonvascular surgery.

Methods: A total of 1340 consecutive patients (mean age =65.5±13.8 years) undergoing noncardiac, nonvascular surgery were prospectively evaluated. Patients older than 85 years who underwent an elective, noncardiac case, open surgical procedure were excluded. Patients with pre-existing renal dysfunction requiring renal replacement therapy or a preoperative serum creatinine higher than 1.4 mg/dL were excluded. The primary outcome of this study was perioperative AKI defined by the following criteria: serum creatinine increase >0.5 mg/dL, urine output failure, loss of function, and end-stage kidney disease.

Results: During the study period, AKI was diagnosed in 128/1340 (9.5%) patients. AKI was associated with a reduced risk of UGIB relative to those taking low-dose ASA without a PPI (OR: 0.02, p<0.001).

Conclusions: These results indicate that low-dose ASA with or without PPI could be beneficial in reducing the risk of UGIB in patients undergoing PCI. HSP27 appears to play protective roles in the process of CIN. Serum HSP60 concentration seems to be a marker of increased risk of CIN development induced by PCI.

The association between brachial-ankle pulse wave velocity and the extent of coronary artery disease in patients with angina

1Sejong General Hospital, Bucheon, Korea, Republic of; 2Inje University, Seoul, Korea, Republic of

Purpose: Arterial stiffness is well known as an important risk factor for cardiovascular disease. Among the variable methods for measuring arterial stiffness, brachial-ankle pulse wave velocity (baPWV) is widely used in clinical research and is a relatively simple and noninvasive test. We assessed the association between arterial stiffness, as determined by baPWV and the extent of coronary artery disease, as detected by coronary angiography (CAG).

Methods: We retrospectively enrolled 651 consecutive South Korean individuals who had been admitted to our institute and had undergone baPWV and elective CAG for suspected coronary artery disease between June 2010 and July 2011.

Results: By multivariable logistic regression analysis, significant predictors of coronary artery disease (CAD, diameter of stenosis>50%) were male gender, age, high density lipoprotein cholesterol, HbA1c and the level of baPWV. When we divided subjects into 3 groups according to clinical outcomes, the value of baPWV showed a significant association with coronary artery disease. The association between baPWV and the extent of coronary artery disease is stronger in men than in women.
baPWV was significantly higher in patients with CAD including those who re-
ceived revascularization than in patients without CAD (p<0.001). But there was no significant difference of baPWV between the groups of intermediate CAD and reflec-
To return the values as if you were reading the text naturally.

**Results:**
After 2-year follow, 11.7% of the patients expired for cardiovascular causes and 1.9 years of follow-up. 
**Conclusion:** Type 2 diabetes mellitus has the same CV risk as a history of CHD in high-risk Japanese hypertensive patients.

**Methods:** Subjects who received coronary angiography (CAG) and did not take any lipid-lowering drugs (n=189) were enrolled. Those who had angiographically confirmed CAD were treated as CAD subjects (n=189). We examined which metabolic parameters recognized as independent coronary risk factors were correlated with the prevalence of coronary artery disease (CAD) and re-

tailed with the primary outcome most significantly.

**Conclusion:** In this 2-year cohort, we discovered that the existence of non-
occult plaque plaques could significantly impose high cardiovascular mortality. Carotid intimal thickness (CIMT) offers an easy access to explore the status of systemic atherosclerosis. In this study, we follow the cohort to figure out the significance of CIMT and other factors, which may impact the clinical outcome of ESRD patients.

**Methods:** This is a cohort study conducted in a tertiary referring medical cen-
tral. All enrollee should be patients of ESRD, who has received maintenance hemodialysis (HD) for more than 3 months. In Feb. 2007, one cardologist fin-
ished the carotid duplex within one week, during which all enrollee received blood sampling for various lab tests. All the patients were closely followed with clinical events recorded. The primary endpoint was cardiovascular death. In statistics, significance is defined by p<0.05.

**Results:** There were 265 patients in this cohort, and the distribution of gender was nearly equal (male vs female: 49.1% vs 50.9%). The age of this cohort is 61.2±12.4 year-old and these patients has been put on HD for 42.7±29.3 months. After 2-year follow, 11.7% of the patients expired for cardiovascular causes and none of them were afflicted with stroke. Those who reached the primary end-
point were 68.2±11.3 vs. 60.3±12.3 year-old, with higher fasting blood sugar (161.1±87.0 vs 117.5±66.1mg/dl), lower sodium (141.2±4.0 vs 144.2±3.3 meq/dl), higher C-reactive protein (CRP) (2.2±4.7 vs 0.8±1.5 mg/L), thicker CIMT over left carotid artery (0.59±0.017 vs. 0.55±0.015 cm) and more carotid plaque (51.6% vs. 24.0%). Those plaques cast 30-50% narrowing of the in-
carotid plaque may improve the primary outcome in this patient population.

**Conclusion:** These results indicate that baPWV is significantly associated with the extent of CAD, although baPWV has limited value in identifying the patients who should receive revascularization among those patients with angiina.

**Methods:** There were 4,703 high-risk hypertensive patients (mean age: 63.8 years) to be analyzed. We divided them into four groups according to base-
line characteristics as follows, non-diabetics with a history of CHD (n=2988), non-diabetics with a history of CHD (n=2988), non-diabetics with a history of CHD (n=2988), and diabetics with a history of CHD (n=203). We used the multivariate Cox regression analysis to estimate the hazard ratios of non-diabetics with a history of CHD and diabetics without a history of CHD (P<0.890). Similar results were observed in terms of the risk of CV events between non-diabetics with a history of CHD and diabetics without a history of CHD (P<0.890). 

**Conclusion:** Type 2 diabetes mellitus has the same CV risk as a history of CHD in high-risk Japanese hypertensive patients.

**Methods:** The CASE-J trial compared the effects of the angiotensin II receptor blocker candesartan and the calcium channel blocker amlodipine on the incidence of CV events in high-risk Japanese hypertensive patients. The CASE-J Extension (CASE-J Ex) was an observational study designed to evaluate their long-term effects, incorporating an additional 3-year follow-up of the CASE-J trial. We have reported that type 2 diabetes mellitus has the same impact on the incidence of cardiovascular (CV) events as a history of coronary heart disease (CHD), as a subanalysis of the CASE-J Trial. We re-examined the impact of type 2 diabetes and a history of coronary heart disease (CHD) on the incidence of CV events with improved statistical power by using the data of CASE-J Ex.

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### Development and psychometric properties of the Heart Failure Knowledge Scale in Japan


**University of Tokyo, Graduate School of Medicine, Tokyo, Japan; 2 Sakaikabara Heart Institute, Tokyo, Japan.**

**Purpose:** Heart failure (HF) knowledge is considered to be a cornerstone for HF management. However, there are no valid and reliable instruments available, with the exception of HF knowledge in Japanese. The purpose of this study was to develop a reliable and valid instrument for the measurement of HF knowledge, and to assess the relationship between HF knowledge and HF self-care behavior.

**Methods:** We developed a questionnaire consisting of 17 items concerning HF knowledge in reference to the previous studies, such as “HF is a condition that the heart is not able to pump sufficient amount of blood through the body”, “Diuretics remove fluids from the body”, and “HF patients had better drink more water than healthy people”. Patients responded these questions with “yes”, “no”, or “I do not know”. A correct answer was scored 1, an incorrect answer or an answer of “I do not know” was scored 0. Scores for each item were summed, giving a range of total scores from 0 to 17. A higher score indicates greater knowledge about HF. Content validity was confirmed by the expert panel including a cardiovascular nurse, a cardiologist, an expert from nursing in cardiovascular area, and the nurse at the heart care unit. Construct validity was assessed through factor validity and concurrent validity. Concurrent validity was evaluated using Pearson product-moment correlation coefficient between the HF knowledge scale and the HF comprehension scale. Reliability was assessed by internal consistency.

**Results:** A total of 178 patients in two independent hospitals completed the self-administered questionnaire. The mean age was 64.3±11.4 years, and males accounted for 70% of the respondents. Mean score of the HF knowledge scale was 9.6±4.5, and the percentage of correct answers ranged from 15% to 79%. Exploratory factor analysis confirmed the one dimensionality of the HF knowledge scale. The contribution to one factor was 61%. Pearson correlation coefficient for concurrent validity was 0.418 (p<0.05). Cronbach’s alpha was measured at 0.88, suggesting adequate reliability. The low HF knowledge score was significantly associated with poor HF self-care behavior, assessed by the European Heart Failure Self-Care Behavior Scale-Japanese version (r=0.256, p<0.01).

**Conclusion:** The HF Knowledge Scale was a valid and reliable one, and this instrument can be used to gain an insight in the effects of education and counseling toward HF patients. Our data suggests that HF knowledge improves HF self-care, although further research is needed to confirm the relationship.

### Comparison of 2, 3, 4 and 16 hour holters

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>2 Hours</th>
<th>3 Hours</th>
<th>4 Hours</th>
<th>16 Hours</th>
<th>Significance vs. 16h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Heart rate</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>p&lt;0.05 vs 16h</td>
</tr>
<tr>
<td>Absolute Difference</td>
<td>+2</td>
<td>+2</td>
<td>+1</td>
<td>+2</td>
<td><strong>NS</strong></td>
</tr>
<tr>
<td>Correlation</td>
<td>0.92</td>
<td>0.93</td>
<td>0.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pauses</td>
<td>0.95</td>
<td>0.98</td>
<td>1.00</td>
<td>1.00</td>
<td>ns</td>
</tr>
<tr>
<td>Add. Difference</td>
<td>0.05</td>
<td>0.02</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correlation</td>
<td>0.97</td>
<td>0.96</td>
<td>0.97</td>
<td></td>
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<td>ns</td>
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</tr>
</tbody>
</table>

This study emphasizes that short duration holter monitoring, even as little as 2 hours may be useful in the clinical setting and have benefits in terms of patient convenience and costs.

### Diagnostic angiography with 5F catheters supports early ambulation and discharge

V. Gatt, M. Borg, J. Agius, A. Fenech, R.G. Xuereb, V. Grech.

**Department Cardiac Services, Mater Dei Hospital, Malta, Msida, Malta.**

**Introduction:** Ischaemic heart disease is mainly diagnosed through coronary angiography. Although the radial artery approach is gaining prevalence the femoral artery access is still very popular. The latter requires longer recovery time compared to the radial approach. Few studies have studied the feasibility of early arterio access early ambulation and the safety of early home discharge.

**Methods:** An initial study with 4F catheters was conducted earlier yielding very good results. This study was published. Then data from 5F diagnostic angiography was prospectively collected over 1 year. The Cath Lab nurses managed sheath removal with manual compression targeting 1 hour bed rest time before ambulation.

**Results:** This study was carried out in 2009 with 262 participants. The mean time from sheath removal to discharge was 161.3 minutes. These results were obtained with minimal access site complications and without major adverse events.

### The evolving role of the angina specialist nurse in a district general hospital in the UK

J. Caton, C. Dereszkiewicz, N. Naqvi. **Department of Cardiology, Royal Albert Edward Infirmary, Wigan, United Kingdom.**

**Purpose:** To assess the changing role of the angina specialist nurse supervising nurse-led rapid access chest pain clinic (RACP) in a district general hospital in the UK.

**Methods:** The angina specialist nurse at hospital supervises a nurse-led RACP since 2002. A protocol was followed which proved to be safe and effective. Patients were managed by initial clinical assessment (history, clinical examination) and exercised on a treadmill utilising the Bruce protocol. Appropriate action was then taken. Details were presented to this Society in 2006. However, with the publication by the National Institute of Clinical Excellence (NICE) of guidelines to manage people presenting with stable chest pain (CG95) in 2010 the protocol of the nurse-led RACP had to change and adapt to these guidelines. The latter is to advocate exercise ECG to diagnose or exclude stable angina in people with unknown coronary artery disease (CAD). The advice is to offer CT calcium scoring, use myocardial perfusion scanning with SPECT, or stress echocardiography, or first-pass contrast-enhanced magnetic resonance (MRI) perfusion or MPI imaging for stress-induced wall motion abnormalities. Following the publication of CG95 a small prospective study was done to test the impact of these guidelines. The study was carried out from March 2011 to May 2011. Facilities for CT calcium scoring are not available at hospital. After initial clinical assessment patients were given a percentage likelihood of CAD as proposed by NICE. Patients were then referred for myocardial perfusion scanning or dobutamine stress echocardiography or treadmill exercise test.

**Results:** 116 patients were audited - 62 Males (mean age 60) and 54 Females (mean age 55). After initial clinical assessment, 8 patients had estimated likelihood of CAD of 61-90% and referred for coronary angiography; 4 patients had 30-60% likelihood of CAD and offered non-invasive clinical imaging. Of these 67 were referred for dobutamine stress echocardiography and 17 for myocardial perfusion imaging; 24 patients had 10-29% risk and referred for exercise test.

**Conclusions:** The angina specialist nurse supervising a RACP now needs to accurately assess the percentage likelihood of CAD and become proficient at assisting the procedure of dobutamine stress echocardiography. Furthermore, NICE indicated facilities for dobutamine stress echocardiography and myocardial perfusion scanning need to be increased. There would still be a role for treadmill exercise stress testing in hospitals where facilities for CT calcium scoring are not available.

### Groin dressing post cardiac catheterization: traditional pressure versus transparent film

R. Al-Shalalah.**Jubail Royal Commission Hospital, Jubail, Saudi Arabia.**

**Purpose of the study:** To determine the efficacy of using a small transparent non pressure dressing compared with the traditional controlled pressure dressing applied to the femoral artery puncture wound site to maintain haemostasis following cardiac catheterization procedures.

**Design:** An experimental design, randomized study.

**Patients:** 80 post cardiac catheterization patients were randomized to have their groins dressed either with pressure dressing (N=40) or TFD (N=40). Patients am-
bullated 8 hours after the procedures. Outcome variables were hematoma formation or bleeding, patient discomfort, and nurse-reported ease of observation of the groin puncture site after the procedure. Five instruments were used for data collection: 1) Demographic and medical data sheet, 2) Hematoma Formation and Bleeding Scale, 3) Skin Integrity Scale, 4) Patient Discomfort and Pain Scale & 5) Nurses Ease of Assessment Scale.

Results: There were no significant differences in base line characteristics and medical data between the two groups. 100% in TFD group vs 55% in pressure dressing group reported feeling very comfortable (p value of 0.003). Hematoma formation was equal in the two dressing groups with no incidence of bleeding complications. Nurses rated the ease of assessing the groin significantly higher for TFD than for pressure dressing (p value of 0.000).

Conclusions: Dressing of the puncture site after cardiac catheterization with TFD was more comfortable than the conventional pressure dressing without any difference in hematoma or bleeding complications. So TFD can be used safely and comfortably after achieving hemostasis.

P4375

PCI in very elderly patients suffering an ACS
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There are few data on safety and outcomes of percutaneous coronary revascularization (PCI) in very elderly patients suffering an Acute Coronary Syndrome (ACS), especially those aged ≥ 85 years old. From January 2009 to December 2011, a total of 108 very elderly patients were admitted at our coronary care unit with a diagnosis of ACS; 44% of these (n = 48) underwent PCI. The average age at intervention was 86.9 years. The most frequent complications were severe chronic renal failure (26%) and COPD (13%). Most of the procedures (47%) was performed for acute myocardial infarction with ST-segment elevation (STEMI), 43% for an acute coronary syndrome without ST-segment elevation with high-risk clinical features. Coronary angiography was performed in 45% of cases with a radial approach. The rate of procedural failure was quite high, with about 20% of PCI ineffective; this finding could be consistent with the high percentage of patients with severe calcific coronary artery disease (CAD).

Complication rate in this population of ultra-elderly was 25%, with a mortality rate of 12.5%, almost entirely attributable to STEMI (83, n=5). The cause of death was attributed to mechanical complications of myocardial infarction; in other patients the cause of death was an arrhythmic event. The only complication attributable to revascularization was an acute contrast nephropathy, which resolved during the hospital stay. Non-fatal complications consist of two cases of severe bleeding and five cases of severe heart failure; a matter of particular concern was the low use of intra arterial counterpulsation balloon pump: in fact, only one patient was assisted with IABP, compared with nine cases of severe heart failure. Our study highlighted how in very elderly patients experiencing an ACS, PCI is a safe procedure, with a single complication attributable to the revascularization procedure, i.e a case of acute contrast nephropathy. With regard to other complications these are mainly correlated to the underlying disease, especially acute myocardial infarction with ST-segment elevation. Careful nursing assessment, with a regular evaluation of main hemodynamic parameters and renal function, may facilitate early recognition of hemodynamic deterioration and its better management.

P4376

Preoperative statin use and postoperative atrial fibrillation after major noncardiac, nonvascular surgery
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Background: Perioperative beta-blockade and statin therapy have been advocated to reduce cardiac risk of noncardiac surgery. The current study investigated the efficacy of a 2-week statin therapy in patients undergoing major noncardiac, nonvascular surgery.

Methods and Results: A total of 1750 patients, undergoing noncardiothoracic, nonvascular surgery were prospectively evaluated. Patients older than 18 years who underwent an elective, nonequivalent case, open surgical procedure were enrolled. Electrocardiography and cardiac biomarkers were obtained 1 day before surgery, and on days 1, 3 and 7 after surgery. Patients with atrial fibrillation were excluded. Demographics, comorbidities, preoperative data (electrocardiography, echocardiography, laboratory results), medications, and intraoperative variables were evaluated for their association with the occurrence of perioperative cardiovascular adverse events. Patients receiving statins were generally older (68.7 vs 62.3 years; P<0.001) and more likely to be receiving a beta-blocker (46.3% vs 19.4%; P<0.001). Statin use was associated with a lower unadjusted rate of atrial fibrillation (2.2% vs 4.2%; P<0.001), myocardial infarction (3.4% vs 6.4%; P<0.001) and mortality (1.1% vs 2.4%; P<0.01). After adjustment for patient risk factors and surgery type, odds for atrial fibrillation (adjusted odds ratio = 0.86; 95% confidence interval = 0.69-0.91; P<0.001) and myocardial infarction (adjusted odds ratio = 0.82; 95% confidence interval = 0.67-0.98; P<0.001) remained significantly lower among statin-treated patients.

Conclusions: Treatment with statins is associated with a lower risk for atrial fibrillation and myocardial infarction following major noncardiac, nonvascular surgery.

P4377

Carperitide can protect against acute kidney injury in patients with chronic kidney disease undergoing coronary angiography
T. Senoo, K. Manabe, S. Umemura, M. Motohiro, H. Kaminishi, T. Iwasaki. Kansai Medical University Hirakata Hospital, Hirakata, Japan

Purpose: Acute kidney injury remains a common complication of coronary angiography (CAG). Although previous study reported that carperitide can reduce renal protective effects after CAG, this has not been a universal finding. We evaluated whether carperitide can reduce renal damage after CAG using urinary Liver-type fatty acid binding protein (L-FABP) expressed after renal ischemia which is a novel marker detecting renal injury more sensitively than the existing marker such as serum creatinine.

Methods: We prospectively randomized 148 patients undergoing CAG who had renal dysfunction (glomerular filtration rate (GFR) < 60 ml/min/1.73m2). Patients were divided into receiving hydration alone (Hyd-group; n=74) and receiving hydration with carperitide (ANP-group; n=74). All patients were treated with hydration for 12 hours before and after CAG. In ANP-group, carperitide (0.0125-0.025g/kg/min) was started for 1 hour before CAG and continued for 24 hours. GFR was estimated by using the MDRD formula and urinary L-FABP measured at baseline, day 1 and 2.

Results: Baseline characteristics of both groups were similar. There were no difference in serum creatinine and GFR between two groups at baseline, day 1 and day 2. However, urinary L-FABP was significantly increased in ANP-group, at day 1 (24.7±24.3 vs 40.4±70.6;Ug/g;p<0.001) and day 2 (15.3±23.4 vs 42.5±83.0; Ug/g;p<0.01).

Conclusions: Prolonged intravenous infusion of sodium chlorediupe carbperitide is more effective than sodium chloride alone for prophylaxis of acute kidney injury after CAG. Sodium chloride plus ANP may be reduced CIN, leading to improvement of long-term prognosis of CKD patients.

P4378

Effects of community-based general practitioners-led care for 12,864 patients with hypertension: study of cardiovascular risk intervention - hypertension (SCRI-HTN) in China
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Background and Objectives: Hypertension is emerging as a leading cause of cardiovascular morbidity, mortality, and disability among adults. General practitioners (GPs) working in the community health service (CHS) organizations are being positionned in the healthcare system to provide long-term follow-up by general practitioners using scheduled consultations and counselling. The intensity of medication treatment was determined by the stratification of risk for cardiovascular disease (CVD). OUTCOME MEASURES: the difference in change in systolic BP, diastolic BP, triglyceride, total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol.

Methods: Data of 12,864 adult patients who had diagnosed hypertension and 196 certificate-trained general practitioners. INTERVENTIONS: cardiovascular risk reduction education; regular, long-term follow-up by general practitioners using scheduled consultations and counselling. The intensity of medication treatment was determined by the stratification of risk for cardiovascular disease (CVD).

RESULTS: The study was carried out over a 5-year period from 2007 through 2011. PARTICIPANTS: 12,864 adult hypertensive patients who had diagnosed hypertension; and 196 certificate-trained general practitioners. INTERVENTIONS: cardiovascular risk reduction education; regular, long-term follow-up by general practitioners using scheduled consultations and counselling. The intensity of medication treatment was determined by the stratification of risk for cardiovascular disease (CVD).

CONCLUSIONS: The SCRI-HTN study showed that adult patients with hypertension undergoing community-based intervention led by GPs on control of cardiovascular risk factors among patients with hypertension in China.

Methods: DESIGN: a longitudinal, pre-post study. SETTING: 98 community health centres (CHCs) in Guangzhou, the most urbanized city in southern China. Multistage cluster sampling method was adopted in identifying the study sites. The study was carried out over a 5-year period from 2007 through 2011. Participants: 12,864 adult hypertensive patients who had diagnosed hypertension; and 196 certificate-trained general practitioners. INTERVENTIONS: cardiovascular risk reduction education; regular, long-term follow-up by general practitioners using scheduled consultations and counselling. The intensity of medication treatment was determined by the stratification of risk for cardiovascular disease (CVD). OUTCOME MEASURES: the difference in change in systolic BP, diastolic BP, triglyceride, total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol.

Methods: Sufficient data were available for 12,864 patients. The mean (SD) patient age was 52.5 (7.5) years, 53.9% were male, and the mean (SD) systolic/diastolic BP was 146.1 (19.4)/84.6 (11.3) mm Hg at baseline. Several main indicators of cardiovascular health improved over the study period: mean systolic BP decreased from 146.1 to 135.1 mm Hg (p<0.001); mean diastolic BP declined from 84.6 to 79.6 mm Hg (p<0.001); mean triglyceride level dropped from 31.7 to 30.1 mg/dl (p<0.005); mean total cholesterol fell from 96.4 to 74.8 mg/dl (p<0.042); mean LDL cholesterol changed from 40.5 to 22.3 mg/dl (p<0.025); and mean HDL cholesterol increased from 28.1 to 46.3 mg/dl (p<0.044).

Conclusions: This SCRI-HTN study showed that adult patients with hypertension receiving GPs-led care in the community health centres achieved statistically and clinically significant and sustained improvements on the cardiovascular markers for as long as 5 years. It demonstrated that the participation of GPs as the core in the multi-disciplinary team to provide hypertension management care at the com-
Anxiety in patients with chronic heart failure: impact of perception of control and acceptance coping

Depressed chronic heart failure patients have impaired sympathetic-parasympathetic activity, a potential contributor to worsened outcomes in depressed CHF patients. The apparent strong influence of social support on cardiac autonomic activity in CHF patients warrants further research.

Acceptance and intervention to improve: Mind, body & behaviour: implications in cardiovascular risk and disease

Purpose: The perception of lack of control has often been associated with anxiety. Studies have indicated that different coping strategies are differentially associated with mood in patients with chronic heart failure (CHF), and that maladaptive coping is generally linked to anxiety. Furthermore, it has been suggested that acceptance may potentially relieve emotional distress. The present study investigates if acceptance coping can buffer the hypothetical impact of perception of lack of control on higher degrees of anxiety. The aim is to clarify if the pattern of control, acceptance, and anxiety has relevance for nursing efforts to provide emotional support for patients with CHF.

Methods: 65 patients diagnosed with CHF in NYHA class II and III were recruited from a heart failure out-patient clinic. The participants filled in forms to measure illness perception (B-IPQ), coping strategies (Brief COPE), anxiety and depression (HADS).

Results: Univariate analysis revealed correlations between Perception of control and Anxiety (r = -0.35, p < 0.05) and Acceptance coping and anxiety (r = -0.27, p < 0.05). However, upon entering both Perception of control and Acceptance coping in a path-analysis as the latter as a mediator, the effect of acceptance coping on anxiety was rendered non-significant.

Conclusion: The majority of surviving heart failure patients reported high adherence to their prescribed beta-blockers. As in previous studies, depression was a significantly correlated with poorer adherence. To our knowledge, this is the first report of geographical differences in adherence in bivariate analyses and should be investigated further.

Depressed chronic heart failure patients have impaired autonomic function

Background: Depression is associated with increased morbidity and mortality in chronic heart failure (CHF) patients. Sympatho-vagal balance might contribute to impaired sympatho-vagal balance and, as measured using heart rate variability (HRV), is unknown in CHF patients.

Purpose: The hypothesis of this study was that, in stable systolic CHF patients, impaired sympato-vagal balance would be independently related to depression and to the severity of depression.

Methods: Participants completed a 30-minute electrocardiogram for HRV analysis (lying, quiet, dimmed room, constant ambient temperature, no caffeine, smoking, alcohol, or exercise) and underwent a clinical interview for major or minor depression according to DSM-IV criteria. Low frequency to high frequency (LF/HF) ratio in the frequency domain, for predominance of sympathetic over parasympathetic activity, was the principal autonomic measure. Regression analyses demonstrated depression had a direct effect on HRV. Social support had both direct and indirect effects on HRV via depression (p < 0.001).

Conclusion: In CHF patients, both minor and major depression are associated with predominant sympathetic over parasympathetic activity, a potential explanation for worse outcomes in depressed CHF patients.

Adherence to beta-blocker therapy in heart failure patients

Background: The hypothesis of this study was that, in the setting of middle-income country, such health states should have similar medical conditions, play a major role in determining HRQoL, we hypothesized that, in the setting of middle-income country, such health states should have similar impacts on HRQoL. The impact of several health states on HRQoL were compared using effect sizes as part of the LIFECAres consortium.

Objective: To examine the impact of lifestyle factors, disease history, and awareness on health-related quality of life in a Thai population.

Methods: Between 2008 and 2009, 4,850 Thais, aged 25-54 years, agreed to participate in an observational follow-up. 1,755 patients died (18.1%). Adherence data was available for 2,520 patients. 208 (90.4%) patients reported perfect (100%) beta-blocker adherence in the previous month. Poorer adherence (<100%) was associated with country of residence (27.3%, 11.7% and 6% of patients were poorly adherent in Slovenia, Serbia, and Germany, respectively; p = 0.046), and with the presence of major or minor depression (20.9% of the depressed vs. 7.0% of the non-depressed patient were poorly adherent; p = 0.005).}

Effects of lifestyle factors, disease history and awareness on health-related quality of life in a Thai population

Background: Health-Related Quality of Life (HRQoL) depends largely on individual perception of their health state, built from social norms and beliefs. Research from developed countries shows that awareness of disease, as well as chronic medical conditions, play a major role in determining HRQoL. We hypothesized that, in the setting of middle-income country, such health states should have similar impacts on HRQoL. The impact of several health states on HRQoL were compared using effect sizes as part of the LIFECAres consortium.

Methods: Between 2008 and 2009, 4,850 Thais, aged 25-54 years, agreed to take part in a health survey. Impact of different health states on HRQoL were compared, using generalized linear models adjusted for age, sex and social status. Cohen’s effect sizes (ES) were calculated, using different health states and compared among each other.

Results: The mean age was 46 years and 72% were male. Physical and Mental Component Summary (PCS and MCS respectively) scores decreased as the number of chronic conditions increased monotonically (p < 0.0001). Liver disease had the highest prevalence, accounting for 11.4%, followed by arthritis (10.4%), asthma (4.9%), cardiovascular disease (CVD) (3.4%) and chronic kidney disease.
Dementia diagnosis seems to be a powerful tool for predicting poor outcomes in the elderly with CVD, thus its diagnosis scale should be applied more often in the cardiology divisions.

Purpose: To evaluate the association between dementia and short-term all-cause mortality rates of older adults hospitalized with CVD during one year of follow-up.

Study design: Prospective cohort study.

Methods: We included a total of 102 consecutive patients aged 65 years or older who were discharged from a cardiology ward of a tertiary-care hospital. Mini mental state examination (MMSE) was applied. Individuals were divided into groups: group 1 with dementia diagnosis, and group 2 without dementia diagnosis. Demographic characteristics, blood analysis and cardiovascular parameters at admission for ACS were compared. Cognitive function was assessed using the MMSE. The scores of group 1 were compared with those of group 2.

Results: The difference of QOL between older and younger patients with atrial fibrillation in Japan

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Introduction: The Atrial Fibrillation Effect on Quality-of-life (AFEQT) Questionnaire was developed and validated to measure the spectrum of quality of life (QOL) affected by atrial fibrillation (AF) and its treatment. We used this AFEQT questionnaire to investigate the QOL differences between AF patients in Japan. In this study, we compared the QOL of Japanese patients to those of Westerners, and focused on the differences in QOL between younger and older age groups.

Methods: 102 consecutive outpatients aged 65 years or older (129 male, 65.6 ± 10.4 years) with AF under anticoagulation therapy received the AFEQT questionnaire, and were divided into two groups: 106 patients in the younger group (YG; age < 70 years) and 62 patients in the older group (OG; age ≥ 70 years). The AFEQT questionnaire includes 20 items, which are divided into 4 domains (Symptom, Daily Activities, Treatment Concern, and Satisfaction). We investigated the overall global score and 4 domains score. The score is a 0 to 100 scale, where a score of 0 indicates the most severe symptoms or disability and a score of 100 indicates no limitation or disability.

Results: The Global Scores of YG and OG were 78.74 ± 15.63 and 77.95 ± 17.00, respectively (P = 0.764, N.S.). The mean score of Symptom was 83.02 ± 17.19 and 84.63 ± 18.15 (YG and OG, respectively, P = 0.566, N.S.). The scores of Daily Activities were 80.72 ± 19.72 and 71.72 ± 23.57 (YG and OG, respectively, P = 0.009). The scores of Treatment Concern were 79.95 ± 17.81 and 81.45 ± 15.71 (YG and OG, respectively, P = 0.046). The scores of Satisfaction were 75.73 ± 18.75 and 75.99 ± 18.05 (YG and OG, respectively, P = 0.931). The score of Daily Activities tended to be higher than Westerners (the previous data showed that the score of asymptomatic patients was 71.2 and the score of patients with severe symptoms was 42.0), and it indicates the Japanese characteristics that they are patient.

Conclusions: Younger patients reported less impairment of daily activities, and more concern about treatment in QOL than older patients in Japan. To younger patients, we should give enough information about the treatment to remove their concern.
Clinical correlations of cognitive impairment in chronic heart failure

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Introduction: Cognitive dysfunction is known to be more common in patients with systolic heart failure than controls. The impact of heart failure severity on cerebral function remains unknown.

Methods: Fifty-three patients with systolic heart failure were included in the study. Patients have answered the Minimental Score and were classified as having normal cognition (25–30), mild (20–24) and moderate (10–19) cognitive impairment (CI). Patients have also completed quality of life scores (Kansas City Cardiomyopathy questionnaire, Duke activity status index), and a depression score (Zung score). Clinical data (age, sex, NYHA class, six minute walk test) and left ventricular ejection fraction (LVEF) were also available.

Results: From the patients screened, only 14 (26%) had normal cognitive function, while 22 (41%) had mild and 17 (32%) had moderate CI. Cognitive dysfunction was strongly associated with sex, NYHA class and depressive symptoms. One out of 11 female vs 14 out of 42 male were classified as having moderate CI (p=0.006). Patients with normal CI had lower zung score (41±11 vs 47±11 for mild CI, vs 54±9 for moderate CI, p=0.05) and higher KCCQ-overall score (57±3 vs 37±2 for mild CI, and 31±2 for moderate CI, p=0.05). Across NYHA class deterioration, mean Minimental score decreases significantly (24±5 for NYHA I, 22±4 for NYHA II, 23±4 for NYHA III, 17±6 for NYHA IV, p=0.023). LVEF, HF cause and six minute walk test did not differ significantly among the CI subcategories.

Conclusions: Cognitive dysfunction is very common in heart failure patients, affecting moderately almost one out of three HF patients. Cognitive dysfunction deterioration along with HF deterioration and this has to be screened, especially when complex medical advice is given.

Symptom profile of hypertensive primary care patients with undiagnosed obstructive sleep apnea - a structured equation model analysis

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Background: Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder associated with hypertension (HT), increased morbidity and mortality. Difficulties to identify patients with OSA have been described in primary care, causing low referral rates to sleep clinics. The Berlin sleep apnea questionnaire (BSAQ) is a validated tool that can help to identify patients.

Aim: To describe and compare (i) cardiovascular signs and risk factors associated with high and low risk for OSA, as measured by the BSAQ, in men and women with HT, as well as (ii) to compare traditional sleep-related symptoms between high and low-risk patients of both genders.

Methods: Cross-sectional design, 480 patients mean age 57.8 yrs (±6.7 yrs; 52% women), of whom 147 had HT were included at 4 primary care centres in Sweden. Clinical examinations (performed by one nurse and one physician specialized in sleep medicine), and the BSAQ, the Minimal insomnia symptoms scale, the Epworth sleepiness scale, the Hospital anxiety and depression scale, as well as the International Physical Activity Questionnaire were used to collect data. Physical activity was measured with validated pedometers.

Results: 71% of the men and 61% of the women had high risk for OSA. 76% of the high-risk men expressed that others were bothered by their snoring compared to 63% of the women (p<0.05). Men with high risk reported that breathing pauses had been noticed more often than women (p<0.05). Men who demonstrated a high risk for OSA had more dyslipidemia (p=0.05-p<0.001), higher mean levels of P-Crea (p<0.001) and lower heredity of CVD (p<0.001) than women. These men also reported more days/week of moderate (p<0.05) and high intensity physical activity (p<0.05), but steps/day did not differ. Medication with ACE inhibitors and angiotensin receptor blockers were more common among high-risk men (p<0.001), but diuretics (p=0.001) and hypotensives (p<0.05) were more common among high-risk women. Low risk was more common among high-risk men compared to men, 42% vs. 25% and 50% (p<0.001). The mean HADS anxiety score and the number of patients above cut-off were significantly higher among women with high risk compared to men (p<0.05). Blood pressure, arhythmias or diabetes did not differ between the risk groups.

Conclusion: Knowledge about gender-specific symptoms, cardiovascular signs and risk factors associated with high OSA risk might help to identify patients in need of sleep respiratory recordings.

Is increased high-sensitive troponin T associated with severity of sleep apnoea syndrome?

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Purpose: With sleep apnoea syndrome (SAS) being a factor for cardiovascular...
morbidity and mortality, we hypothesized that severity of SAS is reflected by elevated high-sensitive troponin T (hsTnT).

Methods: Retrospective analysis of 400 consecutive sleep apnoea patients with regard to hsTnT, sleep and overnight respiratory parameters, CPR, Creatinine/GFR, NTproBNP as well as pulmonary function tests.

Results: Of 400 patients, 65 had positive hsTnT (>14ng/ml). No correlation with severity of sleep apnoea syndrome as defined by apnoea-hypopnoea-index (AHI), oxygen desaturation index (ODI) or lowest saturation during the night was found. Elevated hsTnT was associated with elevated NTproBNP. Creatinine and CPR as well as lower GFR and daytime pCO2. However, during positive airway pressure therapy (CPAP, AutoCPAP or Adaptive Servoventilation) hsTnT decreased significantly (p = 0.046). In patients with long-term follow-up (n=10) within the study period, the decrease of hsTnT was even more pronounced (p = 0.013).

Conclusions: SAS does not lead to elevated hsTnT per se, but co-morbidities as often seen with SAS are associated with positive hsTnT. Nevertheless, treatment of SAS leads to reduction of hsTnT, especially in patients with long-term treatment.

P4394 Adherence to the Mediterranean diet reduces the likelihood of acute coronary syndromes, even among people with high anxiety rates: a case-control study

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Purpose: Adherence to the Mediterranean diet has long been associated with beneficial effects regarding cardiovascular disease, while anxiety exerts the opposite effects. The aim of the present work was to evaluate the association between adherence to the Mediterranean diet and the development of acute coronary syndrome (ACS) in participants with and without symptoms of anxiety.

Methods: During 2008-2010, 500 participants were enrolled; 250 were consecutively patients with a first ACS and 250 population-based, control subjects, matched to the patients by age and sex. Socio-demographic, clinical, psychological, dietary and other lifestyle characteristics were measured. Adherence to the Mediterranean diet was assessed by the validated Mediterranean DietMedScore (theoretical range: 0-55), while trait anxiety with the Spielberger State-Trait Anxiety Inventory form Y-2 (STAI-Y2, range 20-80).

Results: After various adjustments (i.e., age, sex, physical activity, BMI, smoking, education, family history of cardiovascular disease, hypertension, hypercholesterolemia and diabetes mellitus), each 1/55 increase of the MedDietScore was associated with 8% (95%CI: 0.88-0.98) lower likelihood of ACS and each unit increase of the STAI-Y2 with 4% (95%CI: 1.01-1.07) higher likelihood of ACS. When the sample was split according to the presence of trait anxiety, each 1/55 unit increase of the MedDietScore was associated with 8% (95%CI: 0.86-0.99) lower likelihood of having an ACS in subjects with low anxiety and 9% (0.83-0.90) lower likelihood in participants with moderate or severe anxiety.

Conclusions: The protective effect of the Mediterranean diet pattern regarding ACS persisted even in subjects with trait anxiety, highlighting its beneficial role.

P4395 Evaluation of cardiovascular disease patients and healthy subjects as regards risk factors’ knowledge and beliefs

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Purpose: The aim of the present work was to evaluate the perception of the importance of several cardiovascular disease (CVD) risk factors by acute coronary syndrome (ACS) and ischemic stroke patients, as well as by healthy controls.

Methods: During 2008-2010, 1000 participants were enrolled; 250 were consecutive patients with a first ACS, 250 were consecutive patients with a first ischemic stroke and 500 population-based, control subjects, one-for-one matched to the patients by age and sex. Socio-demographic, clinical, psychological, dietary and other lifestyle characteristics were measured. Health perspectives were assessed using a scale of 1 to 9 (1: not important, 9: very important), evaluating the following factors: smoking, passive smoking, sedentary lifestyle, stress, unhealthy dietary habits, obesity, diabetes, hypercholesterolemia or hypertension, family history of CVD.

Results: The ACS patients considered the most important CVD risk factor to be stress, followed by smoking. The ACS-controls rated the most important factor to be smoking and the second one stress. The ischemic stroke patients believed the most important factor to be smoking, followed by presence of diabetes, hypercholesterolemia or hypertension. The control-stroke considered smoking as the most significant factor, followed by stress. The ACS patients, ACS-controls, and stroke-controls considered passive smoking as the least important factor. The stroke patients rated as the least important factors CVD family history and 9% (0.83-0.90) lower likelihood in participants with moderate or severe anxiety.

Conclusions: The protective effect of the Mediterranean diet pattern regarding ACS persisted even in subjects with trait anxiety, highlighting its beneficial role.

P4396 Frequency of returning to work after ST segment elevation myocardial infarction


The aim of the study was to evaluate the occupational functioning and identify the health-related determinants of successful vocational rehabilitation in workers with a recent myocardial infarction (MI).

Material and Methods: The study group consisted of patients (pts) who under- went percutaneous coronary intervention (PCI) for first acute ST-segment eleva- tion myocardial infarction (STEMI) and who were employed before MI. We ex- amined the demographic, clinical and angiographic characteristics of pts who re- turned to employment (group 1), and those who did not return to work (group 2). The subject mental health as well as quality of life and occupational functioning were assessed using the Hospital Anxiety and Depression Scale (HADS), the Brief Revised Nottingham Health Profile (NHP) scale, Beck Depression Inventory and Work Ability Index (WAI). All pts were observed during one year and cardiac events were analyzed.

Results: Among 288 pts (aged 39-64 years) 142 (53%) pts returned to work within 6 months, and 126 (47%) did not. The pts who returned to work after first MI were younger (mean age 49.2 vs 54.3 years), had higher level of education, self- rated health and quality of life than the pts who did not resume their occupational activity. In addition there was no difference in 1-year clinical events in those who returned to work and those who did not.

Conclusion: Age, sociopsychological and occupational factors have the strongest influence on the chance to return to work after myocardial infarction.
Hip fracture and risk of acute myocardial infarction: a nationwide study

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Background: Osteoporotic fractures are associated with increased mortality risk. However, few data are available on the risk of acute myocardial infarction (AMI) following hip fracture. Therefore, we investigated whether hip fracture increased the risk of AMI in a large, nationwide cohort study.

Method: We obtained data from 8,758 patients diagnosed with hip fracture from 2000 to 2009 and from 4 matched controls for each patient from the Longitudinal Health Insurance Database (LHID-2000), Taiwan. Controls were matched for age, gender, comorbid disorders, and enrollment date. All subjects were followed up from the date of enrollment until AMI, death, or the end of data collection (2009). Cox’s regression model adjusted for age, gender, comorbid disorders, and medication was used to assess independent factors determining the risk of development of AMI.

Results: A total of 8,758 subjects with hip fractures and 35,032 controls were identified. Among these patients, 1,183 (257 hip fracture patients and 926 controls) developed AMI during the median 3.2 year (interquartile range, 1.4–5.8 years) follow-up period. Patients with hip fractures had a higher incidence of AMI occurrence when compared to controls (8.71/1000 person-years versus 6.82/1000 person-years). Figure exhibits the results of the log-rank test and Kaplan-Meier survival analysis. During the maximal 10-year follow-up period, the cumulative incidence of AMI was significantly higher in patients with hip fracture than controls (P = 0.001 by log-rank test). Multivariate analysis indicated that hip fracture was associated with a greater risk for AMI development (hazard ratio: 1.29, 95% confidence interval: 1.12–1.48, P = 0.001).

Conclusions: We conclude that hip fracture is independently associated with a higher risk of subsequent AMI.

Secular trends in women with acute coronary syndrome (ACS) referred to coronary artery angiography: a 15-year observation of the University Hospital Bern

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Purpose: It is suggested that the rate of young women suffering from ACS is increasing. We therefore investigated our invasive cardiology database to assess secular trends in the incidence of first ACS and CV risk factors in women classified into different age-groups over the last 15 years (1995 to 2010).

Methods: We extracted data of all women with coronary angiography between 1995 and 2010 for a first ACS event on age, presence, classification of ACS, and cardiovascular risk factors such as smoking, arterial hypertension, diabetes mellitus, dyslipidemia, family history, and obesity. In the age groups 20-49 yrs, 50-59 yrs, 60-69 yrs, 70-79 yrs, and 80-99 yrs, we calculated numbers of first ACS per year and proportion of first ACS per year with regard to the female population (according to data from the Swiss Federal Institute of Statistics) of the referring area (Cantons of BE, SG, FR, and NE). We also calculated the proportion of women with first ACS with CV risk factors. To assess temporal trends within age groups, we performed linear regressions of absolute and relative numbers of first ACS versus time, as well as risk factors versus time.

Results: Absolute and relative time trends showed significant linear increases for all age groups for absolute as well as relative numbers of first ACS events (all p < 0.01, Figure 1). While the increase in the group of the 20-49 year old women was small in absolute and relative numbers, from 1995 to 2010 it was most 5-fold, compared to a 3- and 2-fold increase in the 50-59 yrs and 60-69 yrs age groups, respectively. The increase between 1995 and 2000 in the older age groups was most probably influenced by a change in indication with the advent of PCI. Temporal trends with regard to risk factors showed a significant increase in smoking and obesity in the 60-69 yrs age group.

Conclusions: Our results confirm that there was a small but significant increase of ACS in 20-49 year-old women which, relative to the incidence in 1995, was considerably greater than the increase in the 50-59 yrs and 60-69 yrs age groups. Increases in first ACS in the 60-69 year old women may have been linked to increased prevalence of smoking and obesity.

Physical activity attenuates subclinical atherosclerosis in subjects with chronic spinal cord injury

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Purpose: Cardiovascular diseases are the major cause of death in subjects with chronic spinal cord injury (SCI). Interestingly, SCI subjects present higher carotid intima-media thickness (IMT) than able-bodied individuals, independent of traditional cardiovascular risk factors. The present study investigated the effect of regular physical activity on carotid IMT in men with chronic (> 1 year of injury) SCI.

Methods: We studied 43 SCI men with no voluntary motor activity (30 sedentary, 40% hypertensive; 13 athletes (69% hypertensive) and 24 able-bodied men by clinical, anthropometric, laboratory, blood pressure and ultrasound carotid analysis. All enrolled subjects were normotensive, non-diabetics, non-smokers and non-obese. The studied groups presented similar age, body mass index and body mass index. Data were evaluated by chi-square analysis, Wilcoxon test, 1-way ANOVA followed by Tukey test and coxan analysis and are presented as mean±standard error. A p-value of less than 0.05 was considered significant.

Results: Carotid IMT in SCI athletes (0.63±0.03 mm) was lower than that of SCI sedentary individuals (0.70±0.02 mm; p=0.008), but higher than that of able-bodied subjects (0.49±0.02 mm; p=0.001). SCI athletes still presented lower triglycerides (0.52±1.54 vs. 0.47±1.33 mmol/L, p=0.017) and C-reactive protein (0.49±0.28 vs. 1.17±0.39 mg/dl; p=0.037) levels in comparison to SCI sedentary individuals. Conversely, all other studied variables were similar between the SCI groups. In addition, covariance analysis adjusted by carotid IMT and C-reactive protein levels revealed that carotid IMT was significantly lower in SCI athletes in comparison to SCI sedentary individuals (p=0.009).

Conclusions: Regular physical activity is associated with attenuation of subclinical atherosclerosis in subjects with SCI, independent of hemodynamic, metabolic and inflammatory factors.

Vitamin D deficiency in relation to circulating inflammatory cells and inflammatory markers among apparently healthy individuals

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Purpose: Vitamin D (ViD) insufficiency is widespread all over the world. It is also known that insufficient 25(OH)D3 (vitamin D3) alters metabolite function, that has been related with the development of various clinical disorders [i.e., osteoporosis, diabetes, cardiovascular disease (CVD)]. This study aimed to evaluate the relationship between ViD deficiency and inflammatory cells and markers among apparently healthy adults.

Methods: During 2009, 490 volunteers (46±16 years, 40% male) were consecutively enrolled to the study (participation rate 85%). Biochemical analyses were performed through established procedures, after 12h fasting, and ViD (ng/mL), high-sensitive C-reactive protein (CRP, mg/dL), cytokine C (GycC, mg/L), haptoglobin (Hp, mg/dL) and vitamin D (25(OH)D3, ng/mL) were measured. Anthropometric characteristics were also recorded to account for potential confounders. Participants were classified in ViD sufficiency (i.e., ≥ 30 ng/mL) and ViD insufficiency (i.e., < 30 ng/mL). Logistic regression models were used to evaluate the association of inflammation cells and biomarkers to the likelihood of having ViD insufficiency.

Results: Among participants, 25% were ViD sufficient. Participants with ViD insufficiency had higher values of CRP, GycC and Hp as compared with those with ViD sufficiency (all p’s < 0.05). Logistic regression models, adjusted for age, sex, smoking exposure, family status, physical activity, body mass index and smoking, revealed a positive association between ViD insufficiency and CRP and a negative association with Hp. In particular, 1 mg/dL increase of CRP increase the odds of having ViD insufficiency 3.7 times (95% CI: 1.16-12.0). On the contrary, for every 1 g/dL increase of Hp, the odds of having ViD insufficiency decrease 27% (OR=0.73, 95% CI: 0.57-0.93).

Conclusion: The involvement of ViD in the homeostasis of CVD has been recently evaluated. Results showed that ViD deficiency is a significant risk factor
for the development of atherosclerosis, as it has been related with inflammation markers. Therefore, optimizing VD intake may serve as a potentially effective strategy in CVD prevention.

**P4402 Genetic predisposition to higher blood pressure increases coronary artery disease risk**

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Hypertension is a risk factor for coronary artery disease (CAD). Recent genome-wide association studies (GWAS) have identified 32 single nucleotide polymorphisms (SNPs) associated with higher blood pressure (BP) at genome-wide significance (p<5x10^-8). If elevated blood pressure is a causative factor for CAD, these variants should also increase CAD risk. Analyzing GWAS data from 22,233 CAD cases and 59,405 controls included in the CARDIOGRAM consortium that 88% of these BP-associated SNPs were likewise positively associated with CAD, i.e. they had an odds ratio for CAD ≈ 1, a proportion much higher than expected by chance (p<10^-10). The average relative CAD risk increase per each of the multiple BP-raising alleles observed in CARDIOGRAM was 3.0% for SBP-SNPs (95% confidence interval (CI), 1.8 to 4.3%) and 2.9% for DBP-SNPs (95% CI, 1.7 to 4.1%). In sub-studies, individuals carrying most SBP- and DBP-related risk alleles (lop quinile of a genetic risk score distribution) had 70% (95% CI, 50-94%) and 59% (95% CI, 40-81%) higher odds of having CAD, respectively, as compared to individuals in the bottom quintile. In conclusion, most BP-associated SNPs also confer an increased risk for CAD. These findings are consistent with a causal relationship of increasing BP to CAD. SNPs primarily affecting blood pressure contribute to the genetic basis of CAD.

**P4403 Mitochondrial haplogroups H and J: risk and protective factors for ischemic cardiomyopathy**

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**Purpose:** As mitochondria are the principal source of reactive oxygen species (ROS), these organelles may play an important role in ischämiecardiomyopathy (ICM) development. The mitochondrial genome may influence this disease. The aim of the present study was to test the relationship between IC development and the impact of single-nucleotide polymorphisms (SNPs) in mitochondrial DNA (mtDNA) defining the mitochondrial haplogroups in a population study.

**Methods:** The study complied with the Declaration of Helsinki. DNA samples from 731 unrelated individuals (380 healthy controls and 351 IC patients) were analysed in this study. Haplogroup analysis for the ten major European haplogroups was performed by using the single base extension technique and by polymerase chain reaction-restriction fragment length polymorphism. Frequencies and Odds Ratios for the association between IC patients (n=351) and healthy controls (n=380) were calculated.

**Results:** Compared to healthy controls, the prevalence of haplogroup H was significantly higher in IC patients (40.0% vs 50.4%, p-value=0.005) while the frequency of haplogroup J was significantly lower (10.8% vs 5.7%, p-value=0.015). The haplogroup frequencies for our controls did not differ substantially from those reported in previous studies that analyzed different European populations. The mitochondrial haplogroups distribution between cases and controls, stratified by the major risk factors of ICM (hypertension, diabetes and smoking, and history of myocardial infarction), was similar in both groups. The analysis of the SNPs characterizing the European mtDNA haplogroups showed that the SNP m.10398A>G, which produces a non synonymous amino acid change in NADH dehydrogenase subunit 3 (threonine>alanine), was found to be a protective factor (p-value=0.026).

**Conclusion:** Our results showed suggestive evidence for the association of the mitochondrial haplogroups H and J as risk and protective factors respectively for ischemic cardiomyopathy. Future analysis of the full sequenced mtDNA in these haplogroups and their phenotypic analysis will yield additional insights towards therapeutic targets for ischemic cardiomyopathy pathogenesis.

**P4404 Prediction of ischemic events based on transcriptomic and genomic profiling in patients undergoing carotid endarterectomy**

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**Classical risk factors, including age, smoking, serum cholesterol, diabetes and blood pressure constitute the basis of present risk prediction models, but fail to identify all individuals at risk. The objective of this study was to investigate if genomic and transcriptional patterns improves prediction of ischemic events in patients undergoing carotid endarterectomy.**

Patients were followed for an average of 44 months and 25 ischemic events (18 ischemic strokes and 7 myocardial infarctions) occurred. Blinded leave-one-out cross-validation on Cox regression coefficients was used to assign gene expression based risk scores to each patient. When compared to classical risk factors, addition of gene expression based risk score improved the prediction of future ischemic events from an area under curve (AUC) of 0.66 to an AUC of 0.79. The inclusion of gene expression risk score from peripheral blood mononuclear cells or from 25 established myocardial infarction SNPs alone exhibited marginal effects on the prediction of ischemic events. Prediction of ischemic events is improved by inclusion of gene expression profiling from carotid endarterectomy tissue. These findings alone open the door for individually tailored risk stratification also in patients with atherosclerosis. The method may be developed to identify subjects at very high risk of ischemic events.

**P4405 Genetic variants primarily associated with type 2 diabetes also affect coronary artery disease risk**

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Multiple single nucleotide polymorphisms (SNPs) have been identified to associate with type 2 diabetes (T2DM). If T2DM is a causative risk factor for coronary artery disease (CAD), SNPs increasing T2DM risk should also increase CAD risk. We studied 29 common genetic variants previously associated with T2DM at a genomewide significant level (p<5x10^-8) in CARDIOGRAM, a genomewide data set derived from 22,233 CAD cases and 59,405 controls. Significant associations between T2DM SNPs than expected by chance displayed an odds ratio for CAD >1 (20 out of 29, p<0.031). In fact, 10 T2DM SNPs were nominally significantly (p<0.05) associated with CAD in CARDIOGRAM, a proportion much higher than expected by chance. The average increase in CAD risk observed per individual T2DM risk allele was 1.27% (95% confidence interval (CI), 0.26-3.20%). Studying a weighted genetic risk score in a subgroup of 4500 cases and 5868 controls revealed that individuals in the highest quintile had an 18% higher risk (CI 4.3-4.4%) of CAD as compared to individuals in the bottom quintile of the genetic risk score. Our data indicate that multiple genetic variants associated with T2DM confer a small risk increase for CAD, strengthening the evidence that T2DM may be a causal risk factor for CAD.

**P4406 Impact of arterial stiffness on adverse cardiovascular outcomes and mortality in peritoneal dialysis patients**

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Cardiovascular (CV) disease is a major cause of morbidity and mortality in patients with end-stage renal disease. In recent years, arterial stiffness has taken on great importance in the pathophysiology of CV diseases. The independent predictive value of arterial stiffness for CV events and for all-cause and CV mortality has been demonstrated in the general population and in hemodialysis patients. Our aim in this study was to determine the relationship of arterial stiffness with mortality and fatal and nonfatal CV events in peritoneal dialysis (PD) patients.

**Methods:** In this prospective observational cohort study with 2 years of follow-up, we studied a cohort of 156 PD patients with a mean follow-up of 19.2±6.4 months.
Cardiovascular disease incidence and compliance on treatment strategy in patients with familial hypercholesterolemia

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Introduction: Familial hypercholesterolemics patients are considered high risk patients. Aim: To evaluate the cardiovascular disease incidence and compliance on treatment strategy in patients with familial hypercholesterolemia. Methods: We enrolled 443 consecutive patients, clinically diagnosed with heterozygous familial hypercholesterolemia (172 men), of mean age 40.48±15 years. We measured their biochemical parameters and lipid profile before and after initiation of lipid lowering therapy. We also recorded all major cardiovascular disease events during their follow-up period. Results: Mean period of follow-up was 8 years. 26.6% of the population showed poor compliance to drug therapy. The overall cardiovascular events incidence was 8% (35 events). 16 events occurred on those who showed the poorest compliance on drug therapy and 19 events on those who followed the prescribed instructions (13.5% vs 5.8%, p=0.001). Multi-linear regression showed that increasing age, the cardiovascular events decrease by 1.33%, independently of age, sex, body mass index, arterial hypertension, smoking habits, total and LDL cholesterol levels, previous history of cardiovascular events and compliance to drug therapy. Conclusion: A considerable percentage of heterozygous FH patients show poor compliance to treatment strategy and this finding consists independent prognostic factor of major cardiovascular events.

Association of male pattern baldness with angiographic coronary artery disease severity and collateral development

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Purpose: Although several epidemiological studies have shown an association between male pattern baldness and atherosclerosis, it has never been studied by investigating angiographic presence and severity of coronary artery disease. We aimed to investigate whether there is an association between male pattern baldness and angiographic coronary artery disease severity and collateral development. Methods: Angiographic, coronary artery disease risk factors, lipid parameters, and presence and severity of baldness of 470 male patients were prospectively evaluated. Baldness were defined as five groups (no hair loss, frontal baldness only, frontal baldness with mild, moderate, or severe vertex baldness). Severity of coronary artery disease was evaluated with Gensini and collateral development with Rentrop scores. Results: Although subjects with higher Gensini score had more frequent and severe baldness, they were older than the group with lower Gensini score (60.3±11.7 vs. 56.0±11.7, p=0.001). Bald patients had higher Gensini score when compared with their non-bald counterparts (44.7±14.3 vs. 34.1±13.6, p=0.009). In univariate analysis baldness, smoking and age more than 55 were predictors of a Gensini score more than 20. In multivariate analysis, only age more than 55 (p=0.005, odds ratio: 1.738, 95% confidence interval:1.180-2.561) and smoking (p=0.002, odds ratio: 1.895, 95% confidence interval:1.265-2.843) were independent predictors of a Gensini score more than 20. There were no differences in terms of presence and severity of baldness in subjects with and without adequate collateral development. Conclusion: There was not any relation between presence, severity and age of occurrence of male pattern baldness and Gensini and Rentrop scores which are important markers of presence and severity of coronary artery disease. The potential interaction of male pattern baldness with coronary artery disease needs to be clarified with prospective large scale studies.

Risk factors for coronary plaque progression in patients with far east Asians - A serial volumetric IVUS analysis


Backgrounds: Far East Asians have been reported to be at lower risk of cardiovascular events than Westerners, suggesting the potential racial difference in plaque progression and atherosclerosis. However, few data exist comparing cardiovascular risk factors with volumetric IVUS measurements of coronary plaque progression in Asians.

Methods: Serial volumetric IVUS examinations (baseline and 14-months follow-up, mean measured length; 43mm) were performed for 297 Far East Asian patients with stable angina pectoris. Patients were subsequently treated with a combination of angiotension-II receptor blocking agents (ARBs), β-blockers, calcium channel blockers, glycoprotein control agents and/or statins per physician’s guidance. Serial progression rate of atherosclerosis was compared with the patients’ characteristics during the follow-up periods.

Results: In multiple linear and logistic regression test, age > 65 years, diabetes, and male gender remained as predictors of increased plaque volume by serial IVUS. On the other hand, the use of statins and ARBs were identified as factors associated with decreased plaque volume.

Conclusion: Advanced age, poorly controlled diabetes and male appear to be predictors of atherosclerotic progression in Far East Asians. Statins and angiotension-II receptor blocking agents may play a positive role in potential plaque regression of coronary arteries in this population.

Acute coronary syndrome: a serious threat even at age 40


Purpose: Nowadays, acute coronary syndromes (ACS) are affecting a growing number of young individuals. Are ACS in this population a different entity? Our aim was to assess the prevalence, risk profile, therapeutic approach and outcomes of ACS in a population below 40 years old.

Population and Methods: We studied 4300 patients admitted at a single coronary care unit with ACS, between May 2004 and November 2011. Two groups were considered: A - patients no older than 40 years (n=54, 2.2%), group B - patients above 40 (n=4206).

Results: Compared regarding demographic data, cardiovascular risk factors, lab results, treatment, angiographic findings and prognosis. The median follow-up was 2361 days.

Results: Group A had a mean age of 36.6±3.1 years and included more males (77.7% vs. 68.2%, p<0.05), smokers (59.6% vs. 14.4%, p<0.001) and patients with previous family history of coronary heart disease (25.5% vs. 10.7%, p=0.001), but less with hypertension (40.4% vs. 77.6%, p<0.001), type 2 diabetes (19.1% vs. 34.1%, p=0.002) and dyslipidemia (68.1% vs. 80.2%, p=0.004). Group A was more frequently admitted with ST elevation ACS (51.1% vs. 33.4%, p=0.001). Considering laboratory data on admission, group A had lower creatinine (0.9±0.2 mg/dL vs. 1.2±0.9 mg/dL, p=0.004), but higher hemoglobin (14.7±1.2 g/dL vs. 13.4±1.8 g/dL, p=0.001) and platelet count (259.7±78.6 vs. 224.0±70.3 x 103, p<0.001). Blood glucose and lipid profile were not statically different. Regarding baseline therapy, group A received more GpIIb/IIIa inhibitors (48.9% vs. 30.1%, p<0.001) and less diuretics (10.6% vs. 23.7%, p<0.001). Left ventricular ejection fraction was significantly higher in this group (54.8±11.2% vs. 51.1±11.6%, p=0.007). Group A was also submitted more often to an invasive strategy (80.9% vs. 61.5%, p<0.001) and had a higher prevalence of normal coronary arteries (26.3% vs. 16.5%, p=0.024) and one vessel disease (48.7% vs. 38.3%, p=0.026). The in-hospital mortality was significantly lower for group A (0.0% vs. 5.4%, p=0.020). During the follow up, this group had a trend towards lower mortality rate (6.0% vs. 11.2%, p=0.164).

Conclusion: Younger ACS patients have a particular risk profile, and by being more aggressively treated, are associated with a better short term prognosis.
RENAL DENERVATION THERAPY IN HYPERTENSION

P4411 One year pooled outcomes following renal sympathetic denervation in patients with resistant hypertension: From the Symplicity HTN-2 trial

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Purpose: Renal sympathetic nerve activation plays an important role in the pathogenesis of essential hypertension and selective ablation of the sympathetic nerves through the renal arteries can substantially reduce blood pressure (BP) in patients with treatment-resistant hypertension. The duration of antihypertensive effect and long-term safety of renal denervation (RDN) requires further follow-up.

Methods: This prospective, multicentre, randomised trial evaluated the safety and effectiveness of RDN in patients with an office systolic BP of ≥160 mm Hg while taking ≥3 antihypertensive medications. The control group was managed with medication alone and 6 months after randomization were offered RDN treatment if eligibility was met. Data from all patients receiving RDN was pooled and change in BP at 6 and 12 months, pulse pressure, heart rate, and adverse events were analyzed.

Results: There were 89 patients treated with RDN. At 12 months post-procedure, data are available for 47 patients randomized to immediate RDN and 33 crossover patients. The mean age of patients treated was 58.6 years, 44% were female, mean body mass index was 31.1 kg/m², and mean heart rate at baseline was 73.7 bpm. Approximately one-third of patients had type 2 diabetes. There was one renal artery dissection. No other serious adverse events occurred.

Conclusions: One-year pooled outcomes following renal sympathetic denervation in patients with resistant hypertension were analyzed. Systolic BP change – 12 months post-procedure – 26.3 ± 16.0 mmHg, diastolic BP change – 12 months post-procedure – 11.6 ± 10.4 mmHg, and pulse pressure – 12 months post-procedure – 16.0 ± 25.2 mmHg were observed.

P4412 Percutaneous renal sympathetic denervation exerts a chronic effect on renal hemodynamics using a novel catheter for radiofrequency ablation: data from an animal study

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Purpose: To examine whether renal sympathetic denervation, performed using a novel radiofrequency ablation catheter, exerts a chronic (1 month post ablation) effect on renal hemodynamics assessed by average peak velocity (APV), renal flow reserve (RFR), and resistive index (RI).

Method: In 9 anaesthetized female juvenile farm swines (mean age 6 months, mean weight 34.5 kg), a 0.014 inch Doppler flow wire was introduced in the renal artery for the measurement of the APV under baseline and hyperemic condition that was induced by the bolus intravenous administration of dopamine (50 μg/kg). RFR was calculated as the ratio of hyperemic to basal peak velocity. RI was estimated (peak systolic velocity – end-diastolic velocity)/peak systolic velocity. APV, RFR, and RI were measured before and 1 month after renal sympathetic denervation. The sympathetic denervation was achieved via the lumen of the main renal artery with the novel catheter connected to a radiofrequency generator from ST. Jude Medical according to pre-specified algorithm.

Results: In all animals, APV 1 month after ablation compared to APV before ablation was significantly higher (10.61 ± 9.67 vs 2.50 mm HG; p < 0.001). Moreover, radiofrequency ablation resulted in reduced RFR (1.36 ± 0.25 vs 2.96 ± 1.33, p < 0.001) and RI (0.48 ± 0.15 vs 0.74 ± 0.07, p = 0.003), while no significant changes in the diameter of the renal artery was observed after dopamine administration (p = NS).

P4413 Renal sympathetic denervation - inducing an immediate and persisting blood pressure lowering effect

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Purpose: Renal sympathetic denervation (RDN) has shown to significantly reduce blood pressure (BP) in patients with severe hypertension. According to the Symplicity HTN-1 and -2 trials it is known that the blood pressure lowering effect will take about 1 to 6 months to develop. We studied our carefully investigated early and subsequent blood pressure response to RDN in a cohort of patients with resistant hypertension.

Methods and Results: Our study enrolled 61 consecutive patients (mean age 64.4 ± 9 years, 48.9% women). Baseline values included a mean of 5.8 ± 1.4 antihypertensive medications. A 24h Holter BP monitoring was recorded in every patient 24h before as well as 24h, 3 and 6 months after RDN. BP readings were then averaged according to daytime (7:00am-22:59pm), night (22:00pm-7:00am) and 24 hours intervals. In treated patients mean averaged systolic BP was reduced by 14.3 ± 2.3 mmHg (p < 0.001) during the first 24 hours. Systolic blood pressure reduction appeared to be much higher at daytime (16.2 ± 2.50 mmHg; p < 0.001) compared to night (10.61 ± 2.47 mmHg; p < 0.001) which might indicate the role of sympathetic activity at daytime. A concordant effect on diastolic BP was observed: 6.9 ± 1.7 mmHg (p < 0.001). Systolic BP reduction sustained at 3 (11.7 ± 3.2 mm Hg; p < 0.001) and 6 months (9.3 ± 3.3 mm Hg; p = 0.009) without further decrease – on the contrary a relapse to higher BP was seen.

Conclusion: Catheter-based renal sympathetic denervation augmented APV and decreased RFR and RI, persistently and significantly at 1 month post ablation in healthy swines. These results support the chronic effect of renal artery denervation by the radiofrequency ablation catheters on renal hemodynamic function even in a healthy animal setting.

P4414 Renal denervation for resistant hypertension: real world outcomes

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Purpose: Arterial hypertension is the largest single contributor to global mortal-
Renal sympathetic denervation with brachytherapy using beta-radiation catheter. Results from a feasibility and safety preclinical study

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Background: Renal sympathetic denervation using intravascular radiofrequency ablation has demonstrated significant reduction in systolic and diastolic blood pressure in clinical trials. Local radiation therapy demonstrated the ability to damage the nervous system and is currently used for the treatment of trigeminal neuralgia. This study aimed to assess feasibility and safety of a novel approach for RSD using a clinically available beta-radiation catheter beta-cath™.

Methods: Ten naive Yorkshire swine underwent intravascular brachytherapy using a β-emitting radiation source. Dosages of 25 or 50 Gy was delivered in the proximal renal artery. Animals were followed up to 1- or 2-months and were assessed by angiography, IVUS and histology. Norepinephrine levels were measured in the renal artery and in the renal tissue of the innervated kidneys.

Results: Renal artery intravascular brachytherapy was performed without any procedural complications. No thrombus formed on the catheter and no acute vessel injury was noted by angiography. All animals survived to the predetermined follow up. At 1- and 2-month follow up there was no vascular injury as documented by angiography. IVUS (Figure 1A) and histology studies showed focal hypocellular fascicles with cellular degeneration and some cells having vacuolated cytoplasm as well as mild perineural inflammation with and without fibrosis (Figure 1B). Norepinephrine levels will be available at presentation.

Figure 1

Conclusions: Vascular brachytherapy using the beta-cath™ system in the renal artery in the porcine model is feasible and safe with evidence of sparing damage to the nerve and safety vascular parameters even at high dose of radiation. The results of this study supports clinical evaluation of brachytherapy for the treatment of resistant hypertension.

Effect of renal sympathetic denervation on blood pressure and renal perfusion in a pig model for obstructive sleep apnea

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Objective: Obstructive sleep apnea (OSA) is associated with resistant hypertension and a progression of chronic kidney disease (CKD). Renal sympathetic innervation may contribute to either condition. We investigated the effect of renal sympathetic denervation (RDN) on blood pressure (BP), renal perfusion and neurohumoral responses during and after repetitive obstructive apneas.

Methods: Blood pressure, femoral artery and renal artery flow were measured in 22 spontaneously breathing urethane-chloralose anaesthetised pigs. In 12 pigs, the effect of RDN was investigated. Repetitive tracheal occlusions for 2 min with applied neglable tracheal pressure at ~80 mbar were performed over 3 hours.

Results: Spontaneous breathing attempts during tracheal occlusion caused a strongly intraapneic oscillating pattern of renal perfusion. Renal flow oscillations were more than twofold stronger with a gain between BP and renal flow of 2.9%/mmHg compared with femoral flow that almost showed changes proportional to the BP-alterations (1.3%/mmHg; p<0.0001). Marked postapneic hemodynamic changes – a rise in BP from 120.3 ± 17.2 to 172.8±22.0 mmHg (p<0.00001) together with renal hyperperfusion falling from 190 ± 24 to 105±22 mmHg (p<0.0001) - occurred after application of tracheal occlusion. Renal sympathetic denervation inhibited postapneic BP rises and renal hyperperfusion and attenuated increased plasma renin activity and aldosterone concentration induced by repetitive tracheal occlusions. Additionally, increased urinary protein/creatinine-ratio was significantly reduced by RDN while intraapneic hemodynamic changes were not significantly modified by RDN.

Conclusion: Renal sympathetic denervation inhibits postapneic BP-rises and renal hyperperfusion and attenuates neurohumoral responses and increased protein/creatinine-ratio induced by repetitive obstructive apneas. RDN may therefore provide protection in patients with obstructive sleep apnea, hypertension and renal dysfunction.

Percutaneous renal denervation (PRD) improves central hemodynamics and arterial stiffness - a pilot study

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Background: Percutaneous renal denervation (PRD) is a novel treatment strategy for patients with resistant arterial hypertension. Since central aortic pressures and arterial stiffness are better predictors for future cardiovascular events than peripheral pressures the present study aimed at measuring central pressures and aortic stiffness parameters in patients undergoing PRD.

Methods: 27 patients (18-82 years, mean age 63.0 years) with an office systolic blood pressure of more than 150 mmHg were included. PRD was performed with an PRD radiofrequency ablation catheter system. Central aortic pressure and aortic stiffness was calculated with an oscilometric blood pressure meter.

Results: 21 patients [5±1.3 antihypertensive drugs] were randomized to PRD. Dosages of 43±2 served as control therapy. The systolic blood pressure (SBP) declined significantly in the therapy group after three [156±13 vs. 145±13 mmHg; p<0.05] and six months [156±13 vs. 148±17 mmHg; p<0.05]. Likewise, central systolic blood pressure [161±17 vs. 147±18 mmHg; p<0.01; six month: 161±17 vs. 151±22 mmHg; p<0.05] and pulse wave velocity (PWV) improved significantly [three month: 10.9±1.8 vs. 9.4±1.2 m/s; p<0.01; six month: 10.9±1.8 vs. 9.7±1.8 m/s; p<0.01]. Values did not change significantly in the control group. Univariate analysis of variance (F-test) showed a mean arterial pressure (MAP) independent improvement of PWV in the treatment group.

Conclusion: PRD significantly reduced central aortic pressures and aortic stiffness. Effects on PWV are only partially dependent on blood pressure changes. Thus, PRD may improve cardiovascular outcome beyond blood pressure effects in patients suffering from resistant arterial hypertension.

Age-dependent effects of renal denervation therapy on diastolic blood pressure and pulse pressure

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The hallmark of hypertension in the elderly is a progressive vascular dysfunction. Aging is per se associated with the deterioration in arterial compliance through both structural and functional changes in large arteries. The role of sympathetic nervous dysfunction in a larger proportion of older patients with systolic hypertension is unknown. Renal sympathetic denervation (RDN) via a percutaneous radiofrequency catheter based approach lowers blood pressure (BP) in patients with resistant hypertension. However, the effect of RDN in young vs. elderly patients had never been studied. 24 Patients were selected according to the SIM-
Renal denervation therapy in hypertension / Renin–angiotensin–aldosterone system in hypertension

P4419

Pleiotropic role of angiotensin-converting-enzyme inhibitors on bone remodeling biomarkers in hypertensive subjects

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Objectives: In addition to their well-established efficacy in lowering blood pressure, angiotensin-converting-enzyme inhibitors (ACE-I) have been shown to have an impact on reducing the risk of death, myocardial infarction, stroke and renal complications in patients with coronary artery disease (CAD). Some evidence suggests that high blood pressure is associated with abnormalities of calcium metabolism, leading to an increase in calcium loss and elevation of bone remodeling biomarkers: osteoprotegerin (OPN) and osteopontin (OPG), both in CAD patients and asymptomatic subjects. In our study, we analyzed the role of antihypertensive therapy on OPN and OPG in subjects without a history of CAD.

Methods: We recruited 350 subjects using a population-based approach by stratified randomization with general practitioners. Subjects (n=267) were considered to have hypertension because they were taking antihypertensive agents or had a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Antihypertensive drugs were used in 246 patients as a monotherapy (n=113) or in combination with two (n=95) or three (n=32) drugs. Remaining hypertensive patients (n=47) had masked (or uncontrolled) hypertension. Biochemical parameters were assessed by routine laboratory techniques. Bone remodeling biomarkers were analyzed by commercially available immunoenzymatic assays.

Results: Among analyzed subjects n=287 had defined hypertension, and n=240 of them were treated with antihypertensive drugs. We observed that both OPG and OPG levels were higher in hypertensive subjects in comparison to normoten- sive ones: 3.49±:1.85 vs. 2.83±:1.32 pmol/L (p=0.007) and 88.68±:95.85 vs. 56.58±:69.04 ng/mL (p=0.012). Additional analysis of antihypertensive treatment showed that there was no significant difference in OPG and OPG levels between treated and not-treated hypertensive subjects. However, the patients stratification according to the used antihypertensive drugs revealed that treatment with ACE-I alone significantly reduced OPG levels in comparison to patients treated with other hypertensive drugs: 79.40±:88.72 vs. 139.29±:124.48 ng/mL (p=0.013), or those treated with ACE-I in combination with one another drug: 73.8±:64.21 vs. 106.7±:81.15 (p=0.018). OPG levels were predicted in hypertensive subjects by diabetes and ACE-I treatment, but not by age or body mass index: (p=0.17 (p=0.005) and (p=0.14 (p=0.017), respectively.

Conclusions: Angiotensin blockade inhibits OPN expression in hypertensive asymptomatic subjects, but this mechanism does not involve OPG axis. Combination therapy does not impair the effect of ACE-I on OPN levels.

P4420

The Effect of sRAGE in inhibiting Angiotensin II Mediated Atherosclerosis in Apolipoprotein E deficient mice

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Background: The activation of the renin-angiotensin system (RAS) signaling is a contributing factor for the development of atherosclerosis. Previous studies have shown that activation RAS is associated with increased expression of the Receptor for Advanced Glycation Endproducts (RAGE) at the site of vascular inflammation. The cross talk between RAGE and angiotensin II (AngII) activation may be important in the development of atherosclerosis. Soluble RAGE (sRAGE), a truncated soluble form of the receptor, acts as a decoy and prevents the inflammatory response mediated by RAGE activation. In this study, we sought to determine the effect of sRAGE in inhibiting AngII induced atherosclerosis in apolipoprotein E knockout mice.

Methods and Results: 9 week old ApoE KO mice were infused subcutaneously with AngII (1ug/mg/kg) and saline for 4 weeks using osmotic mini-pumps. The mice were divided into 4 groups. Mice infused with saline group, mice infused with AngII group, mice infused with saline and sRAGE IP injection for 4 weeks. Mice infused with AngII group, mice infused with saline and sRAGE IP injection for 4 weeks. The concentration of sRAGE was varied from 0.5ug, 1ug, 2ug/gly for each group to determine the dose response. We show that atherosclerosis in the AngII infused ApoE KO mice was increased by over 2.5-fold compared to the ApoE KO mice. The treatment of 0.5ug, 1 ug sRAGE in AngII group resulted in the decrease in atheroma plaque area by 35%. In addition, the treatment with 2 ug of sRAGE resulted in 70% decrease in atheroma plaque area in the AngII group.

Conclusion: The results prove that blockade of RAGE activation by sRAGE prevent AngII- induced atherosclerosis. The results from this study suggest that first, RAGE activation is a strong predictor of atherogenesis and cardiovascular events, RDN might be effective independently of age.

P4421

Effect of valsartan or ramipril addition to amiodipine/hydrochlorothiazide combination on left ventricular hypertrophy in hypertensive patients with type 2 diabetes

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Objective: To compare the effect of valsartan (Val) or ramipril (Ram) addition to amiodipine (Ami)/hydrochlorothiazide(HCTZ) combination on left ventricular (LV) mass in type 2 diabetic hypertensive patients with LV hypertrophy.

Design and Method: A total of 180 insulin resistant diabetic hypertensive outpatients with well controlled type 2 diabetes and LV hypertrophy after a 2 week placebo period were treated with Ami 10 mg/HCTZ 12.5 mg for 4 weeks: the 154 patients whose blood pressure BP was not normalized by the dual combination (SBP > 130 mmHg and/or DBP > 80 mmHg) were enrolled in the study and randomized to the addition of valsartan 320 mg or ramipril 10 mg for 12 months. At the third month the non responder patients were discontinued. A total of 142 patients completed the study. Echocardiographic evaluation was performed at the end of the placebo period, of the amiodipine/HCTZ period and after 12 month of combined treatment.

Results: Systolic and diastolic BP were similarly and significantly reduced in both treatment groups (-9.2±:4.4/ 1.85±:2.83 in the Ami group; -9.1±:5.9/-7.5±:3.8 in the ramipril group; all p<0.01 vs Ami/HCTZ combination). LV mass index was reduced significantly in this study (9.4±:6.8 g/m² in the amiodipine group and -7.1±:3.1 g/m² in the ramipril group; p<0.001 vs amiodipine/HCTZ combination). However the reduction was significantly greater with val- sartan than with ramipril (p<0.01). Safety and tolerability were similar across both treatment groups.

Conclusions: Val/HCTZ combination was effective in promoting LV mass regression and such regression was significantly greater than that observed with Ram/Ami/HCTZ, independent of BP lowering. This finding suggests that valsartan is more effective than ramipril in attenuating this measure of myocardial damage in diabetic hypertensive patients with LV hypertrophy.

P4422

Cardioprotective effect by BAY 94-8862, a novel non-steroidal minocorticoid receptor antagonist in a preclinical model of hypertension and diastolic heart failure

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Purpose: High aldosterone levels especially in combination with increased salt intake inappropriately activate the mineralocorticoid receptor (MR). Blockade of the mineralocorticoid receptor (MR) has been shown to be an invaluable therapy in heart failure. Renal impairment is an important co-morbidity of heart failure and application of available steroidal MR antagonists to this group of patients is limited. We aimed to investigate the efficacy of a novel non-steroidal MR antagonist, BAY 94-8862 vs. the steroidal MR antagonist eplerenone in a preclinical model of salt-dependent hypertension and diastolic heart failure.

Methods: Un nephrectomized male SD rats were given 1% NaCl in drinking wa- ter and subcutaneous injections of deoxycorticosterone acetate (DOCA, 30 mg/kg

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Mean ± SEM; p<0.05 vs. baseline, *p<0.05 vs. younger patients. SBP = systolic BP; DBP = diastolic BP; PP = pulse pressure.

<table>
<thead>
<tr>
<th>Age ≤ 65 years (n=11)</th>
<th>Age &gt; 65 years (n=12)</th>
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<tbody>
<tr>
<td>SBP</td>
<td>DBP</td>
</tr>
<tr>
<td>144 before RND</td>
<td>163±:3</td>
</tr>
<tr>
<td>Baseline</td>
<td>162±:3</td>
</tr>
<tr>
<td>1 month</td>
<td>153±:6</td>
</tr>
<tr>
<td>3 month</td>
<td>148±:7</td>
</tr>
<tr>
<td>6 month</td>
<td>142±:3</td>
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Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/655/430798 by guest on 07 February 2019
once weekly) for 10 weeks. The animals were treated with vehicle or three doses of BAY 94-8862 (0.1, 1 and 10 mg/kg/day) and two doses of eplerenone (30 and 100 mg/kg/day) by oral gavage (n=7-12/group). Systolic blood pressure was measured by the tail cuff method during the treatment period of the study. At the end of the experiment, hemodynamic function was measured in the left ventricle by a Millar-Tip (SF) catheter. Plasma samples were taken for subsequent analysis. Organ weights were determined and tissue samples were harvested for histological characterization and gene expression profiling.

**Results:** BAY 94-8862 significantly (p<0.05) decreased cardiac and renal hypertrophy and expression of several renal profibrotic and remodeling biomarker genes (PAI-1, MCP-1, osteopontin, MMP-2) and expression of several renal profibrotic and remodeling biomarker genes (PAI-1, MCP-1, osteopontin, MMP-2) vs. placebo at a dose which induced 1 mmHg reduction in blood pressure (BP). This blood pressure fall was not significant in the LSP group (n=6145) (n=1621) (n=1364).

**Background and aims:** Adiponectin and Retinol-Binding Protein 4 is secreted by adipose tissue and may play a role in cardiovascular disease and insulin resistance. Telmisartan is an angiotensin receptor blocker originally developed for the treatment of hypertension. It can also partially activate peroxisome proliferator-activated receptor γ, which may improve insulin sensitivity. This effect may prove useful in hypertensive patients with insulin resistance or diabetes mellitus. We examined adiponectin and Retinol-Binding Protein 4 levels in patients with type 2 diabetes who treatment with the angiotensin inhibitor telmisartan.

**Methods:** A total of 188 patients with hypertension and diabetes mellitus were assessed at baseline and following 24 weeks treatment with the angiotensin receptor blocker telmisartan (final dose, 80 mg). Adiponectin and Retinol-Binding Protein 4 levels were measured in plasma by radioimmunossay.

**Results:** Adiponectin levels were inversely correlated with systolic (SBP: r = -0.640, P < 0.05) and diastolic (DBP: r = -0.350, P < 0.05) blood pressure at baseline and following treatment with telmisartan. Retinol-Binding Protein 4 levels were correlated with systolic (SBP: r = 0.117, P < 0.05) and diastolic (DBP: r = 0.150, P < 0.05) blood pressure at baseline and following treatment with telmisartan. There was a significant increase in adiponectin levels (0.98% confidence interval (CI), 0.57 to 1.86) microg/ml, P < 0.01) and decrease in Retinol-Binding Protein 4 levels (5.88% confidence interval (CI), 3.28 to 10.10) microg/ml, P < 0.01).

**Conclusion:** Adiponectin and Retinol-Binding Protein 4 levels is correlated with blood pressure in patients with type 2 diabetes. Increased adiponectin and decreased Retinol-Binding Protein 4 are associated with treatment by telmisartan. Given the growing diabetes epidemic, telmisartan that can simultaneously block the angiotensin II receptor and partially activate PPAR-γ have the potential to treat both hemodynamic and biochemical features of insulin resistance.
Phytochemical drugs are the new progress in the Haemodynamic effects of dapagliflozin versus P4427

Phytocomplex drugs are the new progress in the genetical determined arterial hypertension treatment

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Purpose: We compared the hydropertensive effect of valsartan (VAL) and polyphenol complex (PP) and, also, we assessed the efficacy of combination consisting of VAL and PP.

Methods: Male spontaneously hypertensive rats (SHR) (n=34, weight 240-280 g) were selected for study. The experimental animals were given VAL at the doses of 5 mg/kg, 10 mg/kg and 20 mg/kg and PP at the doses of 10 mg/kg, 30 mg/kg and 100 mg/kg. The combinations of VAL plus PP at the doses of VAL 5 mg/kg plus PP 10 mg/kg, VAL 10 mg/kg plus PP 20 mg/kg, VAL 20 mg/kg plus PP 40 mg/kg were tested in animals. The systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were recorded with the non-invasive blood pressure monitor NIBP-8 (Columbus Instruments, USA).

Results: Our results showed the most effective dose of PP is 30 mg/kg. In 3 hours, the SBP and DBP were decreased by 18-22 mm Hg (p<0.007) and 15-19 mm Hg (p=0.002-0.003) respectively. The hydropertensive effect was still present in 24 hours. The largest hydropertensive effect of VAL was recorded at the dose of 20 mg/kg. The reduction was about 20 mm Hg (p<0.003) in the SBP and 15 mm Hg (p=0.002-0.003) in the DBP. The SHR rats which were somewhat greater with DAPA than PBO and HCTZ. Small mean decreases in GFR were noted with all treatments, but the change in GFR was somewhat less with HCTZ than DAPA. Mean changes from baseline in GFR at week 12 were -2.9% (95% CI: -6.8, 1.2), -10.8% (95% CI: -14.8, -6.7), and -3.4% (95% CI: -7.3, 0.6) ml/min/1.73 m² for subjects receiving PBO, DAPA, and HCTZ, respectively.

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Haemodynamic effects of dapagliflozin versus hydrochlorothiazide in subjects with type 2 diabetes mellitus

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Purpose: Sodium-glucose co-transporter 2 (SGLT2) reabsorbs glucose and sodium in the renal proximal tubule. Dapagliflozin (DAPA), an inhibitor of this transporter, targets hyperglycaemia in type 2 diabetes mellitus (T2DM) by increasing renal glucose excretion. The haemodynamic profile associated with administration of DAPA remains incompletely characterised. Therefore we compared the effects of DAPA and hydrochlorothiazide (HCTZ) on 24-h blood pressure (BP) and glomerular filtration rate (GFR).

Methods: In this randomised, placebo-controlled, double-blind trial, 75 subjects with T2DM aged 18–70 years (y), HbA1C 6.6%–9.5%, and seated systolic BP (SBP) 130–165 mm Hg/10 diastolic BP 80–105 mm Hg, on a stable dose of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker and no other antihypertensive medications were randomly assigned to placebo (PBO), DAPA 10 mg/day, or HCTZ 25 mg/day. Change from baseline in 24-h ambulatory BP and GFR, measured by ioehol clearance, was compared with baseline after 12 weeks of treatment.

Results: Subjects’ mean age was 56 years (y), T2DM duration 6.3 y, and HbA1C 7.5%. Treatment with PBO, DAPA, or HCTZ resulted in changes from baseline in 24-h ambulatory mean SBP of -0.9 mm Hg (95% CI: -4.2, 2.4), -3.3 mm Hg (95% CI: -6.8, 0.2), and -6.6 mm Hg (95% CI: -9.9, -3.2) mm Hg, respectively, at week 12. The effects of DAPA and HCTZ on mean SBP were similar during the daytime. Night time mean BP did not differ between DAPA and PBO, and was lower for HCTZ than DAPA. Mean changes from baseline in GFR at week 12 were -2.9% (95% CI: -6.8, 1.2), -10.8% (95% CI: -14.8, -6.7), and -3.4% (95% CI: -7.3, 0.6) ml/min/1.73 m² for subjects receiving PBO, DAPA, and HCTZ, respectively.

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Coronary artery calcification and ECG pattern of left ventricular hypertrophy/myocardial ischemia identify different healthy subjects

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1Odense University Hospital, Department of Cardiology, Odense, Denmark; 2Odense University Hospital, Department of Pulmonary Medicine, Odense, Denmark; 3Odense University Hospital, Department of Endocrinology, Odense, Denmark; 4Sydvestjysk Hospital, Department of Cardiology, Svendborg, Denmark; 5Sydvestjysk Hospital, Department of Cardiology, Esbjerg, Denmark; 6Vejle Hospital, Department of Cardiology, Vejle, Denmark

Purpose: To improve risk stratification several markers have been proposed. Both the presence of coronary artery calcification (CAC), and ECG pattern of left ventricular hypertrophy/myocardial ischemia has been shown to provide prognostic information. In this study we investigated the association between traditionally risk factors, ECG-measurements and presence of CAC.

Method: A random sample of healthy males and females aged 50 or 60 years were invited to the screening study. Traditional risk factors were measured. ECG analysis included 1) left ventricular hypertrophy (LVH) using the Sokolow-Lyon criteria and the Cornell voltage x QRS duration product, and 2) myocardial ischemia based on ST segment depression and T -wave abnormalities. A non-contrast CT scan was performed to assess the CAC score. The association between clinical variables, ECG findings, and the presence of CAC was investigated by means of multivariate logistic regression.

Results: Of 1825 invited subjects 1226 accepted the screening. The prevalence of hypertension was 50%. Hypertensive subjects frequently had LVH and/or myocardial ischemia as compared to non-hypertensive subjects (21% vs. 14% p<0.0001) as well as CAC (52% vs. 38%, p<0.0001). Results from multiple logistic regressions analyses are presented in the table.

Odds ratios for the presence of CAC

<table>
<thead>
<tr>
<th>Hypertension present (n=612)</th>
<th>Hypertension absent (n=614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Male</td>
<td>3.0</td>
</tr>
<tr>
<td>Aged 60 years</td>
<td>2.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.4</td>
</tr>
<tr>
<td>Active smoking</td>
<td>2.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.3</td>
</tr>
<tr>
<td>Family history</td>
<td>1.7</td>
</tr>
<tr>
<td>ECG verified left ventricular hypertrophy</td>
<td>NS</td>
</tr>
<tr>
<td>ECG verified myocardial ischemia</td>
<td>NS</td>
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</tbody>
</table>

Conclusion: Patients with hypertension commonly have CAC. Despite this observation there seem to be no relationship between CAC and ECG suspected LVH and/or myocardial ischemia. Indeed, these risk markers seem to identify different subjects at risk, and together may add to better risk classification.
Background: Many studies demonstrate that systolic blood pressure (SBP) ≤140 mm Hg does not provide renal protection in renal disease with hypertension, but SBP ≤120 mmHg may be able to slow progress of renal disease. However, evidence for SBP ≤120 mmHg in elderly hypertension patients was recommended in Chinese hypertension guideline in 2005. The safety of SBP ≤120 mmHg in elderly hypertension patients is hard to be reported.

Methods: In a prospective, controlled open-label studies, the authors have evaluated the safety and efficacy of five-year treatment on progression of renal disease and risk of development of cardiovascular disease in 122-65 aged hypertensive patients with chronic renal disease III to IV stage and macroproteinuria. Before randomization, all patients have been already treated for one-year with angiotensin converting enzyme inhibitors (ACEI) or angiotensin AT1 receptor blockers (ARBs) and other antihypertensive drugs, but their SBP are above 140 mmHg, less than 150 mmHg. Blood pressure, serum creatinine(Cr) and potas-
sium were monitored every 14 days in the period of follow-up by physician and healthcare nurse and more frequent patient-physician encounters will be improve the patient's health. During the treatment, patients took medication every day at home and adjusted their own medication according to pre-agreed rules.

Results: By the end of five year, medication possession ratio between two groups (49% vs 94%), mean blood pressure group was 116±66±6 mmHg and in control was 146±76±13 mmHg, Cr clearance increased from 51±2.6 to 63±0.01 mm/min (P<0.001) in the group of strict control of SBP ≤120 mmHg, but SBP decreased significantly from 52±1.9 to 40±2.4 mm/min (P<0.01) in the controls. During this time, protein urine excretion decreased from 1.4±0.5 to 0.2±0.3 g every 24 hours (P<0.0001) in the treatment group, but urine protein excretion decreased slightly (from 1.3±0.4 to 1.2±0.6 g) in the controls. Nine patients had got ACS, 11 patients stroke, 18 patients had got pneumonia, 8 patients renal dialysis and six patient died (4 in SCD and 2 in heart failure) in controls but one patient had got ACS, four patient had stroke, five pneumonia, 1 patient renal dialysis and two patients died in non-cardiac causes in the treatment group. Incidence of hyperkalaemia was similar between two groups.

Conclusions: SBP ≤120 mmHg is safe and was more apparently in decreasing proteinuria, slowing the progress of renal disease and reducing the risk of develop-
ment of cardiovascular events and proteinuria in elderly hypertensive patients with chronic renal disease.

Cholesterol control and incident antihypertensive treatment in hypercholesterolemic subjects treated or not with statins: a pharmacoepidemiological report

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Purpose: The aim of our study was to evaluate the association between low-density lipoprotein cholesterol (LDL-C) level, statin treatment and the incidence of new antihypertensive treatment in a large population sample.

Methods: A population-based cohort of 23,849 subjects from two Italian Local Health Units (LHU) aged 18 years or older with at least one LDL-C measure-
m ent during the follow-up period at baseline was followed from the LDL-C date until death or December 31, 2009. The cohort was subdivided into two groups (LDL-C target, LDL-C > target) on the basis of their cardiovascular disease risk. The univariable data analysis was based on Pearson Chi-Square to assess statistical significance of differences between frequencies and rates and to calculate incidence rates to assess statistical significance of differences between means and variances. Logistic regression analyses were performed to evaluate the association of statin treatment with the incidence of new antihypertensive treatment. 

Results: By the end of the follow-up period for no new antihypertensive treatment cases, or the end of the follow-up period for no new antihypertensive treatment cases. 

Conclusion: Long-term, open-label treatment with the triple O/A/H combination, which included dose titration as required, was well tolerated and provided consistent and remarkable antihypertensive efficacy in a large group of moderate-to-
severe hypertension pts. Triple O/A/H therapy got the majority of pts to BP goal and was effective in treatment groups composed of a varying proportion of higher-risk pts.

Conclusions: The addition of cilnidipine rather than amiodipine ameliorated urino-
ary albumin, 8-OHdG, and L-FABP reduction were not correlated with the rate of change in systolic blood pressure.
nary albumin excretion in hypertensive patients already under the treatment with an RAS inhibitor. Furthermore, cilnidipine, but not amlodipine, also decreased urinary 8-OHdG and L-FABP in these patients. These data suggest that cilnidipine has a greater renoprotective effect than amlodipine possibly, at least in part, through the inhibiting anti-oxidative stress.

Does obstructive sleep apnea affect the right heart in patients with resistant hypertension? Echocardiographic study

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Purpose: There are limited data concerning the impact of obstructive sleep apnea (OSA) on the parameters of ventricle in patients with resistant systemic arterial hypertension (RSAH). The aim of the study was to determine the relationship between severity of OSA and echocardiographic parameters of right ventricle in patients with RSAH.

Methods: From 204 patients diagnosed with RSAH hypertension in RESIST-POL study, 155 patients (83M, 62F; mean age 47.5±10.5, range 19-69yrs) with out secondary hypertension were included into analysis. All patients underwent polysomnography and the apnea/hypopnea index (AHI) was calculated. Right ventricular end-diastolic area (RVEDA), right ventricular ejection fraction (RVEF), systolic pulmonary artery dimension (MPAd), RV ejection acceleration time (AcT), systolic velocity from Doppler tissue imagine (s′RV), early diastolic velocity (e′ RV) and tricuspid annular plane systolic excursion (TAPSE) were evaluated.

Results: Patients were divided into 4 groups based on OSA: without OSA (AHI < 5, n=43), with mild OSA (AHI 5-15, n=27), moderate OSA (AHI 15-30, n=27), severe OSA (AHI > 30, n=40); Patients with severe OSA as compared with patients with mild OSA had higher MPAd (26.0±2.2mm vs. 23.1±3.7mm; p<0.001), RVAD (8.7±2.9 vs. 6.8±2.2cm²; p<0.01), RVAD (19.0±3.7vs. 15.0±3.6cm²; p<0.01) and shorter AcT (114.2±15.7 vs. 133.4±22.1ms; p<0.001). There were no differences in RV systolic performance between patients with severe and without OSA. There were no differences between patients with mild or moderate OSA and without OSA in RV echo findings. AHI correlated significantly with MPAd (r=0.22, p<0.05) and AcT (r=0.25, p<0.01) and MPAd (r=0.27p<0.01) and RVAD (r=0.29, p<0.01) but did not with TAPSE, s′RV and e′ RV in a multivariate models including parameters of the right heart, presence of sever OSA, gender, age, BMI and metabolic syndrome, the presence of severe OSA was independently related to MPAd (β=0.22, p<0.05, and AcT (β=0.20; p<0.05).

Conclusions: Severe OSA is an independent factor modifying right heart morphology and RV-MPAd coupling in patients with resistant hypertension.

NOVEL DIAGNOSTIC AND THERAPEUTIC APPROACHES IN STABLE CORONARY ARTERY DISEASE

Utility of high-sensitivity cardiac troponin T in patients undergoing elective coronary angiography


Introduction: High-sensitivity cardiac troponin (hsTn) assays have improved diagnosis of myocardial infarction. It is unknown whether hsTn can improve the diagnosis of obstructive coronary heart disease in patients without acute coronary syndrome.

Methods: This study enrolled 1254 consecutive patients undergoing elective coronary angiography following cardiac stress testing. Obstructive coronary heart disease was defined as a stenosis >75% in at least one of the main native vessels or bypass grafts. Blood samples for hsTnT testing were drawn on admission before coronary angiography and before cardiac stress test. A commercially available hsTn assay with a 99th percentile cut-off point of 0.014 μg/L and a limit of detection of 0.003 μg/L was used.

Results: Plasma levels of hsTnT significantly correlated with the extent of coronary heart disease (r=0.14; p<0.001) but also with left ventricular function (r=0.17; p<0.01), age (r=0.09; p<0.01), and renal function(r=0.18; p<0.001). Out of 1254 enrolled subjects, 64% had a positive stress test and 61% were diagnosed with obstructive coronary heart disease during coronary angiography. The receiver operating curve (ROC) derived optimal cut-off for the diagnosis of an obstructive coronary heart disease was 0.004 μg/L. A positive stress test result was associated with a sensitivity of 69% but only a specificity of 45% for obstructive coronary heart disease. Combining stress test results with hsTnT ≥0.004 μg/L significantly improved the performance for diagnosis of obstructive coronary heart disease (c-statistics from 0.565 to 0.671; p<0.001). The sensitivity of this approach was 67% and the specificity 61%.

Conclusion: Addition of hsTnT improves significantly the performance of cardiac stress testing for diagnosing obstructive coronary heart disease.

Evidence of a synergistic impact of polymorphisms on C-reactive protein and interleukin-6 gene in patients with stable angina pectoris: Effect on inflammatory process


Purpose: Data suggest that novel polymorphisms on different genes of markers of inflammation can simultaneously be involved into mechanisms of atherosclerosis. In the present study we examined the synergistic role of 3872 A→G polymorphism (rs1205) of C-reactive protein gene and -174 G→C polymorphism of interleukin 6 gene (rs1800795) on serum levels of interleukin 6 as well as in the incidence and severity of coronary artery disease (CAD).

Methods: The study consisted of 311 patients with angiographically documented CAD and 160 healthy controls. The 3872 A→G and the -174 G→C polymorphisms were determined by PCR and the restriction enzymes HPYCVII and SFIEN respectively. C-reactive protein (CRP) levels were assessed by specific immunonephelometric method, while serum levels of interleukin-6 (IL-6) levels were assessed by ELISA assay.

Results: The genotype distribution for CRP polymorphism was: GG 42.1%, AG 39.8%, AA 18.2% for CAD group and GG: 48.1%, AG: 39.3%, AA: 12.6% for controls. The genotype distribution for IL-6 polymorphism was: GG: 47%, GC: 35%, CC: 18% for CAD group and GG: 47%, GC: 43% and CC: 8% for controls. Importantly, there was a significant difference in IL-6 levels (pg/ml) between the GG carriers and CC homozygotes both in the CAD group (3.88±2.81 vs 6.07±3.75, p<0.001) and in the control group (3.26±2.24 vs 1.82±1.57, p=0.05). Polymorphism on IL-6 gene and the AA homozygotes of 3872A→G polymorphism on CRP gene were significantly associated with greater incidence of coronary artery disease compared to the other genotypes (RR: 0.945, p<0.0101).

Conclusion: The 3872 A→G polymorphism on C-reactive protein gene is closely related to interleukin-6 levels. These findings suggest that the synergistic impact of these two different polymorphisms is capable of a significant promotion of coronary artery disease via inflammatory mechanisms.

Association between increased levels of cardiac troponin before elective stenting and optical coherence tomography findings in stable angina pectoris


Aims: With the availability of highly sensitive troponin assays, our understanding of minor myocardial damage in various cardiac conditions is challenged. Association between mild elevation of cardiac troponin I (cTnI) before percutaneous coronary intervention (PCI) in stable angina pectoris (SAP) patients and plaque morphology obtained by optical coherence tomography (OCT) was not yet elucidated. The aim of the present study is to investigate the relationship between increased levels of cTnI before elective stenting and OCT findings in SAP.

Methods and Results: We studied 180 native de novo culprit coronary lesions from 166 SAP patients who underwent OCT before elective PCI. Patients were excluded if they had significant left main disease, congestive heart failure, or renal insufficiency with a baseline eGFR < 30 ml/min/1.73m². Patients were divided into two groups according to the presence (n=28; 16%); median 0.15 ng/mL; IQR: 0.08-0.24) and absence (n=152; 84%) of cTnI ≥0.03ng/mL before PCI. Clinical and OCT findings were compared between these two groups. Thin cap fibroatheroma (TCFA) was defined as lipid-rich plaque (one or more quadrants) with fibrous cap thickness ≤70µm. There were no significant differences in the clinical presentation between the two groups including inflammatory markers, eGFR, number of diseased vessel, ejection fraction and Canadian Cardiovascular Society (CCS) grade. In quantitative coronary angiographic analysis (QCA) analysis, there were no significant differences in % diameter stenosis, lesion length, and minimum lu-
men diameter. In OCT analysis, mild CnTnI elevation before PCI was associated with the presence of TCFA (8/28: 29% vs 17/152: 11%, P = 0.032), smallest thinnest cap thickness (median: 65 μm (IQR: 69-120 μm) vs 107 μm (IQR: 73-140 μm), P = 0.01) and lipid quadrants (median: 3 (IQR: 2-3) vs 2 (IQR: 0-3), P < 0.001). Post-PCI CnTnI levels were greater in patients with baseline CnTnI elevation than in those without (median: 0.52 ng/mL (IQR: 0.24 - 4.19 ng/mL) vs 0.33 ng/mL (IQR: 0.12 - 1.06 ng/mL), P = 0.044).

Conclusions: Mild CnTnI elevation was associated with OCT-derived unstable plaque morphology, and may help identify SAP patients at high risk for cardiovascular injury after elective stenting.

Diagnostic performance of cardiac hybrid imaging of single photon emission computed tomography and coronary computed tomography

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Background: Although cardiac hybrid imaging of coronary computed tomography (CCT) and myocardial perfusion imaging with single photon emission computed tomography (MPI) could show the ischemic myocardial area and the culprit vessel, its clinical usefulness has not been clarified. Therefore, we evaluated the incremental clinical usefulness of the hybrid imaging in the diagnosis of coronary artery diseases.

Method: Consecutive patients (n=98) with suspected coronary artery disease who had undergone combined coronary angiography and CCT (90%) and equivocal myocardial ischemia on CCT and equivocal myocardial ischemia on MPI were enrolled. We examined if the hybrid imaging would change the diagnosis on the culprit vessel of myocardial ischemia acquired by side-by-side analysis of CCT and MPI images (Table 1). Hybrid imaging was useful to diagnose correctly the ischemic area at the border of old myocardial infarction or at posterolateral wall that had been overlooked by side-by-side analysis.

Result: In 34 (38%) of 96 patients, hybrid imaging changed the diagnosis acquired by side-by-side analysis of CCT and MPI images (Table 1). Hybrid imaging was useful to diagnose correctly the ischemic area at the border of old myocardial infarction or at posterolateral wall that had been overlooked by side-by-side analysis.

Conclusion: The hybrid imaging of CCT and MPI was more useful than the side-by-side analysis for the correct diagnosis of the myocardial ischemia and its culprit vessel.

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Conclusion: The hybrid imaging of CCT and MPI was more useful than the side-by-side analysis for the correct diagnosis of the myocardial ischemia and its culprit vessel.

Purpose: To assess efficacy of combination therapy with non-maximum dose of beta-blockers and ivabradine compared to up-titration of beta-blockers strategy in patients with intermediate stenosis (FFR > 0.75). FFR and SR were not correlated with plaque characteristics.

Conclusion: For a given stenosis geometry, FFR values decreased and SR values increased with increases in DCV and NCV in patients with hemodynamically significant stenosis. This finding implies that plaque characteristics can affect hemodynamic endpoints in patients with hemodynamically significant coronary lesions.

Plasma cyclophilin A level is a novel biomarker of coronary artery disease

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Purpose: We tested our hypothesis that plasma cyclophilin A (CyPA) levels could be a novel biomarker of CAD.

Background: Oxidative stress, generated by excessive reactive oxygen species (ROS), promotes coronary artery diseases (CAD). We have recently demonstrated that ROS induces secretion of CyPA from vascular smooth muscle cells, which plays a crucial role in the pathogenesis of atherosclerosis, aortic aneurysms, and intimal thickening in mice.

Methods: In consecutive 320 patients undergoing coronary angiography, we examined the relationship between plasma CyPA levels and the severity of CAD. We measured plasma CyPA by an immunoassay based on the sandwich technique.

Results: Plasma CyPA levels were significantly higher in patients with significant coronary stenosis (>50%, >188) compared to those without it (n=131) (P < 0.001). A positive correlation was noted between plasma CyPA levels and significant coronary stenosis both in-stent and even after adjustment for age, sex, hypertension, diabetes, dyslipidemia and smoking. The average number of stenotic coronary arteries and the need for coronary intervention were significantly increased in the quartiles of higher CyPA levels (both P < 0.001). Indeed, plasma CyPA level was a strong predictor of CAD (adjusted odds ratio for CAD, 6.20; 95% confidence interval [CI], 3.14-12.27; P < 0.001). Moreover, plasma CyPA levels were significantly correlated with the number of stenotic coronary arteries, regard-
increased rho-kinase activity in patients with vasospastic angina after the great east japan earthquake disaster.

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Purpose: We have recently demonstrated that Rho-kinase activity in circulating neutrophils is a useful biomarker for the disease activity assessment in patients with vasospastic angina (VSA). Coronary vasospastic activity is known to be enhanced by mental/physical stress. Since we experienced the Great East Japan Earthquake in our Tohoku area on March 11, 2011, we examined whether the Rho-kinase activity was increased in VSA patients after the disaster.

Methods: In 10 patients with proven VSA (mean±SD age 73±6.2±11 yrs) who were hit by the earthquake/tsunami, we examined the Rho-kinase activity in circulating neutrophils before and after the disaster as well as the influence of mental stress by using the questionnaire for post-traumatic stress disorder (PTSD).

Results: In all patients, Rho-kinase activity was increased after the disaster than before (phosphorylated myosin-binding subunit (MBS)/total MBS ratio 1.72±0.25 vs. 1.01±0.36, P<0.001), despite the continued treatment with calcium channel blockers (Figure). Among the 10 patients, 3 complained that the frequency of angina attack and the use of sublingual nitroglycerin were increased after the disaster, in whom both PTSD score (32±7 vs. 3±7, P<0.001) and changes in the Rho-kinase activity from the baseline (268±232% vs. 48±31%, P<0.05) were significantly higher than the remaining 7 patients without worsening symptoms. The changes in the Rho-kinase activity from the baseline were significantly correlated with the PTSD score (r=0.68, P<0.05).

Conclusions: These results indicate that Rho-kinase activity is enhanced in VSA patients by the disaster-related mental stress.

"Heart team" decision making in the management of patients with Coronary Artery Disease; structure, outcomes and reproducibility.

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Purpose: Contemporary guidelines recommend that patients with stable angina and acute coronary syndromes (ACS) with multi-vessel disease are discussed by a multidisciplinary "Heart Team" (HT) to facilitate optimal evidence-based management. However, there is a paucity of data describing the workings of a HT, the actioning of its recommendations and the reproducibility of its decisions.

Methods: We have utilised a HT approach since 2005. We analysed the data for 2010 and describe the HT process. A random sample of cases were scrutinised to identify whether the HT decision had been implemented. Also, cases were represented after 1 year to determine consistency and reproducibility of decision making. The HT panel for the review process excluded members involved in the original discussion.

Results: During 2010, 108 meetings were held, attended by a median of 3 interventional cardiologists, 1 non-interventional cardiologist and 2 cardiac surgeons. 1454 cases were discussed (mean 13.5 cases per meeting). 854 (58.7%) were from our unit, 600 (41.3%) from referring hospitals. 356 (25.5%) were inpatients, 1098 (75.5%) outpatients. 1340 (92.2%) were patients with stable angina or ACS. The HT recommended coronary artery bypass grafting (CABG) ± valve surgery in 429 (32%) cases, percutaneous coronary intervention (PCI) in 303 (22.6%), and optimised medical therapy (OMT) in 264 (19.7%). In the remaining 344 cases (25.7%), further investigation was advised before a HT decision was made; most frequently a pressure wire study, in 151 cases (43.9%). Of 117 cases analysed, the HT recommendation had been fully actioned in 101 (86.3%). In the remaining 16 cases, deviation from the initial plan was due to the patient declining revascularisation (CABG 3, PCI 1), development of new comorbidity (2) or revascularisation of different vessels (6). The reason for deviation was unclear in 4 cases.

Of 50 cases re-presented, the original HT recommendation was the same in 38 (76%) cases. Different decisions in the remaining 12 (24%) included 7 cases (14%) in which further investigation had initially been suggested, and revascularisation was recommended on re-presentation. Conclusions: A well-structured HT allows a large number of cases to be evaluated, while interdisciplinary discussion facilitates consensus with evidence-based and individualised advice. There is a prominent role for pressure wire assessment in the further evaluation of equivocal stenoses. The HT approach appears robust and reproducible in the majority of cases. Variation in decision making reflects the equipoise between suitability of CABG, PCI and OMT in many cases.

Effective radiation dose to obtain coronary morphology and function; comparison of a non-invasive and an invasive strategy.

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Background: Diagnosis and treatment guidance of patients with suspected coronary artery disease (CAD) should rely on combined anatomic and functional data. Yet, there is growing awareness about the detrimental effect of radiation associated with diagnostic procedures.

Aim: To compare the Effective Radiation Dose (ERD) needed to obtain coronary anatomy and function by a non-invasive and an invasive diagnostic strategy.

Methods: Detailed ERD measurements were obtained during two different periods (2005, n=479; and 2010, n=207, after both the coronary computed tomography angiography (CCTA) and the catheter laboratory had been renewed). The non-invasive strategy consisted in the combination of the Coronary Computed Tomography Angiography (CCTA) and 99mTc-MIBI SPECT (MPI). The invasive strategy included Coronary Angiography (CA) and Fractional Flow Reserve (FFR) mea-
poorly studied. We undertook this study to assess whether uric acid level predicts clinical outcome in patients with stable coronary artery disease (CAD) treated with percutaneous coronary intervention (PCI).

**Method:** This study included 8149 patients with stable CAD who underwent PCI. Uric acid was measured in all patients before angiography. The primary end point was 1-year mortality.

**Results:** Quantiles of quartiles of uric acid were: 1.49 to 5.49 mg/dl (1st quartile; n=2032 patients), 5.49 to 6.40 mg/dl (2nd quartile; n=1981 patients), 6.40 to 7.50 mg/dl (3rd quartile; n=2093 patients) and 7.50 to 21.90 mg/dl (4th quartile; n=2043 patients). There were 196 deaths during the 1-year follow-up. The number of deaths (Kaplan-Meier estimates) according to uric acid quartiles were: 35 deaths (1.8%) in the 1st quartile, 30 deaths (1.6%) in the 2nd quartile, 45 deaths (2.2%) in the 3rd quartile and 86 deaths (4.3%) in the 4th quartile (unadjusted hazard ratio HR=1.6, 95% confidence interval [CI] 1.38-1.86, P<0.001 for each standard deviation [SD] increase in the logarithmic scale). Calculated for 1 mg/dl increase in the uric acid level, the unadjusted HR was 1.31 [1.23-2.40], P=0.001, indicating a 31% increase in the unadjusted risk of 1-year mortality with each 1 mg/dl increase in the uric acid level. After adjustment for traditional cardiovascular risk factors, renal function and inflammatory status, the association between uric acid and 1-year mortality remained significant (adjusted HR=1.26, 95% CI 1.17-1.48; P=0.005 for each standard deviation SD increase in the logarithmic scale). Calculated for 1 mg/dl increase in the uric acid level, the adjusted HR was 1.15 [1.06-1.25]; P=0.01 demonstrating a 15% increase in the adjusted risk for 1-year mortality for every 1 mg/dl increase in the uric acid level. Uric acid improved predictive power of the multivariable model regarding mortality (P=0.040).

**Conclusion:** In patients with stable CAD treated with PCI, elevated uric acid level predicts the increased risk of death independently from cardiovascular risk factors, status of renal function or inflammatory burden. Thus uric acid, a readily available test, has the potential to risk stratify the large group of patients with stable CAD in terms of mortality prediction.

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**Prognostic impact of uric acid in patients with stable coronary artery disease**

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**Background:** The association between uric acid and cardiovascular disease is

**Conclusion:** Prior stroke was an independent predictor of 5-year outcome in stable CAD patients with a 47% increased mortality rate in clinical practice.
Lack of concordance between image stress tests and invasive functional evaluation with pressure wire in patients with stable angina

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Background: Current guidelines suggest that coronary lesions should be treated when there is a previous ischemia stress test implying the involved myocardial area. However, sensitivity and specificity of non invasive stress tests (NIST) be less than expected, when compared with invasive functional invasive evaluation of lesions, using a pressure wire, particularly in patients with multivessel disease.

Purpose: To investigate the diagnostic value of NIST in patients with stable angina, compared with the invasive functional study (fractional flow reserve – FFR – evaluated with a pressure wire) during coronary angiography.

Methods: Patients with stable angina admitted for coronary angiography and with ischemia identified on a previous NIST, were included. The functional relevance of identified coronary lesions was determined by FFR evaluation (Pressure-Wire®), St. Jude Medical), under adenosine coronary hyperemia. An FFR<0.75 was considered as functionally significant.

Results: 57 lesions, from 36 patients (mean age 61.6±9.5 years, 24 males) were included. The NIST was myocardial perfusion scan in 28 (81%) patients and stress Echo in 7 (19%). Concordance between NIST and FFR was present in only 24 (42%) of the evaluated lesions. For the defined FFR value (<0.75), NIST sensitively 75%, specificity 94%, positive predictive value 16.2% and negative predictive value 90%. There were no identifiable variables affecting the concordance between NIST and functional invasive evaluation (including age, gender, cardiovascular risk factors, presence of multivessel disease or ischemia affected territory). However, there was a trend for an increase in the concordance between non invasive and invasive tests when lesion where divided according to angiographic severity: for lesions <69%, 70-89% and >90%, the concordance was, respectively, 51%, 31.6%, 50.0% and 100% (p=0.007).

Conclusions: NIST have a low concordance with the invasive functional evaluation of lesions with a pressure wire, usually oversestimating the presence of ischemia. The lack of concordance between non invasive and invasive test tends to decrease in more severe lesions. These results should be tested in larger trials, since they might change the present recommendations for coronary lesions revascularization.

Effects of ranolazine and ivabradine on exercise stress test and on coronary and peripheral vascular function in patients with refractory microvascular angina

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Purpose: Iviabradine and ranolazine are novel anti-ischemic drugs with known beneficial effects in patients with stable angina and obstructive coronary disease. In this study we assessed their effects on exercise stress test (EST), coronary microvascular function and systemic vascular function in patients with microvascular angina (MVA).

Methods: We randomized, in a double-blind way, 46 MVA patients (defined by the presence of effort angina, positive maximal EST, normal coronary arteries at angiography and coronary flow response [CFR] to adenosine <2.5), who reported symptoms related to effort (dyspnoea, angina, other symptoms) to receive ivabradine (5 mg b.i.d.), ranolazine (375 mg b.i.d) or placebo (b.i.d.) for 4 weeks. Maximal EST, CFR to adenosine and to coldpressor test (CPT) in the left hand, microvascular function (flow-mediated dilation [FMD] and nitrate-mediated dilatation [NMD] of the brachial artery in response to post-ischaemic hyperaemia) were assessed at baseline and after treatment.

Results: No significant differences among groups in EST parameters, CFR to adenosine and to CPT, and FMD and NMD. Compared to placebo, time to 1 mm ST-segment depression and exercise duration were significantly improved by ranolazine (p<0.05), but not by ivabradine. No significant changes were detected in CFR to adenosine and to CPT, as well as in FMD and NMD in any group after treatment (table).

Conclusions: Ranolazine, but not ivabradine, was able to delay the appearance of ischemic ST-segment changes and improve exercise tolerance in MVA patients. This effect was not related to significant improvement in coronary microvascular function or in endothelial systemic function.

Impact of metabolic syndrome on the outcome of patients with stable coronary artery disease submitted to different types of treatment: 10-year follow-up of the MASS II study

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Purpose: Metabolic syndrome (MetS) is understood as a condition that promotes atherothrombosis and confers an additional risk of adverse cardiovascular events in patients with coronary artery disease. The prognosis of this syndrome in this subset of patients in a long term follow up is inconclusive. Evaluate the impact of metabolic syndrome on cardiac death in patients with symptomatic chronic multivessel coronary artery disease.

Methods: Patients randomized in MASS II study submitted to coronary artery revascularization (CABG, PCI) or medical treatment (MT) were evaluated for the presence of MetS and followed prospectively for 10 years. We evaluated the incidence of overall and cardiac death in this period.

Results: Criteria for MetS were fulfilled in 283 patients of 583 (54%) randomized to three therapeutic strategies. The presence of MetS was associated with an increased cardiac related death in studied population. During a 10-year follow-up, the probability cardiac mortality free survival was significantly different among patients in the 2 groups (MetS = 81.6% x non-MetS = 91.3% P=0.004). Stratifying patients with MetS by therapeutic approach we identified a statistical difference in cardiac death free survival comparing interventional approaches (CABG and PCI) to MT: 82.4% for CABG, 86.2% for PCI and 75.9% for MT (P=0.003). Besides, there is a group with best prognosis: patients without MetS submitted to CABG presenting 98.7% of patients free of cardiac death in a 10-year follow-up.

Conclusions: MetS confers high rates of cardiac death in patients with stable coronary artery disease irrespective of therapeutic strategy used. In patients with MetS, interventional approaches (PCI or CABG) seem to confer more protection against cardiac death in a 10-year follow-up.
P4453  YKL-40 is associated with long-term mortality in patients with stable coronary artery disease

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Objective: We investigated whether the inflammatory biomarker YKL-40 could improve the long-term prediction of death caused by common risk factors plus high-sensitivity C-reactive protein (hs-CRP) and N-terminal-pro-B natriuretic peptide (NTproBNP) in patients with stable coronary artery disease (CAD).

Background: Non-hospitalized CAD patients are usually followed in general practice. There is a need for identify biomarkers which could help to foresee the prognosis of these patients. Elevated serum YKL-40 is a short-term predictor for myocardial infarction (MI), cardiovascular mortality and all-cause mortality in patients with stable CAD.

Methods: Serum YKL-40, hs-CRP, and NTproBNP were measured in 4265 (97.6%) of the 4372 patients with stable CAD included in the CLARICOR trial, and death was registered in a 6-years follow-up period.

Results: After adjustment for type of intervention, risk factors (age, sex, hyperten-

sion, diabetes, smoking status, and previous MI) and medical treatment (diuret-
cals, digoxin, and statin) serum YKL-40 (transformed as ln(max [82, YKL-40 (µg/L)]) was significantly associated with all-cause mortality (hazard ratio (HR) = 1.55, 95% CI = 1.39-1.73, p<0.001). After additional adjustment for ln(hs-CRP) and ln(NTproBNP) this was still true [HR = 1.38, 95% CI = 1.21-1.53, p<0.001].

Conclusions: Serum YKL-40 is a predictor of long-term mortality in patients with stable CAD independent of common risk factors and ln(hs-CRP) and ln(NT-

proBNP). Serum YKL-40 can be used for prognostication in these patients.

P4454  Coronary plaque characteristics that indicate distal embolization during percutaneous coronary intervention in patients with stable angina-virtual histology intravascular ultrasound study


Background: Distal embolization (DE) is a serious complication of percutaneous coronary intervention (PCI) in patients with stable angina.

Purpose: The purpose of this study was to evaluate the coronary plaque character-

istics that indicate DE during PCI in patients with stable angina using virtual histology intravascular ultrasound (VH-IVUS).

Methods: Three hundred and sixty-four consecutive stable angina patients who underwent PCI were enrolled in this study. The patients were divided into the two groups as follows: patients exhibiting DE (DE group, n=10) and patients with-

out DE (non-DE group, n=354). The culprit coronary plaque compositions were calculated by receiver operating characteristic curve and evaluated by univariate logistic regression analysis.

Results: The FF ratio (28±17% vs. 11±9%, p<0.0001) was higher in the DE group compared with in the non-DE group. None of the other VH parameters were different between the two groups. The best cut-off value of FF ratio for prediction of DE was 20%, with a sensitivity of 0.80 and a specificity of 0.81 (odds ratio; 17.1, 95% confidence interval 3.56-82.5, p=0.0004).

Conclusions: Coronary plaques with high FF ratio may be the predictor of indicating DE in patients with stable angina during PCI.

P4455  Effects of ranolazine and ivabradine on angina status and quality of life in patients with microvascular angina

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Purpose: Aim of this study was to assess the effects of ranolazine and ivab-

drine on angina symptoms and quality of life (QoL) in patients with microvascular angina (MVA: effort angina, positive exercise test, normal coronary arteries and coronary flow reserve <2.5).

Methods: We randomized 46 MVA patients under usual antiangina therapy to re-

ceive ivabradine (5 mg b.i.d.), ranolazine (375 mg b.i.d.) or placebo for 4 weeks. The Seattle Angina Questionnaire (SAQ) and EuroQol scale were assessed be-

fore and after treatment.

Results: Basal SAQ scores and EuroQol scale did not differ among groups. Both ranolazine and ivabradine improved outcome variables compared to placebo; fur-

thermore, ranolazine was more effective than ivabradine in improving most SAQ items and EuroQol scale (table).

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<td>68.8±16.4</td>
<td>75.8±14.9</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>84.4±14.3</td>
<td>90.8±8.5</td>
<td>74.2±13.9</td>
</tr>
<tr>
<td>Disease perception</td>
<td>Baseline</td>
<td>49.5±23.5</td>
<td>45.0±16.9</td>
<td>60.0±22.3</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>62.5±25.8</td>
<td>79.4±14.4</td>
<td>57.2±23.3</td>
</tr>
<tr>
<td>EuroQol</td>
<td>Baseline</td>
<td>66.6±13.6</td>
<td>61.3±16.8</td>
<td>65.7±16.7</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>72.5±16.8</td>
<td>79.3±12.9</td>
<td>64.3±18.6</td>
</tr>
</tbody>
</table>

*p<0.05 for differences in changes vs. ivabradine.

Conclusions: Our data show that both ranolazine and ivabradine may have a therapeutic role in MVA patients. Ranolazine appeared more effective than ivabra-

dine in achieving a better control of symptoms.

P4456  Low testosterone levels correlate with the angiographic extent of coronary artery disease in patients with stable angina and/or abnormal stress test

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Purpose: Low testosterone concentration is associated with endothelial dysfunc-


tion and increased cardiovascular risk. The relationship between total testosterone (TT) levels and extent of coronary artery disease (CAD) in patients with chest pain and/or abnormal stress test has not been fully elucidated.

**Methods:** 116 subjects (mean age, 60.5±9 years) with stable angina and/or stress echocardiography considered positive for myocardial ischemia were enrolled prospectively for coronary angiography. According to the angiographic findings they were divided into 4 groups: group A (no coronary stenoses < 50%, n = 12), group B (1-vessel CAD, n = 56), group C (2-vessel CAD, n = 40) and group D (coronary ectasia, n=8). TT levels were measured in all patients.

**Results:** Concentration was significantly lower in group C as compared to group A or B (left figure). This last relationship remained significant in multivariate analysis (p<0.005 by ANCOVA, post hoc P<0.05) after adjusting for age, blood pressure, lipids and blood glucose. Interestingly, when patients with coronary ectasia (group D) were compared with patients who had significant stenosis in at least one artery (groups B and C), no significant differences were found in TT levels. TT concentration was also inversely associated with extent of coronary atherosclerosis as assessed by modified Gensini’s score (right figure). Receiver operating curve analysis showed that TT ≥ 3.2 ng/ml was the optimal cutoff value to predict 2/3 vessel CAD (AUC: 0.702, CI: 0.610-0.805, sens:62%, spec:79%, PPV:82% and NPV:67%).

**Conclusions:** Coronary angiographic findings correlate significantly with TT levels. This may reinforce the link between low testosterone and increased cardiovascular risk.

**Abstract P4457**

**Markers of prognosis, incidence of sudden cardiac death and heart failure in coronary artery disease**

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**Purpose:** To evaluate in patients with stable angina, ST and non ST elevation acute coronary syndromes (ACS) platelet inhibitory biomarkers and the effects on outcomes included sudden cardiac death, heart failure readmission and left ventricular systolic dysfunction.

**Methods:** In 400 patients (pts) with stable angina and ACS, platelet inhibitory biomarkers: endothelial dysfunction (Von Willebrand factor activity, flow mediated dilatation), plateleters hyperactivity (ASPItest, ADPtest by multiple electrode aggregometry), oxidative stress (Total antioxidant status, Anti Myeloperoxidase antibodies -MPO Ig G ELISA), were evaluated in correlation with incidence sudden cardiac death, heart failure and other major acute cardiovascular events (MACE) for 2 years of follow up. Statistical analysis: chi square test, multiple regression.

**Results:** See Table.

**Conclusions:** Higher aggregation values of ASPItest/ADPtest/ATP, higher Von Willebrand factor activity plasma values, lower values of flow mediated vasodilatation, lower serum levels of total antioxidant status and higher serum level of myeloperoxidase Ig G antibodies, were correlated with significant increased incidence of sudden cardiac death, cardiovascular death, nonfatal AMI, heart failure and recurrent angina with readmission; significant higher incidence of left ventricular systolic dysfunction in patients with acute coronary syndromes at 2 years of follow up. Endothelial dysfunction, plateletiers hyperactivity and oxidative stress are the most important factors in atherosclerotic plaque instability and evolution with major acute cardiovascular events.

**Abstract P4458**

**Extracorporeal shockwave myocardial revascularization therapy (ESMR): an alternative for patients with end-stage coronary artery disease and chronic refractory angina pectoris?**

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**Purpose:** Patients with chronic refractory angina complaints on maximum tolerable medication and no further revascularization options represent a difficult therapeutic challenge. Extracorporeal Shockwave Myocardial Revascularization therapy (ESMR) might improve symptoms and alleviate ischemia by stimulating collateral growth in chronic ischemic myocardium in patients with end-stage coronary artery disease. A shockwave is a single pressure pulse with a short (<1 ms) positive spike with an amplitude up to 100 MPa followed by a lower amplitude tensile part lasting several microseconds. The highly localized physical forces of shockwaves increase capillary density in ischemic myocardium. This prospective study was performed to evaluate the feasibility and safety of ESMR.

**Methods:** We recruited 50 patients (40 male, mean age 66.6±9 years, mean left ventricular ejection fraction 53.12%) 175 patients with end-stage coronary artery disease, chronic angina pectoris and reversible ischemia on myocardial single photon emission tomography (SPECT). ESMR was applied to the ischemic zones (3-7 spots/session, 100 impulses/spot, 0.09 mJ/mm²) in an echocardiography-guided and ECG-triggered fashion. The protocol included a total of 9 treatment sessions (3 treatment sessions within one week at baseline, and after 1 and 2 months). Exercise test, angina score (CCS class), nitrate use and SPECT 1 and 4 months after the last treatment session were used to evaluate the effect of the ESMR.

**Results:** One and 4 months after ESMR, the angina complaints diminished (CCS class 3.2±0.2 to CCS class 2.1±0.7, p<0.001 and p=0.001, respectively). Sublingual nitrate use diminished from 35.8±8.1% at baseline to 2.1±3.4% week to 1.5±2.5% week (p<0.001 and p=0.001, respectively). This clinical improvement was in line with improved myocardial uptake on stress SPECT at 4 months follow up (54.4±9.3% to 56.1±10.6%, p=0.023) and with an increased exercise tolerance at 1 and 4 months follow up (from 8.2±3.2 to 9.2±3.8 to 9.6±3.8 minutes, p=0.028 and p=0.02, respectively). No clinically relevant side effects were observed.

**Conclusion:** ESMR improved symptoms and reduced ischemia burden in patients with end-stage coronary artery disease. The non-invasive character of ESMR in combination with absence of relevant side effects makes ESMR a promising treatment modality for patients with chronic refractory angina pectoris.

**Abstract P4459**

**The prevalence of refractory angina in patients undergoing coronary angiography for stable ischemic heart disease**

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**Background:** Epidemiological studies of refractory angina do not always take into account the number of angina episodes during a certain period of time in separate patient groups. The severity of refractory angina is not always known. Aim of the study: To evaluate the prevalence and severity of refractory angina in real clinical practice in patients with stable ischemic heart disease undergoing coronary angiography.

**Methods:** 418 patients (301 male (72%) and 117 female (28%)) undergoing coronary angiography due to chronic stable angina were consecutively screened during a one-year period. Several aspects of ischemic heart disease were analyzed. In patients with angina refractory to medical and surgical treatment frequency of chest pain episodes was recorded using standardized one-week diaries.

**Results:** Amongst all 418 patients 6 (1.4%) had Class I angina (CCS Angina Grading Scale), 288 (68.9%) – Class II, 121 (28.9%) – Class III, 3 (0.7%) – Class IV. 29 patients (6.9%) had no detectable lesions of coronary arteries, 138 patients (33%) had non-significant lesions, 82 (19.6%) patients were diagnosed with significant (Ⅲ/Ⅳ) coronary artery disease, 98 (23.4%) – with multiple-vessel disease. Myocardial revascularization was indicated in 251 patients (60.1%), 117 of them (46.6%) undergoing PTCA, 79 (31.5%) – CABG. Cardiac surgeons refused to operate (due to various contraindications and/or high risk) in 26 patients (10.4%), 29 patients (11.6%) refused to be operated because of fear of operation.
Totally 55 patients were considered as having angina pectoris refractory to surgical and medical treatment, which is 21.9% of all patients with stable angina in whom revascularization was indicated. The frequency of angina attacks in this group ranged from 0 to 24 episodes per week with median of 5 episodes. 27 patients (49% of all refractory angina patients) had less than two angina attacks a week, the rest 28 patients (51%) had an average of 8 attacks of angina per week. Therefore, the majority of the patients considered refractory control and only 28 patients had a refractory angina which is 6.7% of all 481 patients undergoing coronary angiography.

Conclusions: Amongst all patients with stable angina undergoing coronary angiography 6.7% had a refractory angina which is substantial. Usage of other tools apart from CGS Angina Grading Scale can help to evaluate severity of angina: standardized diaries, special tools for measurement of quality of life, etc.

An analysis of the proportion of visits in which BP was controlled to <75% and ≥75% is important for understanding the potential impact of improved BP control on cardiovascular outcomes. A retrospective analysis of the ACTION database demonstrated the importance of consistent blood pressure (BP) to be below 140/90mmHg. This further analysis evaluates the benefits of sustaining “tight” BP control, the levels recommended by current guidelines for this “high risk” patient population. The analysis was limited to those patients who had complete BP measurements over the first year of the study (4 recordings) and excluded those who had an event during this period. The patients were then divided into 4 groups according to the proportion of visits in which BP was in controlled to <130/80 mmHg, <75%, ≥75%, 50% to <75%, 50% to >75% and >75%. Data were analysed for the major pre-specified ACTION outcomes by unadjusted clinical outcomes: thus, % of patients with outcome by proportion of visits with BP control. Data were also analysed estimating the hazard ratios (HR) for each outcome relative to the consistency of BP control in the group with BP control >25% of visits as reference. Only 18.1% of patients achieved a BP control rate (<130/80 mmHg) for more than 75% of visits and, in the first year, 46.0% were controlled at fewer than 25% of visits. With the exception of coronary angiography, the rate of all of the pre-specified cardiovascular endpoints declined as the proportion of visits with BP control increased. The risks for primary outcome (HR: 0.63; 95% CI: 0.53 to 0.75), all cardiovascular events (HR: 0.63; 95% CI: 0.53 to 0.76), myocardial infarction (HR: 0.69; 95% CI: 0.51 to 0.92), and stroke (HR: 0.34; 95% CI: 0.18 to 0.63) were less in the group with >75% of visits with BP control compared with the group with <25% of visits with BP control. These findings were not significantly modified when the data were analysed on the basis of two treatment groups (placebo or nifedipine GITS).

These retrospective analyses highlight the importance of the current recommendations for the treatment of hypertension. The present study shows that CSWT application to the ischemic myocardium in patients with refractory angina pectoris, improved symptoms and reduced severity of ischaemic areas at 6 months follow-up, compared to baseline. No side-effects were observed. We recommend further studies to confirm the results.

**UPDATE ON INNATE AND ADAPTIVE IMMUNITY IN CORONARY ARTERY DISEASE**

**P4463**

**Interleukin-6 promoter genetic polymorphism is associated with the presence and the severity of coronary artery disease**

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**Purpose:** Interleukin 6 (IL-6) is marker of inflammatory process, closely related to the initiation and evolution of atherosclerosis. However, it remains unclear, whether common polymorphisms within the IL-6 gene affect the mechanisms of atherosclerosis. In the present study we examined the impact of the common polymorphism G-174C on IL-6 gene promoter on the severity of coronary artery disease (CAD) as well as on endothelial function.

**Methods:** The study population consisted of 272 patients with angiographically documented coronary artery disease (CAD) and 160 healthy controls. The G-174C polymorphism was determined by PCR and digestion with SFAN1 restriction enzyme. Endothelial function was assessed by flow mediated dilation (FMD).

**Results:** The genotype distribution among the CAD patients was GG: 47.4%, GC: 30.5%, CC: 22.5%, and GG: 47.8%, GC: 43.8%, CC: 8.4% for the healthy controls. Our results showed that the CC polymorphism was associated with the presence of CAD (RR=1.11, 95% CI: 1.03-2.0; p=0.05). Importantly, the present polymorphism was also associated with the angiographic extent of CAD (X2 =11.64, p<0.001). Although, the CC homozygosity was associated with lower FMD compared to the G allele carriers, this difference did not reach statistical
Lipoprotein-associated phospholipase A2 (Lp-PLA2) expression is inversely correlated with memory T cell expression in patients with CAD.

**Methods:** We studied 30 patients with a first STEMI treated with percutaneous coronary intervention. Memory T cells were serially determined by flow cytometry before reperfusion (basal) and further CD4CXCR3 and CD4CCR4 in the first 96 hours of reperfusion. Lp-PLA2 was measured in circulating monocytes of patients and healthy subjects. The relationship between T memory cells with MVO in reperfused STEMI.

**Results:** A rise of T memory cells was significantly associated with MVO after reperfusion (Figure). In the subgroup of patients with severe multivessel coronary artery disease (MVD), T memory cells were associated with more MVO compared to patients with fewer MVO.

**Conclusions:** Lp-PLA2 expression in memory T cells and cytokine receptors expression is closely related to MVO and it could be a pathophysiological mechanism to explain MVO plugging in reperfused myocardium. Further studies will be needed to determine if T cell number during the first stages of MI could be a useful predictor of MVO.

**Figure 1**

**P4466**

Memory T cells are related with microvascular obstruction in ST segment acute myocardial infarction

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**Purpose:** In ST segment elevation myocardial infarction (STEMI) successful restoration of epicardial coronary artery flow might result in microvascular obstruction (MVO). The pathophysiology of this process and its relationship with lymphocyte trafficking has not been fully defined. The aim of this study was to determine the relationship between T memory cells with MVO in reperfused STEMI.

**Methods:** We studied 30 patients with a first STEMI treated with percutaneous revascularization. Distinct subtypes of memory T cells: T naive (CD45RA/CD4/CD62L-), and memory: T effector memory (TEM) (CD45RO/CD4/CD62L+), and chemokine receptors: CXCXR3 and CCR4 were serially determined by flow cytometry before reperfusion and 24 h and 30 days afterwards; values were compared with 30age- and sex-matched control subjects with normal coronary arteries. Cardiac magnetic resonance was used to detect microvascular obstruction during the first week after the infarction.

**Results:** In comparison with controls, patients displayed more circulating TEM cells. In STEMI patients there was a significant increase of TEM cells during first 30 hours compared with basal levels (p<0.05). T naive cells was associated with more MVO (Figure 1). An increment of TEM cells was correlated with lymphocyte trafficking after 24 hours with further TEM cells and further CD4CCR4 (132±94 vs 242±82 cells/μl) and CD4CCR4 (132±94 vs 242±82 cells/μl) (p<0.001 in both cases).

**Conclusions:** Lymphocyte trafficking understood as an increase of memory T cells and chemokine receptors expression is closely related to MVO and it could be a pathophysiological mechanism to explain MVO plugging in reperfused myocardium. Further studies will be needed to determine if T cell number during the first stages of MI could be a useful predictor of MVO.

**Figure 1**
Role of CD31 and CD38 in innate and adaptive immunity in patients with chronic stable angina

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Purpose: CD38 is a molecule implicated in leukocyte transendothelial migration and immunomodulation by TCR inhibition. CD31 is involved in homophilic and heterophilic binding interactions with different ligands like CD38. CD38 is a functionally pleiotropic molecule implicated in transmembrane signaling and adhesion of immune cells. Recent studies have highlighted the importance of innate and adaptive immunity in acute coronary syndromes (ACS).

We aim to evaluate CD31 and CD38 expressions by different monocyte and T-cell subsets in patients with ACS compared to chronic stable angina (SA). We also analyzed CD31 signaling in CD4+T-cells after TCR stimulation.

Methods: Consecutive patients with Non-ST elevation ACS (n=12) and SA (n=16) were enrolled. CD31 and CD38 were assessed by median fluorescence intensity (MFI) of different monocyte subsets, total CD4+ and CD4+CD28null T-cells was assessed by flow cytometry. In T-cells, CD31 signaling was assessed by ZAP-70 phosphorylation after TCR stimulation with CD3/CD28 and CD31 monoclonal antibody.

Results: Data are presented as mean ± SE. ACS patients had lower CD31 expression on monocyte and T-cell subpopulations as compared with SA (see Table), but there were no differences in CD38 expression. Moreover, ACS patients showed a reduced TCR inhibition after stimulation with CD31 monoclonal antibody of both total CD4+ T-cells (ACS=6.2% vs SA=19.2% P<0.001) and CD4+CD28null T-cells (ACS=10.5% vs SA=26.8% P=0.005). Thus, in ACS the reduced expression of CD31 is related to an impaired control of the immune response.

Conclusions: In ACS, the altered CD31/CD38 expression and the reduced function of CD31 pathway suggest a defective immunomodulation which could contribute to the impaired control of inflammation. Our data also support the importance of CD31-mediated signaling in modulating low-grade inflammation in SA.

Figure 1. Cox regression results for the IAP group.

Erythrocyte aggregation portends worse outcomes in unstable angina patients undergoing percutaneous coronary interventions

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Background: We have previously reported a correlation between the time from symptom onset to the appearance of an inflammatory response and erythrocyte aggregation (EA) in the peripheral blood of acute coronary syndrome (ACS) patients. We now analyze the added prognostic value of EA determination in ACS patients undergoing percutaneous coronary interventions (PCI).

Methods: We performed an analysis on prospectively collected data at a tertiary hospital and catheterization laboratory between 2006-2011. Cox regression analysis were used to determine the relationship.

Results: There were 119 patients (46%) with at least two atherosclerosis risk factors of atherosclerosis, with and without CAD were patients undergoing percutaneous coronary interventions (PCI).

Purpose: High sensitivity C-Reactive Protein (CRP) and endothelin (ET-1) are biomarkers of cardiovascular risk in patients with and without coronary artery disease. The dynamic response of retinal vessel diameter to flicker-light is a measure of endothelial function. In this study, we sought to determine the relationship of flicker-light induced retinal arteriolar dilatation (FI-RAD) with CRP and ET-1.

Methods: Patients with risk factors of atherosclerosis, with and without CAD were recruited (n=258). FI-RAD was measured in both eyes after pupil dilatation using the Dynamic Vessel Analyzer (DVA) and expressed as percentage increase over baseline diameter in response to flicker light. CRP was measured by the rate turbidity method and ET-1 by radioimmunoassay method. Pearson’s correlation and linear regression analysis were used to determine the relationships.

Results: There were 119 patients (46%) with at least two atherosclerosis risk factors but no CAD, 78 patients (30%) with stable CAD and 61 patients with an acute coronary syndrome (ACS, 24%). The mean age of the total sample was

Update on innate and adaptive immunity in coronary artery disease
58±11 years (mean±SD) and 175 patients were male (68%). The sample included 73% of patients with hypertension, 78% with dyslipidemia and 36% with diabetes. The BMI was 32.6±7 kg/m², total cholesterol 4.5±1.3 mmol/l, fasting glucose 6.4±2.4 mmol/l, CRP was 8.3±14.5 mg/l and ET-1 was 2.5±0.7 pmol/l (mean±SD). In the overall sample FI-RAD was inversely correlated with CRP (r=-0.13; p=0.04) and ET-1 (r=-0.16; p<0.01). For each 1 mg/l increase in CRP, FI-RAD decreased by 0.19% (95% CI -0.30, -0.08; p=0.04). For each 1 pmol/L increase in ET-1, FI-RAD decreased by 0.44% (95% CI -0.78, -0.1; p=0.01). After adjustment for age, gender, hypertension, systolic blood pressure, BMI, dyslipidemia, cholesterol and glucose, the association between FI-RAD and CRP or ET-1 remained unchanged within 12-24 hours after PPCI (r²=0.8; p=0.0001). This ACS-related attenuation of retinal arteriolar diameter changes to flicker light. The relationship between FI-RAD and ET-1 was only present among ACS patients. These data suggest that plasma markers of endothelial function and vascular inflammation are linked to retinal microvascular vasodilator function.

### P4472 Myocardial injury induces AIM2 inflammasome expression in neutrophil granulocytes in patients with acute coronary syndrome

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**Background:** Early priming and recruitment of neutrophil granulocytes (PMN) play a major role in myocardial injury following acute coronary syndrome (ACS). Molecular mechanisms of PMN activation after myocardial ischemia and reperfusion remain largely unknown. In-vitro and animal studies could show that specific intracellular protein complexes, so-called inflammasomes (e.g. Nlrp3 or AIM2) can initiate an inflammatory response by sensing host-derived danger signals (DAMPs), such as ATP and other cellular components released during tissue injury. The aim of the present study was to investigate the inflammation activation in PMN and its role in induction of the sterile inflammatory response in patients with ACS.

**Methods:** 75 patients (pts) with chronic heart disease (CHD) were included into this study. 50 pts with ACS (25 with STEMI, 25 with NSTEMI) and 25 pts with stable CHD were analyzed before and 12-24 hours after primary percutaneous coronary angioplasty (PPCI) or prior to elective coronary angiography, respectively. 20 healthy volunteers were enrolled as controls (Ctrl). In an in-vitro cell culture model PMN from healthy donors (n=5) were stimulated with ATP and dsDNA. Expression of the inflammasome-associated genes was analyzed using quantitative real-time PCR (relative copy number, RGN). Protein expression was quantified using Western Blot analysis.

**Results:** Expression of mRNA for AIM2 inflammasome was significantly higher in ACS as opposed to stable CHD pts (RCN 88.1±7.7 vs. 59.4±5.4; p=0.02) or healthy controls (88.1±7.7 vs. 88.3±3.7; p=0.001). This ACS-related activation remained unchanged within 12-24 hours after PPCI (r²=0.8; p=0.0001). AIM2 expression was higher in NSTEMI than in the STEMI group (84.1±4.7 and 83.5±8.1; p=0.009 and p=0.0001 vs. Ctrl). Protein expression analysis confirmed significant induction of AIM2 in STEMI (fold-change vs. Ctrl: 5.6±1±10; p<0.0001). NSTEMI pts. (7.2±6.7; p=0.001). In-vitro PMN stimulation with injury-associated DAMPs, dsDNA and ATP, resulted in a 5-fold increase in AIM2 protein expression.

**Conclusion:** Our results identify the first time enhanced expression of AIM2 inflammasome in PMN in patients with acute coronary syndrome. Our data suggest that inflammation activation in PMN contributes to the early ischemia-triggered inflammatory response. Measuring inflammasome activation may therefore provide a novel clinical parameter for improved diagnosis and risk assessment in patients with ACS.

### P4473 Monocyte chemotractant protein-1 release does not respond to acute variations of background inflammation and lipid peroxidation, but it is subjected to circadian variations

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**Purpose:** Monocyte chemotactrant protein-1 (MCP-1) is an important player in atherosclerosis-related inflammatory response, released by various organs including the adipose tissue. However it is still unclear whether acute inflammation and the resulting lipid peroxidation regulates the release of MCP-1 in humans.

We investigated the effects of acute inflammation on MCP-1 release in healthy subjects. 

**Methods:** Eighty healthy individuals were randomized to receive Salmonella Typhi vaccine (S.typhi) or placebo vaccine and followed up for 24 hours. Circulating levels of MCP-1, interleukin-6 (IL-6, marker of acute inflammation) and malondialdehyde (MDA, marker of lipid peroxidation) were measured at baseline (at 08:00) and 0.5% (95% CI post-intervention. Serum MCP-1 and IL-6 were measured by ELISA, while plasma MDA by using a fluorometric method.

**Results:** Acute inflammation was documented by an increase in serum IL-6 at 6h in the group receiving S.typhi vaccine (B) but not in the placebo group (A). Importantly MCP-1 levels followed a distinctively different pattern, not being affected by acute inflammation, but being significantly decreased at 6h post-intervention in both groups (E, F).

**Conclusions:** Acute inflammation is not a strong regulator of circulating MCP-1 levels in healthy subjects. Despite the increase in circulating proinflammatory cytokines and stimulation of lipid peroxidation, MCP-1 levels are not affected by acute inflammation. On the contrary, circulating MCP-1 is subjected to circadian variations which might have important clinical implications in atherosclerosis-related vascular inflammation.

### P4474 Increased YKL-40 levels in patients with isolated coronary artery ectasia

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**Background:** YKL-40, new biomarker of localized inflammation, is secreted by macrophages in the atherosclerotic plaques. Coronary artery ectasia (CAE) is a clinical entity characterized with localized or diffuse dilatation, of the coronary arteries, greater than 1.5 times diameter of adjacent segments. Although the etiopathogenesis is not clearly understood, some studies have revealed that CAE may be a form of atherosclerosis that has greater inflammatory properties than atherosclerosis. The goal of this study was to investigate whether YKL-40 and C-reactive protein (CRP) are increased in patients with isolated CAE compared to patients with coronary arterial disease (CAD).

**Methods:** Forty-nine patients with isolated CAE (mean age: 60±10 years) and 30 age- and gender-matched control participants with NCA, but without CAE (mean age: 61±10 years) were included in the study. The relationship between YKL-40, CRP levels and the presence of CAE was investigated.

**Results:** Serum YKL-40 levels were significantly higher in CAE group compared to NCA group (144±68 vs. 110±53 μg/L, p=0.015). CRP was not significantly different between two groups (0.67±0.63 vs. 0.53±0.39, p=NS). In addition, there were not any statistically significant differences, with respect to age, gender, the presence of hypertension or diabetes mellitus, and the smoking status (p=0.05), except creatinine levels (0.89±0.21 vs. 0.79±0.11 mg/dL, p=0.012). When we performed multiple logistic regression analysis, YKL-40 level was still significantly elevated (odds ratio, 8.04, 95% CI: 1.01-0.026, p=0.029) independent of CRP and the other study parameters.

**Conclusion:** This is the first study displaying an significantly elevated YKL-40 level in patients with isolated CAE. We believe that further studies are needed to clarify the role of YKL-40 in patients with isolated CAE.
Inflammation of peri-coronary adipose tissue may affect plaque destabilization in patients with non ST segment myocardial infarction

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Background: Extravascular expression of inflammatory mediators may adversely influence coronary lesion formation and plaque stability through outside-to-inside signaling. It has been previously shown, that maximal standardized uptake value (SUV) of 18-fluorodeoxyglucose (FDG) detected by positron emission tomography in peri-coronary adipose tissue (PVAT) is greater in patients with stable coronary artery disease (CAD), than in controls. It also correlates with % of coronary stenosis. We sought to investigate, whether PVAT may influence plaque composition.

Methods: 20 coronary arteries (LM, RCA, LCX, LAD) have been investigated in non-diabetic patients with moderate and low risk NSTEMI (GRACE < 140). SUV was measured in fat surrounding coronary arteries on the sections corresponding to proximal and medial segments. PVAT thickness was measured in two perpendicular dimensions on axial cuts separately for the LM, RCA, LAD and LCX, using steady state free precession cine imaging. Additionally SUV was measured in subcutaneous fat (SC), visceral thoracic fat (VS), epicardial fat over right ventricle (EPI). Conventional and virtual histology intravascular ultrasound (VH-US) was performed to assess plaque composition, which were classified as calcified, fibrous, fatty, or necrotic core. PET/CT sections were further examined in segments corresponding to coronary plaques.

Results: PVAT SUV in NSTEMI patients was significantly greater than in other fat locations (LM SUV: 1.54; RCA SUV: 1.42; LCX SUV: 0.98; LAD SUV: 2.34 vs SC SUV: 0.60; VS SUV: 0.80; EPI SUV: 0.98; p<0.01; ANOVA). There was no significant correlation between PVAT thickness and plaque composition. In contrast PVAT SUV positively correlated with necrotic core plaque rate r (r = 0.67, p<0.05), and negatively correlated with fibrous plaque rate (r = -0.50, p<0.05). There was also positive correlation between PVAT SUV and % plaque volume (r=0.32, p<0.05).

Conclusions: Inflammatory activity of peri-coronary adipose tissue reflected by SUV is greater than in subcutaneous, visceral thoracic, or epicardial tissue in NSTEMI patients; There is no association between amount of pericoronary fat and plaque composition; PVAT SUV correlates with necrotic core component of coronary plaque and plaque volume in patients with NSTEMI; In conclusion, pro-inflammatory activity of PVAT in patients with NSTEMI may contribute to plaque formation, vessel narrowing and plaque rupture, supporting the hypothesis of the outside-to-inside signaling.

Low-grade inflammation and post-operative clinical outcome in elective coronary artery bypass surgery: the emerging role of monocyte chemoattractant protein 1

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Background: Low-grade inflammation is strongly involved in the pathophysiology of coronary artery disease. However, the role of low-grade inflammation on clinical outcome post-coronary bypass surgery (CABG) is unclear. We explored the role of key components of low-grade inflammation such as interleukin 6 (IL-6), C-reactive protein (hsCRP) and monocyte chemoattractant protein 1 (MCP-1) in clinical outcome of patients undergoing elective CABG.

Methods: We recruited 181 patients scheduled for elective CABG. The morning before the operation, following an 8-hours fasting period, blood samples were obtained andobined and CRP and monocyte chemoattractant protein 1 (MCP-1) in clinical outcome of patients undergoing elective CABG.

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Results: Higher MCP-1 (A) and IL-6 (B) but not hsCRP (C) levels were associated with increased length of hospital stay for those patients. In co-regression, MCP-1 (A) was a strong predictor of the length of hospital stay (p<0.01), independently of risk factors, Euroscore, extend of coronary artery disease and left ventricular ejection fraction preoperatively.

Conclusions: Low MCP-1 levels are associated with decreased length of stay following CABG, whereas CRP levels (the most commonly used inflammatory biomarker) failed to predict the length of hospitalization in these patients. These
Purpose: To established levels of CXCR4+ reparative monocytes and monocyte-derived endothelial progenitor cells (EPCs) derived from distinct monocyte subsets in STElevation MI(STEMI) and non-STEMI.

Methods: CXCR4+ cells and CD34+KDR+ EPCs, attributable to individual monocyte subsets (Mon1, Mon2, Mon3), were measured by flow cytometry in patients with STEMI, NSTEMI, and stable CAD (Table). Left ventricular ejection fraction (LVEF) was measured within 6 weeks after STEMI onset.

Results: CXCR4+ cells derived from Mon1 and Mon2 were increased in STEMI. CXCR4+Mon3 were increased in NSTEMI. Only EPC derived from Mon3 were increased in both STEMI and NSTEMI. In STEMI CXCR4+Mon1 and CXCR4+Mon2 decreased by 1 month, with similar trend seen for Mon3-derived EPC. After adjustment for age, sex, diabetes and troponin levels only CXCR4+Mon3 (taken as average of the 4 time points) were independently predictive of LVEF (p=0.05, p=0.02).

Conclusions: Only specific monocyte subsets contribute towards upregulation of reparative and angiogenic monocytes in MI. CXCR4+Mon2 are independently associated with cardiac recovery post MI. These cells may represent a new therapeutic target in the future.

The association of neutrophil/lymphocyte ratio with coronary flow and in-hospital mace in patients with STEMI undergoing primary PCI

Purpose: With the growing understanding of the role of inflammation in the atherosclerosis, studies have focused on hs-CRP and other inflammatory markers in the management of ST segment elevation myocardial infarction (STEMI). In this study, we aimed to investigate the role of neutrophil/lymphocyte (N/L) ratio and in-hospital major adverse cardiac events (MACE) in patients with STEMI undergoing primary PCI.

Methods: A total of 961 consecutive female patients (pts) underwent the ACH provocation test were enrolled. The pts were divided into two groups according to the level of hs CRP. Cut off value of hs CRP was defined as 1mg/dL. (high hs CRP >1 mg/dL and low hs CRP ≤1mg/dL)

Results: At baseline characteristics, the incidence of old age was higher in the pts with high hs CRP . At multivariate regression analysis, N/L ratio was still independent predictor of no-reflow (OR 1.537, 95% CI 1.343–1.759; p < 0.001) and in-hospital MACE (OR 1.137, 95% CI 0.981–1.315; p =0.043).

Conclusions: N/L ratio which is a cheap and easily measurable laboratory variable is independently associated with the development of no-reflow and in-hospital MACE in patients with STEMI undergoing primary PCI.
Suppression of iron metabolism pathway and Low T3 syndrome and inflammation in patients with acute myocardial infarction did not result in increased adverse clinical events. Routine biohumoral exams including haemoglobin, creatinine, TH, C-reactive protein (CRP), fibrinogen dosage and erythrocyte sedimentation rate (ESR) were not found in the erythropoietin group. Left ventricular ejection fraction was significantly increased after 6 months of the onset of myocardial infarction in the control group (Figure). However, these changes were not found in the erythropoietin group. Conclusions: LT3S is associated with a worse clinical status, a greater degree of inflammatory activation and a lower ejection fraction in patients with STEMI. In these subjects, an altered TH metabolism and enhanced inflammation may contribute to post-ischemic myocardial dysfunction and progression towards heart failure.

Methods:

Aim of this study is to evaluate the relationship between LT3S and inflammatory activation and cardiac function during ischemia. Interleukin-6/hepcidin system for cardiac injury and protection during ischemia. Conclusions: LT3S is associated with a worse clinical status, a greater degree of inflammatory activation and a lower ejection fraction in patients with STEMI. In these subjects, an altered TH metabolism and enhanced inflammation may contribute to post-ischemic myocardial dysfunction and progression towards heart failure.

Purpose: Erythropoietin has been shown to have anti-apoptotic and tissue protective effects on the myocardium in experimental studies. However, the clinical effects of administration of erythropoietin on myocardial infarction are controversial. We conducted a prospective, randomized, placebo-controlled single-blind study to assess the effects of erythropoietin administration on iron metabolism substances and cardiac function in patients with acute myocardial infarction.

Methods and Results: This study included 36 patients (61±11 years, 6 females) with acute myocardial infarction who received successful percutaneous coronary intervention within 24 hours after the onset of myocardial infarction. Patients were randomly assigned to receive intravenous injection of either erythropoietin (12,000 IU/body) or saline placebo within 24 hours after coronary intervention. The serum levels of interleukin-6, hepcidin, and ferritin were increased, and the iron levels were decreased on day 4 after the onset of myocardial infarction in the control group (Figure). However, these changes were not found in the erythropoietin group. Left ventricular ejection fraction was significantly increased after 6 months of the onset of myocardial infarction in the erythropoietin group (from 51±20% to 59±15%, P<0.02), but was not changed in the control group (from 47±16% to 51±16%, P=NS). Erythropoietin administration did not result in increased adverse clinical events.

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A gene expression was estimated by the number of mRNA copies per one microgram of total RNA sample.

**Results:** The gene expression of TGFβ1 and its receptors in peripheral blood mononuclear cells was estimated with QRT-PCR technique in the study group - patients with ACS and in the control group of healthy subjects - Table 1.

**Conclusion:** Significantly reduced gene expression of TGFβ1 and its receptors in PBMC of patients with severe stable CAD than in healthy controls. Alterations of these transcripts may reflect the level of disease severity.

**Introduction:** The epicardial thrombus burden and distal macro- and microembolization are associated with perfusion deterioration during acute phase of ST-segment elevation myocardial infarction (STEMI) but their influence on microvascular obstruction remains poorly understood. We sought to investigate the quantitative impact of ex vivo measured fibrin clot properties and platelet function on microvascular obstruction.

**Methods:** Plasma clot permeability (Ks) and passive permeability of clot surface (Km) were measured as % of infarct size and reduced clot permeability.

**Results:** During acute phase of STEMI pore size of fibrin clot was lower by 28% (5.6 vs. 7.1 μm, P<0.001) and clot lysis time was prolonged by 20% (10.7 vs. 8.9 min, P<0.001) as compared to follow-up measurements. The area of MVO was also significantly smaller (40.3 vs. 55.7 μm², P<0.001) and clot lysis time was longer by 20% (10.7 vs. 8.9 min, P<0.001) as compared to follow-up measurements. The area of MVO was also significantly smaller (40.3 vs. 55.7 μm², P<0.001) and clot lysis time was longer by 20% (10.7 vs. 8.9 min, P<0.001) as compared to follow-up measurements.
Prevalence of microvascular obstruction after primary percutaneous coronary intervention is higher in male patients with hypogonadism.

**Background:** Testosterone deficiency afflicts approximately 30% of Men aged 40-79 years. Recent studies claimed that androgen deficiency contributes to the onset and progression of cardiovascular disease. Microvascular obstruction (MO) is a common event associated with a worse prognosis and unfavorable left ventricular remodeling after primary percutaneous coronary intervention (P-PCI). However, mechanisms involved in MO have not been fully elucidated yet. We evaluated the importance of gonadal function in the onset of MO.

**Methods:** We studied 54 patients with stable effort angina and known positive exercise stress test (EST) results in patients with microvascular angina (MVA) compared to patients with obstructive coronary artery disease (CAD). Patients underwent 2 maximal treadmill ESTs on 2 separate days, in a random sequence, after withdrawing all medications: one EST without any interference (control EST) and one EST after sublingual administration of isosorbide dinitrate (5 mg, ISDN-EST). CBF response to nitroglycerin (25 μg) was assessed in the left anterior descending coronary artery by means of transonic echo-Doppler.

**Results:** ST-segment depression >1 mm (STD) at the control EST was induced in 26 (90%) and in 24 (90%) of MVA and CAD patients, respectively (p=0.41), whereas at the ISDN-EST, STD was induced in 25 (86%) patients with MVA, but in only 14 (56%) patients with CAD (p=0.01). At control EST maximal STD was similar in MVA and in CAD patients (1.5±0.7 vs. 1.3±0.4, respectively, p=0.07); at ISDN-EST maximal STD did not change in MVA patients, whereas it was significantly reduced in CAD patients (1.5±0.7 vs. 1.3±0.6, p=0.15 and 1.3±0.4 vs. 0.6±0.6, p<0.01, respectively). In MVA patients, rate-pressure product (RPP) at 1 mm STD at ISDN-EST and at the control EST was 2129±5438 and 2081±4286 bpm·mmHg, respectively (p=0.35); the same RPP values in CAD patients were 22650±5014 and 20731±6091 bpm·mmHg, respectively (p=0.03). In MVA patients, time to 1 mm STD at ISDN-EST and at the control EST was 308±160 and 284±136 s, respectively (p=0.19); the same values in CAD patients were 474±112 and 367±163 s, respectively (p=0.01). CBF response to NTG was significantly lower in MVA compared to CAD patients (1.4±0.3 vs. 1.7±0.3, p=0.01); in MVA patients a significant correlation was found between CBF response to NTG and heart rate at STD during ISDN-EST (r=0.40, p=0.04).

**Conclusions:** In MVA patients, short-acting nitrates improve EST results in CAD, but not in MVA patients. A lower NTG-induced coronary microvascular dilatation seems to contribute to EST positivity after nitrate administration in patients with MVA.
Objective: We investigated the correlation between IMR and infarct size in anterior and non-anterior STEMI.

Method: We investigated 104 patients who underwent successful pPCI for STEMI within 12 hours after onset between April 2009 and March 2011. CK-MB was measured 1, 2, 4, 6, 9, 12, 18, 24, 48, 96 hours after pPCI, and the area under the curve of CK-MB (CK-MB AUC) was calculated as the index of infarct size. We evaluated the IMR as the quantitative index of microvascular dysfunction. After successful pPCI, IMR was measured using a PressureWireTM Certus (St. Jude Medical, USA) at maximal hyperemia.

Result: There was a significant correlation between IMR and infarct size in anterior STEMI. However, this finding was not observed in non-anterior STEMI.

Conclusion: IMR may predict infarct size in only anterior STEMI, but not in non-anterior STEMI.

P4496

Quantitative analysis of microvascular obstruction is best related to clinical prognosis than clinical markers at a 1 year follow-up: a contrast-enhanced MRI study

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Objectives: To evaluate the clinical prognostic value of a cardiac magnetic resonance (CMR) assessment soon after a first ST-segment elevation myocardial infarction (STEMI).

Background: Clinical factors such as gender, age, blood pressure, heart beat, heart and renal failure have already been described as related to poor clinical prognosis at follow-up. For now, the prognostic value and weight of CMR parameters is not well-defined.

Methods: We followed for 1 year up to 168 consecutive patients with a first STEMI treated with primary angioplasty. We performed CMR at day 5±2 and 3 months to assess LV volumes. We used delayed enhancement imaging to assess the infarct size and the presence of MVO. We defined severe MVO as MVO extent being superior to its median value (28.2 gr).

Results: 13 major adverse cardiac events (MACE) including 2 cardiac deaths, 1 non-fatal myocardial infarctions, 8 readmissions for heart failure and/or stroke were documented. In univariate analysis, the MACE was related to age, creatin kinase peak, heart failure, MVO and LV volumes. In a complete multivariate analysis, age (hazard ratio 1.075, p=0.003), end-diastolic LV volume (HR 0.74, p=0.017), end-systolic LV volume (HR 1.046, p=0.039), MVO presence (HR 8.867, p=0.041; Log hazard ratio 1.075, p=0.003), end-diastolic LV volume (HR 0.74, p=0.017), end-systolic LV volume (HR 1.046, p=0.039), MVO presence (HR 8.867, p=0.041; Log rank = 9.195, p=0.002) and severe MVO (HR 9.906, p=0.002; Log rank = 18.090, p<0.001) were the only independent prognostic variables. Of note, clinical marker such as heart failure was strongly related to age and found as non significant in multivariate analysis.

Conclusion: A comprehensive CMR assessment is useful for stratifying risk soon after STEMI: baseline LV volumes and severe MVO are the stronger independent prognostic factor. This result supports the clinical interest of a quantitative assessment of MVO.

P4496

Coronary microvascular function is impaired in diabetic patients with normal coronary arteries and correlates to renal function

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Purpose: Endothelial dysfunction is thought to represent a common pathogenetic mechanism of impaired coronary flow reserve (CFR) and renal dysfunction in patients with type 2 diabetes mellitus (DM), yet no data are available on the relationship between CFR and renal function in these patients.

Methods: In the same day, while off drugs, we studied endothelial-dependent, during cold pressor test (CPT), and independent (dipyridamole infusion (Dip) 0.84 mg/kg over 6 minutes) CFR using transthoracic Doppler echocardiography of the left descending coronary artery in 23 DM (12 men; age 62±10; and 25 non DM patients (17 men; age 61±10), matched for all other cardiovascular risk factors. Glomerular filtration rate (GFR) was estimated by Cockcroft Gault formula in the same day of CFR studies. All patients had no significant coronary artery disease (CAD) at invasive coronary angiography performed within 7 days from CFR.

Results: CPT-CFR (1.46±0.26 in DM vs 1.70±0.33 in non DM; p=0.007) and Dip-CFR (2.38±0.74 in DM vs 2.76±0.04 in non DM; p=0.04) were significantly lower in DM patients. GFR did not statistically differ between DM and non DM patients (85.28 vs 86.25 ml/min/1.73m2, respectively; p=0.96) with 42% of patients in class I and 58% in class II-III renal dysfunction. In DM patients a significant direct correlation was found between GFR and CPT-CFR (r=0.55; p=0.007), but not between GFR and Dip-CFR. In DM patients with GFR above the median (75 ml/min/1.73m2), CPT-CFR was significantly higher (1.52±0.19) than in DM patients with GFR below the median (1.33±0.20; p=0.00), whereas no difference was found for Dip-CFR (2.48±0.75 vs 2.30±0.70; p=0.57). Moreover, a weak significant correlation was found between fasting glyceremia and CPT-CFR (r=0.34; p=0.016) but not with Dip-CFR.

Conclusion: In DM patients without epicardal coronary stenosis microvascular function is significantly impaired compared to non DM patients with similar risk factors. However, only endothelial dependent CFR significantly correlates to GFR. These findings support the role of endothelial dysfunction as common pathogenetic mechanism of renal and myocardial dysfunction in DM patients.

P4497

The Impact of ECG Change during Intracoronary Acetylcholine Provocation Test on the 12 months Clinical Outcomes in Korean patients

S.W. Rha1, J.Y. Park2, S.K. Ryu1, J.W. Choi1, B.G. Choi1, A. Elnagar1, S.I. Im1, S.W. Kim1, C.U. Choi1, D.J. Oh1. 1Korea University Guro Hospital, Seoul, Korea, Republic of; 2Eulji University, Seoul Eulji Hospital, Seoul, Korea, Republic of

Background: The ischemic electrocardiography (ECG) changes are known to be a predictor of ischemic heart disease. However, whether the ischemic ECG changes occurred during acetylcholine (Ach) provocation test is associated with clinical outcomes is largely unknown. We evaluated the impact of ischemic ECG changes occurred during Ach test on Ach induced coronary artery spasm (CAS) and 12 months clinical outcomes.

Methods: A total 2441 consecutive pts without significant coronary artery disease who underwent the Ach test were enrolled between November 2004 and October 2010. Ischemic ECG changes were defined as ST elevation, ST depression, and deep T wave inversion. The patients were divided two groups according to ischemic ECG changes occurred during Ach test (ischemic ECG changes group: n=88, control group: n=1305).

Results: At baseline characteristics, there were no differences between two groups. At angiographic characteristics, the incidence of basal spasm (43.8% vs 30.7; p=0.010), multivessel (58.4% vs 36.9%; p=0.003) and diffuse (92.1% vs 81.0%; p=0.001) spasm were higher in the pts with ischemic ECG changes. At 12 month clinical outcomes, the incidence of cardiac death (2.3% vs 0.0%, p=0.001) and myocardial infarction (1.1% vs 0%, p=0.003) were significantly higher in the pts with ischemic ECG changes (table). Multivariate analysis showed that the ischemic ECG change was an independent predictor of mortality (odds ratio: 125.3, 95% confidence interval: 3.4-447.2, p=0.008) up to 12 months.

Table 1. 12 months clinical outcomes

<table>
<thead>
<tr>
<th>Ischemic ECG change (n=88)</th>
<th>Control (n=1305)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2 (2.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (2.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>PTCa</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>CKd</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Conclusion: In this study, ischemic ECG change occurred during Ach test was associated to 12-month clinical outcomes. Therefore, if the ischemic ECG change was observed during Ach test, intensive antianginal treatments and close clinical follow up would be needed.

P4498

Association of myocardial bridge and acetylcholine induced coronary artery spasm and 12-months clinical outcomes

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Background: Myocardial bridge is known to be a strong predictor of coronary artery spasm (CAS). However, whether myocardial bridge (MB) is associated with clinical outcomes is largely unknown. We evaluated the impact of MB on CAS induced by acetylcholine (Ach) provocation test and 12 months clinical outcomes.

Methods: A total 2441 consecutive patients (pts) without significant coronary...
Twelve months clinical outcomes of diffuse coronary artery spasm as compared with focal coronary artery spasm

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Background: There are limited data regarding features & outcome of diffuse coronary artery spasm (CAS) in patients (pts) with vasospastic angina. We investigated whether diffuse CAS have specific procedure related features and its clinical outcome as compared with focal CAS.

Methods: A total 1384 consecutive pts [Men: 721 (52.1%), mean age: 55.1±11.6 years], who underwent intracoronary Acetyl choline (Ach) provocation test. Provocation test was performed by intracoronary injection of incremental dosages (20, 50, 100ug) of Ach. The study population were divided into focal spasm group (2004±30mm) and diffuse spasm group (11.6±55.6mm). Significant CAS was defined as transient >70% luminal narrowing with chest pain and/or ST segment changes.

Results: Baseline clinical characteristics were similar between the two groups except that diffuse spasm group had a higher body mass index (24.3±3.2 vs 23.9±2.9, p=0.067) & lower ejection fraction (58.6±4.2 vs 59.1±2.7, p=0.049). Regarding procedure related characteristics, diffuse spasm group had a higher incidence of chest pain, multi-vessel spasm, and ischemic EKG changes. At twelve months clinical follow up, there was a trend towards higher MACCE in focal spasm group (Table 1).

Conclusion: In our study, MB was associated with ACH induced CAS, and multivessel and diffuse spasm. But MB was not associated with the 12-months clinical outcomes.

Table 1. 12 months clinical outcomes

MB (n=367) Control (n=1027) p-value

<table>
<thead>
<tr>
<th>Variable</th>
<th>MB</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE</td>
<td>5 (1.4)</td>
<td>8 (0.7)</td>
<td>0.31</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (0.2)</td>
<td>3 (0.3)</td>
<td>0.95</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>0 (0.0)</td>
<td>2 (0.2)</td>
<td>0.39</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0.0)</td>
<td>1 (0.0)</td>
<td>0.50</td>
</tr>
<tr>
<td>PTCA</td>
<td>2 (0.5)</td>
<td>6 (0.5)</td>
<td>0.93</td>
</tr>
<tr>
<td>CVR</td>
<td>2 (0.5)</td>
<td>2 (0.2)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Impact of alcohol on coronary artery spasm as assessed with intracoronary acetycholine provocation test

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Background: There are limited data regarding impact of chronic alcohol use on vasospastic angina. We evaluated the impact of alcohol use on coronary artery spasm (CAS) as assessed with intracoronary acetylcholine (Ach) provocation test.

Methods: A total 3034 consecutive patients [pts, Men 1457 (48.0%), mean age 54.5±12.4 years] who underwent coronary angiography with Ach provocation test were enrolled. Study population were divided into current alcoholic (912, 30.1%) vs. non alcoholic (2101, 69.2%) groups. Significant CAS was defined as transient >70% luminal narrowing with chest pain and/or ST segment changes.

Results: Baseline clinical characteristics were balanced except non alcoholic had more hypertension (49.3% vs. 40.4%, P=0.001), diabetes (13.6% vs. 10.2%, P=0.009), peripheral vascular disease (6.3% vs 3.2%, P=0.001), history of CVA (3.5% vs.2.1%, P=0.041), congestive heart failure (2.0% vs.5.5%, P=0.004) whereas alcoholic group were mostly men (76.5% vs.35.8%,P<0.001) and had more current smokers (42.8% vs. 13.6%,P<0.001). Although the alcoholic group showed higher multivascular, bridge, Ach induced CAS, and severe narrowing on QCA on univariate analyze, however, after adjusting the baseline differences, all clinical and angiographic parameters of Ach provocation test were not different between the two groups (Table).

Conclusion: In our study, current alcohol use was not associated with clinical and angiographic characteristics of CAS as assessed with Ach provocation test.

CONDITIONING AND OXYDATIVE STRESS: FROM BENCH TO PRACTICE

Exendin-4 postconditioning is not effective in hearts isolated from hypertensive SHR-S rats with left ventricular hypertrophy

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Purpose: Exendin-4 (ex4) postconditioning has been shown to limit reperfusion injury (RI) in experimental [1] and clinical [2] settings. Left ventricle hypertrophy (LVH) may be associated with increased RI. Few studies have addressed the efficacy of various conditioning treatments for RI in LVH. We studied ex4-postconditioning in hearts isolated from SHR-S (hypertensive LVH) rats.

Method: Hearts isolated from WKY (control) and SHR-S rats (11-15 weeks old) were subjected to 35 min LAD occlusion-2 hrs reperfusion, with ex4 0.3 nM present during the first 15 min in treated hearts. Evans blue/TTC method was used to determine area-at-risk (AAR) and infarct size (% of AAR). Akt phosphorylation (Akh-P) was measured on western blots after 3 min of reperfusion. Arterial blood pressure (BP) was measured in conscious animals by tail cuff method.

Results: BP and heart/body weight ratio were increased in SHR-S compared to WKY rats (169±3 vs 129±4 mmHg, N=8-10; and 3.43±0.05 vs 2.35±0.03, N=15-18; P<0.001 for both parameters). Infarcts were larger in SHR-S than in WKY (65±3.3 vs.3.7±0.9, N=10 respectively; P<0.05). Infarct size diminished following ex4-postconditioning of WKY hearts (to 21.8±5.6; N=8; P<0.05), but not SHR-S hearts (64.0±4.7; N=7). In WKY hearts, ex4 treatment decreased diastolic contracture (1099±168 to 518±162 min mm Hg, N=8; 7; P<0.05) and increased left ventricle developed pressure (3195±184 to 3914±253 min mmHg, N=10; P<0.05), measured as area under the curve over the last hr of reperfusion. Following ex4 treatment, left ventricle developed pressure measured as a percentage of its prescisma value was increased in
WKY hearts (34±2.3 vs 27.7±1.6, N=10-8; P<0.03), but not in SHR-SP hearts. Following exed, Akt-P was increased by 22% in exed-treated WKY, but not SHR-SP hearts snap-frozen after 3 min of reperfusion. Akt-P appeared reduced by approximately 50% in SHR-SP hearts with or without exed-treatment.

Discussion: These data suggest that hypertensive LVH may be associated with a loss of efficacy of exed postconditioning, as shown earlier for erythropoietin [3] and ischemic [4] preconditioning. Insufficient Akt-mediated signaling might contribute to this impairment.


**Impact of ischemic postconditioning in acute myocardial infarction patients with preconditioning**

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**Background:** Both ischemic preconditioning and postconditioning have been found to reduce myocardial damage in acute myocardial infarction (AMI). How-ever, in animal models of ischemia and reperfusion, additive cardioprotective effects by ischemic preconditioning and postconditioning were unexpectedly con-tradicted. The present study aimed to determine whether postconditioning would provide more power ful cardioprotection in AMI patients with prodromal angina.

**Method:** The consecutive 82 AMI patients with single vessel occlusion, gained successful reperfusion, were recruited. Twenty-eight patients with postcondition-ing under 60s and 30s 60s are divided into two groups, with prodromal angina (PA(+)) and without (PA(-)). Cardiac kinase-MB (CK-MB) were determined serially every 4 hour 24 hours after AMI onset.

**Results:** Both ischemic preconditioning and postconditioning were unexpectedly contradictory. The present study aimed to determine whether postconditioning would provide more powerful cardioprotection in AMI patients with prodromal angina.

**Conclusion:** We demonstrated that cardioprotective effects of ischemic postconditioning were significantly and additively enhanced in AMI patients with pro-dromal angina, opposite to previous experimental studies of animal models.

**Effect of hydrogen gas inhalation on lipid metabolism and left ventricular remodeling induced by intermittent hypoxia in mice**

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**Background:** Intermittent hypoxia (IH) relevant to sleep apnea syndrome (SAS) produces reactive oxygen species and increases cardiovascular events. Among others hydroxyl radicals are highly toxic for cellular proteins and ribonucleic acids, and might affect lipid metabolism. Recently, hydrogen (H2) gas has been reported to scavenge hydroxyl radicals in rat model of cerebral infarction. The aim of this study was to examine the dyslipidemia and cardiac remodeling induced by IH in mice and to evaluate the efficacy of hydrogen gas inhalation as a novel therapeutic strategy.

**Methods:** Male C57BL/6J mice at 8 week of age (n = 60) were exposed to IH (repetitive cycle of 1 min periods of 5 and 21% oxygen for 8 h during daytime) for 7 days. H2 gas (1.3 vol%) was given either at the time of reoxygenation, during hypoxic conditions, or throughout the experimental period. Plasma lipoproteins were analyzed using a high-performance liquid chromatography system. The heart was excised for light and electron microscopic examination, immunohistochemistry, and RT-PCR.

**Conclusion:** H2 gas inhalation attenuated the dyslipidemia and the development of IH-induced LV remodeling at least partly through the suppression of oxidative stress. Inhalation of H2 gas during hospitalization might be potentially useful for preventing cardiovascular events in patients with SAS.

**APE1/Ref-1 decreases ROS generation and myocardial infarction in a mouse model of acute myocardial infarction**

J.O. Jeong, S.A. Jin, S.J. Park, J.H. Park, J.Y. Yoon, S.K. Kim, R.R. Khambhatia, H.E. Botkeb, 1Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2University of Oxford, Department of Cardiovascular Medicine, Oxford, United Kingdom

**Purpose:** Remote ischemic conditioning (RIC) by 3 times 5-minutes upper arm ischemia and 15 minutes reperfusion and measured by venous occlusion plethys-mography after 3 min of reperfusion. Akt-P appeared reduced by venous occlusion plethys-mography at baseline, and either 24 hours after a single RIC treatment (Second Window RIC) or after 14 days with daily RIC (Chronic RIC).

**Results:** In both groups, I-R injury significantly reduced Bf response to acetylcholine, an endothelium-dependent vasodilator (n=8, p<0.05 and n=8, p<0.05). Both Second Window RIC and Chronic RIC abolished the reduction in Bf re- sponse after I-R injury (n=8, p<0.01 and n=8, p<0.01 compared to baseline).

**Conclusion:** This is the first study to show Second Window RIC and Chronic RIC protection against I-R injury in human resistance vasculature in vivo. While yet to be proved effective in other organs, the ability to maintain a chronic pre-conditioned state using RIC may have therapeutic implications as a potentially valuable strategy of prophylaxis for individuals at high risk of I-R injury, e.g. stroke and myocardial infarction.

**Second window and chronic remote ischemic conditioning prevent endothelial injury by ischemia-reperfusion in humans**

K. Pryds1, S. Rasalingam1, H. Contractor2, M.R. Schmidt1, R.K. Khambhatia3, H.E. Botkem, 1Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2University of Oxford, Department of Cardiovascular Medicine, Oxford, United Kingdom

**Purpose:** Remote ischemic conditioning (RIC) by 3 times 5-minutes upper arm ischemia induces early protection against endothelial ischemia-reperfusion (I-R) injury in humans. The objective of this study was to assess whether there is a sec-ond window RIC and whether repeated application of RIC (Chronic RIC) induces persistent protection against I-R injury.

**Methods:** In a randomised, single blinded parallel group study, 16 healthy vol-unteers were randomised to either a second window or Chronic RIC. Vascular function was assessed by forearm blood flow (FBF) before and after 20 minutes ische mia and 15 minutes reperfusion and measured by venous occlusion plethys-mography at baseline, and either 24 hours after a single RIC treatment (Second Window RIC) or after 14 days with daily RIC (Chronic RIC).

**Results:** In both groups, I-R injury significantly reduced Bf response to acetylcholine, an endothelium-dependent vasodilator (n=8, p<0.05 and n=8, p<0.05). Both Second Window RIC and Chronic RIC abolished the reduction in Bf re- sponse after I-R injury (n=8, p<0.01 and n=8, p<0.01 compared to baseline).

**Conclusion:** This is the first study to show Second Window RIC and Chronic RIC protection against I-R injury in human resistance vasculature in vivo. While yet to be proved effective in other organs, the ability to maintain a chronic pre-conditioned state using RIC may have therapeutic implications as a potentially valuable strategy of prophylaxis for individuals at high risk of I-R injury, e.g. stroke and myocardial infarction.
Effect of sildenafil on mitochondria in rat myocardial infarction model - morphological and property changes utilizing atomic force microscopy

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Objectives: Many studies showed that sildenafil have cardioprotective effects mediated by nitric oxide and ischemic preconditioning. Mitochondria play critical roles in both the life and death of cardiac myocytes. We tested whether sildenafil could make the rat hearts resistant to infarction through mitochondrial protection using atomic force microscopy (AFM).

Methods: To prove the cardiac protective effect of sildenafil and investigate the morphologic and property analysis of mitochondria by AFM in the rat myocardium, in-vivo myocardial infarction (MI) model were used. Rat hearts were subjected to 40 min local ischemia by ligation of the left anterior descending (LAD) coronary artery and examined by AFM 7 days after infarction. The isolated mitochondria were treated with 10 μM sildenafil for 40 min local ischemia by ligation of the left anterior descending (LAD) coronary artery. The effect of sildenafil on mitochondria was measured by AFM imaging, image analysis and multivariate Cox regression. Pre-specified sub-group analyses by ejection fraction were performed.

Results: Thirty-one % had QRS ≥ 120 ms, and 56% of these had left bundle branch block. Strong independent predictors of QRS ≥ 120 ms were higher age, male gender, dilated cardiomyopathy, longer duration of HF, and lower EF. One-year survival was 77% in QRS ≤ 120 ms vs. 82% in QRS > 120 ms, and 5-year survival was 42 and 51%, respectively (p < 0.001, figure). The adjusted hazard ratio for all-cause mortality was 1.11 (95% CI, 1.04-1.18, p<0.001) for QRS ≥ 120 vs. <120 ms. There was no statistically significant interaction between QRS width and ejection fraction.

Conclusions: We studied QRS width and 40 other clinically relevant variables in 25,171 patients (age 75±12 years; 40% women) between 2000 and 2011. Correlates with QRS width were assessed with multivariate logit regression. Association between QRS width and all-cause mortality was assessed by Kaplan-Meier analysis and multivariate Cox regression. Pre-specified sub-group analyses by ejection fraction were performed.

Prevalence and incidence of myocardial dysfunction and CHD, systolic blood pressure 0.0001). Whereas sildenafil reduced the mitochondrial area (7,428 ± 3,682 nm² vs. 9,305 ± 4,384 nm², p < 0.0001), the mitochondrial swelling (1,495 ± 3,179 nm vs. 2,734 ± 4,109 nm, p < 0.0001). However, no differences were observed in mitochondrial activity, membrane potential, and oxidative stress.

Conclusions: In MI rat model, cardioprotective effect of sildenafil pretreatment associated with a mitochondrial protective mechanism.

Prevalence and incidence of myocardial dysfunction and chronic heart failure in the patients with type 1 diabetes: a 7-year prospective cohort study

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Purpose: To evaluate the prevalence and incidence of MD and HF in long lasting (over 10 years) type 1 diabetes (T1DM) without cardiovascular disorders or with hypertension and/or coronary disease (CHD). Research design and Methods: 1617 T1DP (baseline: mean age 51 years, mean diabetes duration 35 years) following initial evaluation (clinical symptoms, echocardiography, NT-pro BNP levels) underwent a 7 year follow-up in terms of MD, HF (its diastolic and systolic forms), under a 7 year follow-up in terms of MD, HF (its diastolic and systolic forms), and CVD. Strong independent predictors of QRS ≥ 120 ms, and 5-year survival was 42 and 51%, respectively (p < 0.001, figure). The adjusted hazard ratio for all-cause mortality was 1.11 (95% CI, 1.04-1.18, p<0.001) for QRS ≥ 120 vs. <120 ms. There was no statistically significant interaction between QRS width and ejection fraction.

Conclusions: In this registry, QRS prolongation was associated with other markers of severity in heart failure but was an independent risk factor for all-cause mortality. QRS prolongation was more common with lower ejection fraction, but the risk associated with QRS prolongation was similar regardless of ejection fraction, which may be important for future studies of CRT in preserved ejection fraction.

Prevalence of increased heart rate, links with clinical status and therapy in outpatients with heart failure with preserved ejection fraction in modern Poland: results of preserved-DATA-HELP study

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Prevalence, correlates and prognostic significance of QRS prolongation in heart failure with reduced and preserved ejection fraction

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Methods: We studied QRS width and 40 other clinically relevant variables in 25,171 patients (age 75±12 years; 40% women) between 2000 and 2011. Correlates with QRS width were assessed with multivariate logit regression. Association between QRS width and all-cause mortality was assessed by Kaplan-Meier analysis and multivariate Cox regression. Pre-specified sub-group analyses by ejection fraction were performed.

Results: Thirty-one % had QRS ≥ 120 ms, and 56% of these had left bundle branch block. Strong independent predictors of QRS ≥ 120 ms were higher age, male gender, dilated cardiomyopathy, longer duration of HF, and lower EF. One-year survival was 77% in QRS ≤ 120 ms vs. 82% in QRS > 120 ms, and 5-year survival was 42 and 51%, respectively (p < 0.001, figure). The adjusted hazard ratio for all-cause mortality was 1.11 (95% CI, 1.04-1.18, p<0.001) for QRS ≥ 120 vs. <120 ms. There was no statistically significant interaction between QRS width and ejection fraction.

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Conclusions: In MI rat model, cardioprotective effect of sildenafil pretreatment associated with a mitochondrial protective mechanism.
ferent β-blockers (all p<0.02). There were no associations between HR and daily doses of β-blockers, investigated separately in subgroups of patients receiving the particular β-blocker (all p>0.2).

Conclusions: Increased HR is common in patients with HFpEF, regardless of NYHA class. There is no association between the most common HR reducing therapy (β-blockade) and resting HR among these patients. There is a substantial group of patients with HFpEF in whom the classification of β-blockade on/and the introduction of other HR reducing strategies could be considered.

**P4510** Old tools in new combination: combined stress echocardiography cardiopulmonary exercise testing in early detection of diastolic dysfunction

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**Background:** Echocardiography is shown to be very important clinical tool for detection of diastolic dysfunction (DD) at rest in patients with hypertensive heart disease. However, simple diagnosis and stratification of patients according to severity of DD can underestimate the functional impairment in patients with exertional dyspnea and normal baseline values, without cardiopulmonary exercise testing (CPET). Relationship between diastolic function (DF) and CPET during combined stress testing has still remained underdefined.

**Objective:** To assess integrated simultaneous evaluation of both echocardiographic variables and parameters of CPET in pts with hypertension, exertional dyspnea and normal baseline systolic and DF.

**Methods:** We studied 100 pts (68 male, mean age 51±14 years, with the history of essential hypertension, exertional dyspnea and normal baseline echo characteristics (including normal baseline systolic and DF). They all underwent CPET with supine ergospirometry with incremental ramp protocol (15W/min), with breath by breath gas analysis, in combination with simultaneous echo monitoring during CPET. We assessed systolic and diastolic function at baseline and at maximal exercise. DF was assessed by analyzing transmitral flow pattern using pulse Doppler and tissue Doppler (TDI) of mitral annulus. Mitral E wave/E wave of mitral annulus > 8 was cut off for impaired DF.

**Results:** All patients had ventricular ejection fraction > 50%, and none of them had exercise induced myocardial ischemia. Worsening of DF was found in 45% pts during combined CPET stress echo test. Patients with DD were older (p=0.001), and had lower peak VO2 (p=0.001), shorter time to VAT (p=0.006) and shorter total exercise time (p=0.017), and higher VE/VCO2 slope (p=0.0011). However multivariate analysis showed that only VE/VCO2 was independent predictor of DD during CPET (p=0.001; RR 1.68; 95%CI: 1.24 -2.24). We also found the strong correlation between VE/VCO2 slope and E/Em (r=0.70; p=0.0001) which can be also used for stratification of pts with DD.

**Conclusion:** Integrated evaluation of both exercise induced echocardiographic changes and expiratory gas analysis during combined stress CPET stress echo improves detection and clinical assessment of DD in patients with exertional dyspnea and normal baseline LV function. It adds more information to echo and CPET as a single test. The best predictor of development of DD during CPET was VE/VCO2 slope, showing the strong relationship with E/Em as a determinant of DF.

**P4511** Anthracycline cardiotoxicity: incidence at present time


**Purpose:** Chronic Anthracycline cardiotoxicity (AC) characteristically presents within the first year after treatment with a peak of incidence 3 months after the treatment. Chronic Anthracycline cardiotoxicity (AC) characteristically presents within the first year after treatment with a peak of incidence 3 months after the treatment. Chronic AC expressed as asymptomatic diastolic dysfunction and 38 pts (47%) developed diastolic dysfunction which was permanent in 29pts (36%). Twenty nine pts (36%) didn't develop significant diastolic changes.

**Conclusions:** Chronic AC expressed as asymptomatic diastolic dysfunction is common. However incidence of subclinical systolic dysfunction with current chemotherapy schemes and pts selection is lower than previously published data and it doesn't carry relevant clinical consequences.

**P4512** Relation between diastolic function in rest and during stress and peak exercise capacity among heart transplant recipients

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**Purpose:** Several studies have shown that diastolic dysfunction impairs exercise capacity despite normal left ventricular ejection fraction (LVEF). This may also be a contributing factor in the limited physical performance of heart transplant recipients (HTX). We studied whether diastolic dysfunction at rest and during exercise is related to exercise capacity and the ability to improve exercise capacity after training intervention.

**Methods:** 23 stable HTX pts (mean age 50.4±14.8) with normal LVEF underwent maximum bicycle exercise test and semi supine exercise stress echocardiography. 13 patients underwent 6 weeks aerobic interval training and had echocardiography and exercise test repeated. Standard resting echocardiography included pulsed Doppler LV inflow at apical 4 chamber (E, A, dec. time) and pulsed TDI (e' calculated as mean of lateral, septal, anterior and posterior cor- ner of mitral annulus). Acquisitions were repeated at 30% and 60% of maximum workload and during recovery.

**Results:** VO2peak increased from (mean ± sd): 23.8±7.0 to 28.3±6.4 ml/kg/min (p<0.001) after training. Only few of the patients exhibited diastolic dysfunction at rest, but during stress echocardiography E/e' increased and deceleration time decreased, unmasking sign of diastolic dysfunction. Diastolic dysfunction during rest and stress or the change in diastolic measures from rest to 60% did not predict workload at VO2peak at baseline or improvement in VO2peak.

**Conclusion:** In contrast to previous studies of other cardiac patients, we found no correlation between diastolic function in rest and during stress echocardiography and VO2peak or improvement in VO2peak after 6 weeks aerobic interval training in heart transplant patients. Diastolic dysfunction may not be a limiting factor for exercise capacity when chronotropic response is impaired.

**P4513** Diastolic dysfunction in a population-based study sample

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**Background:** Left ventricular (LV) diastolic dysfunction has been reported to be associated with exercise capacity in heart failure and in patients referred for exercise testing. However, this relationship has not been studied extensively in the general population.

**Methods:** Data of 1,344 subjects (737 women, 607 men) aged 25-85 yrs from the population-based Study of Health in Pomerania (SHIP) in Germany with echocardiographic data on systolic and diastolic LV function and without reduced LV systolic function (LVEF<50%) were included in the analyses. All subjects volunteered symptom-limited cardiopulmonary exercise testing. The association of diastolic dysfunction with exercise capacity as assessed by peak oxygen uptake

**Abstract P4512** – Table 1. Measures of diastolic function at rest and during stress and their correlation with baseline VO2peak and improvement in VO2peak

<table>
<thead>
<tr>
<th>E' (cm/s)</th>
<th>VO2peak baseline Corr. coef.</th>
<th>Improvement VO2peak</th>
<th>E' (cm/s) Corr. coef.</th>
<th>Improvement VO2peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>E' (cm/s)</td>
<td>(mean ± sd)</td>
<td>(p-value)</td>
<td>(mean ± sd)</td>
<td>(p-value)</td>
</tr>
<tr>
<td>E' (cm/s)</td>
<td>84±25.4</td>
<td>0.08 (0.70)</td>
<td>0.11 (0.73)</td>
<td>136.5±28.6</td>
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<tr>
<td>A (cm/s)</td>
<td>51.8±12.1</td>
<td>0.17 (0.61)</td>
<td>0.02 (0.74)</td>
<td>54.5±13.4</td>
</tr>
<tr>
<td>Dec/Time/ms</td>
<td>176±65</td>
<td>-0.05 (0.83)</td>
<td>-0.17 (0.58)</td>
<td>112±21.7</td>
</tr>
<tr>
<td>E/A</td>
<td>2.0±0.6</td>
<td>0.06 (0.92)</td>
<td>-0.01 (0.96)</td>
<td>2.3±0.3</td>
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<tr>
<td>E'/e'</td>
<td>8.3±2.9</td>
<td>0.17 (0.43)</td>
<td>-0.04 (0.90)</td>
<td>10.3±4.0</td>
</tr>
</tbody>
</table>
Diastolic dysfunction: epidemiology and mechanism / Heart failure with preserved ejection fraction—echo investigation

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(VO2peak) and minute ventilation changes as a function of the pulmonary carbon dioxide output (VE/VO2 slope) was analyzed by multivariable regression models adjusted for age, gender and hypertension. Furthermore, analyses were stratified by the presence of obesity (BMI ≥ 30 vs. < 30 kg/m²).

Results: Diastolic dysfunction was present in 550 subjects (40.9%). After adjustment for age, gender and hypertension diastolic function was associated with a reduced exercise capacity. Thus, subjects with diastolic dysfunction had lower values of VO2peak (24.9 ± 26.3 ml/min*1kg⁻¹, p < 0.001) and higher values of VE/VO2 slope (25.6 ± 24.6, p < 0.001), respectively, as compared to those without diastolic dysfunction. Stratified analyses revealed that these associations were only present in non-obese subjects (VO2peak 26.4 ± 27.4 ml/min*1kg⁻¹, p < 0.022; VE/VO2 slope 25.4 ± 24.4, p = 0.001) but were not statistically significant in the presence of obesity.

Conclusion: In this sample from a population-based study we found an association between left ventricular diastolic dysfunction and a reduced exercise capacity in non-obese but not in obese subjects. These results may point towards a putative functional significance of diastolic dysfunction in relatively healthy individuals.

The association between computed tomography-derived three-dimensional pericardial adipose burden, cardiac structural alteration and diastology

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Purpose: Pericardial adipose tissue had been shown to exert their local effect on adjacent cardiac structures. However, data regarding three-dimensional volume measurements of such visceral adipose burden on myocardial diastolic function remained largely unknown.

Methods: We consecutively assessed pericardial fat tissue (PCF) by volume-based three-dimensional measure utilizing computed tomography (Aquarius 3D Workstation, TeraRecon, San Mateo, CA, USA) from 286 subjects after exclusion of decompensated heart failure. Diastolic parameters including left atrial (LA) diastolic filling pressures. Our study suggested the possible link between excessive peri-cardial fat accumulation, altered cardiac geometry and diastolic dysfunction.

Analysis showed that prolonged IVRT, reduced E', elevated E/e' and enlarged LA diameter were all related to increasing PCF (all p < 0.05). In the multivariate regression analysis after adjusting for age, gender, body mass index, LV mass, and clinical variables, increasing PCF was independently associated with reduced E' (Coef: -0.03, p < 0.05), borderline elevated E/e' (Coef. 0.95, p = 0.077) and LA enlargement (Coef. 0.05, p = 0.05).

Conclusion: Increasing pericardial visceral burden was independently associated with impaired diastolic function, leading to left atrial dilation and elevated filling pressures. Our study suggested the possible link between excessive pericardial fat accumulation, altered cardiac geometry and diastolic dysfunction.

A risk-factor based porcine model of heart failure with preserved ejection fraction (HFPEF)

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Background: Heart failure with preserved ejection fraction (HFPEF) results from the accumulation of cardiovascular risk factors. So far, no clearly effective treatment of HFPEF could be established, which in part relates to the lack of suitable animal models. We aimed to model HFPEF in pigs by induced hypertension and western diet.

Methods/Results: Eight landrace pigs were implanted with subcutaneous 90 day release DOCA pellets (an aldosterone analog), and subsequently fed a high salt/high lipid/high sugar diet for 90 days (DOCA). Eight weight-matched pigs (no DOCA, regular diet) served as controls. After 90 days, tail-cuff systolic blood pressure during light sedation was 139 ± 11 mmHg in DOCA vs 95 ± 6 mmHg in control (p < 0.05). Echocardiography demonstrated pronounced concentric hypertrophy in DOCA. LV function was assessed during deep anaesthesia by pressure-volume (PV) analysis. In DOCA vs control, baseline cardiac output (6.0 ± 0.2 vs 6.6 ± 0.5 l/min) and heart rate (95 ± 5 vs 84 ± 6 bpm) were not different, while LV ejection fraction (68 ± 3 vs 51 ± 3%) was higher (p < 0.05). The end-systolic and end-diastolic PV relationships (ESPVR and EDPVR) were markedly shifted leftwards in DOCA (see graph). Right atrial pacing both at baseline and during low-dose dobutamine infusion (2.5 μg/kg/min) revealed a lower increase of cardiac output in DOCA.

Conclusion: This risk factor based animal model for the first time reproduces two major characteristics of HFPEF: (i) a leftward shift of the ESPVR and EDPVR and (ii) a limited cardiac reserve.

Heart failure with preserved ejection fraction—echocardiography investigation

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Background: Clinical features of heart failure with preserved EF (HFPEF) have not been well characterized. It is reported that peak atrial systolic mitral annular velocity (A') predicts left atrial (LA) systolic function. The aim of the present study was to investigate the relation between LA systolic function and left ventricular (LV) performance in HFPEF.

Methods: Out of 327 patients who presented to the emergency department because of acute pulmonary congestion during the last 5 years, those with EF ≥ 50% upon admission comprised the HFPEF patients (n=56) were enrolled in this study.
Patients with atrial fibrillation or mitral valvular disease were excluded in this study. A control group (Gr-C) consisted of consecutive 30 hypertensive patients with EF of 50%. We recorded tissue Doppler-derived peak early diastolic and atrial systolic velocity of mitral annulus (E and A) respectively in the chronic stage. Other echo parameters (LA diameter (LAD) and LV diastolic diameter (LVDD) and E/E') were measured at the same time. The HFPEF patients were divided into the good LA function group (Gr-G) (A' > 6cm/s, n=30) and the poor LA function group (Gr-P) (A' < 6 cm/s, n=21) depending on the score of A'.

Results: E/E' was correlated with A' (r=0.92, p=0.069) in the HFPEF patients. A and E were the lowest and E and E' were the highest in Gr-P (table).

LA systolic function and LV performance

<table>
<thead>
<tr>
<th>A' (cm/s)</th>
<th>E (cm/s)</th>
<th>E/E'</th>
<th>LAD (mm)</th>
<th>LVDD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr-C</td>
<td>8.5 ± 1.6</td>
<td>6.4 ± 1.7</td>
<td>10.9 ± 2.0</td>
<td>38 ± 4.5</td>
</tr>
<tr>
<td>Gr-G</td>
<td>7.0 ± 1.9</td>
<td>5.0 ± 1.4</td>
<td>13.2 ± 3.3</td>
<td>41.5 ± 4.9</td>
</tr>
<tr>
<td>Gr-P</td>
<td>4.2 ± 0.8*</td>
<td>3.7 ± 0.6*</td>
<td>17.8 ± 4.3*</td>
<td>45.9 ± 2.3*</td>
</tr>
</tbody>
</table>

*p<0.05 vs Gr-C and Gr-G, *p<0.05 vs Gr-C.

Conclusions: The progression of LA systolic dysfunction was associated with the impairment of LV diastolic function and may play an important role in the pathogenesis of HFPEF.

Radial ventricular dyssynchrony on exercise in patients with heart failure and normal ejection fraction


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Background: Longitudinal dyssynchrony has been shown in patients with heart failure and normal ejection fraction (HFNEF). We hypothesised that radial dysynchrony may also be present in these patients on exercise and contribute to LV dysfunction.

Methods: We studied 57 patients with the clinical diagnosis of HFNEF (39 female, age 73 ±7 years, EF 61 ±6%) and 30 healthy controls (23 female, age 70 ±7 years, EF 62 ±7%). All underwent echocardiography at rest and on supine exercise. Images were acquired and analysed off line. Radial strain and time to peak radial strain in a six segments model were studied. Standard deviation for six radial segments was calculated (SDradial) to assess segmental radial dyssynchrony. A cut-off of 24.6ms at rest and 18.6ms on exercise (mean ±2SD of controls) were used to diagnose dysynchrony.

Results: Radial strain was comparable at rest (44.0 ±15.1% versus 48.2 ±11.2%, p=0.191) but significantly lower in patients on exercise (49.6 ±14.2% versus 58.0 ±8.2%, p=0.018). SDradial was also comparable at rest (14.1 ±1.3ms versus 10.5 ±0.7ms, p=0.150). Controls achieved significant reduction in SDradial on exercise (8.4 ±5.1ms) which was not seen in patients (13.5 ±5.9ms) (p=0.008). Radial dyssynchrony was detected in 12% of patients at rest which increased to 29% patients on exercise. SDradial on exercise correlated with Radial strain on exercise (r=0.246, p=0.022).

Conclusions: HFNEF is associated with LV radial dysfunction and dyssynchrony as well as longitudinal particularly on exercise and which is not present at rest.

LV and RV diastolic function during follow up in patients with systemic sclerosis

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Systemic sclerosis (SSc) is characterized by vascular changes and fibrosis of the skin and internal organs. There are limited data on left (LV) and right ventricular (RV) diastolic function in SSc patients particularly in follow up and their relations to parameters of collagen metabolism.

Purpose: To analyze LV and RV diastolic function during follow up in patients with SSc and its relation to serum TIMP 1 (tissue inhibitor of metalloproteinase 1) levels, a biomarker of matrix remodeling.

Methods: We prospectively studied 69 consecutive pts (64F, 5M mean age 55.5±13.8yrs) with SSc (mean SSc duration 9±12yrs) at baseline and after at least 1 year of follow up (3±1yrs). TTE (Philips IE 33) for assessment of LV and RV diastolic function was performed. We also measured serum TIMP–1 (human TIMP-1 immunoassay R&D Systems) levels. At fu we observed significant determination of Doppler parameters of LV but no RV diastolic function. Mean TIMP-1 serum concentration was higher at SSc follow up patients (204.6±167.1 ng/ml, p=0.0001). In SSc fu group TIMP-1 correlated positively to mitral lateral and septal E/E' (r=0.4, p=0.0019 and r=0.32, p=0.01), and negatively to early diastolic lateral velocity E' (−0.46, p=0.0003) and early diastolic septal velocity E' (−0.38, p=0.003).

Conclusion: Our data support the hypothesis that calibrated CIB, a surrogate for myocardial fibrosis, identifies HFPEF patients at risk of death or HF hospitalization.

Prognostic significance of calibrated integrated backscatter in patients with heart failure and preserved ejection fraction

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Introduction: Calibrated integrated backscatter (CIB), a surrogate for myocardial fibrosis, is deteriorated in hypertrophic, ischemic cardiomyopathy or in systolic heart failure (HF). Whether CIB may differentiate patients with heart failure and preserved ejection fraction (HFPEF) at risk of death or HF reoccurrence has never been investigated.

Methods: 35 patients admitted for HFPEF (Framingham criteria, EF > 50% and BNP level > 100 pg/ml) were imaged by echocardiography 2 months following an acute decompensation. We measured left ventricular function, atrial dimensions and calibrated Integrated Backscatter (CIB) which was obtained from parasternal long axis by subtracting pericardial CIB intensity from myocardial CIB intensity of the LV anteroseptal and posterior walls (figure). Measurements of calibrated CIB, expressed in decibels, were performed at QRS complex onset. The primary endpoint was the occurrence of death or hospitalization for HF at 12-month FU.

Results: 10 patients reached the primary endpoint (3 deaths and 7 hospitalizations for HF). In this group at risk, patients had more chronic obstructive pulmonary disease (p=0.03) and coronary artery bypass (p=0.008). Despite similar EF (57.3±7.3% vs. 60.4±9.7%), we observed larger left atrial diameter (49.7±6.9 mm vs. 44.7±6.4 mm, p=0.050) and area (25.8±6.2 cm2 vs. 24.5±5.1 cm2, p=0.044) in patients with endpoint vs. no endpoint. Patients with clinical endpoint showed more anteroseptal and posterior wall myocardial ultrasound reflectivity (-12.3±6 dB vs. -22.7±8.1 dB, p=0.0024 and -14.9±6.1 vs. -21.1±8.0 dB, p=0.031) as compared with event-free patients.

Conclusion: Our data support the hypothesis that calibrated CIB, a surrogate for myocardial fibrosis, identifies HFPEF patients at risk of death or HF hospitalization.

LV and RV diastolic function in SSc pts

Parameter

<table>
<thead>
<tr>
<th>SSc (n=69)</th>
<th>SSc follow-up (n=69)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral E/A</td>
<td>0.99±0.3</td>
<td>0.92±0.3</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>120±56</td>
<td>188±36</td>
</tr>
<tr>
<td>PVF V (cm/s)</td>
<td>59±14</td>
<td>63±16</td>
</tr>
<tr>
<td>S/G</td>
<td>1.21±0.2</td>
<td>1.38±0.3</td>
</tr>
<tr>
<td>PVF Ar (cm/s)</td>
<td>29.5±7.4</td>
<td>33.3±8.1</td>
</tr>
<tr>
<td>Mitral E’ lateral</td>
<td>7.5±3.1</td>
<td>6.9±2.5</td>
</tr>
<tr>
<td>Mitral E’ septal</td>
<td>9.4±3.3</td>
<td>9.5±3.4</td>
</tr>
<tr>
<td>Tricuspid E’</td>
<td>1.05±0.2</td>
<td>1.02±0.2</td>
</tr>
<tr>
<td>Tricuspid E’</td>
<td>4.75±1.35</td>
<td>4.83±1.54</td>
</tr>
</tbody>
</table>

Conclusion: LV but not RV myocardial relaxation deteriorate during follow up. TIMP-1 is significantly correlated with echocardiographic parameters suggesting a potential link for LV diastolic dysfunction and matrix remodeling in patients with SSc.
Heart failure with preserved ejection fraction-echo investigation

**P4521**

**Left ventricular torsion during exercise in patients with and without increase in left ventricular filling pressures**

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Left ventricular torsion (Tor) is increased in patients (pts) with diastolic dysfunction but little is known about the effect of exercise (Ex) on Tor in them. We aimed to assess Tor during Ex in pts with and without increase in left ventricular filling pressures.

**Methods:** We studied 132 consecutive pts with normal LV ejection fraction (LVEF>-50%), and normal Ex echocardiography. Speckle imaging was performed at rest (R) and at peak (Pk). Tor was defined as maximal apical rotation – basal rotation (°)/LV length (cm). Confident tracking assessment was achieved in 107 pts (81%). Volumetric LVEF and the ratios of early translaminar flow early diastolic flow at the septal mitral annulus waves (E/e') at R and Pk were also measured.

Twenty-six pts had E/e' ratio >15 (G-HEe) and 81 pts <15 (G-NHe).

**Results:** G-HEe pts were older (67±9 vs 56±14, p=0.001) and achieved less METs (8.8±3.7 vs. 11.0±4.0, p=0.02). A history of coronary artery disease was equally frequent (8% in G-HEe and 21% in G-NHe, p=0.15). LVEF at R was higher in G-HEe (70±9 vs 66±8, p=0.04) whereas it was similar at Pk (74±9 vs 70±11, p=0.05). E/e'values at R were 24±20.3 in G-HF and 10±2 in G-NHe (p=0.001), whereas at Pk were 18.9±11.1 and 9.8±2.9, respectively (p=0.001). Rotation parameters were similar between groups except for apical rotation which was higher at R and Pk in G-HEe.

Conclusions: In conclusion, characteristics of pts with high E/e'values include old age, low functional capacity, and increased apical rotation at R and at Pk.

**P4522**

**Ventricular-arterial coupling and arterial stiffness in hypertensive subjects with diastolic heart failure**

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**Objective:** To compare ventricular-arterial coupling (Ea/Ei) and arterial stiffness indices in hypertensive subjects with and without heart failure with preserved ejection fraction (HFPEF).

**Methods:** The study included 66 hypertensive patients with stable NYHA class II-II HFPEF (26 male, age 71.8±8.7 years, clinic BP 130±190/80±30 mmHg, EF 61±9%, HFPEF was confirmed by NT-proBNP >100 pg/ml (Me 873, min 112 - max 3000 pg/ml). Control group included 20 hypertensive patients (5 male, 61.7±7.9 years, clinic BP 136±207/80±12 mmHg) without symptoms of HF and NT-proBNP (Me 1044, min401 - max2241 pg/ml). All patients underwent central pulse wave analysis (PWA) and pulse wave velocity measurement (PWV) (Sphygmocor, AtCor, Australia) and echocardiography (Vivid 7, GE). Ventricular-arterial coupling index was calculated as Ob i = End Systolic Pressure (ESP)/Stroke Volume, Elv=Ei/End Systolic Pressure (ESP)/Stroke Volume. Results are presented as M±SD. Spearman correlation analysis was performed.

**Results:** Diastolic function indices in patients with HFPEF were IRVT 177±40.5 ms, E/A 1.0±0.8, E/E' 8.6±3.3, DT 201±87.7 ms, in control group 110±42.5 msec; 0.7±0.1; 6.7±1.7; and 173.8±49.3 msec, respectively. In control group all patients had asymptomatic type 1 diastolic dysfunction. Age-adjusted PWA represented arterial stiffness differences between patients with HFPEF and control subjects: central BP 126±19±79±12 vs 121±18±81±8 mmHg, pulse pressure (PP) augmentation index (HRR75 beats/min 27.4±9±5 vs 25.0±8.9, PWV 121±3-7 vs 10.4±2.4 m/s, respectively. Central PP was significantly higher in HFPEF than in control subjects (48±16 vs 39±14 mmHg, P=0.045), PWV -12 m/s was observed more often in HFPEF (41% vs 15%, P<0.05). Ea/Ei was similar (0.63±0.2 vs 0.62±1.5, respectively), Ea/Ei -0.6 was found in 37.8% in subjects with HFPEF and in 30% in control group. Significant correlation was found in patients with HFPEF between EA and PWV (r=-0.28, p=0.04) and PWV and NT-proBNP (r=0.51, p=0.02).

Conclusions: The obtained results suggest similar rates of ventricular-arterial uncoupling in hypertensive subjects with HFPEF and asymptomatic diastolic dysfunction. HFPEF is associated with increased arterial stiffness.

**P4523**

**Moving toward an ejection fraction paradox: the ratio between left ventricular and left atrial volume**

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**Background:** We hypothesize that the ratio between left ventricular end-diastolic volume (LVEDV) and end-systolic left ventricular volume (LA; LVLA ratio) may better estimate the severity of the HF, being a sum of a long term history of systolic-diastolic dysfunction.

**Methods:** Out-patients attending a community HF service between 2008 and 2010 were enrolled. HF was defined as the presence of relevant symptoms and signs and objective evidence of cardiac dysfunction: either a left ventricular ejection fraction (LVEF) <45%, or the combination of both left atrial (LA) dilatation (>4 cm) and raised amino-terminal pro-brain natriuretic peptide (NTproBNP) >400 pg/ml.

**Results:** Amongst the 693 patients included, median age was 73 years, 33% were women and HF was confirmed in 568. LV-LA ratio (SD) in patients with no HF (n=125) was 2.1 (0.8). The mean LV-LA ratio for each quartile in patients with HF was 3.8 (1.2) vs. 2.3 (0.2) vs. 1.6 (0.2) vs. 1.0 (0.2). Comparing patients with HF in the lowest and highest quartile of LV-LA ratio, those in the highest quartile were older, had more signs of HF, were more likely to have atrial fibrillation and to be treated with diuretics, had higher pulmonary pressures but had more negative values (better function) for global longitudinal strain (GLS, -12.3 (4.3) % vs. -7.4 (3.3) %, p<0.001) and higher LVEF (54 (12) % vs. 32 (9) %, p<0.001). LV/LA diameter was larger (22.3 (5.1) vs. 17.6 (3.3) mm, p<0.001) and NTproBNP plasma levels were more elevated (1966 (IC: 1139-3727) vs. 1044 (401-2241) ng/l, p<0.001). During M67 (IQR: 413 - 736) days of follow up there were 158 events (78 patients were admitted to hospital with heart failure and 80 died due to CV causes). The Kaplan-Meier curves show that patients in the highest quartiles of LV-LA ratio have the higher risk of adverse outcome and this risk decreases accordingly with the increasing LV-LA ratio. In a multivariable Cox regression model, including NTproBNP, LV-LA ratio, but not LVEF, was an independent predictor of worse outcome.

Conclusions: In patients with chronic HF with or without a reduced LVEF, the LV/LA ratio identifies patients with higher NTproBNP and worse outcome who paradoxically have higher LVEF.

**P4524**

**Deceleration time of early diastolic velocity by tissue Doppler velocity image: a novel index of left ventricular end-diastolic pressure**


**Purpose:** This study aimed to examine the diagnostic utility of the deceleration time (DT) of early diastolic velocity of mitral annulus by tissue Doppler imaging, a method for the assessment of left ventricular end-diastolic pressure.

**Methods:** Simultaneous left ventricular catheterization and Doppler echocardiography were performed to compare the left ventricular end-diastolic pressure (LVEDP) and DT in 57 patients who were scheduled for diagnostic coronary angiography. They were admitted to our hospital for the assessment of heart disease including cardiomyopathy (n=26) and coronary artery disease (n=31). We excluded the patients with atrial fibrillation and mitral valvular disease and who undergone mitral valvaral surgery. Color-coded tissue Doppler images were acquired at apical 4 chamber view, and DT of early diastolic velocity measured at mitral annulus were assessed. DT was also evaluated in 15 healthy subjects.

**Results:** DT is successfully measured in all subjects. DT in the patients with elevated LVEDP (>18mmHg) (69±12ms, n=14) was significantly shorter than those with LVEDP<18mmHg (94±18ms, n=43) and healthy subjects (100±11ms). DT is inversely proportional to LVEDP (r=-0.7, p<0.0001). With a cut-off value of DT of 80 ms, which was determined by receiver operating characteristic curve, the

Figure 1. DT measurement
sensitivity and specificity of DT to detect elevated LVEDP were 90 and 85%, respectively.

Conclusions: DT of early diastolic velocity of mitral annulus could be an efficient novel index of LV end-diastolic pressure.

Impact of gender difference on the relation between arterial stiffness and left ventricular diastolic function in healthy subjects

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Background: Diastolic heart failure has been reported to occur more often in elderly women rather than elderly men. Several studies have reported a relation between arterial stiffness and left ventricular (LV) diastolic function. Recently, it was reported that this relation was stronger in women than in men among individuals with cardiovascular risk factors. However, the impact of gender difference on this relation is still poorly understood.

Methods: Study subjects were selected from 447 who had echocardiography and examination of arterial stiffness. Among them, 95 men (mean age, 47±11 years) and 72 women (mean age, 47±10 years) without atherosclerotic risk factors (hypertension, dyslipidemia, diabetes mellitus) were analyzed. We measured brachial ankle pulse wave velocity (baPWV), carotid augmentation index (AIX) and radial AIX as arterial stiffness parameters immediately after the echocardiographic examination.

Results: Peak early diastolic mitral annular velocity (e') was significantly correlated with baPWV (Men: r= -0.42, p<0.01, Women: r= -0.54, p<0.01), carotid AIX (Men: r= -0.26, p=0.01, Women: r= -0.57, p<0.01) and radial AIX (Men: r= -0.35, p<0.01, Women: r= -0.36, p=0.01). E/e' had a significant correlation with each arterial stiffness parameter in women, but not in men. Multivariate regression analysis revealed carotid AIX (β= -0.26, p=0.02) was a significant independent predictor of e' in women, but not in men.

Conclusion: Our results suggested that LV diastolic function was more affected by arterial stiffness in women than in men among healthy subjects. This might partially account for a higher incidence of diastolic heart failure in women than men.

Increased prevalence of diastolic heart failure can be identified by impaired global longitudinal strain in patients with rheumatoid arthritis

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Background: Risk of heart failure is increased in patients with rheumatoid arthritis (RA) and is more likely to occur in RA patients with a preserved ejection fraction. Until now little is known about the prevalence of diastolic heart failure (HFNEF) in RA. In the RA population, therefore we examined RA patients for diastolic heart failure using measurement of NT-proBNP level and echocardiography, including strain imaging.

Methods: In this prospective cross-sectional observational study we examined 155 patients (68% female, mean age 60±13 years, 56% hypertension, median BMI 29 kg/m²) with RA according to the current ACR/EULAR criteria in our outpatient clinic for rheumatic diseases. Echocardiography including strain imaging and blood sampling for NT-proBNP were done. HFNEF was diagnosed if (1) symptons and (2) E’/E ratio > 15 or (2) NT-proBNP > 220 pg/ml with (3) E’/E ratio > 8 or (3) atrial fibrillation existed.

Results: There was a surprising high rate of HFNEF (21%) in our RA cohort. The systolic LVEF was reduced in only 4% of patients. LV mass index was increased in 44% of pts and 18% of pts with HFNEF, mostly due to concentric hypertrophy. In the strain imaging we found a significant reduction in the global longitudinal strain in patients with HFNEF with a threshold of -18%.

Logistic regression analysis of HFNEF

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate OR (95% CI)</th>
<th>p</th>
<th>Multivariate OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global longitudinal strain &lt; -18%</td>
<td>7.9 (3.3-20.8)</td>
<td>&lt;0.001</td>
<td>14.6 (6.8-31.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &gt; 65 years</td>
<td>19.0 (6.7-58.8)</td>
<td>&lt;0.001</td>
<td>21.6 (6.0-101.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>6.0 (2.0-20.3)</td>
<td>0.005</td>
<td>21.6 (3.0-140.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>RA activity (DAS28 = 2.6)</td>
<td>4.0 (1.7-10.2)</td>
<td>0.002</td>
<td>7.3 (2.0-24.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>5.9 (2.3-18.8)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>3.2 (1.0-9.4)</td>
<td>0.037</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentric LV hypertrophy</td>
<td>4.1 (1.7-9.8)</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of CVD</td>
<td>7.5 (2.1-30.7)</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of RA &gt; 15 years</td>
<td>3.32 (1.45-7.72)</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: This finding in addition to the conventional echocardiographic measurements in HFNEF suggests the role of fibrotic endocardial changes in diastolic heart failure in RA. Markers of RA activity (DAS28) were significant risk factors beyond classical risk factors like age, female gender, hypertension and diabetes mellitus type 2.
Differing relations of the clinical responder rate to the left ventricular reverse remodelling and changes in left ventricular filling pattern in patients receiving cardiac resynchronization therapy

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Background: Clinical responder rate (CRr) and left ventricular (LV) reverse remodelling (RR) are regarded valuable markers for long-term favourable effects of cardiac resynchronization therapy (CRT). Besides the aforementioned parameters, the improvement of LV diastolic function (LVDF) might also be another valuable predictor of the long-term response to CRT.

Aim: To assess the relation of the CRr to the LVRR and to the improvement of LVDF evaluated by improvement in LV diastolic filling pattern (ILVFP) in pts receiving CRT. To investigate the survival of pts according to RR and ILVFP.

Patients and methods: 139 pts with CRT-P (51%) or CRT-D (49%) followed prospectively for 38.8±23.8 months. Age:64.1±10.6 years, male:81.2%, ischemic:37.4%, diabetes mellitus:35.4%, atrial fibrillation:23.6%, NYHA:2.8±0.8, blood pressure:116.4±21.6/72.6±12.8mmHg, LV ejection fraction (LVEF):29.9±7.9%, LV enddiastolic diameter (LVEDD):74.2±17.9mm, LA area cm²18±32.8, central regurgitation:1.7±0.9, estimated GFR:58±32.3ml/min/1.73m², QRS width:159.9±32.4ms, left bundle branch block: 89.4%. Treatment: beta-blockers 95.6%, ACEI/ARBs 95%, aldosterone antagonists:71%, direct vasodilators:72%, furosemide:89%, digoxin:33%.

Results: The cumulative survival rate at 1, 2 and 3 years: 97.6%, 92.5% and 78.6%, respectively. CRr (alive, improved):1 NYHA, and not hospitalized: at 6 months 82%, at 12 months 78%. RR (LVEF increases ≥5% and LVEDD decreases≥5%): at 6 months 36.8%, at 12 months 40.4%. ILVFP (deceleration time increases≥10% and E/A decreases≥10%): 35.8% at 6, and 34.4% at 12 months. Investigation of the relations between the aforementioned parameters showed, that ILVFP correlated significantly (p<0.05) to CRr, while no correlation was found between RR and CRr. LVDF was associated with 100% of CRr in lack of ILVFP CRr was 54.1%. Either in presence, or in absence of RR, the CRr was almost the same, i.e. 82% and 76%, respectively. Differences between surviving and not surviving pts according to RR and ILVFP, were nearly the same: in surviving pts RR in 37.5%, ILVFP in 29.2%, in not surviving pts RR in 17.1%, ILVFP in 16.1%. However these differences did not reach the level of significance: p=0.102 and 0.092 for RR and ILVFP, respectively.

Conclusions: In the effect of CRT, CRr and LVRR were not concordant with each other. On the other hand, the changes in LV diastolic filling pattern significantly correlated with CRr. Besides RR, the changes in LVDF may have a value also in predicting the long-term effect of the CRT on clinical outcome. Investigation its value in a larger pts’ population seems to be reasonable.
Adaptive servo ventilation improves long-term prognosis in heart failure patients with preserved left ventricular ejection fraction and sleep disordered breathing

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Background: Effective pharmacotherapy for heart failure (HF) with preserved left ventricular ejection fraction (LVEF) is still unclear. Sleep disordered breathing (SDB) may cause cardiac diastolic dysfunction. A high prevalence of SDB has been documented in HF patients with preserved LVEF. Adaptive servo ventilation (ASV) improves SDB including Cheyne-Stokes respiration. However, it still remains unclear whether ASV improves cardiac function and long-term prognosis of HF patients with preserved LVEF and SDB.

Methods: Twenty five HF patients with preserved LVEF (defined as LVEF of > 45%) and moderate-severe SDB (defined as apnea hypopnea index > 15 h) were enrolled. Study subjects (apnea hypopnea index 39.3±15.2/h) were divided into two groups: 10 patients treated with conventional medications for HF and ASV (ASV group) and 15 patients treated with conventional medications alone (Non-ASV group). BNP, LVEF, and right ventricular systolic pressure (RVPs) were determined before and 6 months after treatments. Patients were followed to register cardiac events after discharge (average follow up period 728 days).

Results: Although, LVEF did not improve in both groups, BNP and RVPs significantly reduced in ASV group (BNP: 195.6±101.3 to 161.8±62.1 pg/ml, RVPs: 40.5±16.3 to 32.1±8.1 mmHg, P<0.05, respectively), but not in Non-ASV group. Eight events (death 5, re-hospitalization 3) occurred in this follow up period. Importantly, event free rate was significantly higher in ASV group than in Non-ASV group (90.0% vs. 53.3%, logrank P<0.01; TMF patterns: i.e., 0.362, P<0.01; TMF patterns: P<0.05).

Conclusions: Serum CysC is associated with diastolic dysfunction in patients with various cardiac diseases and preserved ejection fraction without renal dysfunction. Our study also suggests that serum CysC become a surrogate biomarker of cardiac diastolic dysfunction in patients with various cardiac diseases and preserved ejection fraction.

Diastolic dysfunction and treatment / Heart failure with preserved ejection fraction: biomarkers

Serum vitamin D and CRP levels are independently associated with diastolic dysfunction

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Objective: We hypothesized that vitamin D (25(OH)D) levels would be inversely associated with inflammation and with diastolic dysfunction. We therefore investigated the link between vitamin D levels and i) diastolic dysfunction (as a surrogate of left ventricular diastolic function) and ii) inflammatory parameters. We aimed to elucidate whether low vitamin D levels are predictive for diastolic dysfunction.

Methods: The study included 281 patients who were referred for coronary angiography. We measured in all patients 25(OH)D serum levels, C-reactive protein (CRP) and fibrinogen and performed standardized LV echocardiograms. Echocardiographic data were used for classification of systolic and diastolic dysfunction. Results: 25(OH)D deficiency (<30 ng/ml) was common among our study population (77.8%). Patients with severe diastolic dysfunction had a lower vitamin D levels (14.7±5.7 ng/ml, P<0.01), higher CRP levels (P<0.01), higher prevalence of hypertension (P<0.032), diabetes (P<0.01) and higher left ventricular mass index (LVMi) (P=0.021). In multivariate analysis, decreased vitamin D (β = −0.154, P<0.012) and elevated CRP (β = 0.124, P = 0.035) was associated with e/e’ ratio after adjustment for potential confounders.

Conclusions: Serum levels of 25(OH)D are significantly associated with LV diastolic dysfunction suggesting that vitamin D supplementation is a promising approach in the prevention of diastolic dysfunction.
Heart failure with preserved ejection fraction: biomarkers / Pharmacotherapy

P4537 Pulmonary hypertension and collagen metabolism in patients with heart failure and preserved ejection fraction

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Purpose: Pulmonary hypertension (PH) is a strong predictor of mortality in patients with heart failure with preserved ejection fraction (HFpEF). This study was designed to evaluate the association between circulating biomarkers of collagen metabolism and PH as assessed by pulmonary artery catheterization, in patients with HFpEF.

Methods: Plasma matrix metalloproteinase-2 and -9 (MMP-2 and MMP-9), tissue metalloproteinase inhibitor 1 (TIMP-1) and C-terminal propeptide of type I procollagen (CIPC) values, and Doppler echocardiography images were obtained from 21 patients with HFpEF and 21 control subjects with hypertension without HF. Patients with pulmonary artery systolic pressure (PASP) >50 mmHg were proposed to undergo a right heart catheterization.

Results: Compared to controls, HFpEF patients had higher circulating levels of MMP2 (252.6±13 ng/mL vs. 211.1±4 ng/mL, p=0.002) and CIPC (106.1±7 ng/mL vs. 79.5±4 ng/mL, p=0.016), but no significant differences in MMP9 or TIMP1. Among the HFpEF group, PH was present in 16 patients (76%). 13 of them underwent a right heart catheterization, showing PASP 74.15±24 mmHg, PAPD 27.9±11 mmHg, pulmonary capillary wedge pressure (PCWP) 18.4±5 mmHg, cardiac Index 2.7±1 L/min/m², pulmonary vascular resistance 6.3±4 Wood Units. Among patients with HFpEF and PH, MMP2 levels showed a linear correlation with PASP (r=0.87, p=0.004) and PAPD (r=0.71, p=0.047). Circulating CIPC values showed a linear correlation with PASP (r=0.56, p=0.04), PAPD (r=0.64, p=0.018) and with pulmonary vascular resistance (r=0.70, p=0.007).

Conclusions: Patients with HFpEF had increased values of MMP2 and CIPC compared to hypertensive controls. Their levels showed a significant linear correlation with the invasive measurements of PH. These data suggest that MMP2 and CIPC might be useful as markers of PH development and progression in patients with HFpEF.

P4538 Expression of connective tissue growth factor in diastolic heart failure patients and canine models

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Background: Diastolic heart failure (DHF) is characterized by myocardial interstitial fibrosis and left ventricular hypertrophy. Connective tissue growth factor (CTGF) is an emerging marker for tissue fibrosis. The study investigated the association between CTGF and DHF from animal model to clinical indices.

Methods: A total of 120 patients with a diagnosis of DHF confirmed by echocardiography and 60 matched controls were recruited. Soluble plasma levels of CTGF were measured in all subjects and the associations with diastolic function parameters were calculated. Canine model of DHF was induced by aortic banding. Left ventricular (LV) pressures, LV volumes, and transmural Doppler were obtained before and after pressure loading (at baseline and after 6 months). Myocardium tissues were collected, and western blotting was used to detect the protein expression of CTGF for each dog. The correlation for CTGF and the severity of diastolic dysfunction was then calculated.

Results: Patients with DHF presented significantly higher CTGF levels than the controls. Significant correlations (all P < 0.05) were found for CTGF and E/e’ (r = 0.55), E/A (r = 0.5) in advanced DHF patients (E/e’ > 15). After 24 weeks in canine models, the protein expression of CTGF from LV myocardial tissue was significantly increased (p<0.01) compared with the controls (sham dogs). Moreover, the expression of CTGF paralleled the severity of LV diastolic dysfunction parameters and hemodynamic changes.

Conclusions: Both Plasma and myocardium CTGF levels had significant correlations to the severity of DHF. Our study offered the evidence to apply novel therapies for DHF patients aim to down-regulate the overexpression of CTGF.

P4540 Continuous infusion of the novel chimeric natriuretic peptide cenderitide in the Dahl salt sensitive rat model of hypertension and renal dysfunction: evidence for renoprotection

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Purpose: Cenderitide (CD-NP) is a chimeric natriuretic peptide created by fusing the 22 amino acid human C-type natriuretic peptide (CNP) with the 15 amino acid C-terminus of Dendroaspis natriuretic peptide (DNP). The peptide was developed to have natriuretic, diuretic, antihypertensive and antioxidative effects through binding of both guanylyl cyclase (GC)-B and GC-A receptors. Continuous administration of CD-NP is of interest for fluid management in patients with heart failure and impaired renal function. The purpose of this study was to deter-

P4539 Resveratrol, a SIRT1 activator, prevents cardiomyopathy in dystrophin-deficient mice by down-regulation of p300

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Background and purpose: Heart failure is a main cause of death in patients with Duchenne muscular dystrophy (DMD), a disorder caused by defective gene for dystrophin. However, there is no effective therapy for prevention of heart failure in DMD. The aim of this study was to examine whether activation of SIRT1, an NAD+-dependent histone/protein deacetylase, by use of resveratrol prevents cardiomyopathy due to dystrophin deficiency.

Methods and results: We used dystrophin-deficient mice (mdx) as a model of DMD and C57BL/10 mice as controls. Mdx were untreated or orally treated with resveratrol (400 mg/kg/day) from 3 weeks of age. Diastolic left ventricular (LV) thickness (0.72±0.02 vs. 0.82±0.03 mm), heart-to-body weight ratio (4.1±0.6 vs. 5.4±0.8 mg/g), and atrial natriuretic peptide (ANP) mRNA level (4.3-fold) were significantly increased in 40-week-old mdx mice compared with those in the control. Echocardiography showed that diastolic LV posterior wall movement, an index of LV diastolic function, was significantly slower in the untreated mdx than in the controls (21.1±1 vs. 30.2±2 mm/sec), though LV dimension and LV ejection fraction were similar in the two groups. Ventricular fibrosis and collagen gene expressions were increased in the mdx group. These phenotypes of mdx mice were significantly suppressed by treatment with resveratrol. Resveratrol reduced myocytes acetyl-histone H3 levels determined by immunohistochrometry and immunoblot in mdx hearts, indicating activation of SIRT1, Phospho-ERK1/2 and TGFβ1 mRNA levels in mdx hearts were not reduced by resveratrol. However, resveratrol suppressed the expression of p300 level of the transcription co-activator p300, a pro-hypertrophic and pro-fibrotic histone/protein acetyl-transferase, in the mdx myocardium. In vitro experiments demonstrated that p300 dose-dependently increased ANP promoter activity, which was suppressed by overexpression of wild-type SIRT1. Wild-type SIRT1, but not deacetylase inactive mutant SIRT1, reduced p300 protein level, which was blocked by the proteasome inhibitor MG132. In addition, SIRT1 was found to promote p500 deacetylation and polyubiquitination.

Conclusion: Resveratrol attenuates both cardiac hypertrophy and fibrosis and improves diastolic LV function in the mdx presumptively by SIRT1-mediated down-regulation of p300. SIRT1 activation may be a novel strategy in treatment of cardiomyopathy in DMD.
Antibodies to C-ending (intracellular) fragment of the Tranilast reduces pathological cardiac fibrosis and the contributions of blood pressure lowering and direct tissue protective actions. Histopathologic assessment revealed a dose dependent trend of im-
mals. CC was increased in the CD-NP treated animals, though not to statistical
significance. Long term subcutaneous dosing of CD-NP had an antihypertensive
effect in the DSS rat model. In addition, treated animals exhibited less renal
damage and reduced proteinuria. Further studies are warranted to understand the
contributions of blood pressure lowering and direct tissue protective actions of
this novel peptide.

**Results:** Continuous CD-NP administration dose-dependently decreased BP,
reaching statistical significance at 170 ng/kg/min (172.4±5.2 vs. 163.8±4.4 vs.
148.5±4.7 mm Hg for groups 1, 2, and 3, respectively at week 5). At week 6,
there was a statistically significant reduction in albuminuria in both CD-NP treated
groups (95.8±10.16 vs. 72.8±10.23 vs 70.1±5.44 mg/day for groups 1, 2, and 3,
respectively). Proteinuria was similarly reduced at week 6 in the treated ani-
mals. CC was increased in the CD-NP treated animals, though not to statistical
significance. Histopathologic assessment revealed a dose dependent trend of im-
poved renal tissue morphology, specifically in terms of tubulo-interstitial changes and
glomerulopathy.

**Conclusions:** Long term subcutaneous dosing of CD-NP had an antihyperten-
sive effect in the DSS rat. In addition, treated animals exhibited less renal
damage and reduced proteinuria. Further studies are warranted to understand the
contributions of blood pressure lowering and direct tissue protective actions of
this novel peptide.

Antibodies to C-ending (intracellular) fragment of the angiotensin II type 1 receptor and endothelial NO synthase: the pathophysiologic significance of these antibodies in patients with congestive heart failure: **first clinical experience**

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**Background:** Antibodies to C-ending (intracellular) fragment of the angiotensin II type 1 receptor and endothelial NO synthase are a principally new classes of neurohumoral modulators. The aim of our study was to investigate the efficacy and safety of combination these antibodies (anti-AT1+E-NO-synthase) in pts with congestive heart failure (CHF).

**Methods:** 60 pts (mean age 56.9±1.3 years) with CHF (NYHA class II-IV, mean 2.7±0.07, mean ejection fraction 29.6±0.9%) were included into the randomized, single-blind, placebo-controlled study. Baseline therapy (ACE inhibitor, β-blocker, diuretics) wasn't changed during the study. Pts with CHF were randomly assigned to anti-AT1+E-NO-synthase 3 tabs/day (group I, n=30) or placebo (group II, n=30).

**Results:** After 6 months of therapy with anti-AT1+E-NO-synthase NYHA class reduced to 42.6% (p<0.008), in placebo group to 52.4% (n.s.). Significant in-
crease in left ventricular ejection fraction was noted in both groups: group I +25.47% (p<0.0001); group II +6.29% (n.s.). Significant increase both exercise time (+34.7%, p<0.0005) during treadmill-test and distance during 6-min walking test (+24.50%, p=0.0002) was noted only in the group I. Adverse events related with anti-AT1+E-NO-synthase were not observed.

**Conclusions:** The adding of combination of antibodies to C-ending (intracellular) fragment of the angiotensin II type 1 receptor and endothelial NO synthase to standard therapy is a promising way for treatment pts with CHF. Large clinical trials are indicated.

**Transplant reduces pathological cardiac fibrosis and improves diastolic function following kidney dysfunction: implication for cardio-renal syndrome**

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**Background:** Kidney dysfunction in heart failure (HF) is associated with in-
creased mortality, morbidity and cost of care known as cardio-renal syndrome (CRS). Fibrosis plays an important role in disease progression in HF in patients with CRS. We examined the effect of the anti-fibrotic agent, transplant, on amelio-
rating these processes.

**Methods:** 5/6 subtotal nephrectomy (STNx) was induced in male Sprague Daw-
ley (SD) rats. Animals were randomized to receive either transplant (300mg/kg/day, p.i.) (n=14) or vehicle (n=16) for 12 weeks. Sham operated control animals also received vehicle (n=9). Glomerular filtration rate (GFR) was measured with a single shot Trc99m-DTPA clearance. Blood pressure was measured by tail-cuff plethys-
omography. Echocardiogram was performed to assess cardiac function before car-
diac tissues were harvested for immunohistochometric analysis.

**Results:** Transplant treatment had significant effect on blood pressure (vs STNx+Vehicle, P<0.05) and reduced collagen I and III deposition (vs STNx+Vehicle, P<0.05) in the heart post STNx. (Table)

**Conclusion:** Transplant reduced cardiac fibrosis, renal function and blood pressure in STNx rats as well as improved diastolic function. These findings support the use of direct antifibrotic strategies in CRS.
Methods: Twenty-four patients (age 74±9 yrs; left ventricular ejection fraction 40.2±17.6%) with AHF were enrolled and were treated with intravenous low dose hANP. When adequate diuresis was not obtained by 4 hours after administration despite increasing the dose of hANP twice, low dose DA (1-3μg/kg/min, n=12) or low dose furosemide (F, 10-30mg injection, n=12) was randomly added. Serum creatinine, a novel reno-tubular marker, urinary L-type fatty acid-binding proteins (L-FABP) and an oxidative stress marker, urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) were measured on admission and after additional DA or F administrations.

Results: Heart rate did not change in both groups. Systolic blood pressure decreased significantly in DA and F groups (137.3±15.8, P<0.001, 137.1±29.4 to 108.3±16.1 mmHg, P=0.007, respectively). Urine volume increased significantly in both groups (fig). Urinary L-FABP and 8-OHdG decreased significantly in DA but not in F (fig). Serum creatinine did not change in both groups.

Conclusion: The combination therapy with low doses of hANP and DA might be a reno-protective strategy for AHF management.

P4547 Cardiac iron and function by CMR in thalassemia major patients treated with combined deferiprone and desferrioxamine regimen versus monotherapies: a multi-center, observational and prospective study


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Purpose: To the limited data available in literature, the aim of this multi-centre study was to prospectively assess in thalassemia major (TM) the efficacy of combined deferiprone (DFP) and desferrioxamine (DFO) regimen versus DFP and DFO in monotherapy by cardiovascular magnetic resonance imaging (CMR) over a follow up of 18 months.

Methods: Among the first 1135 TM patients in the MIOT (Myocardial Iron Overload in Thalassemia) network, we evaluated those who had been received combined regimen (N=51) or DFP (N=39) and DFO (N=74) monotherapies between the two CMR scans. Iron overload was measured by T2* multiecho technique. Biventricular function parameters were quantitatively evaluated by cine images.

Results: The percentage of patients that maintained a normal global heart T2* value was comparable between DFP+DFO versus both groups. Among the patients with myocardial iron overload at baseline, the changes in the global heart T2* and in biventricular function were not significantly different in DFP+DFO versus the DFP group. The changes in the global heart T2* were significantly higher in the DFP+DFO versus DFO group, without a difference in biventricular function.

Conclusions: In TM patients at the dosages used in the real world, combined DFP+DFO regimen was more effective in removing cardiac iron load only versus the DFO group. Combined therapy did not show an additional effect on heart function.

P4548 Evaluation of safety, tolerability, PK and hemodynamic properties of JNJ-39588146 (strescopin) in healthy and HF subjects: a phase 1 ascending dose randomized multicenter trial

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Purpose: JNJ-39588146/human Stresscopin (SCP) is a member of the corti-
cortisol releasing factor family of peptides. It is a highly selective agonist of CRFR2. This three part study assessed the safety, PK, and hemodynamics of SCP in healthy subjects (HS) and heart failure (HF) subjects. 

Methods: In Part 1, 30 male HS were randomized to receive continuous IV infusions of either SCP (0.1 to 144 ng/kg/min, N=25) or placebo (N=5) for 7.5 hours (h), with increases in dose at 2.5 and 5h. In Part 2, 20 subjects with HF with EF > 40% were randomized to receive either SCP (0.3 to 54ng/kg/min, N=13) or placebo (N=7) for 7.5h, with 2 increases in dose. In Part 3, 26 male and female HS were randomized to receive a constant IV infusion of either SCP (54ng/kg/min, N=20) or placebo (N=6) for 24 or 72h. Heart rate (HR) and Cardiac index (CI) were measured by impedance cardiography. HR was noted to decrease during the infusion for placebo subjects. This “placebo effect” was considered when analyzing the HR and CI data for SCP treated subjects.

Results: SCP was safe and well tolerated with no notable changes in ECG parameters and no ventricular arrhythmias. The proportion of subjects with AEs who received SCP at doses >36 ng/kg/min was similar to those in subjects receiving placebo. The mean baseline CI in the HS and HF subjects was 3.2 and 2.9L/M2. In HS who received SCP (0.1 to 36ng/kg/min), no notable change in CI, HR, or BP was seen compared to placebo. In HF subjects who received SCP (0.3 to 36ng/kg/min), a higher mean CI (7-15%), was seen compared to placebo. Though numerically lower BP was seen in HF subjects dosed with SCP compared to placebo, no notable change in BP and no dose relationship was observed. At doses >36 ng/kg/min, a dose-related increase in HR was seen in both HS and HF subjects. In HF subjects, the increase in HR was 7-8 bpm at the highest dose (54ng/kg/min) compared to placebo. A greater proportion of subjects who received >36 ng/kg/min of SCP had AEs compared to placebo; the most common AEs in SCP treated subjects were: headache, back pain, feeling hot, nausea, vomiting, and catherter site pain or inflammation. In general, SCP showed linear pharmacokinetics as the systemic exposures increased with the infusion rate. The elimination was multi-phasic, with initial rapid decline of SCP (112-10-15 min) followed by a slower terminal phase. No antidrug antibodies were detected.

Conclusion: IV infusions of SCP were safe and well tolerated in HS and HF subjects. SCP showed linear PK that was similar between HS and HF subjects.

Pragmatic Study of Aldosterone Antagonist Epleronone in Heart Failure Patients with Adequate Heart Rate Control

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Purpose: Recent studies indicated that heart rate was an important target for Chronic heart failure (CHF) treatment, whereas the importance of doses of beta-blockers and had adequate heart rate control had the best survival prognosis. We should make an effort to achieve the target doses of the beta-blockers, even the heart rate is well controlled.

Methods: A. Sukonthasarn. Chiang Mai University, Faculty of Medicine, Chiang Mai, Thailand

Figure 1

Conclusions: The CHF patients who both achieved the target doses of beta-blockers and had adequate heart rate control had the best survival prognosis. We should make an effort to achieve the target doses of the beta-blockers, even the heart rate is well controlled.
in decompensated HF. Interestingly, as many as 26% of patients with pulmonary oedema received inotropes and 20% were given vasopressors whereas only 15% of pulmonary oedema patients had systolic blood pressure <120 mmHg. CPAP was used only in 50% of pulmonary oedema patients.

Conclusion: The management of AHF differs between ESC clinical classes. The use of IV nitrates and CPAP was lower than expected whereas there was overseuse of inotropes and vasopressors especially in pulmonary oedema.

Continuous furosemide infusion versus furosemide manitol infusion in acute congestive heart failure

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Background: Loop diuretics remain the cornerstone for fluid mobilization in patients with acute congestive heart failure (CHF) although there is little evidence regarding the ideal dosing strategies and method of administration. Data on the use of mannitol for prophylaxis and/or treatment of acute CHF is controversial and the role of this implicit selection bias on mortality remains unclear.

Methods: A retrospective study of 233 patients with CHF (N=108 who received treatment with continuous furosemide-manitol infusion (FM) and N=125 with continuous furosemide infusion) was performed. Infusions were administered intravenously for a period of 1-4 days. Dose titration was protocol-driven and based on urine output. Outcomes of diuresis achieved, death during hospitalization, dialysis in patient, length of hospital stay, effects on kidney function and electrolytes were assessed. Data are reported as mean±SD.

Results: In the comparison of continuous furosemide infusion, there was no significant difference in patients’ weight (-4.71±1.9 kg and -4.84±2.03 kg, p=0.02) or in the mean creatinine level (0.53±0.3 mg/dl vs 0.40±0.2 mg/dl, p=0.33), respectively; P=0.45. There was no significant difference between these groups in the need for dialysis (9.6% and 9.2%, p=0.98), in hospital death (10.4% and 10.1%, p=0.99) and duration of hospitalization (6.9±1.2 and 6.0±1.5 days, p=0.61). Patients who required diuresis had a lower diuretic response (FM (-0.8±0.3 kg vs 4.9±1.9 kg, p=0.02); furosemide (-0.7±0.2 kg vs 4.8±1.3 kg, p=0.03)), higher baseline creatinine (FM [2.8±1.6 mg/dl vs 2.5±1.2 mg/dl, p=0.05]; furosemide [2.9±1.3 mg/dl vs 2.6±1.6 mg/dl, p=0.04]), higher BNP on admission (FM 2120±990 vs 1735±860, p=0.05; furosemide 2340±560 vs 1650±590, p=0.06) and a higher incidence of acute kidney injury on admission (FM 40%, p=0.001; FM 100% vs 76%, p=0.002)

Conclusion: FM is equally efficacious as furosemide infusion in severe CHF. Mortality continues to be high in CHF patients with underlying kidney failure.
Efficacy of ivabradine therapy on right heart parameters in patients with severe systolic chronic heart failure

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The aim of study was to assess the efficacy of ivabradine (I, up to 15 mg) therapy on prognosis, right ventricular (RV) and atrial (RA) functional parameters, BNP, NT-proBNP and high sensitivity C reactive protein (CRP) levels in patients (pts) with III-IV NYHA FC systolic CHF in sinus rhythm.

Methods: 76 pts (age 57.4) were randomly assigned to group A (n=38, receiving I) and group B (n=38, receiving placebo, I), in addition to ACE inhibitors, beta-blockers, digoxin and diuretics. Assessment of RV EF, myocardial mass (MM), myocardial mass index (MMI), fractional area change (FAC), tricuspid annulus plane systolic excursion (TAPSE), right atrial index (RAI) and RA transmural caval flow velocities, deceleration time (DT) of E wave, overall filling time (OFT), pulmonary artery (PA) ejection ET and pre-ejection (PET) times, RA functional index (FI) and fractional contribution (FC), BNP, NT-proBNP and hsCRP levels was performed at baseline and 12 months.

Results: 1-year mortality, hospitalization rate and combined endpoint of mortality and hospitalization (%) were, respectively, 34.2%, 55.3 and 89.5 and 21.1, 31.6 and 52.6 in groups A and B. Event-free analysis showed lower right ventricular mortality (RR 0.76, CI 0.65-0.89, p<0.001). This positive association was mostly due to a lower CV death (HR 0.76, CI 0.65-0.89, p<0.0002). In addition, patients on I had a lower risk of a first hospitalization for stroke. In contrast, atrial size was associated with a slightly higher rate of non-CV hospitalizations (HR 1.16.; CI 1.02-1.33, p=0.02).

Conclusions: In patients with post-MI acute HF, I therapy was associated with a lower risk of all-cause and CV death, but with a higher risk of non-CV hospitalizations. Although clinical trials prospectively randomizing patients to I are required to validate these findings, our results suggest that patients with acute HF complicated by or may benefit from being on I therapy.

Are there relationships between high resting heart rate and not optimal doses of beta-blockers in patients with systolic heart failure in contemporary Poland? Results of DATA-HELP study

E.A. Jankowska1, B. Kurian2, W. Baniasik3, P. Ponikowski1 on behalf of On behalf ofOf DATA-HELP study (Diagnostic And Therapeutic methods, used in patients with systolic heart failure. Living in Poland) investigators.

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Background: Resting heart rate (HR) is associated with poor outcome, and its reduction due to both β−adrenergic and if current blockade has provided survival benefits in patients with systolic heart failure (HF). The magnitude of contemporary European population of patients with systolic HF and HR, and links between applied therapy and achieved HR in everyday practice are unclear.

Methods: Registry DATA-HELP was performed in X-II-2009 in Poland in a randomly selected representative sample of 5563 outpatients with clinical diagnosis of HF and LVEF<45%; resting HR was available in 5513 subjects (99%).

Results: We analyzed 3620 patients with systolic HF in a sinus rhythm (65% of the whole cohort; age: 66±11 y, BMI: 28.2±4.2 kg/m², men: 64%, NYHA class III-IV: 31%, previous MI: 61%, diabetes: 33%). Mean±SD HR was 75±13 bpm, median with upper/lower quartiles 72 (68-80) bpm. HR >70 bpm and ≥75 bpm were found in 68% and 47% of patients, respectively, with increasing frequency among NYHA classes (II/III/IV - HR >70 bpm: 65%/67%/74%/77%, HR >75 bpm: 42%/45%/53%/60%, both p<0.001). In a multivariable stepwise regression model, high HR was related to high syst Bp (p<0.001), presence of pulmonary congestion (p<0.05) and peripheral oedema (p<0.001), advanced NYHA class (p<0.01), and longer age (p<0.001). A close association was found between the left and the right side of the heart (r=0.80). HR >70 bpm and ≥75 bpm were found in 68% and 47% of patients received β-blockers; bisoprolol, carvedilol, metoprolol, nebivolol and others were used in 52%, 30%, 12%, 3% and 2% of subjects, respectively, in an average daily dose of 5.4±3.9, 21.5±14.1, 63.2±37.1, 4.4±1.5, respectively for 4 major β-blockers (i.e. 41±34% of daily recommended dose). There were no differences in HR between those treated vs not treated with β-blockers, and between those treated with different β-blockers (all p>0.2). There was no association between HR and the % of daily recommended dose, and there were no correlations between HR and the daily dose of bisoprolol, carvedilol, metoprolol, nebivolol (analysed separately) (all p>0.2). There was an inverse relationship between HR and the daily dose of carvedilol, which remained significant after adjustment for clinical status (p<0.05).

Conclusions: Polish registry demonstrates high prevalence of increased resting HR and low doses of β-blockers used in outpatients with SHF in a sinus rhythm, and no relationship between HR and the dose of β-blockers (in spite of carvedilol). HR is not sufficiently controlled in the majority of these patients, and it is reliable to consider also alternative therapies reducing HF (e.g. ivabradine).

Subcutaneous furosemide can prevent hospitalization in fluid overload decompensation of chronic heart failure

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Purpose: Chronic heart failure (CHF) is a high prevalent disease, a main cause of admission and it supposes a high economic cost. The basis of treatment for fluid overload consists of diuretics. Furosemide is the most widespread. When oral treatment is not enough, the endovenous route is the most frequent access, but many patients require admission. Relevant differences between bolus and perfusion have not been proved. We tested ambulatory continuous infusion of subcutaneous furosemide (SF) with elastomeric pumps in order to prevent hospitalization in patients with fluid overload decompensation of CHF.

Methods: 25 patients (p) (76% male, 74±10±10 years-old) in 42 episodes of fluid overload were treated by subcutaneous system of furosemide continuous infusion in a heart failure department. Elastomeric pumps with UFA filter were prepared with different dilutions of furosemide (in 2, 4 or 5 days of infusion. Analytical, clinical and functional data were prospectively registered.

Results: 52% suffered hypertension, 24% diabetes, 36% chronic renal failure; mean creatinine 1.58±0.6, 72% atrial and 71% were on beta-blockers therapy, 81% on angiotensin- converting enzyme inhibitors/angiotensin-receptor-antagonists II and 24% were on aldosterone- antagonist treatment. Mean dose of furosemide was 110±50 mg, 92% were in NYHA class III-IV. 52% had severe left ventricle impairment and 44% severe pulmonary hypertension by echocardiogram. Mean NT-proBNP was 6476±5762 pg/ml. After therapy (9±4 days) with furosemide (150±40 mg), mean weight loss was 2.11±2.9kg (79.05 vs 76.93 kg, p=0.001). Creatinine levels were stable (1.58 vs 1.53, p=0.3) and no clinical relevant hypokaliemia happened (2% (1p) had ≥3mmEq (2.9 mEq/dl) but no clinical events). Only 17% (7p) needed hospitalization due to fluid overload during therapy and no deaths during therapy occurred. Main adverse events were local complications at the infusion point without clinical significance (pain 5%, irritation 10%, disconnection 5%, infection 7% and local bleeding 3%). NYHA class was improved in 61% of episodes, it did not differ in 37% and it worse in just 2% (1p).

Conclusion: Ambulatory continuous infusion of subcutaneous furosemide by elastomeric pumps is effective and safe to prevent hospitalization in patients with fluid overload decompensation of CHF. No relevant renal, ionic or clinical complications occurred. Frequent minor local complications were observed. So, this alternative route of diuretic administration could have a beneficial economic impact.

Do early and late nephroprotective effects differ with different inhibitors of renin-angiotensin-aldosteron system in chronic heart failure patients?

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Overall, 3095 patients (47%) had a statin prescribed at baseline. Cox regression models were fit to assess the association between statin intake at baseline and outcome, with adjustment for all baseline characteristics. Cox regression models were fit to assess the association between statin intake at baseline and outcome, with adjustment for all baseline characteristics.

Conclusions: In patients with post-MI acute HF, statin therapy was associated with a lower risk of all-cause and CV death, but with a higher risk of non-CV hospitalizations. Although clinical trials prospectively randomizing patients to statins are required to validate these findings, our results suggest that patients with acute HF complicated by CHF may benefit from being on statin therapy.

Conclusion: In post-MI heart failure patients, a lower HR is not sufficiently controlled in the majority of these patients, and it is reliable to consider also alternative therapies reducing HF (e.g. ivabradine).
ure (CHF) patients treated with angiotensin-converting enzyme inhibitor (ACEI), angiotensin-II receptor blocker (ARB), and direct renin inhibitor (DRI).

Methods: 155 patients with CHF of different etiology and NYHA class II or III, with chronic kidney disease (CKD) stage I to III, and with uncorrected arterial hypertension, were randomized after getting informed consent into three treatment arms: 1st – with ACEI enalapril (n=49), 2nd – with ARB losartan (n=47), and 3rd – with DRI aliskiren (n=59). The patients were evaluated at baseline, after two weeks and after one year of treatment, for systolic and diastolic blood pressure (BP), microalbuminuria (MAU), and glomerular filtration rate (GFR) by Cockcroft-Gault equation. Overall there were 6 drop-outs from groups due to patients’ decision and no cross-over of assigned treatment arms at follow-up. Mean daily doses at one year evaluation were 19.1 mg for enalapril, 65.4 mg for losartan, and 274.5 mg for aliskiren. All patients were on beta-blockers and aldosterone antagonists, and 86% on diuretics in comparable doses. ANOVA for independent and dependent samples was used for statistical analysis with 0.05 alpha-error cut-off.

Results: After one year of treatment there was no significant difference between groups in achieving BP control: BP < 140/90 mm Hg was observed in 65.8±6.8% of patients in the 1st group, 72.6±6.5% – in the 2nd, and in 73.1±6.5% – in the 3rd. Slight decrease in MAU (by 24-27 mg per day) was already seen after two weeks of treatment; it became more pronounced and statistically significant (p<0.05) at one year evaluation within each group but more or less similar between the respective groups: by 66.9±8.1% and 71.2±9.5% vs 62.8±6.9% higher GFR was also noted in two weeks in all groups, and reached statistical significance in each group up to one year. At one year evaluation, however, there was no significant difference in GFR (by 11.2±1.3 ml/min) as compared to enalapril group (by 5.4±1.2 ml/min). There was only a tendency for higher nephroprotection of aliskiren over losartan after one year of treatment. Tolerability of drugs was good in all treatment arms.

Conclusion: In CHF patients with CKD and arterial hypertension the nephro-protective effects may differ with different types of renin-angiotensin-aldosterone system inhibition, being somewhat greater in terms of higher GFR with aliskiren and losartan as compared to enalapril after one year of treatment.

Secondary Prevention: From Awareness to Action

Effect of valsartan and amlodipine on heart failure and left ventricular mass in Japanese hypertensive patients with glucose intolerance: a subanalysis of the Nagoya heart study


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Purpose: The Nagoya Heart Study was a multicenter, prospective, randomized, open labeled, blinded endpoint trial that was performed to compare the beneficial effects of valsartan and amlodipine on cardiovascular events in Japanese hypertensive patients with glucose intolerance without apparent heart failure. Although the blood pressure levels were well controlled in both groups and remained similarly throughout the trial, valsartan had more favorable effect on heart failure than amlodipine. We analyzed the details about heart failure patients and assessed comparability throughout the trial, valsartan had more favorable effect on heart failure than amlodipine.

Methods: We enrolled 1168 hypertensive patients with type 2 diabetes mellitus or impaired glucose tolerance. These patients were randomly assigned to the valsartan or amlodipine treatment group (after informed consent was obtained). As an initial dose, either valsartan 80mg or amlodipine 5mg once daily was administered. The primary outcome was a composite of acute myocardial infarction, admission due to heart failure, coronary revascularization, or sudden cardiac death. Laboratory tests were performed every 6 months and echocardiography were performed every 12 months.

Results: Patients were randomly assigned to the valsartan group (n=575) or the amlodipine group (n=575), and a total of 1117 patients (97%) completed the follow-up throughout the study. The mean follow-up period was 3.2 years. In baseline, there were no significant differences between exclusion criteria (EF) and left ventricular mass (LVMass) between the valsartan and amlodipine group (EF: 62.5±8.2% vs 63.1±9.1%, LVMass: 206.6±68.22g vs 209.47±64.8g, respectively). However, EF at the last visit was higher than baseline in valsartan group but with chronic kidney disease (CKD) stage I to III, and with uncorrected arterial hypertension, improved LVMass better than amlodipine did (LVMass: 192.96±60.68g vs 215.66±66.60g) at the end of this study. Furthermore, EF of the heart failure in the valsartan group seemed to be preserved better than in the amlodipine group. Conclusions: In Japanese hypertensive patients with glucose intolerance, valsartan significantly reduced the incidence of heart failure. In addition to that, not only the EF was well preserved but also significant improvement in LVMass was observed in valsartan group. These results could be considered as the reasons for the reduction of heart failure and suggest that valsartan would be more effective in the treatment of diabetic hypertensive patients with incipient LV dysfunction than amlodipine.

Prevalence, co-prevalence and awareness of cardiovascular risk factors - results from the population based Gutenberg Health Study

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Purpose: Classical cardiovascular risk factors (CVRF) explain a substantial part of the risk for cardiovascular diseases. In past decades, prevalences of CVRF have changed. The presence, awareness and medical treatment of CVRF may differ strongly. Current data from large-scale population-based studies are limited.

Methods: We investigated a sample of 10,000 participants from the age - gender and residence-stratified, population-based Gutenberg Health Study, examined from 2007 to 2008. Data were obtained from self-reported data, computer-assisted personal interviews, blood pressure measurements and blood sampling (fasting values) according to standard operating procedures with detailed quality control.

Results: The sample comprised 4,983 women (w) and 5,017 men (m), aged 35 to 74 years. The overall prevalence was: hypertension 46.0% (m:50.2%, w:41.9%), dyslipidemia 27.7% (m:35.6%, w:19.9%), obesity 24.1% (m:25.3%, w:16.1%), diabetes 16.6% (m:20.8%, w:14.6%), smoking 21.6% (m:26.1%, w:17.0%), alcohol history 16.6% (m:14.7%, w:18.5%), and physical inactivity 16.6% (m:14.7%, w:18.5%). Co-prevalence of hypertension and obesity was 42.4% in women (m:45.5%, w:39.3%) and 45.9% in men (m:45.9%, w:42.4%). Co-prevalence of hypertension and diabetes was 16.5% in women (m:17.9%, w:15.1%) and 19.4% in men (m:19.4%, w:17.0%). Co-prevalence of hypertension and smoking was 43.4% in women (m:45.9%, w:41.0%) and 47.3% in men (m:47.3%, w:44.9%). Co-prevalence of hypertension and alcohol history was 25.5% in women (m:29.5%, w:21.4%) and 28.1% in men (m:28.1%, w:22.9%). Smoking 20.8% (m:22.7%, w:19.0%), family history of myocardial infarction 16.6% (m:15.6%, w:17.0%) and diabetes 6.1% (m:7.7%, w:4.5%). Analysis of co-prevalences showed lower co-prevalences than single CVRFs. Highest co-prevalences were found for prevalent diabetes, obesity and dyslipidemia with hypertension (82.3%, 68.0% and 57.8%), lowest for smoking with diabetes (50.4%). Analysis of co-prevalences showed a comparison to women lower increase of CVRF by age revealed an increase of all risk factors with increasing age (BMI, systolic and diastolic blood pressure, LDL, HDL, triglycerides, Glucose, HbA1c) in women (all p<0.001).

Mean, however, showed a compared to women lower increase of CVRF by age revealed an increase of all risk factors with increasing age (BMI, systolic and diastolic blood pressure, LDL, HDL, triglycerides, Glucose, HbA1c) in women (all p<0.001), except for BMI, triglycerides and diastolic blood pressure, where no association was found. Analysis of awareness showed that approx. 3 out of 4 (74.3%) hypertensive individuals were aware of having hypertension, although just 24.4% were treated sufficiently. Hypertension was untreated in 51.3% of the hypertensive individuals. The prevalence of unknown diabetes was nearly twice as high in men as in women with diabetes (m:10.4%, w:5.3%) whereas sufficient antidiabetic treatment was less prevalent in men (m:21.6%, w:24.9%). The preva-
Use of lipid lowering therapy in primary care across Europe: results from the European study on cardiovascular risk prevention and management (EURINA)1,2,4,5,6,7,8

1. P.J. Holme1, F. Tubach1, J.R. Bangæs2, C. Borghy4, J. Dallongeille5, G. De Backer2, J. Perk1, P.G. Steg1, F. Rodríguez-Artalejo1, E. Guarra1 on behalf of The EURIKA investigators.

Purpose: Current European guidelines recommend that patients free from cardiovascular disease (CVD) but estimated to be at high (>5%) 10-year risk of CVD mortality should be more vigorously pharmacologically treated than those at lower risk. The recommended target level of low-density lipoprotein cholesterol (LDL-C) is <2.5 mmol/l, or <1.8 mmol/l for those at very high risk (VHR; those with diabetes mellitus [DM] or ≥10% 10-year mortality risk). We examined the use of lipid lowering therapy (LLT) and achievement of LDL-C level targets in routine clinical practice in Europe.

Methods: The European Study on Cardiovascular Risk Prevention and Management in Daily Practice (EURINA) (NCT00883326) was a cross-sectional study conducted simultaneously in 12 European countries from May 2009 to January 2010. Amongst 32841 patients aged >50 years who were free of classical cardiovascular disease but had at least one cardiovascular risk factor (dyslipidaemia, hypertension, DM, smoking or obesity), ten-year CVD mortality risk was estimated using the Systematic Coronary Risk Evaluation (SCORE) algorithm. LDL-C levels were measured and use of LLT was noted, including the agents and doses used. Statin therapy was classified as low-intensity (LIS; pravastatin, simvastatin, lovastatin, fluvasitatin, atorvastatin <40 or rosuvastatin <20 mg) or high-intensity (HIS; atorvastatin >40 mg or rosuvastatin >20 mg).

Results: We identified 3278 individuals who were receiving any form of LLT, of whom 3040 (92.7%) were receiving a statin. Of the 4363 patients not receiving LLT, 1741 (39.9%) had a DM or a SCORE risk ≥5%. LDL-C levels were available for 3151 participants receiving LLT, for whom LDL-C levels were not targeted (<2.5 mmol/l) in 1931 (61.3%). Only 8.9% of patients on LLT were receiving HIS. Of the participants with at least one cardiovascular risk factor, only 39.8% had an LDL-C level <2.5 mmol/l. A subset of 2970 patients were at VHR, of whom only 1469 (49.5%) were receiving any form of LLT. LDL-C levels were targeted (<1.8 mmol/l) in 171.7% of these patients. Only 0.9% of VHR patients on LLT were receiving HIS. Of the VHR patients receiving LIS, only 17.1% had achieved LDL-C levels <1.8 mmol/l.

Conclusion: Approximately 40% of patients aged ≥50 years with at least 1 cardiovascular risk factor who are not currently receiving LLT are at high risk of CVD (DM or SCORE ≥5%). Furthermore, well over half of all those receiving LLT and more than 80% of VHR patients receiving LLT did not achieve recommended LDL-C levels. These results demonstrate that there is potential for major improvements in lipid level management in patients at risk of CVD in Europe.

Low levels of IgM antibodies against phosphorylcholine (anti-PC) increase the risk of ischemic cardiovascular events among European men at high risk of cardiovascular events

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Purpose: IgM antibodies against phosphorylcholine (anti-PC) reduce the uptake of oxidized LDL and inhibit the effect of inflammatory phospholipids, thereby exerting an atheroprotective effect. Previous studies have shown that low anti-PC serum levels increase the risk of cardiovascular (CV) events. The aim of the present study was to investigate the association of low levels of anti-PC with the incidence of CV events and the progression of intima media thickness (IMT) in a large cohort of European men at high risk of cardiovascular disease and to evaluate the risk associated with low anti-PC levels contained in the IMPROVE study, a prospective multicenter European study.

Methods: 3711 subjects (age 54-79) with at least three established cardiovascular risk factors at enrollment. Serum levels of anti-PC were measured at baseline on all the study participants by ELISA (CV Define, Athera Biotechnologies AB, Stockholm Sweden). Carotid ultrasound investigations were performed at baseline and after 15 and 30 months of follow-up. The risk of ischemic cardiovascular events and IMT progression associated with low anti-PC levels was tested by a Cox regression and a logistic regression analysis, respectively. Risk estimates were adjusted by center, gender, age and the conventional cardiovascular risk factors.

Results: 3516 were included in the present analysis and 198 incident ischemic cardiovascular events were recorded during a 3 year follow up. Anti-PC levels (UI/ml) were classified into quartiles [Q1 <40, Q2 >40-64, Q3 >64-<102, Q4 >102] and the highest quartile (Q4) was taken as reference. Presence of low levels (Q1 vs Q4) of anti-PC was associated with an increased risk of CV events in men with a multivariately adjusted HR of 1.76 and 95%CI (1.02-3.03). In men, low levels of anti-PC were found to be associated with the highest (>90th) percentile of the fastest IMT progression, i.e. the segment showing the fastest progression over 30 months in the whole carotid tree, with an OR of 1.42 (95%CI:1.03-1.98). No significant associations were found in women.

Conclusions: These results suggest that low anti-PC serum levels increase the risk of cardiovascular events in men partly through effects on progression of atherosclerosis.

Fasting and postprandial triglycerides are independent cardiovascular risk markers in non-obese coronary artery disease patients with normal glucose tolerance

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Background: Risk prediction with fasting triglycerides (TG) in high cardiovascular disease (CVD) risk patients with remains uncertain. The role of postprandial serum triglycerides as a risk modifier in secondary prevention is unknown. We hypothesized that the postprandial TG increase is a superior risk predictor compared to fasting TG in patients with coronary artery disease (CAD).

Methods: An oral triglyceride (OT, 75g cream fat) and glucose tolerance test (OGT, 75g glucose) was developed to obtain standardized measurements of postprandial TG in an observational, prospective study on 514 consecutive patients (83% male, 95% on statin) with angiographically confirmed stable coronary artery disease. Patients with medical treatment for diabetes mellitus (DM) received the OGT only; all others ingested the OGT and the OGT 3 hours later in a sequential test protocol. Lipid and glucose parameters were measured at fasting, 3, 4, and 5 hours after the OGT/OGT.

Results: Metabolic characterization revealed that 126 patients had normal glucose tolerance (NoDM), 388 had impaired glucose tolerance (IGT) or DM, 95 patients had a normal BMI (<25kg/m²) and 419 were obese. Both, IGT/DM and obesity were associated with elevated fasting and postprandial triglycerides. Follow-up was 24 months and the primary outcome was the composite of cardiovascular death and cardiovascular hospitalization for coronary or cerebrovascular events. Cox proportional hazards regression models were used to calculate multivariable-adjusted hazard ratios (HR) and confidence intervals (95%-CI) in time-to-event analyses. In the total cohort and in patients with IGT/DM or obesity, neither fasting nor postprandial TG predicted event-free survival independently. After stepwise adjustment for baseline characteristics, cardiovascular risk factors, and metabolic parameters, fasting TG >150mg/dl (compared to <106mg/dl) were independently associated with event-free survival in normoglycemic and non-obese patients (NoDM: HR 3.50, CI 1.90-6.40, p=0.004; Lean: HR 3.71, CI: 1.30-10.0, p=0.02). The area under the curve (AUC) is an integral measure of serum triglycerides from fasting to the postprandial TG peak. An AUC above 120mg/dl (compared to ~750mg/dl), also predicted risk independently (NoDM: HR 2.62, CI 1.00-6.98, p=0.05; Lean: HR 3.12, CI 1.00-9.81).

Conclusions: In normoglycemic, non-obese CAD patients, both, fasting and postprandial TG independently predict cardiovascular outcomes. The findings of the study are of great clinical relevance with respect to the identification of high risk patients, who may benefit from TG-lowering therapies.
Methods: The subjects replaced 20 g/d of their regular fat intake with the test spread with (staged group) or without (controls) plant stanol esters (3 g/d of plant stanols). Compliance was verified with measuring serum plant stanols. Arterial stiffness was measured using the pulse wave velocity and the obtained variables were carotid-ankle vascular index (CAVI) and augmentation index (AI), and endothelial function was measured as reactive hyperaemia index (RHI) using peripheral arterial tonometry. Serum sterols were analysed with gas-liquid chromatography. The study was performed according to the principles of Declaration of Helsinki of the World Medical Association, and the Ethics Committee of the Hospital District of Helsinki and Uusimaa had accepted the study protocol.

Results: The mean age of the study population was 50.8±1.0 (SEM) years with 38% of males. At baseline, mean LDL cholesterol was 3.5±1.0 mmol/l, HDL cholesterol and serum triglycerides were within the reference values, CAVI was 8.7±0.1, AI 9.1±1.9, and RHI 2.2±0.1, respectively. The intervention was well tolerated without any side-effects, and compliance was good. LDL cholesterol was reduced in the staged group by 7.9±1.6% from baseline and by 10.2±2.7% from controls (P<0.05 for both). AI changed significantly differently between the groups: it was increased in the controls and decreased in the staged group (P=0.04 between groups). CAVI was decreased in men with weight loss by 1.1±1% and increased in control men by 3.2±2% so that the difference was significant (P=0.007). In the staged group, the change in RHI was inversely related to the change in LDL cholesterol level suggesting that the more LDL cholesterol was reduced, the more RHI was increased (n=0.452, P<0.001).

Conclusions: Six-month consumption of 3 g plant stanols as esters decreased arterial stiffness and increased endothelial function by reducing LDL cholesterol by 10.2±2.7% compared to controls. This study is dedicated to the memory of Professor Tatu A. Miettinen.

**P4659 Reduced blood pressure and risk of future cardiovascular disease from structured care algorithm in primary care patients with persistent hypertension: a multicentre randomised controlled trial**

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Purpose: To determine the impact of reduced systolic and diastolic blood pressure (BP) on the risk of cardiovascular disease achieved in primary care patients with persistently elevated BP randomised to enhanced usual care (UC) or an algorithm to optimise risk profiling and BP control in the Valsartan Intensified Primary Care Reduction of Blood Pressure (VIPER-BP) Study.

Methods: Prospective, multi-centre randomised controlled trial involving 119 primary care clinics and 2185 patients. The VIPER-BP intervention comprised automated risk profiling plus standardised guideline-based, stepwise pharmacological treatment (initial angiotensin receptor blocker (ARB) monotherapy or two forms of single pill ARB combination therapy) and computer assisted intensified follow-up and treatment titration. Using 26 week follow-up data (intention to treat) we used -a) change in risk profile (age as a constant) and b) age, initial systolic and diastolic BP and change in BPs, we calculated the impact of VIPER-BP intervention on absolute 5 year cardiovascular risk score (ACVRS) and relative risk (RR) of a future coronary artery disease (CAD) or stroke event.

Results: Overall, 1962 patients (aged 59±12 years, 62% men, 67% prior hypertension and BP 150±17/88±11 mmHg) who remained above their individualised BP target (national guidelines) were randomised (1:2 ratio) to UC (n = 524) or VIPER-BP intervention (n = 1438). During follow-up, BP was reduced in the VIPER-BP group from 150±17/88±11 to 136±15/81±10 mmHg in the VIPER-BP group vs. 149±17/87±11 to 139±15/81±10 mmHg in the UC group. Accordingly, at 26 weeks 72.1% UC vs. 81.4% VIPER-BP patients had a lower systolic BP (< 130 mmHg) in favour of VIPER-BP - p<0.001. For both systolic (R2 0.39) and diastolic (R2 0.28) BP there was a strong linear relationship with greater falls (± 75 mmHg) in those with the highest initial BP. Mean falls in calculated ACVRS from baseline were greatest in VIPER-BP patients (3.7±4.5%), -2.6±4.5%, adjusted mean difference -1.13 95 CI -1.63 to -0.64%, p<0.001. Similarly, the adjusted risk of CAD (R 0.75±0.36 vs. 0.81±0.39; p<0.001) and stroke (R 0.69±0.49 vs. 0.75±0.49; p<0.001) was attenuated most in the VIPER-BP group.

Conclusions: VIPER-BP is one of the largest studies of its type ever undertaken and reflects real-world practice. In those patients with persistently elevated BP being managed in primary care, a structured care algorithm not only results in lowered BP (those with higher BPs benefiting most) but reduces absolute and relative risk of future cardiovascular disease.

**P4660 Successful weight loss following gastric sleeve surgery improves vascular function in obese individuals**

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Background: The risk of premature atherosclerosis rises with obesity and previ-
Comprehensive assessment of diastolic function from velocity-encoded cardiac magnetic resonance in patients with hypertrophic cardiomyopathy

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Purpose: To assess the value of velocity and flow rate-related parameters obtained by cardiac magnetic resonance (CMR) for evaluation of left ventricular (LV) diastolic function in patients (pts) with hypertrophic cardiomyopathy (HCM).

Methods: CMR was performed in 26 HCM pts and 24 healthy volunteers (HV) matched for age, gender, body surface area (BSA) and blood pressure. Diastolic parameters were obtained using a semi-automated software enabling extraction of transmural flow, including transmural E' and AV flow peaks, isovolumic relaxation time (IVRT) and early peak diastolic longitudinal myocardial velocity E' obtained using 2D phase contrast-CMR. LV mass and volumes were measured from cine CMR images.

Results: Mean age was 47.0±20.2 years in HCM pts and 47.5±16.1 in HV (p<0.05). LV mass, mass/end-diastolic volume and LA volumes were increased in HCM pts compared to HV. The ratio between areas of the peaks of IVRT and AV was measured in 20 HCM pts. While there was no significant difference in E/A ratio, myocardial energy metabolism alterations.

Conclusions: Comparison of HCM pts with HV by CMR showed significantly altered LV diastolic function and increased LA volumes related to increased LV mass. Assessment of diastolic function may be considered for routine comprehensive evaluation of left heart function in HCM.

High energy myocardial metabolism in patients with different causes of left ventricular hypertrophy by 31P magnetic resonance spectroscopy


Purpose: To elucidate the role of cardiovascular magnetic resonance (CMR) in the diagnosis and management of restrictive pericarditis.

Methods: In 47 patients with a clinical diagnosis of restrictive pericarditis a complete CMR exam was performed to assess biventricular volumes, function, minor atrial diameters both in systole and in diastole in a four-chamber view (FSRL). The results were compared with echocardiography (E). We estimated LV stroke volume (SV), ejection fraction (EF) and mass by CMR tools.

Results: Patients with pericardial effusion (PE) showed FSRL and FAC significantly reduced compared to patients without PE (p<0.0000001). LA volume was higher in patients with constrictive pericarditis. The CMR diagnosis was compared with echocardiography and the final diagnosis (based on clinical, multimodality imaging, catheterization, as well as cardiac surgery for those who underwent pericardiectomy) in order to assess sensitivities and specificities in the CMR diagnosis of constrictive pericarditis. The telephonic follow-up of all patients was performed to assess the incidence of major events (surgery and death).

Conclusions: CMR resulted as specific as echocardiography (100%) but significantly more sensitive (91.2% vs 50%) in the diagnosis of constrictive pericarditis. The positive predictive value was 100% in both techniques, but the negative predictive value was significantly higher for CMR (97.2%) than for echocardiography (50%). The most sensitive and specific parameter resulted a pericardial thickness >3 mm. Sigmoid motion of the interventricular septum was a specific (97.1%) but not very sensitive (51.6%) parameter. A CMR diagnosis of pericardial constriction was a significant predictor of mortality (p<0.0039).

Role of cardiovascular magnetic resonance in the diagnosis and management of constrictive pericarditis

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Purpose: To elucidate the role of cardiovascular magnetic resonance (CMR) in the diagnosis and management of constrictive pericarditis.

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Late gadolinium enhanced cardiac magnetic resonance (CMR) is a standard noninvasive tool for the identification of myocardial fibrosis which is a histological hallmark of heart failure and an independent predictor of adverse outcome. Late gadolinium enhancement (LGE) by cardiac magnetic resonance (CMR) is a standard noninvasive tool for the identification of focal fibrosis. Diffuse fibrosis, however, cannot be quantified by LGE. Recently, it was shown that diffuse myocardial fibrosis is strongly related to post-contrast longitudinal relaxation (T1) time. The aim of our study was to assess the prevalence of diffuse myocardial fibrosis by CMR T1 mapping in patients with serum NT-proBNP levels >125 pg/ml and preserved left ventricular ejection fraction (EF≥50%).

Methods: NT-proBNP serum levels were obtained in 1939 (36%) MYBPC3 carriers, all TNN2 carriers and 1/5 (20%) LMNA carriers; midwall patterns of LGE located at the basal and/or mid-ventricular septal wall were the most commonly seen pattern in all gene mutations (57% of all LGE data). In our study, T1 mapping can be performed 10 minutes after a gadolinium bolus using an inversion recovery sequence. The quantitative extent of LGE was defined as a signal intensity of 2 standard deviations above the mean intensity of the remote myocardium in the same slice. The mitochondrial protein mRNAs were quantified using real-time quantitative reverse transcription-PCR in 46 patients.

Results: Patients were divided into two groups on the basis of presence (LGE group, n = 27) or absence (non-LGE group, n = 32) of LGE. Patients with LGE had lower cardiac index (2.9±0.6 vs. 2.6±0.5 L/min/m², P<0.027), LV ejection fraction (37.1±2 vs. 31.1±10%, P = 0.042) and higher BNP values (97±113 vs. 210±242 pg/ml, P = 0.032) than those without LGE, while CVF did not correlate with these parameters. Mean CVF was significantly higher in LGE group than in non-LGE group (7.2% ± 6.3% vs 3.3% ± 2.9%, P = 0.0002). Late gadolinium enhancement rate and CVF were not associated with LVPd/dtmax as an index of LV contractile function, but with LVPd/dtmin as an index of LV relaxation (r = 0.432, P = 0.028 and r = 0.363, P = 0.008, respectively). Multivariate analysis revealed that not CVF but LGE rate was an independent determinant of LVPd/dtmin. The abundance of mRNAs for mitochondrial enzymes inversely correlated with LGE rate and CVF. Focal fibrosis rather than interstitial fibrosis is more strongly associated with LV dysfunction. Noninvasive CMR is more useful to predict LV dysfunction than invasive histological assessments in NICM.

Conclusion: LGE is a common finding in cardiomyopathy patients with known gene mutations, most prominently expressed with basal and/or mid-ventricular septal midwall patterns. Its presence seems to be independent of the symptomatic stage of the disease or its phenotypic manifestation.

Uniformity of circumferential strain and strain delay index are the most relevant left intraventricular dysynchrony indices to identify patients with impaired left ventricular function

Cardiac magnetic resonance across the spectrum of cardiomyopathy
**POSTER SESSION 6**

**ARRHYTHMIA MECHANISMS AND ANTIARYRHRHYMIC DRUGS**

**P4690**

**Ranolazine modifies the electrophysiological effects of acute myocardial stretching**

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**Purpose:** Mechanoelectrical feedback is an arrhythmogenic factor and several mechanisms have been implicated in this effect, involving the stretch-activated ion channels, autocrine/paracrine events or the activation of beta-adrenergic receptors as a result of the stretch-mediated release of catecholamines from intramyocardial nerve endings. Ranolazine inhibits the late inward Na+ current, but we do not know whether it also modulates the electric responses to myocardial stretch-in acute cardiac ventricular stretching produces modifications on the cardiac electrophysiological properties such as an increase of dominant frequency (DF) during ventricular fibrillation (VF). The aim of this study is to analyze and to compare the acceleration of VF activation frequency under perfusion of this drug.

**Methods:** In eighteen Langendorff-perfused rabbit hearts VF recordings were obtained using epicardial multiple electrodes on the left ventricle free wall under control (n=9) and during perfusion of ranolazine (50μM) (n=9). VF was induced by pacing at increasing frequencies, without interrupting coronary perfusion. After the induction of VF, stretching was applied and maintained for ten minutes and after this period, local stretching was suppressed. DF during VF was determined using spectral techniques and spectral concentration (SpConc) was calculated as a percentage of the total energy contained in the interval of DF=0.5 Hz.

**Results:** In control series, myocardial stretch increased DF of VF from 13.6±1.2 Hz to 19.1±3.1 Hz (p=0.001), with a SpConc that decreased from 29±8% to 18±3% (p=0.001). These parameters returned to baseline values 3 minutes after injection of drug.

**Conclusion:** The inhibition of the late inward Na+ current with ranolazine reduces the ventricular electrophysiological modifications produced by acute myocardial stretching.

**P4691**

**Novel electrophysiological properties of dronedarone: Inhibition of human cardiac two-pore-domain potassium (K2P) channels**

C. Schmidt, F. Wiedmann, P. A. Schweizer, R. Becker, H. A. Katus, D. Thomas. University Hospital of Heidelberg, Department of Cardiology, Heidelberg, Germany

**Purpose:** Dronedarone is currently used for the treatment of paroxysmal and persistent atrial fibrillation (AF). Pharmacological inhibition of cardiac two-pore-domain potassium (K2P) channels results in action potential prolongation and has recently been proposed as a novel antifibrillatory strategy. We hypothesized that blockade of human K2P channel contributes to the electrophysiological efficacy of dronedarone in AF.

**Methods:** Two-electrode voltage clamp electrophysiology was used to record K2P currents from Xenopus oocytes. The inhibition of the late inward Na+ current with ranolazine reduces the ventricular electrophysiological modifications produced by acute myocardial stretching.

**Results:** All functional human K2P channels were screened for dronedarone sensitivity, revealing significant and concentration-dependent inhibition of cardiac K2P2.1 (TREK1; IC50 = 26.7 μM) and K2P3.1 channels (TAS1K; IC50 = 18.7 μM) with maximum current reduction of 60.3% and 65.5%, respectively. The molecular mechanism of action was studied in detail. Dronedarone block was voltage-independent and affected open and rapid-closed channels. K2P3.1 currents were reduced in frequency-dependent fashion in contrast to K2P2.1. Mutagenesis studies revealed that amino acid residues implicated in K2P3.1 drug interactions were not required for dronedarone blockade, indicating a novel pharmacological binding mode.

**Conclusion:** The class III antiarythmic drug dronedarone targets multiple human cardiac two-pore-domain potassium channels, including atrial-selective K2P3.1 currents. K2P current inhibition by dronedarone represents a previously unrecognized mechanism of action that is expected to suppress AF by prolonging atrial refactoriness in vivo.

**P4692**

**Mechanisms of antiarythmic activity of new class III agent Nifedilide in patients with supraventricular arrhythmias**


**Background:** Nifedilide (Nf) is a new potassium channel blocker that inhibits transient outward and delayed rectifier currents. Preclinical studies showed that Nf increases effective refractory periods (ERP) in atria more than in ventricles. High affinity of Nf to atrial myocardium is thought to contribute to high efficacy in supraventricular arrhythmias and to low risk of ventricular proarythmya.

**Objectives:** To evaluate electrophysiological mechanisms of antiarythmic effect of Nf in patients with paroxysmal supraventricular tachycardia (PSVT).

**Materials and methods:** Effects of Nf (0.2g/kg intravenously) were studied in 24 consecutive patients (14 males with PSVT (12 orthodromic tachycardia in WPW syndrome, 8 AV-nodal reentrant tachycardia, 4 orthodromic tachycardia due to concealed bypass tract) during endocardial electrophysiological study. Termination of sustained paroxysms of SVT by Nf could be investigated in 18 patients and prevention of reinduction of PSVT in 22 patients.

**Results:** Nf terminated PSVT in 77.7% and prevented reinduction in 72.7% of patients. Nf increased ERP of right atrium (by 22.88%), left atrium (by 20.09%), right ventricle (by 12.33%) and accessory pathways (antegradely by 21.47%; retrogadely by 32.83%). Nf did not affect sinus node and atrioventricular conduction. Nf significantly increased relative refractory period (RRP) of His-Purkinje system (by 33.41%), Nf prolongs QT (by 24.5%; p<0.01) and QTC (by 17.31%; p<0.05) intervals. One patient developed short runs of tordse de pointes shortly after injection of drug.

**Conclusions:** Prolongation of ERP, predominantly in atria and accessory pathways, and RRP in His-Purkinje system are main electrophysiologic effects of Nf. New drug showed high antiarythmic efficacy and good safety profile in patients with PSVT.

**Abstract P4693**

**Table 1. Effect of flecainide on exercise testing**

<table>
<thead>
<tr>
<th></th>
<th>On BB (N=10)</th>
<th>Same patients but on BB plus flecainide (N=10)</th>
</tr>
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<tbody>
<tr>
<td>p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minutes of exercise</td>
<td>9.2±2.2</td>
<td>10.7±2.3</td>
</tr>
<tr>
<td>Maximal arrhythmia</td>
<td>3.0±0.8</td>
<td>0.9±0.6</td>
</tr>
<tr>
<td>VAB/AUC and total ventricular extrasystoles</td>
<td>242±67/221±64.7±15.1</td>
<td>12.3±13.3 and 5.6±6.4</td>
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<td>Threshold of any ventricular arrhythmia＜bpm and etage</td>
<td>114.4±9.1 and 2.7±1.3</td>
<td>124.0±18.4 and 4.0±0.7</td>
</tr>
<tr>
<td>Threshold of maximal ventricular arrhythmia＜bpm and etage</td>
<td>122.3±11.4 and 3.2±1.0</td>
<td>129.5±10.6 and 4.0±0.9</td>
</tr>
</tbody>
</table>

**References:**

- Dronedarone is currently used for the treatment of paroxysmal and persistent atrial fibrillation (AF). Pharmacological inhibition of cardiac two-pore-domain potassium (K2P) channels results in action potential prolongation and has recently been proposed as a novel antifibrillatory strategy. We hypothesized that blockade of human K2P channel contributes to the electrophysiological efficacy of dronedarone in AF.
- Dronedarone block was voltage-independent and affected open and rapid-closed channels. K2P3.1 currents were reduced in frequency-dependent fashion in contrast to K2P2.1. Mutagenesis studies revealed that amino acid residues implicated in K2P3.1 drug interactions were not required for dronedarone blockade, indicating a novel pharmacological binding mode.
- The class III antiarythmic drug dronedarone targets multiple human cardiac two-pore-domain potassium channels, including atrial-selective K2P3.1 currents. K2P current inhibition by dronedarone represents a previously unrecognized mechanism of action that is expected to suppress AF by prolonging atrial refactoriness in vivo.
- Nifedilide (Nf) is a new potassium channel blocker that inhibits transient outward and delayed rectifier currents. Preclinical studies showed that Nf increases effective refractory periods (ERP) in atria more than in ventricles. High affinity of Nf to atrial myocardium is thought to contribute to high efficacy in supraventricular arrhythmias and to low risk of ventricular proarythmya.
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- Nf terminated PSVT in 77.7% and prevented reinduction in 72.7% of patients. Nf increased ERP of right atrium (by 22.88%), left atrium (by 20.09%), right ventricle (by 12.33%) and accessory pathways (antegradely by 21.47%; retrogadely by 32.83%). Nf did not affect sinus node and atrioventricular conduction. Nf significantly increased relative refractory period (RRP) of His-Purkinje system (by 33.41%), Nf prolongs QT (by 24.5%; p<0.01) and QTC (by 17.31%; p<0.05) intervals. One patient developed short runs of tordse de pointes shortly after injection of drug.
- Electrophysiological effects of Nifedilide
- Prolongation of ERP, predominantly in atria and accessory pathways, and RRP in His-Purkinje system are main electrophysiologic effects of Nf. New drug showed high antiarythmic efficacy and good safety profile in patients with PSVT.
F 16915 prevents heart failure induced atrial fibrillation and systemic embolism, and for major bleeding, intracerebral hemorrhage occurred with equal frequency for all agents and regimens except for rivaroxaban (higher risk than dabigatran 110 mg bid, p=0.070). Myocardial infarction occurred less frequently with rivaroxaban and apixaban compared to either dose of dabigatran (all p<0.05). All-cause mortality was not different for any agent or regimen. In the absence of head-to-head comparisons, this network meta-analysis suggests that apixaban and dabigatan 110 mg bid may offer the best benefit-risk balance for stroke prevention in non-valvular atrial fibrillation. Dabigatran 150 mg bid may be preferred for patients in a high-risk for embolism.

### Value-based pricing for dabigatran, rivaroxaban and apixaban in patients with non-valvular atrial fibrillation in Germany

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Warfarin effectively reduces the incidence of ischemic stroke in patients with non-valvular atrial fibrillation (AF) but increases the risk of major and intracerebral bleeding. 

The three new oral anticoagulants (NOAC) dabigatran (110mg bid and 150mg bid, D110 and D150), rivaroxaban (20mg od, R20), and apixaban (5mg bid, A5) showed equivalent or superior efficacy and safety compared to warfarin in these patients. We aimed to analyse the value-based price (in Euro) for Germany for these NOACs from a social health perspective.

The data of the outcomes of ischemic cerebral and non-cerebral embolism, major and intracerebral hemorrhage, myocardial infarction, and mortality were taken from dabigatran’s RE-LY (D110 and D150), rivaroxaban’s ROCKET (R20), and apixaban’s ARISTOTLE trials (A5). All were randomized and prospective trials and compared the NOAC with dose-adjusted warfarin including more than 6.000 patients. The quality-adjusted life-years (QALYs), costs (in Euro 2012 for Germany), and incremental cost-effectiveness ratios (ICER) for the NOACs were calculated with adjusted-dose warfarin as comparator. The societal willingness-to-pay was set conservatively at 50.000 Euro per QALY.

A Markov decision model was adopted using the Tree Age Pro 2011 program.

The current daily cost of D110, D150, and R20 in Germany account for about 3.20 Euro for Germany, and incremental cost-effectiveness ratios (ICER) for the NOACs were calculated with adjusted-dose warfarin compared to warfarin in these patients. We aimed to analyse the value-based price (in Euro) for Germany for these NOACs from a social health perspective.

Our results are robust in a wide range of sensitivity analyses. The daily value-based price of D150/warfarin, 12.32/12.05 for R20/warfarin, and 11.74/11.5 for A5/warfarin. Total costs were higher for all NOACs compared to warfarin. With this calculations ICER was found for all NOACs in a range of about 50.000 Euro per QALY. Provisionally calculated increased prices for the NOACs compared to dose-adjusted warfarin ranged from 1.25 Euro to 2.50 Euro per day.

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### Network meta-analysis of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with non-valvular atrial fibrillation

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The three new oral anticoagulants (NOAC) dabigatran (two doses), rivaroxaban, and apixaban showed equivalent or superior efficacy and safety compared to warfarin in patients with non-valvular atrial fibrillation. A head-to-head clinical trial comparison of these NOACs is highly unlikely to be performed given the expense of such an investigation. Therefore, there is a need for an unbiased comparative assessment of the benefits and risks of the NOACs, based on the available trial data. Appropriate statistical tools for such an analysis is mixed treatment comparison (MTC) network meta-analysis (NMA).

A NMA of the 3 new oral anticoagulants was performed extracting the data of the RE-LY study of dabigatran 110 mg bid and dabigatran 150 mg bid, the ROCKET-trial of rivaroxaban and the ARISTOTLE-trial of apixaban for the composite outcome ischemic stroke and systemic embolism with the same rate of intracerebral bleeding, mortality and myocardial infarction. The NMA was performed to compare these endpoints using odds ratios and confidence intervals.

Dabigatran (150 mg bid) showed superior efficacy in preventing ischemic stroke plus systemic embolism to dabigatran (110 mg bid, p=0.036) and rivaroxaban (p=0.038). Apixaban had equivalent efficacy with rivaroxaban and dabigatran (either dose). Apixaban was safer (less major bleeding) than dabigatran (150 mg bid, p=0.036) or rivaroxaban (p=0.002). Intracerebral hemorrhage occurred with equal frequency for all agents and regimens except for rivaroxaban (higher risk than dabigatran 110 mg bid, p=0.070).

Myocardial infarction occurred less frequently with rivaroxaban and apixaban compared to either dose of dabigatran (all p<0.05). All-cause mortality was not different for any agent or regimen. In the absence of head-to-head comparisons, this network meta-analysis suggests that apixaban and dabigatan 110 mg bid may offer the best benefit-risk balance for stroke prevention in non-valvular atrial fibrillation. Dabigatran 150 mg bid may be preferred for patients with a high-risk for embolism.

### Administration of vernakalant in a highly sensitive model of proarrhythmia caused by prolongation of myocardial repolarization without increased vulnerability to arrhythmias


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Purpose: Vernakalant (VER) is a novel and relatively atrial-selective antiarrhythmic drug that inhibits potassium and sodium channels frequency-depending. Previous studies demonstrated conversion of atrial fibrillation (AF) to sinus rhythm by VER. The present study investigated whether VER in escalating high doses in a highly sensitive rabbit model of proarrhythmia.

Methods: Eight endo- and epicardial monophasic action potentials (MAP) and 12-lead ECGs were recorded simultaneously at baseline conditions and from 7 rabbits treated with VER, compared to 13 rabbits treated with sotalol (SOT).

Results: Administration of VER (10 μM and 30 μM) showed a significant prolongation of QT-interval compared to baseline (10 μM: < 25 ms, 30 μM: < 51 ms, p<0.05) and an enhanced action potential duration (APD90, 10 μM VER: + 18 ms; 30 μM VER: + 20 ms). APD90 prolongation was accompanied by a distinctive decrease in effective refractory period (ERP, 10 μM: + 40 ms, 30 μM: + 50 ms, p<0.05) leading to a significant increase in postrepolarization refractoriness (PRR) defined as the difference between the ERP and APD90. Dispersion of repolarization was not altered by VER. Intradirectional conduction in hearts with mechanical pacing in 5 rabbits, reduced potassium concentrations did not lead to early afterdepolarizations (EAD) or polymorphic ventricular tachycardia despite significant QT-prolongation. Application of SOT (100 μM) caused prolongation of QT-interval (+ 52 ms) and APD90 (+ 33 ms) along with an increased ERP (+ 49 ms) and PRR (+ 15 ms). In contrast to VER, SOT enhanced dispersion of repolarization (< 19 ms, p<0.05) and evoked EAD in 12 of 13 rabbits and torsades de pointes (TdP) in 9 of 13 rabbits after lowering of potassium level.

Conclusions: The present study showed that administration of VER and SOT caused comparable prolongation of myocardial repolarization. PRR was increased by both drugs. In contrast to SOT, VER did not affect dispersion of repolarization nor generate EAD and thus did not provoke ventricular tachyarhythmias. In summary, administration of VER seems to be safe despite significant prolongation of QT-interval.
was not associated with significant modification of any hemodynamic parameters. Ventricular infarct size was determined at the end of the experiment and was assessed by histological analysis (Masson staining). F 16915 significantly reduced the extent of infarct size (31.3±3.9%, n=5 vs. 56.8±14.6%, n=5; p<0.001). In conclusion, in an ischaemia-induced heart failure model in the rat, F 16915 prevented the structural remodelling of the left atria associated with an increased left ventricular function. Therefore, F 16915 constitutes a new emerging opportunity as up-stream therapy for the treatment of AF.

**P4698 Zooming in on the focus: flecainide inhibits atrial fibrillation maintained by aconitine**

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**Background:** The contribution of focal discharges for the maintenance of atrial fibrillation (AF) is under discussion. Aconitine (ACO) is used in a model for focal AF. To find mapping criteria for focal discharges during AF, we performed high density mapping of AF maintained by flecainide and investigated the effect of flecainide.

**Methods and results:** In open chest experiments in goats (n=6), we performed high density epicardial mapping to investigate the interaction of focal tachycardias induced by ACO with activation pattern during AF. The topological application of ACO-crystals on the left atrium in the middle of the mapping area induced rapid focal discharges with radial spread of activation exactly at the place of ACO-application. In a cycle length (CL): 242±15 ms, Local electrograms at the site of earliest activation did not show R-waves. S1S1-stimulation (basic cycle length (BCL): 200 ms) from two different directions showed no blocklines and no change of conduction velocity (CV) (80±3 cm/s vs. 80±3 cm/s, n.s.), During experimental period of 30 min. after ACO-application, neither atrial effective refractory period (BCL=200 ms: 135±2 ms vs. 135±4 ms, n.s.) nor left atrial effective refractoriness was changed significantly. Episodes of burst-induced AF became longer (470±65 sec. vs. 269±40 sec., p<0.01), but ACO-crystal was not changed significantly (131±5 ms vs. 134±5 ms, n.s.). During AF the number of breakthroughs increased more than 10-fold (1.4±0.14 per cycle vs. 0.08±0.03 per cycle, p<0.01). However, breakthroughs occurred remote from the sites of ACO-application. The mean of epicardial coupling intervals of breakthroughs and dominant interval at the site of ACO-application were slightly shorter than the mean of AFOC (131±3 ms and 131±2±5 ms respectively vs. 133±5 ms, p<0.05). During AF, more than 80% of all local electrograms at the site of breakthroughs showed R-waves, but just 44% of them could be explained by transmural conduction (contralateral activation within 8 ms). Flecainide inhibited ACO-induced rapid focal discharges at the site of ACO-application. After flecainide, AF was not inducible anymore. Summary: Topical application of ACO on the left atrium induced focal discharges. During burst-induced AF, the incidence of breakthroughs increased and AF became more stable without changes in AERP or CVCL. However, the sites of breakthroughs during AF differed from the site of highest affinity to focal discharges, suggesting a complex underlying interaction. Flecainide inhibited ACO-induced focal discharges and AF-inducibility.

**P4699 Absence of cyclase-associated protein 2 leads to marked atrial and ventricular conduction delays and ventricular arrhythmias**

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**Purpose:** Cyclase-associated protein 2 (CAP2) is an evolutionarily conserved protein that plays a major role in regulating the actin cytoskeleton and in signal transduction. CAP2 is predominantly found in the nucleus of undifferentiated cardiomyoblasts and at the M-line of adult cardiomyocytes. Recent studies showed that the expression of CAP2 by a gene trap approach (CAP2gt/gt) results in right ventricular cardiomyopathy and increased mortality in a mouse model. We hypothesised that CAP2gt/gt would affect the morphology and the electrophysiological parameters of these cells. We further investigated whether CAP2gt/gt affects the viability and the inducibility of arrhythmias.

**Results:** In comparison to WT, CAP2gt/gt showed a reduction in basal heart rate (403±59.9±0 ms vs. 465±3.3±0 ms, p<0.03), prolongation in PQ time (45.4±3.6 ms vs. 39.0±6.3 ms; p=0.02), QRS time (15.0±1.7 ms vs. 12.7±1.5 ms; p<0.01) and QT time (35.3±3.9 ms vs. 30.7±3.5 ms; p<0.002). Functional testing revealed an extension in atrio-ventricular refractory period in CAP2gt/gt+ (53.1±6.9±0 ms vs. 41.7±12.1 ms; p<0.01). The ventricular refractory period (VRP) was slightly prolonged in CAP2gt/gt (33.1±12.2 ms) and significantly in CAP2gt/gt (36.7±5.8 ms) compared to WT (28.7±5.2 ms; p=0.03). The probability of induction of ventricular tachycardias (VTs) was significantly raised in CAP2gt/gt+ (16% vs. 5% in WT; p<0.001). Interestingly, in CAP2gt/gt the probability of induction of VTs (7%) was as low as in WT. The inducibility of atrial fibrillation (AF) did not differ among the groups.

**Conclusions:** Loss of CAP2 results in marked changes in heart rate, atrial and ventricular conduction times and refractory periods. This points towards a significant involvement of CAP2 in a normal sinus node function as well as a normal conduction system. CAP2gt/gt leads to impaired automaticity with a lack of further increase in the incidence of VTs in CAP2gt/gt may originate from a further prolongation of VRP with antiarrhythmic effects. Cases of right ventricular cardiomyopathy with no real cause of an underlying disease may be due to dysfunction of CAP2, so further evaluation of its influence on cardiomyopathy and arrhythmogenesis should ensue to fully understand its functioning.

**P4700 NRDc regulates circulatory dynamics through modulating sinus node automaticity and cardiac sympathetic innervation**

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We identified nardilysin (NRDc), a zinc protease of the M16 family, as a specific binding partner of H6-EGF, and demonstrated that NRDc enhances ectodomain shedding of multiple membrane proteins through activation of ADAM. To explore the physiological functions of NRDc, we generated NRDc-deficient mice (Nrd1−/−) and found that NRDc regulates axonal maturation and myelination in the CNS. We also showed that Nrd1−/− mice have increased sympathetic nerve firing (NRF) and that the role of NRDc in the cardiovascular system, however, has not been clarified.

Nrd1−/− showed hypolipidemic heart and severe Bradyadry with Nrd1−/+ (H/R; Nrd1−/+ vs. Nrd1−/−: 719±44 vs. 579±44/min; p<0.001). ECG monitoring by telemetry system demonstrated the remarkable bradycardia of Nrd1−/− throughout the day. Pharmacological blocking of autonomic nervous system by the simultaneous treatment with metoprol and atropine showed that the intrinsic heart rate of Nrd1−/− is significantly lower than that of Nrd1+/+. Quantitative PCR showed that the mRNA level of HCN4 in Nrd1−/− heart, which is essential for the sino node automaticity, was significantly lower than that of Nrd1+/+ heart, indicating that the automaticity of the Nrd1−/− sinus node is impaired. Analysis of the heart rate variability demonstrated that Nrd1−/− show higher ratio of low-frequency to high-frequency, indicating that the sympathetic nervous system is hyperactive in Nrd1−/−. Next, we examined patterning of sympathetic innervation in Nrd1−/− ventricular myocardium by immunostaining of tyrosine hydroxylase, a marker of sympathetic nerve. While cardiac sympathetic nerves were located subepicardially in Nrd1+/+ ventricles, Nrd1−/− ventricular myocardium was uniformly innervated from epicardium to endocardium. Taken together, the hyperactive sympathetic nervous system and the aberrant innervation pattern of Nrd1−/− might compensate the lower intrinsic heart rate. To gain further insight into the molecular mechanism of the aberrant innervation pattern, the expression of p75NTR, critically involved in the cardiac sympathetic innervation, was examined in Nrd1−/− hearts. The full-length form of p75NTR was clearly increased and the cleaved form of p75NTR was decreased, indicating that p75NTR shedding was impaired in Nrd1−/− ventricles. Given that the regulated p75NTR shedding is required for appropriate developmental apoptosis of sympathetic neurons, these results strongly suggested that NRDc is involved in sympathoadrenal system regulating apoptosis of sympathetic neurons. In summary, NRDc critically controls circulatory dynamics through modulating sinus node automaticity and cardiac sympathetic innervation.

**P4701 Decreased connexin43/Nav1.5 expression and reduced sodium current through downregulation of desmoplakin by small RNA interference in HL-1 cardiomyocytes**

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**Purpose:** Desmosomes and gap junctions are situated in the intercalated disc and ensure the integrity of mechanical coupling and electrical impulse conduction between cells. In addition to these cell-cell junctions, there are other molecules such as voltage-gated sodium channel (Nav1.5) also located in the intercalated disc. Some cardiac disorders, such as arrhythmogenic right ventricular cardiomyopathy (ARVC), have mutations in genes encoding proteins of the desmosome with occurrence of fatal arrhythmias. The desmosomal plakin protein, desmoplakin (DSP), plays an important role in the stability of these components interconnecting. The mutant proteins in ARVC may lead to the loss of desmosomal integrity, but it cannot be explained why life-threatening arrhythmias occur early in the course of the disease before cardiac dysfunction becomes evident.

We here sought to characterize whether the presence of DSP is necessary for the normal function and localization of the gap junction protein connexin (Cx) 43 and Nav1.5.
Validation of an increased Tpeak-Tend interval in a large series of Brugada syndrome patients as a highly and independently ECG parameter related to symptoms and cardiac events

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Methods: We used small RNA interference to downregulate DSP specifically in HL-1 cells derived from the AT-1 mouse. The expression and content of Cx43 and Nav1.5 were determined by western blot and flow cytometry. The location and distribution of Cx43 and Nav1.5 were evaluated by immunofluorescent staining and observed under laser scanning confocal microscopy. The function of Cx43 gap junctions were assessed by scrape loading dye transfer (SLDT) and sodium current were recorded with the whole-cell and patch clamp technique.

Results: Western blot and flow cytometry experiments showed that the expression of connexin43 and Nav1.5 were decreased following DSP silencing. Immunofluorescence studies demonstrated that loss of DSP expression led to an abnormal distribution of connexin43 and Nav1.5. SLDT found a decrease in dye transfer through gap junctions in DSP siRNA treated cells. Furthermore, a decrease in peak current density, a shift in voltage dependence of steady-state inactivation, and a prolongation of time-dependence of recovery from inactivation of sodium current were observed in DSP silenced cells.

Conclusion: This is the first demonstration of association between three components of the intercalated disc: DSP, gap junctions c43, and the voltage-gated sodium channel Nav1.5 complex. It indicates that impaired mechanical coupling largely affects electrical synchrony, partially explaining the pathogenesis of ARVC.

P4702

Ranolazine suppresses atrial fibrillation in an experimental model of chronic heart failure due to development of atrial postreperfusion remodeling and slowing of conduction velocity

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Introduction: In recent years, ranolazine (RAN) was reported to be effective and safe in converting atrial fibrillation (AF) to sinus rhythm by intake of a single dose (“pill in the pocket”) in patients with structural cardiac abnormalities. The apparent electrophysiologic safety and the ability to use it in patients where other Na+ channel blockers are contraindicated could have enormous economic implications. This is the first experimental study to investigate the electrophysiologic mechanisms for the antiarrhythmic benefit of RAN application in chronic heart failure (CHF).

Methods and results: In 7 female rabbits CHF was induced by 4 weeks of rapid ventricular pacing leading to a significant decrease in ejection fraction. 12 rabbits were sham-operated and served as controls. Isolated failing and sham hearts were perfused using the Langendorff method and were paced with cycle lengths from 350 to 150 ms in the atrium. In addition, burst pacing was used to induce atrial fibrillation. Two monophasic action potential recordings on the left- and right epicardium showed an increase of atrial action potential duration (aAPD) and effective refractory period (aERP) in CHF hearts as compared with controls. Addition of acetylcholine (1μM) and isoproterenol (1μM) led to a significant shortening of aERP but a significant increase of aAPD in sham- and in failing hearts. RAN had no effect on aERP but led to a significant increase of aERP in sham- and failing hearts. RAN had no effect on aAPD but led to a significant decrease of aERP in sham- and failing hearts. RAN had no effect on aAPD but led to a significant decrease of aERP in sham- and failing hearts. Moreover, RAN reduced the incidence of atrial fibrillation and significantly increased conduction velocity in sham (+14ms) and failing (+16ms) hearts, respectively. aERP was also significantly increased in failing hearts and aERP application significantly increased conduction velocity in sham (+14ms) and failing (+16ms) hearts, respectively.

Conclusion: In the present study, administration of RAN has been shown to be effective in suppressing AF not only in sham- but also in failing hearts. The antiarrhythmic effect is due to development of aPRR and a marked effect on conduction velocity. RAN might be a new safe option to reduce the burden of AF in CHF, where other antiarrhythmic drugs are contraindicated. The described electrophysiologic mechanism should be adopted as a fascinating novel antiarrhythmic option in heart failure.

P4703

Induction of torsades des points is facilitated by stimulation of extra-cardiac alpha-adrenergic receptors

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Introduction: Torsades des Points is a potentially lethal ventricular arrhythmia and is known for adverse effect of many drugs secondary to block of the rapidly activating delayed rectifier potassium current, IKr. Novel antiarrhythpic drugs have reduced proarrhythmic potential compared to drugs with comparable IKr blocking characteristics, which may be secondary to the additional block of α1-adrenergic receptors.

Methods: α1-Adrenergic receptor affinities were quantified by prazosin displacement studies. Electrophysiological recordings were made in isolated canine Purkinje fibers (n=24) using methoxamine (0.1-10 μM) and doxofiline (300 nM).

EGC were recorded from anesthetized rabbits treated with methoxamine (15 μg/kg/min), clotrimazol (51 μg/kg/min) and various antiarrhythpic (all 0.5 mg/kg bolus).

Results: The Ki for I1A affinity of the antiarrhythpic were risperidone,<ihaloperidol and olanzapine. In canine Purkinje fibers a I1A stimulation prolonged APD (265±12 to 302±14 ms at 1 Hz pacing, p<0.05). Block of IKr more profoundly prolonged APD (263±8 to 453±17 ms, p<0.05) and predicted any effect of a I1A stimulation. Early or delayed afterdepolarizations were not observed upon slowing cycle length to 5 s. In anesthetized rabbits, IKr block alone did not result in arrhythmias but combined IKr block and a I1A stimulation caused conduction (188±7 to 509±82 ms, p<0.05) and TdP in 8 of 10 rabbits. Pretreatment with antiarrhythpic with various combinations of IKr block and a I1A blocking properties reduced the incidence of drug-induced TdP to 0/10 (risperidone) and 2/10 (sertraline), p<0.05; whereas haloperidol (4/10, p=0.2) and olanzapine (5/10, p=0.3) did not reduce TdP incidence at the tested dose.

There was a statistically significant positive correlation between a I1A antagonism and antiarrhythmic efficacy (Spearman’s correlation, p<0.05) independent of QT intervals.

Conclusions: a I1A-stimulation causes APD prolongation in vitro and contributes to TdP in vivo. In the present model, risperidone and sertraline have antiarrhythmic effects. The absence of afterdepolarizations in Purkinje fibers after IKr block and a I1A stimulation suggests involvement of non-cardiac a I1A in the induction of TdP.

P4704

Myofibroblasts do not contribute to the substrate for atrial fibrillation. A study of human left atrial appendages


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Introduction: The contribution of myofibroblasts to the substrate of atrial fibrillation (AF) is unknown. The electrical coupling between myocytes and myofibroblasts reverts these changes. We hypothesize that myofibroblasts may promote arrhythmogenicity through a decrease of conduction velocity (CV). Ablation of myofibroblasts with Latrunculin-B (LatB) in cell cultures of myocytes and myofibroblasts reverts these changes. We hypothesize that myofibroblasts...
Contribute to the AF substrate and that administration of LatB increases CV in the left atrial appendage (LAA) of patients with AF.

Methods: The LAA of patients undergoing thoroscopic surgery for AF was excised. The LAA preparation was superfused with Tyrode's solution in a tissue bath and optical mapping was performed with di-4-ANEPPS. The LAA was paced at 100bpm and exposed to LatB for 1 hour and CV was measured every 5 minutes. Immunohistochemical staining for alpha-SMA and connexin 43 was performed to identify myofibroblasts in tissue preparations and differentiate myofibroblasts from vascular smooth muscle cells.

Results: A total of 21 LAAs were studied (0.1 and 1 micromol LatB and control, 7 per group). No spontaneous activity was observed. Longitudinal CV was 0.27-1.43mm/ms and transversal CV was 0.04-1.11 mm/ms. LatB did not affect CV irrespective of the type of AF. Run down of the model, characterized by a reduction of CV in time, was observed. Concordantly with the outcome of the electrophysiological experiments, myofibroblasts were not detected with immunohistochemical staining of LAA.

Conclusion: Exposure of human LAA preparations to LatB does not change CV. Furthermore, immunohistochemical staining does not reveal the presence of myofibroblasts in LAA of AF patients. These data suggest that myofibroblasts do not play a major role in the pathophysiological substrate of human AF.

Cervical vagal nerve contains sympathetic ganglion...
mechanistic insights into potential efficacy of pharmacological and electrophysiological interventions. The anatomic relationship between the right and left ventricular outflow tracts: its relevance in catheter ablation

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Purpose: Premature ventricular contractions, ventricular tachycardia and initiating beats for ventricular fibrillation have all been localized at the level of the right and left ventricular outflow tracts (RVOT and LVOT). Catheter ablation at and around the junction between the outflow tracts and the great arteries is being increasingly performed. Detailed anatomic information of these structures may be useful to perform the ablation techniques in a safer and more efficient way.

Methods: Fifteen structurally normal human hearts (10m, 47±5 years) were carefully studied by sagittal and horizontal histological sections. The junction between the LVOT and RVOT were serially sectioned at 10-μm thickness, and stained with Goldner and Masson trichrome an interdigitated light microscope. The minimal distance between the endocardium of the right and left ventricles was 7.2 mm (range 4.1-14 mm) being in 3 hearts (20%) greater than 10 mm.

Figure 1. RVOT-LVOT anatomic relationship

Conclusions: The myocardial thickness at the level of the RVOT and LVOT may be greater than 10 mm. An endocardial ablation approach of idiopathic outflow tract tachycardias can be unsuccessful due to this anatomic finding, suggesting the need of an epicardial approach in selected cases.

Acute block of Kv1.5 channels by DHA increases rabbit atrial refractory period

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Kv1.5 is considered to be a potential molecular target for treatment of atrial fibrillation or flutter. Polynsaturated fatty acids such as docosahexaenoic (DHA) and eicosapentaenoic acids could exert anti-arrhythmic activity in animal models as well as in human. Thus by means of patch clamp technique we investigated a potential regulation by DHA on Kv1.5 channels stably transfected in HEK 293 cells. Among mono-, polyunsaturated and saturated fatty acids, DHA was the most effective in reducing IKv1.5 with an IC50 of 6.6 μM with a 95% confidence interval of [4.5;10.0] μM. DHA fastened the apparent slow inactivation in a concentration-dependent manner leaving peak current nearby unaffected and slowed the deactivating tail current leading to a cross-over phenomenon This is consistent with an open channel block mechanism. For a simple channel open-state block model, derived values of Kon and Koff are 3.1 μM-1 s-1 and 8.4 s-1, respectively leading to a KD of 2.7 μM. Bi-exponential fit of recovery from inactivation showed that time constants were significantly increased with \( \Delta t \) and tslow values of 36.5±1.2 ms and 1713.6±270.0 ms in control and 89.4±21.5 ms and 4134.9±450.5 ms in the presence of 10μM DHA. In order to test whether the inhibition of IKv1.5 may have physiological implication, we developed a rabbit model of atrial effective refractory period (AERP) using a conventional pacing protocol through epidural electrodes placed on the left atrium. Quantitative RTPCR demonstrated the presence of Kv1.5 in left and right rabbit atria. Direct injection of monounsaturated fatty acid (oleic acid, 20 mg/kg) in atrium failed to affect AERP in contrast to flecainide (1.25 mg/kg, +15.0±2.1%, n=6, P<0.05). DHA (20 mg/kg) significantly increased AERP by +10.7±2.3% (n=6, P<0.05). As a conclusion, among mono-, polyunsaturated and saturated fatty acids, DHA exerted the most powerful inhibition of IKv1.5 that appears to be sufficient to significantly increase AERP in anesthetized rabbit. Such a lengthening of AERP may be of therapeutic benefit in atrial fibrillation.

Depletion of connexin45 and connexin30.2 deteriorates AV-nodal conduction in the murine heart

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Introduction: Connexin (Cx) 30.2 provides physiological conduction slowing in the murine AV-node. Cx45 has been proposed to maintain basal AV-nodal conduction. The interaction of the predominant connexins Cx45 and Cx30.2 in the murine AV-node has not yet been systematically evaluated as Cx45 deficient mice are embryonic lethal.

Methods: We interbred a transgenic mouse line cardiacly depleted for Cx45 (Cx45/-) with Cx30.2 knock out (KO) mice (Cx30.2/-), resulting in Cx45/-Cx30.2/- double KO offspring. In these and control wildtype (WT) littermates, we performed telemetric ECGs and in vivo electrophysiological investigations (EPI) using transvenous catheterization to assess standard EPI-parameters (n=14).

Results: In Cx45/-, AV conduction was impaired in Cx45/-:PQ-intervals were significantly prolonged in the Holter ECG-recordings of Cx45/- compared to their WT littermates (41.0±2.2 ms vs. 36.4±1.1 ms, p<0.05). When Cx30.2 was additionally deleted in Cx45/-:Cx30.2/-, PQ was more prolonged as compared to Cx45/-: (43.5±1.1 ms vs. 41.0±2.1 ms, p<0.05). In vivo EPI showed prolongation of the A-His interval as surrogate of supraventricular conduction disturbances in Cx45/- versus WT (33.3±5.3 ms vs. 26.9±2.1 ms, p<0.05), which was more pronounced in the double KO versus their WT littermates (48.3±4.6 ms vs. 33.3±5.3 ms, p=0.02). AVNR was shortened in the double KO. Spontaneous AV-Blocks did not occur in none of the genotypes. Inducibility of atrial and ventricular arrhythmias was equal among the groups.

Conclusions: Our data show prolonged AV-intervals and impaired AV-nodal conduction under fast heart rates in mice with conditional cardiac deletion of Cx45. These findings support the thesis of Cx45 as a provider of basal AV-nodal conduction. When Cx30.2 is additionally missing, AV-nodal conduction is more severely impaired as in the Cx45 single knock out. These results proof that predominantly expressed Cx45 and Cx30.2 are crucial for maintaining AV-nodal conductivity.
Dexametomidine and clonidine inhibit ventricular tachyarrhythmias in a rabbit model of acquired long QT syndrome


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Purpose: We hypothesized that alpha-2 AR agonists have an inhibitory effect on abnormal repolarization-related ventricular tachyarrhythmias (VTs).

Methods: Effects of dexametomidine and clonidine on the occurrence of VTs were assessed in a methoxamine-sensitized rabbit model of acquires long QT syndrome (n=45). To verify that VTs in this animal model is triggered by early afterdepolarization (EAD), monophasic action potential on the left ventricular surface was recorded in 28 open-chest rabbits.

Results: Incidence of VT significantly decreased during the treatment with dexametomidine (1 μg/kg/min: 5/12 [p<0.01 vs. control]) or with clonidine (33.3 μg/kg/min: 10/18 [p<0.01]), as compared with that in control rabbits (14/15). EAD-like hump was less frequently detected during DNA synthesis with clonidine or dexametomidine (2/14) than in saline-treated rabbits (9/10, p<0.005). Presence of hump was significantly related with the advent of VTs (p<0.05).

Conclusion: Alpha-2 AR agonists have an inhibitory effect on VTs in the rabbit long QT model.

Lymphocytic cell infiltration of myocardium is associated with the episode of ventricular fibrillation in patients with Brugada syndrome

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Purpose: Brugada syndrome is a disease known to cause ventricular fibrillation (VF) with a structurally normal heart and is linked to SCN5A gene mutation. The existence of myocarditis on endomyocardial biopsy samples in patients with Brugada syndrome is still debated. The aim of the present study was to investigate the existence of myocarditis on endomyocardial biopsy samples in patients with Brugada syndrome.

Methods: We studied consecutive 73 patients (71 males; mean age 48±11 years) with Brugada syndrome. All patients underwent cardiac ultrasonography, coronary and ventricular angiography, endomyocardial biopsy from right ventricular septum, electrophysiological (EP) study, and DNA screening of the SCN5A gene. The lymphocytic cell infiltration of myocardium was determined by the presence of over five inflammatory cell infiltration by CD45RO immunohistochemical staining associated with necrosis or degeneration of adjacent myocytes in high power field image.

Results: SCN5A mutation was detected in 15 patients. VF episode was detected in 17 patients. Lymphocytic cell infiltration of myocardium was detected in 7 patients (2 patients with SCN5A mutation and 5 without SCN5A mutation) out of all patients and was detected in 4 patients out of 17 patients with episode of VF. The existence of lymphocytic cell infiltration was associated with the VF episode in patients with Brugada syndrome (P=0.047), but not with SCN5A mutation, syncpe, family history, or VF induction in EP study.

Conclusion: Lymphocytic cell infiltration was detected in patients with Brugada syndrome in both of SCN5A positive and negative group. And the existence of lymphocytic cell infiltration is associated with VF episode in patients with Brugada syndrome.

False tendons are possibly associated with genesis of J-waves: prospective study in young healthy men

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Background: Recent studies showed that J-wave was associated with vulnerability to ventricular fibrillation. While J-waves are also observed in the healthy population, the mechanisms responsible for J-wave are still under investigation. On the other hand, the possible association of false tendon (FT) with fascicular tachycardia suggested the presence of the arrhythmogenic slow conduction zones in FT. Recently, we reported the association between the FT and J-waves in the general population (Heart Rhythm, in press).

Methods: We prospectively studied 30 young healthy men. The FTs were detected by the echocardiogram and classified into 3 types on the basis of their points of attachment: type 1 (longitudinal type), type 2 (diagonal type) and type 3 (transverse type) as shown in figure. 12-lead ECG and the signal averaged ECG were recorded. J-wave was defined as terminal QRS notchting or slurring.

Results: The FT was detected in 70% of all subjects. The incidence of J-wave was significantly higher in the subjects with type 1 and 2 FTs than type 3 FT and without FT (100, 50, 20%, respectively, p<0.005). Late potential was not recorded in all subjects, however, the presence of late potential determined by SAECG was significantly longer in the subjects with type 1 or 2 FTs than the others (p<0.05).

Conclusions: These results suggested that FT was related to the genesis of J-waves and may have a potential arrhythmogenic property with conduction abnormality.

Partial blockade of IK1 destabilizes the rotation center of spiral wave reentry without enhancement of wavefront-tail interactions in the arm


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Background: It was previously reported that partial blockade of the inwardly rectifying potassium current, IK1, reduced dominant frequencies and facilitated initiation of reentry induced after application of 10 μM Ba2+, but we hypothesized that partial IK1 blockade destabilizes the rotation center of spiral wave (SW) reentry in favor of its early termination.

Methods: A 2-dimensional ventricular muscle layer was made in Langendorff-perfused rabbit hearts and excitation patterns were imaged by high-resolution optical mapping. In different series of experiments, action potentials were recorded from isolated superfused papillary muscle of rabbit ventricles by conventional glass-microelectrode technique.

Results: In Langendorff-perfused hearts, Ba2+ (10 and 50 μM) caused a dose-dependent prolongation of the action potential duration (APD) during constant pacing at 2.5-5 Hz (from 136±8 ms to 148±5 ms at 10 μM and 164±9 ms at 50 μM at 5 Hz, n=11, P<0.05) without significant changes in conduction velocity. SW reentry induced after application of 10 μM Ba2+ rotated around a longer I-shaped functional block line (FBL, length 6.8±0.7 mm vs. 3.2±0.8 mm, n=7, P<0.05) than in controls. After 50 μM Ba2+, the FBL was further prolonged (9.4±3.2 mm, n=7) and showed prominent beat-to-beat changes in shape in 2 of 7 episodes, resulting from decremental conduction close to the rotation center. A phase-mapping analysis revealed that the number of phase singularities remained ~1 after 10 and 50 μM, indicating minimal interactions between wavefront and wave tail in the SW arm. In papillary muscles, Ba2+ caused a dose-dependent depolarization of the resting potential (from -82.2 mV to -81.8 mV at 10 μM and -78.5 mV at 50 μM, P<0.05). The maximum upstroke velocity of the action potential was unchanged 199±10.2 V/s vs. 199±8.6 V/s at 1 Hz at 10 μM Ba2+ but was significantly decreased (156±9.8 V/s, P<0.05) at 50 μM Ba2+.

Conclusions: Partial blockade of IK1 destabilizes the rotation center of SWs without enhancement of wavefront-tail interactions in the SW arm.
Effects of renal sympathetic denervation on heart rate and atrioventricular conduction in patients with resistant hypertension

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Introduction and Hypothesis: Renal sympathetic denervation (RDN) reduces sympathetic activity and blood pressure (BP) in patients with resistant hypertension. The present study was aimed to investigate the effects of RDN on HR and other electrophysiological parameters.

Methods: 136 patients aged 62.2±9.0 years (58% male, BP 177±293±11 mm Hg) with resistant hypertension underwent RDN. BP and a 12-lead electrocardiogram (ECG) were recorded before, 3 months (n=129), and 6 months (n=84) after RDN.

Results: After 3 months (3M) and 6 months (6M), systolic BP was reduced by 25.5±2.4 mm Hg (p<0.0001) and 28.1±3.1 mm Hg (p<0.0001). HR at baseline was 66.1±1.1 beats per minute (bpm) and was reduced by 2.6±0.8 bpm after 3 months (p=0.001) and 2.1±1.1 bpm after 6 months (p=0.046). Change of HR correlated with HR at baseline: patients with HR at baseline between 60-71 bpm and ≥71 bpm had a reduction of 2.9±7.6 bpm (p=0.008) and 9.0±8.6 bpm (p=0.001), respectively, whereas in patients with baseline HR ≥60 bpm HR increased after 3 months (2.7±8.4 bpm; p=0.035). Neither baseline HR nor change of HR correlated with changes of systolic BP. The PR interval was prolonged by 11.3±2.5 ms (p=0.0001) and 10.3±2.5 ms (p=0.0001) at 3 and 6 months after RDN. Patients with a PR change ≥10 ms had a shorter baseline PR duration (159.7±3.6 ms vs. 171.4±4.4 ms; p=0.043) and a greater reduction of heart rate (3M: 4.1±1.5 bpm vs. -0.1±1.1 bpm; p=0.022). Duration of ventricular depolarisation was not significantly affected by RDN.

Conclusion: RDN significantly reduced heart rate and PR interval, as indicators of cardiac autonomic activity, in patients with resistant hypertension. The changes did not correlate to BP reduction.

Distribution of J waves on 87-lead body surface map in patients with interstitial early repolarization syndrome

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Purpose: J waves in the inferior lead reportedly relate poor prognosis in patients with interstitial early repolarization syndrome (ERS). However, little is known about the body surface distribution of J waves and the significance of J wave localization in ERS patients with ventricular fibrillation (VF).

Methods: This study consists of 15 patients (13 males, mean age 33.6±9.5 years) with ERS and a prior VF who underwent multiple recordings of 12-lead electrocardiogram (ECG) and 87-lead body surface map (BSM) during sinus rhythm. Locations of J waves on ECG were compared with distributions of J waves on the body surface and the clinical characteristics of patients. J wave was defined as an elevation at least 1 mm (0.1 mV) of the J point or at least 2 leads, either as QRS slurring or notching in the inferior lead (II, III, aVF), lateral lead (V4-V6), and high lateral lead (I, aVL) followed by ST elevation. Type 1 Brugada syndrome was excluded from this study.

Results: J waves were noticed on extensive body surface area, not only in the lower anterior chest but also in the lower back where the excitation of left ventricle is reflected in 9 patients with inferior J waves. In contrast, they were noticed in the restricted area of left mid lateral chest in 11 patients with lateral J waves, and in the left upper chest in 5 patients with high lateral J waves. Two patients with J waves in global leads had much wider J wave distribution on BSM. During 11.5±4.14 years follow-up, 14 patients received implantable cardioverter-defibrillator and 7 of 15 (47%) patients had recurrences of VF with a rate of 80%, 46%, and 33% in patients with high lateral, lateral, and inferior J waves, respectively.

Conclusion: Patients with J waves in the inferior or global leads on ECG exhibited wider distribution of J waves on the body surface, although high lateral J waves tended to link with poor outcome in ERS patients with VF.

QT peak prolongation predicts cardiac death following stroke

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Introduction and Hypothesis: Cardiac death has been linked in many populations in patients with acute myocardial ischemia (AMI). However, little is known about the body surface distribution of J waves and the significance of J wave localization in ERS patients with ventricular fibrillation (VF).

Methods: ECGs were recorded from 296 stroke patients (152 male), mean age 67.2 (SD11.6) approximately 1 year after the event. These ECGs were digitised by one observer who was blinded to patient outcome. The distribution of J waves was systematically studied over the 87-lead body surface map.

Results: Four patients with J waves in the inferior or global leads on ECG exhibited a greater reduction of heart rate (3M: 4.1±1.5 bpm vs. -0.1±1.1 bpm; p=0.022). Duration of ventricular depolarisation was not significantly affected by RDN.

Conclusion: QT peak prolongation predicts cardiac death in stroke survivors. Further studies are required to elucidate the mechanism that may lead to their cardiac death, and test the hypothesis that interventions might reduce the risk of cardiac death in these patients.

Changes in QRS duration in ECG leads with ST segment elevation differentiate acute pericarditis and acute transmural myocardial ischemia

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Purpose: Transmural myocardial ischemia prolongs the duration of the QRS complex in ischemia-related ECG leads. Theoretically, these changes should not occur in acute pericarditis because the injury is not transmural, but this is not well known. This study aims to assess whether QRS duration is affected differently in patients with acute pericarditis and in those acute transmural myocardial ischemia.

Methods: The clinical records and the admission 12-lead ECG at x2 magnification were analyzed in 79 patients with acute pericarditis and in 28 patients with anterior and inferior acute STEMI (ST-segment elevation myocardial infarction). The QRS interval duration was measured in leads with ST segment elevation and in those with isoelectric ST segment and differences among the three groups were statistically tested.

Results: The magnitude of ST segment elevation was lower (P<0.001) in patients with pericarditis (0.1±0.06 mV) than in patients with STEMI (anterio: 0.2±0.16 mV; inferior: 0.2±0.15 mV). However, the number of leads with ST segment elevation was larger (P<0.001) in pericarditis (6.5±2.0) than in STEMI (anterio: 5.8±2.14; inferior: 4.8±1.78). Patients with pericarditis show comparable QRS duration in leads with isoelectric ST segment and in those with elevated ST segment (80.4±12.12 ms vs 81.4±11.36 ms; P=0.281). However, patients with STEMI showed a significant longer QRS duration in leads with ST segment elevation than in leads with isoelectric ST segment (anterio: 83.3±3.15 ms vs 78.1±12.58 ms, p<0.005; inferior: 87.2±14.67 ms vs 83.1±12.12 ms; P<0.009).

Conclusion: Patients with STEMI but not patients with pericarditis show prolongation of QRS duration in leads with ST segment elevation. Present data afford new ECG criteria for the differential diagnosis between acute pericarditis and acute coronary artery occlusion.

Is QRS axis pattern associated to the type of surgical repair in adults with operated tetralogy of Fallot?

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Introduction: Until the development of the transatrial-transpulmonary approach, surgical repair of Tetralogy of Fallot (ToF) was achieved through a right ventriculotomy causing right ventricular (RV) conduction disturbance. We studied QRS
morphology in adults with repaired ToF to predict the presence and location of RV surgical scar.

Methods: All adults with ToF repair who had a cardiac MRI were included in the absence of pacemaker. Surgical history was obtained from hospital records. Electrocardiographic measures (maximum PR, QRS and QT duration, QRS axis) were analyzed manually from standard 12-lead electrocardiograms and delayed enhancement MRI was used for scar location.

Results: Twenty nine patients were included (72% male, 33±13 years). All patients but one had a transventricular repair (37% had a transannular patch, 60% had a transannular fenestration). Ventriculotomy with transventricular patch. Mean MRI right and left ventricle indexed end diastolic volumes were respectively 150±29 and 71±17 mL/m². Mean QRS duration was 156±16 ms with a RBBB pattern for all patients. There was no significant difference concerning BMI, MRI measures nor QRS duration between different sub-groups. All patients from the ventriculotomy group had a normal or right ECG axis pattern (axis between 34 and 160°).

Nine patients (90%) from the transannular group had a left ECG axis pattern (axis between -10° and 76°) (Figure 1).

Conclusion: QRS axis pattern in adults with repaired ToF correlates to the type of surgery: patients with ventriculotomy have normal or right ECG axis pattern while patients with transannular patch have a left ECG axis pattern.

P4723 The prognostic value of sinoatrial block of Wenckebach type (Mobitz I) in patients with symptoms suggestive of paroxysmal cardiac arrhythmias

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Introduction: In the literature, there is no work on the prognostic value of the sinoatrial block II of Wenckebach type (Mobitz I) - block W, that appears at different times of the day during Holter monitoring. The aim of the study was to determine the clinical significance of the block W identified in the Holter study in patients with symptoms suggestive of cardiac arrhythmias.

Methods: The study group included 300 consecutive patients (mean age 54±19 years, 130 women) with symptoms suggestive of cardiac arrhythmias who underwent Holter monitoring. Patients who were found to experience the block W episodes had re-performed 24-hour ECG Holter monitoring after 12 and 24 months. All patients underwent medical examination, assessing their clinical condition at 12 month intervals.

Results: The block W was diagnosed in 88 persons (29%). In 37 patients the block W occurred only during sleep and in 51 during sleep and during daily activity. Prospective observation time averaged 41±11 months, the survival without a diagnosis of sinus node disease was 26±10 months, and survival without pacemaker implantation 28±8 months. The sinus node disease was diagnosed in 25 people: in 1 person (2%) in the group with the block W only during sleep, in 19 patients (37%) in the group with the block W during the daily activity and in 5 patients (10%) in the group without the block W. The incidence of the block W during activity occurred in 20 patients: 1 person (2.7%) with the block W only at night, in 16 patients (31.3%) with the block W in activity during the day and in 3 patients (1.4%) with no identifiable block. Variables (age > 60 years, male gender, structural heart disease, the block W during the day), which in univariate analysis showed association (p < 0.05) with sinus node disease and the necessity for permanent pacing were subjected to Cox multivariate analysis. Results of Cox multivariate analysis revealed that the block W occurring during the daily activity is an independent predictor of future diagnosis of sinus node disease (relative risk: 17.61 [3.92-46.25]; p < 0.014), and the emergence of indications for permanent cardiac pacing (relative risk: 7.92 [2.79-24.52]; p < 0.028). During the follow-up 25 people died. There were no differences between groups in mortality.

Conclusions: The block W during daily activity in patients with symptoms suggestive of cardiac arrhythmias indicates an increased likelihood of future diagnosis of sinus node disease and indications for permanent pacing.

P4724 Cardiac autonomic disturbances in patients with vasovagal syndrome: comparison between 123I-metaiodobenzylguanidine myocardial scintigraphy and heart rate variability

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Purpose: The aim of this study was to examine autonomic disorders in patients with different types of vasovagal syndrome by performing both a cardiac sympathetic innervation evaluation, and a head-up tilt-test with heart rate variability (HRV) analysis.

Methods: We enrolled 60 patients with vasovagal syncope (32 women, mean age 40±16 years), and 20 age matched controls. We assessed pathologic changes in the integrity and function of the myocardial presynaptic nerve endings and in the sympathetic activity, using 123I-metaiodobenzylguanidine (MIBG) scintigraphy and time domain indexes of HRV.

Results: A significantly lower heart/mediastinum ratio was found in the syncope patients compared to the control group both at 10 minutes (1.9±0.25 versus 3.6±1.7, p=0.02) and at four hours (1.79±0.12 versus 2.07±0.19, p=0.04), whereas washout rate was significantly greater in syncope patients (5.5±3.7 versus 2.2±0.19, p=0.04). There were no significant differences in any of the above parameters between patients with different types of syncope. No significant difference was found in any of the HRV time domain indexes depending on the type of syncope. However, a correlation was found between MIBG and washout rate in syncope patients (r=0.256, p=0.48).

Conclusion: Patients with vasovagal syncope induced by tilt test, reveal a high degree of disturbance of myocardial adrenergic innervation, which appears to be associated with a reduction in parasympathetic tone. This suggests a possible predominance of cardiac adrenergic activity in those with abnormal cardiac MIBG scintigraphy.

P4725 Early repolarization patterns in young healthy individuals: prevalence, morphological characteristics and impact of gender, ethnicity and physical activity

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Purpose: Early repolarization (ER) is commonly observed in athletes and young healthy individuals. Recently, ER in the inferior and lateral leads has been associated with sudden cardiac arrest from idiopathic ventricular fibillation. We studied the prevalence, distribution and morphology of ER patterns in inferior and lateral leads in young healthy individuals.

Methods: 12-leads electrocardiogram (ECG) was performed at rest in 1929 young healthy individuals (age range 13-38 years) between February and September 2011. We evaluated the impact of gender, ethnicity and physical activity on ER. Individuals were divided into physically-active (exercise > 2 hours/week) and sedentary. Early repolarization was defined as notched or slurred J-point elevation of at least 0.1mV from baseline, in ≥ 2 contiguous inferior or lateral leads; anterior ER patterns were not considered in this study. The morphology of ST-segment was classified as rapidly ascending/up sloping or horizontal/descending.

Results: The mean age of participants was 17.9±4.4 years, of which 1406 (73%) were male, 1557 (80%) were physically active and 1780 (92%) were Caucasians. ER pattern in inferior and lateral leads was present in a total of 382 (19.8%) cases; of these 40% were in the inferior leads, 35% in lateral leads and 25% in both. Notched ER pattern was more prevalent compared to slurred morphology, and more commonly associated with ascending/up sloping ST-segment elevation. ER was significantly more prevalent in males compared to females (20% vs. 12%, p=0.003), in physically-active people compared to sedentary (20.4% vs. 14.8%, p=0.013), and in Afro-Caribbeans compared to Caucasians (31.2% vs. 19.9%, p=0.012). In addition, voltage criteria for left ventricular hypertrophy and sinus bradycardia were a common associated finding in individuals with ER pattern compared with those without (p=0.0001 and 0.0001 respectively). Only 5% of individuals with ER had J-point elevation of >0.2mV.

Conclusion: Early repolarization is a common finding in young healthy individuals, and is more prevalent in males, physically-active individuals and those with Afro-Caribbean ethnicity. The inferior leads were more commonly involved but the difference was not statistically significant. Notched ER pattern with ascending ST-segment elevation was the most commonly observed morphological pattern. More research is required to understand precise long term implications of such repolarization changes in young individuals.
Screening for arrhythmogenic myocardial substrate by 12-lead ECG, high resolution ECG and T-wave alternans in patients with low to intermediate sudden cardiac death risk

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Aims: Increased QRS score, wide spatial QRS-T angle, T-wave alternans (TWA), and late potentials by signal averaged electrocardiogram (SAECG) are independent predictors of cardiovascular mortality in the general population. We analyzed whether these electrocardiographic (ECG) parameters enable screening of patients for myocardial scar features implicated in sudden cardiac death risk.

Methods and results: We screened a 6-month interval of the entire 2-month ECG database of Johns Hopkins Hospital and identified 800 patients age >70 years from non-critical care areas and no record of reduced life expectancy who had QRS >120 ms and spatial QRS-T angle >10°, as well as left ventricular ejection fraction (LVEF) <35%. All individuals were invited to participate, of whom 77 enrolled in the study and underwent clinical examination, SAECG, 30-minute ambulatory ECG recording for TWA, and complete late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) study to determine scar presence and pattern as well as to characterize gray zone, core, and total scar size.

The mean patient age was 60±10 years, with 70% males and no known heart disease in 43% of the study population. Patients’ mean LVEF was 58±8%. Previously unreported myocardial scar was present in 41 (53%) patients, of whom 19 (48%) exhibited a typical ischemic pattern. Median and inter-quartile range for scar, core scar, and gray zone extent were 8% [4; 12%], 5% [3; 8%], and 2% [1; 7%] of left ventricle (LV), respectively. QRS-T angle but not QRS score was associated with the presence of scar and ischemic scar pattern. QRS score was related to total scar size and gray zone size (R²=0.18; P=0.001) and gray zone size (R²=0.10; P=0.005, respectively). There was a significant independent association between TWA level with total scar size (R²=0.2, P=0.005) and gray zone size (R²=0.12; P=0.002, respectively). There was a significant independent association between TWA level with total scar size (R²=0.18; P=0.001) and gray zone size (R²=0.12; P=0.002, respectively). There was a significant independent association between TWA level with total scar size (R²=0.18; P=0.001) and gray zone size (R²=0.12; P=0.002, respectively).

Conclusions: ECG screening by QRS score >5, QRS-T angle >105°, and TWA identifies patients with preserved LVEF but previously unreported myocardial scar with arrhythmogenic potential.

Prevalence, electrocardiographic characteristics and variations of early repolarization syndrome on a population of healthy subjects

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Background: Infero-lateral repolarization has been considered benign for a long time, however recent studies have demonstrated a possible association with sudden death.

Purpose: Our data are consistent with previous studies concerning early repolarization syndrome. Given the high prevalence and important fluctuations of early repolarization, every patient who presents with this syndrome cannot be considered to be at risk of sudden death. Further research is needed to identify the electrocardiographic forms of this syndrome which are associated with an increased risk of mortality.

The fragmented QRS complex in patients with idiopathic ventricular fibrillation

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Introduction: Fragmented QRS (fQRS) on 12-lead ECG, a marker of myocardial conduction delays, predicts arrhythmic events in patients with ischemic or non-ischemic cardiomyopathy. We aimed to assess the clinical implications of fQRS in patients with idiopathic ventricular fibrillation (IVF).

Methods: 12-lead ECGs were studied in 52 patients with IVF (>13 years old) and 156 controls without structural heart disease matched for age and sex. The fQRS was defined by the presence of >1 notching in the R or S wave in ≥2 contiguous leads.

Results: The fQRS was more frequently detected in patients with IVF compared to the controls (25/52, 48% versus 21/156, 13%; P=0.001). The fQRS was detected primarily in inferior leads (16/52, 31%) and followed by precordial (9/52, 17%) and lateral leads (15/52, 29%). During the mean follow-up of 20 months after defibrillator implantation in IVF group (n=52), significantly higher proportion of patients with fQRS experienced appropriate shock compared to those without fQRS (47/52, 90% versus 4/52, 8%; P=0.001). However, there was no significant inappropriate shock between the 2 subgroups (5/25, 20% versus 5/27, 19%; P=1.0).

Conclusions: The fragmented QRS complex might reflect the presence of arrhythmic substrate in IVF patients.

Various morphological ventricular premature beats with fragmented QRS waves on a 12 lead Holter ECG had a positive relationship with the left ventricular fibrosis on CT in hypertrophic cardiomyopathy

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Purpose: Various morphological kinds of ventricular premature beats (VPB) with fragmented QRS waves and often observed in subjects with hypertrophic cardiomyopathy (HCM) but its significance is not clear.

Methods: Retrospective analysis acquired from a total of 24 consecutive HCM subjects (17 male, mean 64±12 yrs) who underwent enhanced ECG gated CT (Aquilion one or Light Speed Ultra 16) and a 12 lead Holter ECG (RAC-2103, Nihon Koden) within 3 months. Evaluation of coronary artery and characteristics of left ventricular myocardium were performed. If there was a contrast defect in myocardium in early phase, late phase acquisition was added, and if abnormal late enhancement was observed in the corresponding site, we diagnosed myocardial fibrosis.

Results: Correlation coefficients (CCs) of numbers of morphological kinds of 1) all VPB (blue bar) and 2) fragmented VPB (red bar) against the patient’s characteristic factors and CT findings are represented in the Figure. Positive CCs were observed between numbers of kinds of both all VPB and fragmented VPB and the frequency of diabetes mellitus and fibrosis in left ventricular myocardium on CT and negative CCs were observed between numbers of kinds of both all VPB and fragment VPB and luminal stenosis ≥50% in any coronary arteries and each coronary artery on CT. There were no significant differences between numbers of kinds of all VPB and fragmented VPB concerning their relationship with the patient’s characteristic factors and CT findings.

Conclusion: Numbers of morphological kinds of fragmented VPB on a 12 lead Holter ECG may have a positive relationship with the occurrence of fibrosis in left ventricular myocardium but a negative relationship with coronary arteries stenosis on CT in HCM subjects as well as those of all VPB.

Association of sudden cardiac death and ambient temperature in Scotland

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Purpose: Freezing temperatures in early 2012 have claimed more than 200 lives...
in Eastern Europe. Several studies have investigated the effect of seasonality and sudden cardiac death (SCD). Less commonly investigated has been the short-term effects of change in ambient temperature and SCD. We investigated the association between hourly and mean daily change in ambient temperature and SCD.

Methods: We evaluated the effect of ambient temperature and the risk of SCD, comparing data from the Heart Start registry with local hourly measurements of atmospheric temperature in Scotland from January 1995 to December 2004, using a case-crossover design.

Results: 29,854 victims suffered a SCD in the studied time frame. Across all distances and all time lags, there was an increase in risk of SCD with lowering of ambient temperature. There was a 7.6% (95% CI 2.7% – 12.3%) increase in the risk of SCD per 10 degree lowering of the ambient temperature. The association with temperature remained up to 24hours (Lag 0-1 days) prior to the SCD with sensitivity analysis showing patients ≥65 years and those with known heart disease (Figure 1) being more vulnerable.

Conclusion: These preliminary results of a prospective registry show that MFI based QRS-fragmentation in addition to the ejection fraction is able to identify patients who are more likely to get a life-threatening ventricular tachycardia. Further studies to evaluate the use of this parameter for pts. with only moderate ejection fraction are planned.
The role of non-invasive methods in determining the arrhythmic risk in myotonic dystrophy type 1

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Purpose: In myotonic dystrophy type 1 (MD1) the risk of cardiac death is higher than in the general population and atrial or ventricular arrhythmias are frequent. The aim of this study was to assess the determinants of arrhythmic risk in patients with MD1 using non-invasive methods.

Methods: Eighty-four patients (62% males; age 41±15 years) with a clinical-genetic diagnosis of MD1 (class E1±11%; E2±75%; E3±14%) were enrolled. All patients underwent cardiovascular evaluation, 12-lead ECG, echocardiography, 24-hour ECG/Holter with heart rate variability (HRV) and neurological assessment at entry. During a mean follow-up of 46±28 months (≥2 visits) echo-ECG-Holter data and arrhythmic events were collected.

Results: During the follow-up 8 patients (9%, incidence 2/100-year) died (age at death 48±11 years). Six (75%) of the deaths were cardiac: 2 sudden deaths (SD), 1 aborted SD i.e. ICD shock on ventricular fibrillation (VF), and 3 deaths due to heart failure. Four patients (5%) developed major arrhythmic events (ST/SDS/SDVF, sustained or non-sustained ventricular tachycardia, and 7 patients (8%) atrial flutter/fibrillation (AF). According to current guidelines, 7 patients received pacemaker or ICD. The incidence of cardiac death was associated with prolonged PR and QRS intervals at baseline ECG (544±48 msec vs 189±34, p=0.003 and 126±23 msec vs 96±21, p=0.002 respectively), with presence of AF (50% vs 11%, p=0.009) at baseline or during follow up, with lower SDNN (100±22 vs 174±45, p=0.06) and SDANN (81±15 vs 132±41, p=0.04) values at HRV. Patients who developed major arrhythmic events had a trend toward a longer QRS duration at baseline ECG (118±13 msec vs 97±23, p=0.07) and more frequent premature ventricular beats/PVbs at ECG-Holter (252±4817 vs 499±1579, p=0.018). Patients who developed AF were characterized by older age (51±17 years vs 39±14, p=0.047), longer PR interval at baseline ECG (257±49 msec vs 198±32, p=0.03), and higher HRV (RR 1086±197 vs 837±84, p=0.008; SDNN 176±45 vs 139±39, p=0.04; RMSSD 89±53 vs 43±21, p=0.001).

Conclusions: In MD1 patients cardiac-deaths are associated with conduction disturbances at baseline ECG, presence of AF and HRV data suggesting increased sympathetic activation. Major arrhythmic events are associated with intraventricular disturbances at ECG and frequent PVbs at Holter. Atrial fibrillation is more frequent in patients with baseline atrio-ventricular conduction disturbances and vagal prevalence. Non-invasive cardiological evaluation is important for arrhythmic risk assessment, identifying patients who can develop major tachyarrhythmic events.

The importance of atrioventricular conduction and myocardial function in ventricular arrhythmogenesis in lamin A/C mutation carriers

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Purpose: Mutations in the Lamin A/C gene may cause dilated cardiomyopathy (DCM), typically accompanied by atrioventricular block (AVB) and high risk of ventricular tachycardia (VT). VT may occur before development of DCM and risk stratification is challenging. Mechanisms of arrhythmias in these patients are not fully understood.

Methods: We included 41 Lamin A/C mutation carriers. PQ interval from resting ECG and occurrence of VT were recorded. Myocardial function was assessed by echocardiography as ejection fraction (EF) and by speckle tracking strain from 16 LV segments as global longitudinal strain. Regional function in the interventricular septum was assessed by averaging strain from 4 septal segments and defined as septal strain.

Results: VT was documented in 21 patients (51%). Importantly, 13 patients without evident DCM had VT (62%). Prolonged PQ interval (p=0.001), presence of AVB (p=0.001) and reduced global longitudinal strain (p=0.01) were markers of VT, while EF was not (p=0.53). By ROC analysis, PQ interval ≥230 ms showed the best ability to discriminate between those with and without VT with a sensitivity and specificity of both 87%. PQ interval was an independent predictor of VT in multivariable analysis (OR=1.35, p=0.01). Septal strain was markedly reduced compared to the rest of LV segments (-16.7% vs. -18.7%, p=0.001). Prolonged PQ interval correlated with reduced septal function (R=0.41, p=0.03).
Conclusion: Prolonged PQ interval was the best predictor of VT and may help arrhythmic risk stratification in Lamin A/C mutation carriers. Myocardial function was most decreased in the septum and correlated to prolonged PQ interval. These findings indicate that reduced septal function and AVB are involved in mechanisms of ventricular arrhythmias in Lamin A/C mutation carriers.

Left atrial strain predicts postoperative atrial fibrillation in patients waiting for aortic valve replacement for aortic stenosis

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Background: The occurrence of atrial fibrillation (AF) is a common and dangerous complication in patients undergoing aortic valve replacement (AVR); Speckle tracking echocardiography (STE) has recently enabled the quantification of longitudinal myocardial LA deformation dynamics. Our aim was to investigate by STE the eventual pre-existent subclinical mechanical atrial dysfunction in patients who develop AF after AVR.

Methods: 75 patients with aortic stenosis in sinus rhythm, undergoing AVR, were prospectively enrolled. Conventional echocardiographic parameters, and peak atrial longitudinal strain (PALS) were measured in all subjects the day before surgery. PALS values were obtained by averaging all segments measured in the 4- and 2-chamber views (global PALS).

Results: All patients received a biological valve prosthesis and a standard postoperative care. Postoperative AF occurred in 15 patients (20.0%). Among all clinical and echocardiographic variables analyzed, global PALS demonstrated the highest diagnostic accuracy (AUC of 0.90) and, with a cutoff value less than 16.9%, good sensitivity and specificity of 86% and 91%, respectively, to predict postoperative AF episodes. LA volume indexed and E/E' ratio presented lower diagnostic accuracy (AUC 0.76 and 0.51, respectively).

Conclusions: STE analysis of LA myocardial deformation could be considered a promising tool for the evaluation of LA subclinical dysfunction in patients undergoing AVR, giving a potentially better risk stratification for the occurrence of postoperative AF.

Clinical aspects and prognosis of type 1 ECG pattern of Brugada syndrome

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Purpose: This study investigated the clinical aspects and long-term prognosis of type 1 ECG pattern of Brugada syndrome (BS).

Methods: The clinical data of 68 apparently healthy individuals (55 males, age 44.7 ± 12.7 years) with spontaneous (n=27) or drug-induced (n=41) type 1 ECG pattern of BS were retrospectively analyzed.

Results: Twenty-eight subjects were symptomatic with a history of syncope (41.2%) and 18 displayed a positive family history of BS and/or sudden cardiac death (26.5%). Electrophysiological study was performed in 37 subjects, and programmed right ventricular stimulation induced ventricular tachycardia/fibrillation in 25 of them (67.5%). A cardioverter defibrillator (ICD) was implanted in 27 individuals (39.7%). During a mean follow-up period of 5.0 ± 3.5 years, five symptomatic subjects suffered appropriate ICD discharges due to ventricular arrhythmias (7.4%, 1.7% per year in total population, 3.55% per year in symptomatic individuals), and one died due to non-cardiac causes. None of the asymptomatic individuals had syncope or ICD therapies. A history of syncope (p = 0.005) as well as a prolonged QRS duration in leads II (p = 0.026) and V2 (p = 0.001) were significantly associated with ventricular arrhythmic events during follow-up. Sinus node dysfunction and atrial arrhythmias were observed in 8.8% and 20.6% of subjects, respectively.

Conclusions: In this study population, the mean arrhythmic event rate per year in symptomatic individuals with BS phenotype was 3.55%. Asymptomatic subjects with type 1 ECG pattern of BS display a benign clinical course.

T-wave alternans is helpful for predicting recurrence of fatal arrhythmias in ventricular fibrillation survivors

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Backgrounds: T-wave alternans (TWA) is useful for predicting the occurrence of ventricular tachyarrhythms in various heart diseases. However, little is known about the clinical significance of TWA measurement in patients with past history of ventricular fibrillation (VF).

Methods: We studied 22 VF survivors (15 males, mean age 58 years) who received implantable cardioverter-defibrillator implantation. The patients of J-wave syndrome were excluded from this study. We measured plasma B-type natriuretic peptide (BNP) and assessed left ventricular ejection fraction (LVEF) by echocardiography. Additionally, QRS duration and QTc interval were measured in electrocardiogram. TWA value was calculated by the time-domain moving average method. All subjects were divided into two groups based on whether TWA value was above 65 μV (n=11, Group-A) or not (n=11, Group-B). We compared these parameters and the appearance of ventricular arrhythmias requiring appropriate shock therapy in the observation term (8.8 ± 5.9 months) between two groups.

Results: BNP and LVEF were not different between two groups (BNP, 213 ± 42 pg/ml vs. 175 ± 154 pg/ml; LVEF, 42.4 ± 14.8% vs. 46.6 ± 16.3%). QRS duration and QTc interval were not different between two groups (QRS duration, 121.3 ± 23.2 msec vs. 107.2 ± 16.1 msec; QTc interval, 454.8 ± 12.7 msec vs. 431.6 ± 54.1 msec). However, ventricular arrhythmias requiring appropriate shock therapy occurred more frequently in Group-A than in Group-B (55% vs. 9%, P < 0.05). In Kaplan-Meier actuarial curves for arrhythmic event-free rates, Group-A had lower event-free than Group-B (P < 0.05).

Conclusions: These results suggest that T-wave alternans is useful for predicting the recurrence of ventricular arrhythmias or adverse outcomes in patients with past history of VF.
Utility of magnetocardiography for detection of delayed potentials, epsilon waves, with arrhythmogenic right ventricular cardiomyopathy

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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by hypokinetic areas involving the free wall of the right ventricle, with fibro-fatty replacement of the right ventricular myocardium, with associated arrhythmias originating in the right ventricle. Diagnostic ECG finding includes epsilon wave, which is interpreted as a delayed potential in RV. Some cases are difficult to identify the delayed potentials. The aim of this study was to visualize the delayed potentials and compare the delayed potential point using magnetocardiography (MCG).

Methods: This study included 14 cases with ARVC who were diagnosed by Task Force of WHO/ISH (1996) and biopsy, echocardiography and imaging, they were examined 64-channel MCG waveforms. 64-channel MCG waveforms were examined before electrophysiological study and ablation for ventricular premature contraction or ventricular tachycardia. 6 of them showed typical abnormal potential representing the epsilon wave at the end of QRS complex and right in front of T wave on electrophysiological (ECG). 8 cases were difficult to detect the delayed potentials by 12-leads ECG. A current arrow map (CAM) depicted the propagation of the delayed potentials. The locations of the delayed potentials identified by MCG were compared with ablation successful site tagged on the electroanatomical map.

Results: 6 of 8 (75%) with undetectable delayed potential cases could identify the delayed potentials at the end of QRS complex, using MCG. The origins of the delayed potentials deduced CAM agreed with that from the invasive study in 12 of 14 patients.

Conclusion: Magnetocardiography was useful for detecting the presence of delayed potential, epsilon wave, and estimating delayed potential points before the catheter ablation.

SYNCOPE

P4740

Home orthostatic training is not effective in elderly patients With vasovagal syncope - a prospective randomised controlled trial

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Objective: To assess the effect of home orthostatic training (HOT) on autonomic reflexes in elderly patients with vasovagal syncope (VVS).

Design: A single blind randomised controlled trial.

Setting: Eastbourne District General Hospital, East Sussex NHS Trust.

Interventions: The over 65 group were randomised 1:1 to active HOT (O65+) or sham HOT (O65-). The U65 group received active HOT. Participants performed HOT/sham HOT and recorded their training and symptoms. Patients had a repeat tilt test at 3 months.

Main outcome measures: Time to syncope at repeat tilt table testing, low-frequency heart rate variability (LF-HRV), high-frequency HRV (HF-HRV), mean upstroke baroreflex sensitivity (BRS) and mean downslope BRS were assessed.

Results: Symptomatic benefit occurred in 4 (31%) of the O65+, 4 (29%) of the O65-, and 6 (50%) of the U65. None of the autonomic measures changed significantly in any group (table 1). 50% of the O65+ group stopped training due to back pain. Time constraint (25%) was the most common reason for cessation in the U65 group.

Conclusions: Despite good tilt training compliance no improvement in autonomic measures in any group was shown. The most common reason for cessation of training was back pain the elderly groups. This study does not support the use of HOT in elderly patients.

P4741

Additional diagnostic value of very prolonged observation by implantable loop recorder in patients with unexplained syncope

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Introduction: In the literature, the average diagnostic yield of the implantable loop recorder (ILR) is reported to be 35% over an observation period generally less than 18 months. The aim of this study was to evaluate the diagnostic value of ILR during very prolonged observation.

Methods and Results: Consecutive patients who had received one or more (in the case of battery exhaustion before diagnosis) ILR (Reveal/plus/DX, Medtronic Inc.) from 2001 to 2010 were included. The diagnostic ECG was classified according to the ISSUE classification. We analyzed 157 patients (87 males, 69±14 years): 70 of these were followed up for ≥18 months. The estimated cumulative diagnostic rates were 30%, 43%, 52%, and 80% at 1, 2, 3, and 4 years, respectively. 26% of diagnoses were made after 18 months. The diagnostic yield was independent of structural heart disease, bundle branch block, number of syncope episodes, and gender; the median time to diagnosis of ISSUE type 1 patients was shorter than that of the others (4 [2;10] vs. 16 [6;23] months; P < 0.003). During the observation period, 3 patients (1.9%) died and none suffered arrhythmic death.

Conclusions: Prolonging observation up to 4 years increased the diagnostic value of ILR in syncopal patients and was safe. A quarter of patients diagnosed needed more than 18 months of follow-up. As consequence, when a strategy of prolonging monitoring is chosen, monitoring should be maintained even for several years until diagnosis is established.

P4742

Vasovagal syncope mediated by emotional distress associated with increased risk of cardiovascular events

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The aim of the study was to assess whether vasovagal syncope mediated by emotional distress (emotional-VVS) is associated with an increased risk of cardiovascular events (CVEs).

Methods and Results: The study group consisted of consecutive 2248 Cardiology Clinic outpatients aged 61±12.1 years (604 patients with and 1644 patients without CVE). 28.3% of the studied population reported at least one episode of syncope, 8.7% had emotional-VVS. The median age of CVE was 59, the interquartile range 52-66 years. The median time between the first emotional-VVS and CVE was 7 years, interquartile range 25-44 years. The median time between the first emotional-VVS and date of the visit in cardiology outpatient clinic in patients without CVE was 41 years (interquartile range 25-49 years). Emotional-VVS was significantly more frequent in patients with CVE than in those without (35% vs 26% P < 0.01). For each patient an index date was established. The index date was the one of the first CVE or, in the case of patients without CVE, the date of their visit to the clinic. Survival free of CVE to the index date estimated according to Kaplan-Meier method showed lower probability of survival in patients with emotional-VVS and the survival curves began to drift apart at the age of 50. Multiple Cox regression analysis revealed that shorter CVE free survival was related to male gender, diabetes, an hypercholesterolemia above 240 mg/dL, family history of premature cardiovascular disease (CVD) and positive history regarding the emotional-VVS.

Table. Cox regression survival analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male gender</th>
<th>Smoking</th>
<th>Family history</th>
<th>Diabetes</th>
<th>Total cholesterol (mg/dL)</th>
<th>Emotional-VVS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>HR</td>
<td>coefficient</td>
<td>p</td>
<td>HR</td>
<td>coefficient</td>
<td>p</td>
</tr>
<tr>
<td>CVE</td>
<td>1.75±0.65</td>
<td>1.75±0.65</td>
<td>1.75±0.65</td>
<td>1.35±0.65</td>
<td>1.35±0.65</td>
<td>1.35±0.65</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.001</td>
<td>&gt;0.001</td>
<td>&gt;0.001</td>
<td>&gt;0.005</td>
<td>&gt;0.005</td>
<td>&gt;0.005</td>
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</tbody>
</table>
Classification and Regression Trees (CART) analysis revealed that emotional-VVS is a factor of increased risk of CVE in men.

**Conclusions:** 1. Emotional-VVS is associated with an increased risk of CVE, independently of other risk factors and seems to be a risk factor only in men. 2. The survival curves between patients with and without emotional-VVS begin to drift apart at the age of 50.

3. The causal relationship between emotional-VVS and CVE requires further studies.

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**P4743**

Two-year diagnostic yield of implantable loop recorder in patients with neurally-mediated syncope enrolled in the ISSUE3 trial

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Since the diagnostic yield of implantable loop recorders (ILLRs) is a function of the length of observation, this rate increases by prolonging the observation period. We assessed the diagnostic yield among the 284 patients (pts) enrolled in ISSUE3 trial who completed the 2-year follow-up period. Eligible pts who have >3 seizures or any of the following were referred for a HUTT study: 1. Past resuscitation for syncope; 2. History of presyncope; 3. Severe syncopal episodes of suspected or certain neurally-mediated syncope (NMS) in the prior 2 years without significant electrocardiographic and cardiac abnormalities. Within 2 years from implantation, 76 pts (27%) had syncope recurrence with asystolic pause ≥3 s (457) or asystolic pause ≥3 s without syncope (419). 49 pts (17%) had a diagnosis of tachycardia or syncope due to non-arrhythmic cause and 159 pts (56%) had no diagnosis. No baseline clinical variables (table 1) was able to predict the outcome except a positive HUTT (TTR) response which was predictive of neurally-mediated syncope, 51% of those with non-asystolic syncope and in 36% of those without diagnosis (p=0.003).

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**Clinical characteristics**

<table>
<thead>
<tr>
<th>Asystolic</th>
<th>No asystolic</th>
<th>No diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=76</td>
<td>n=49</td>
<td>n=159</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>66 (11)</td>
<td>66 (13)</td>
</tr>
<tr>
<td>Men, No. (%)</td>
<td>37 (49)</td>
<td>22 (45)</td>
</tr>
<tr>
<td>Syncopy events; median (IQR)</td>
<td>6 (1-15)</td>
<td>6 (4-15)</td>
</tr>
<tr>
<td>Events in the last year, median (IQR)</td>
<td>3 (3-4)</td>
<td>3 (3-4)</td>
</tr>
<tr>
<td>Events in the last year without syncope</td>
<td>2 (0-4)</td>
<td>2 (0-4)</td>
</tr>
<tr>
<td>History of syncope, n (%)</td>
<td>43 (57)</td>
<td>25 (51)</td>
</tr>
<tr>
<td>Hospitalization for syncope, n (%)</td>
<td>45 (59)</td>
<td>30 (61)</td>
</tr>
<tr>
<td>Injuries related to fainting, n (%)</td>
<td>3 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Major injuries (fractures, brain concussion)</td>
<td>6 (8)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Minor injuries</td>
<td>30 (40)</td>
<td>16 (33)</td>
</tr>
<tr>
<td>Tilt testing performed, No (%)</td>
<td>65 (86)</td>
<td>45 (92)</td>
</tr>
<tr>
<td>Positive of those performed, No. (%)</td>
<td>39 (66)</td>
<td>23 (51)</td>
</tr>
</tbody>
</table>

In conclusion, about a half of pts receiving an ILLR for suspected or certain NMS has a diagnosis within 2 years of observation. Of these, about a half may benefit from pacemaker therapy due to a documented long asystolic pause. The pts with a positive response to TTT are more likely to benefit from an ILR strategy.

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**Incidence, etiology and predictors of adverse outcomes in 43315 patients presenting to the emergency department with syncope: an international meta-analysis**

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**Background:** Syncope remains challenging for Emergency Department (ED) physicians due to difficulties in assessing the risk of future adverse outcomes.

**Objective:** The aim of this meta-analysis was to establish the incidence and etiology of adverse outcomes as well as the predictors.

**Methods:** Studies reporting multivariate predictors of adverse outcomes in patients presenting with syncope to the ED were included and pooled, when appropriate, using a random-effect method. Adverse events were defined as “incidence of death, or ophthosipitalization and interventional procedures because of arthrythmia, ischemic heart disease or valvular heart disease”.

**Results:** 11 studies were included. Pooled analysis showed 42% (CI 95%; 32-52) of patients were admitted to hospital. Risk of death was 4.4% (CI 95%; 3.1-5.1) and 1.1% (CI 95%; 0.7-1.5) had a cardiovascular etiology. One third of patients were discharged without a diagnosis, while the most frequent diagnosis was situational, orthostatic or vasovagal syncope in 29% (CI 95%; 12-47). 10.4% (CI 95%; 7.8-16) were diagnosed with heart disease, the most frequent type beingbradyarrhythymia, 4.8% (CI 95%; 2.2-6.4) and tachyarrhythmia 2.6% (CI 95%; 1.1-3.1). Post-syncope preceding syncope, exertional syncope, a history consistent of heart failure or ischemic heart disease, and evidence of bleeding were the most powerful predictors of an adverse outcome.

**Conclusion:** Syncope carries a high risk of death, mainly related to cardiovascular disease. This large study which has established the most powerful predictors of adverse outcomes, may enable care and resources to be better focused at high risk patients.

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**The risk of clotting induced by orthostatic stress patients with vaso-vagal syncope**

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**Aim of study:** Analysis of prevalence of endothelium-dependent clotting and fibrinolysis, as a response to orthostatic stress during head up tilt test (HUTT) in patients with vaso-vagal syncope (VVS).

**Study population:** 40 pts (15 men, 25 women) aged 18-72 yrs (median of age: 35 yrs. IQR 27-55,6) with VVS referred to HUTT with or without VVS referred to HUTT. Cardio- and neurogenic reasons of syncope were previously included in all pts.

**Methods:** All pts underwent HUTT acc. to standard Westminster protocol. Before HUTT and at the onset of HUTT provoked syncope blood sample was collected for analysis of clotting and fibrinolysis parameters. We measured: prothrombin time, expressed as international normalized ratio (INR), activated partial thromboplastin time (APTT), serum concentrations of: fibrinogen (FIB) d-dimer (D-Dim) serum, tissue plasminogen activator (tPA) plasminogen activator (inhibitor-1) (PAI-1) and von-Willebrand antigen (VWF:Ag) described as % of normal values.

**Results:** Significant decrease of APTT (30.9 to 25.6 s; p<0.0001), INR (1.1 vs 1.03; p<0.001) and PAI-1 (4.6 vs 3.4 ng/ml; p<0.03) as well as increase of serum levels of FIB (3.1 to 3.3 g/l; p<0.006), D-Dim (263.0 vs 379.0 ug/l; p<0.001), vW-BAg (57.1 vs 81.6%; p<0.01) and IPA (5.0 vs 9.8 ng/ml; p<0.001) were observed in fainters during HUTT. APTT showed 36% of pts, FIB increased in 43% of pts, and PAI-1 decreased in 75% of patients. Fibrinogen concentration rises during HUTT in 76% of pts, d-Dimer – in 86.6% of pts, vWBI – in 69.2% of pts ant IPA – in 71.8% of patients. In patients with negative HUTT only significant decrease of PAI-1 serum level was observed (6.8 vs 4.4 ng/ml; p<0.04). Changes of values of measured parameters during HUTT did not correlate with age of pts. Observations changed in clotting related to the orthostatic stress resembles changes occurred during haemorrhage. Only activation of fibrinolysis simultaneously to
clotting provoked by orthostatic stress may prevent against dangerous thromboembolic complications in patients with vasovagal syncope. **Conclusions:** 1. Syncope induced by orthostatic stress during head-up tilt test lead to potentially dangerous activation of clotting in patients with vasovagal fairs. 2. Simultaneous activation of fibrinolysis processes by orthostatic stress prevents against dangerous thromboembolic complications in patients with vasovagal syncope. 3. Endothelium-dependent activation clotting and fibrinolysis in response to orthostatic stress seems to play an important role in pathogenesis of vasovagal syncope.

**Incidence of permanent atrioventricular block in patients with syncope and bifascicular block**

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**Introduction:** In patients with syncope and bifascicular block (BBF), syncope is likely to be attributable to paroxysmal atrioventricular block (AVB). Therefore, a pacemaker implantation is recommended by current guidelines. However, it remains unclear if and at which time point a permanent blockade of atrioventricular (AV) conduction occurs and if pacemaker with AV management are useful in these patients.

**Methods:** 106 patients with either syncope with bifascicular block (group 1, n = 34) or paroxysmal AVB with (group 2, n = 51) or without BBF (group 3, n = 21) were included in the study. All patients received a pacemaker with AAI-SafeFit™, Symphony®, Sorin SPA, Milano, Italy) and were follow-up in a six-months-interval (mean follow-up 20±2 months). The primary end-point was the time to permanent switch to DDD-, DDI-, or VVI-mode.

**Results:** 46% of patients in group 1, compared to 70% in group 2 and 77% in group 3 had episodes of intermittent switches to ventricular pacing modes (p=0.065). Proportion of ventricular pacing was significantly higher in group 2 (40%) and group 3 (32%) compared to group 1 (17%) (p=0.02). The primary end-point occurred in 16% patients in group 1, 56% patients in group 2, and 53% patients in group 3 (p=0.001). Time to primary end-point was not significantly different between the groups (17.5±12.3 vs. 11.3±3 months; p=0.633). Documented paroxysmal AVB before pacemaker implantation was a significant predictor of the primary end-point (hazard ratio 4.86; 95% confidence interval 95% CI: 1.88-12.5; p=0.01). No other clinical or electrophysiological variables were predictive for the primary end-point.

**Conclusion:** Only 16% of patients with syncope and bifascicular block lose permanent AV conduction compared to 56% of patients with paroxysmal AVB.

**Prevalence of depression syndrome in patients with vaso-vagal syncope**

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The aim of study was analysis of factors influencing on the prevalence of depression syndrome (DS) in patients with vaso-vagal syncope (VVS). **Study population:** We observed 650 pts (386 women, 264 men) aged 18-72 (median of age 41.5yrs, with VVS referred to head-up tilt test (HUTT).

**Methods:** All pts underwent HUTT performed acc. to standard Westminster or Italian protocols. Before HUTT the Depression Beck Score questionnaire was applied to all pts for evaluation of presence of DS. Mild DS was diagnosed if Beck Score ranged between 10 and 19, mild 20-25 and severe SD – with Beck Score 26 and higher. During HUTT regional saturation (rSO2) of frontal lobes of brain was measured using INVOS cerebral oximeter in all pts. Changes of rSO2 during HUTT was expressed as a relative decrease (in%) of rSO2 in left and right channels in relation to the baseline value of rSO2. Univariate and multivariate analysis were performed for evaluation of the influence of age and gender, number of syncope and presyncope episodes, duration of disorder. **Conclusions:** 1. Depression syndrome is relatively frequent in patients with syncope. 2. Occurence of depression syndrome, in spite of age correlation, is also related to intensity of syncope and duration of the disorder and may be related to the type of vaso-vagal response to orthostatic stress during HUTT. 3. Cardioinhibitory response to the orthostatic stress during head-up tilt test occurred significantly more frequent in patients with diagnosed severe depression syndrome.

**The CHADS2 risk score predicts long-term outcome after first admission for syncope - A nationwide study**

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**Background:** The CHADS2 is an important risk stratification tool for risk of stroke in patients with atrial fibrillation and may also be predictive for other major cardiovascular events. We investigated if CHADS2 score could be applied as a risk stratification tool for predicting cardiac events after an episode of syncope.

**Methods and results:** All patients admitted with a first diagnosis of syncope from 2001 to 2009 who identified from nationwide administrative registers in Denmark. Risk of major cardiovascular events (acute myocardial infarction or implantation of pacemaker/ICD) and all-cause or cardiovascular death according to CHADS2 score was analyzed by multivariable Cox proportional-hazard models. A total of 88,355 patients were included (median age 64 years (IQR: 47.5-80.5) and 47.6% were males. There were a total of 19,011 deaths of which 10,389 (54.6%) were cardiovascular. The event rate of cardiovascular death was 5.25 per 1000 person-years for the group with CHADS2 score=0. The risk of cardiovascular death was significantly increased with increasing CHADS2 score when CHADS2 score was analyzed by multivariable Cox proportional-hazard models.

**Conclusion:** The CHADS2 score significantly predicts risk of cardiovascular death, all-cause mortality and major cardiovascular events in patients admitted with syncope, and may be used for risk stratification in combination with other risk score systems. A CHADS2 score of 0 is associated with a very low long- and short-term mortality.**
Purpose: To quantify the resource use associated with unexplained syncope in a real-world setting, before a clinical decision to implant an implantable loop recorder (ILR) was made.

Methods: PICTURE is a prospective, observational registry on Implantable Loop Recorders (ILR) and diagnostic tests for unexplained syncope, carried out in 570 patients at 83 sites in 11 EU countries. PICTUREEconomics is based on PICTURE and a UK micro-costing study to quantify the burden of investigation and understand actual 'bottom-up' costs of each test. The previous history of healthcare contacts and investigations were captured. Types and volumes of 17 predefined diagnostic tests were recorded. Patients then received ILRs and were followed until a symptomatic event or a clinically scheduled visit (35-65 months after implant).

Results: The mean number of tests before ILR implant was 17 (95% CI 16.08 – 17.04) while the median was 13 (IQ Range 9 – 20). The minimum number of diagnostics observed was 0 while the maximum was 203. Among the top 25% of healthcare resource users, the median tests were 27 (IQ Range 22–36). Based on the tag-on micro-costing study, the mean expenditure per patient was £1,613.15 (€1,879.5 – 95% CI £1,552.68 – £1,674.08). The median was £1,113.86 (€1,297.77 – IQ Range £568.97 – £2,426.22), while the costs escalate up to £7,417.89 (£8,642.66). The cost of a patient receiving every type of the 17 investigations once, including e.g. ECG, Holter, blood pressure provocation, TILT test, neurological evaluation, coronary angiography, MRI, CT, invasive testing etc., would have been £3,007.81 (€4,669.54). Should ESC Guidelines have strictly been adhered to (as was the case in 12% of the PICTURE Study population), the investigations to be highly significant and most patients having moderate consumption than suggested in guidelines. PICTUREEconomics showed the costs of implementing an ILR may be higher than suggested in guidelines. PICTUREEconomics showed the costs of implementing an ILR may be higher than suggested in guidelines.

Conclusions: Our data show a high incidence of artefact in the early phase after ILR implantation resulting in multiple recordings. Staff time to process, report and communicate data was 5.3 minutes per transmission.

Remote monitoring of implantable loop recorders: high artefact in the early phase following implant

Freeman Hospital, Newcastle upon Tyne, United Kingdom

Purpose: Implantable loop recorders (ILRs) are increasingly used in the investigation of unexplained syncope. Remote monitoring of ILRs has recently become available. We report our initial experience with the practical aspects of remote monitoring of ILRs.

Methods: For the period of August 2011, patients were offered remote monitoring using the Medtronic Carelink system at the time of Reveal XT ILR implant. Scheduled transmissions were planned weekly for 8 weeks, then monthly. Patients were asked to make scheduled transmissions after a symptomatic episode. Time taken to download, review and report results to patients was recorded. Data from existing patients using Carelink after Reveal implant was also analysed; these patients made ad-hoc transmissions.

Results: 19 patients were enrolled, mean age 49.5 years. 18 successfully made a test transmission; there were technical difficulties in 1 patient resulting in 4 missed transmissions. 2 other patients missed a total of 3 transmissions. 134 scheduled transmissions were made; 2039 automatically detected episodes were recorded, all false positives. The majority of the episodes occurred in 2 patients. 1570 episodes of asystole were recorded in 1 patient due to artefact as a result of the autogain feature. In another patient, 401 episodes were detected as AF due to frequent atrial ectopics. Staff time requirements are shown in Table 1. Three patients made recordings after symptoms but no abnormality was identified.

Nine patients already using Carelink sent ad-hoc/symptomatic transmissions only. 44 transmissions were received; 23 VT episodes in 1 patient and 2575 AF episodes in another patient; all were artefact, 9 symptomatic recordings were made; 1 patient received a pacemaker, all were artefact.

Conclusions: Our data show a high incidence of artefact in the early phase after ILR implantation resulting in multiple recordings. Staff time to process, report and communicate data was 5.3 minutes per transmission.

The influence of the menstrual cycle on the tilt testing result

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The fluctuation of the female sex hormones level may change the susceptibility to the neurocardiogenic reflex provocation throughout the menstrual cycle. The aim of the study was to assess the distribution of the positive tilt testing (TT) results through menstrual cycle as well syncope and presyncope and finally to determine if the phase of menstrual cycle contribute to the duration of the loss of consciousness during TT induced syncope.

Material and methods: The study group consisted of 138 premenopausal, women aged 29.5 ± 6.8 years. The menstrual cycle was divided into 4 phases based on the first day of the last menstruation (Premenstrual (P), Periovulatory (F), preovulatory (O) and postovulatory (L)). The clinical characteristics and TT results are shown in the table:

<table>
<thead>
<tr>
<th>Group</th>
<th>Premenstrual phase (M)</th>
<th>Periovulatory phase (F)</th>
<th>Periovulatory phase (O)</th>
<th>Postovulatory phase (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=49</td>
<td>n=56</td>
<td>n=54</td>
<td>n=39</td>
<td>n=41</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.4 ± 10.8</td>
<td>29.0 ± 10.2</td>
<td>30.0 ± 10.3</td>
<td>28.4 ± 7.4</td>
</tr>
<tr>
<td>Syncpe spells</td>
<td>2 (1.5)</td>
<td>3 (1.5)</td>
<td>4 (1.10)</td>
<td>4 (1.10)</td>
</tr>
<tr>
<td>Positive TT (%)</td>
<td>82 ± 9</td>
<td>89 ± 5</td>
<td>95 ± 5</td>
<td>85 ± 5</td>
</tr>
<tr>
<td>Syncope duration (sec)</td>
<td>41 ± 26</td>
<td>30 ± 10*</td>
<td>20 ± 15*</td>
<td>25 ± 12*</td>
</tr>
</tbody>
</table>

Conclusions: 1. The distribution of the positive and negative TT results as well syncope and presyncope as a TT result does not differ through the menstrual cycle. 2. The duration of the loss of consciousness is longer during perimenstrual phase of the menstrual cycle independently from the higher syncope number and lower heart rate at TT termination. 3. The fluctuation of the female sex hormones levels does not change the susceptibility to the neurocardiogenic reflex provocation but provoked influence on its course.

The cardiodepressive type of neurocardiogenic reaction was more frequently per-
PERCUTANEOUS CORONARY INTERVENTION: INVASIVE IMAGING/DEVICES AND TECHNIQUE

P4754

Head to head comparison of fully drug-free biodegradable PLA and bare metal stents in normal porcine coronary: a six-month angiography and OCT follow-up study

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Background: The concept of fully bioresorbable polyactic (PLA) stent is now perceived as a potential attractive alternative to metallic stent. The aim of this study is therefore to evaluate a drug-free PLA stent in the porcine model as compared to a bare metal stent (BMS).

Methods: Twenty-nine BMS (Vision®, Abbott, Inc: 3.12 mm) and 29 PLA stents (ART, Noisy le Roi, France, 3.11 mm) were implanted in porcine coronary arteries. QCA and OCT analysis were performed immediately after stent implantation, and repeated 1 (n=22), 3 (n=28), and 6 (n=6) months later. The primary end-point was in-stent diameter by OCT, and the secondary end-points were acute recoil and late lumen loss (LLL).

Results: Acute recoil was not significantly different between PLA and BMS groups (3.6±0.2% vs. 4.7±5.3%, respectively, p=NS). In-stent diameter was closely similar immediately after stent implantation in PLA and BMS groups (2.99±0.08 mm vs. 3.05±0.18 mm, respectively). BMS in-stent diameter remained constant throughout 6-month follow-up (2.99±0.21, 2.95±0.21, 3.14±0.21 mm at 1, 3, and 6 months, respectively). In contrast, in-stent diameter significantly increased at 3 and 6 months in the PLA group indicating late positive remodeling (2.87±0.08, 2.99±0.10, 3.13±0.08 mm at 1, 3, and 6 months, respectively). Similarly, LLL was initially significantly higher in the PLA group (0.08±0.14 mm vs. 0.16±0.23 mm, p=NS). However, LLL significantly increased at 3 and 6 months in the PLA group indicating late positive remodeling (2.87±0.08, 2.99±0.10, 3.13±0.08 mm at 1, 3, and 6 months, respectively). In contrast, in-stent diameter significantly increased at 3 and 6 months in the PLA group indicating late positive remodeling (2.87±0.08, 2.99±0.10, 3.13±0.08 mm at 1, 3, and 6 months, respectively). In contrast, in-stent diameter significantly increased at 3 and 6 months in the PLA group indicating late positive remodeling (2.87±0.08, 2.99±0.10, 3.13±0.08 mm at 1, 3, and 6 months, respectively).

Conclusions: OCT and QCA analysis of bare PLA stent indicated favorable 6-month outcomes as compared to BMS in porcine coronary arteries. Interestingly, PLA strut degradation is associated with positive remodeling at 3-6 months, and late lumen gain.

P4757

Nine months optical coherence tomography evaluation of neointimal coverage of a strategy of paclitaxel-eluting balloon plus bare metal stent

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Background: Drug-eluting balloon (DEB) predilatation followed by bare metal stent (BMS) implantation represents an innovative treatment for coronary artery disease. Yet, the safety of this strategy has still to be demonstrated.

Methods: Frequency-domain optical coherence tomography was performed at 9 months in a registry of 30 consecutive patients who underwent elective stenting with a BMS (Prokinetic, Biotronik) after predilatation with a DEB (Elutax, Aachen Resonance). Patients with clinical restenosis (n=3), or with suboptimal images (n=4) were excluded. Quantitative strut level analysis was performed at 0.4-mm intervals (every other frame) along the entire target segment. A total of 23 lesions in 23 patients were analyzed. The center of the luminal surface of the strut blooming was determined for each strut, and its distance to the lumen contour was calculated automatically to determine strut-level intimal thickness (SIT). Struts covered by tissue had positive SIT values whereas uncovered or malapposed struts had negative SIT. The number of struts without coverage was counted for each frame analyzed, and the total number of frames with uncovered struts was recorded. Strut malapposition was determined when the negative value of SIT was higher than 100 micron (60). Proximal strut thickness, plus a correction factor of 40μ, to account for strut blooming).

Results: A total of 4304 struts were analysed. In total, 131 struts (3%) in only 2 lesions (123 in one, 8 in the other) were found to be uncovered. Malapposed struts were 105 (2.4±3.2%). Percentage net volume obstruction was 30.2±5.6%.

Conclusions: BMS implantation plus DEB is a safe strategy, as it is associated with a percentage of malapposed/uncovered struts which compared favourably with BMS historical controls. Neointimal regrowth (after the exclusion of clinical restenosis patients) is also comparable to historical data.

P4758

Intravascular ultrasound guided everolimus eluting stent implantation resolves the disadvantage of thin strut cobalt chromium platform in patients with diabetes


Background: Though efficacy of everolimus-eluting stent (EES; Xience V) is well-established by many clinical evidences, several trials failed to show superiority in diabetic subset. We hypothesized that inappropriate stent expansion in complex lesion of diabetes due to thin cobalt chromium platform may be one of the reasons. The purpose of this study is to investigate this hypothesis using intravascular ultrasound (IVUS).

Method: Consecutive 130 de-novo lesions (61 EES and 69 paclitaxel-eluting stent (PES; Taxus Express2, stainless steel thick platform)) treated by elective IVUS-guided PCI for stable patients were recruited in this study. Stent size was determined according to pre-procedural IVUS findings. After stent deployment using standard technique, IVUS procedure was repeated and stent diameter and cross-sectional area (CSA) were measured. If stent expansion was inadequate,
post dilation was performed using short-length high pressure balloon and again IVUS was performed. IVUS findings were then compared with estimated diameter and CSA calculated from each stent compliance chart.

**Result:** In EES, there were significant differences of stent expansion and symmetry index between diabetic and non-diabetic just after stenting. However, these findings were not observed in PES. According to IVUS findings, 75% of diabetic cases in EES group required post balloon dilation to obtain optimal stent expansion. After post dilation, difference between diabetic and non-diabetic did not appear in EES.

**Conclusion:** In EES, asymmetrical stent underexpansion was observed in diabetic patient after stent deployment, however, IVUS-guided post-dilation resolved this disadvantage. IVUS-guided EES implantation can improve clinical outcome in patients with diabetes.

### Table 1. Results

<table>
<thead>
<tr>
<th></th>
<th>IVUS Findings</th>
<th>EES (N=61)</th>
<th>P</th>
<th>EES (N=61)</th>
<th>P</th>
<th>PES (N=69)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum/Estimated stent diameter (mm²)</td>
<td>0.715 0.776 0.002 0.794</td>
<td>0.867 0.52 0.757 0.776</td>
<td>0.34 0.835 0.823 0.56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum/Estimated CSA (mm²)</td>
<td>0.633 0.700 0.019 0.734</td>
<td>0.748 0.61 0.680 0.722</td>
<td>0.13 0.799 0.786 0.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symmetry index</td>
<td>0.802 0.855 0.007 0.842</td>
<td>0.842 0.21 0.842 0.835</td>
<td>0.72 0.866 0.859 0.66</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Results

<table>
<thead>
<tr>
<th></th>
<th>BMS (n=15)</th>
<th>SES (n=19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of OCT imaging after stent implantation, month*</td>
<td>100±23</td>
<td>33±14</td>
<td>0.011</td>
</tr>
<tr>
<td>Lipid-rich neointima, n (%)</td>
<td>13 (87) 15 (79)</td>
<td>0.558</td>
<td></td>
</tr>
<tr>
<td>TCF-like neointima, n (%)</td>
<td>7 (73) 7 (73)</td>
<td>0.633</td>
<td></td>
</tr>
<tr>
<td>Micro-channels, n (%)</td>
<td>11 (73) 12 (63)</td>
<td>0.521</td>
<td></td>
</tr>
<tr>
<td>Neointimal disruption, n (%)</td>
<td>9 (60) 6 (32)</td>
<td>0.096</td>
<td></td>
</tr>
<tr>
<td>Thrombus, n (%)</td>
<td>9 (60) 7 (37)</td>
<td>0.179</td>
<td></td>
</tr>
<tr>
<td>Stent malaposition, n (%)</td>
<td>0 (0) 5 (26)</td>
<td>0.032</td>
<td></td>
</tr>
<tr>
<td>Calcification within neointima, n (%)</td>
<td>3 (20) 0 (0)</td>
<td>0.041</td>
<td></td>
</tr>
</tbody>
</table>

Values are given as n (%) or *mean ± SD. BMS = bare-metal stent; OCT = optical coherence tomography; TCF = thin-cap fibroatheroma.

### Conclusion:

In late clinical event related lesions, atherosclerotic change such as TCFA formation and calcification within neointima is often demonstrated in BMS and stent malaposition might be related in DES.
Sex-related differences in percutaneous coronary interventions for chronic total occlusions

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Purpose: The aim of this study was to assess sex-differences in percutaneous coronary intervention (PCI) for chronic total occlusions (CTO).

Methods: The study included all consecutive patients undergoing PCI for CTO at 3 tertiary PCI centres between January 2004 and December 2011. A multivariable mixed effect logistic regression for clustered data was used to assess the impact of female sex on PCI success after adjustment for clinical and procedural characteristics, CTO lesion difficulty, vessel size, and procedural techniques. CTO lesions were graded as easy (score of 0), intermediate (score of 1), difficult (score of 2), and “very difficult” (score of ≥3), according to the J-CTO score on the basis of calcification, bending, blunt stump, occlusion length ≥20 mm, and previously failed lesion.

Results: Among 1261 patients, median age 63 yrs-old (25th-75th percentile, 55-72), undergoing PCI for 1418 CTO, 176 (13.9%) were women. Women, as compared to men, were significantly older (70.5 yrs-old (61-77) vs 62 (55-72), more frequently diabetics (33.5% vs 26.1%, p=0.04), hypertensive (71.0% vs 56.8%, p=0.04), less frequently smoker (15.3% vs 28.8%, p=0.001), and had less frequent a previous coronary artery bypass graft surgery (2.8% vs 8.1%, p=0.01). In a lesion-based analysis, left anterior descending artery as the treated vessel, was more common (36.5% vs 26.4%) and left circumflex artery was less frequent (15.6% vs 23.8%) among women (p=0.03). The prevalence of J-CTO score ≥3, according to the J-CTO score on the basis of calcification, bending, blunt stump, occlusion length ≥20 mm, and previously failed lesion.

Conclusion: The newly developed covered stents performed well in terms of creating less intramural hyperplasia and in the embolization effect without disturbing branching vascular flow.
Germany) followed by bare-metal CoCr stent implantation (Prokinetic, Biotronik, Berlin, Germany) (PEB-CoCr-stent group) versus implantation of everolimus-eluting stent (Xience, Abbott Vascular, Redwood City, CA) (DES group) in the treatment of de-novo stenosis in native coronary artery.

Methods: The study, randomized, single center, was planned to enroll 366 pa-
tients, 188 patients per arm, with stable angina, undergoing percutaneous coro-
nary intervention of a de-novo stenosis less than 15mm in length in a native coronary artery. Primary endpoint, in a non inferiority study design, was 9-month binary angiographic restenosis. Combined antiplatelet treatment was to be con-
tinued for 3 months in PEB-CoCr stent group and 12 months in DES group.

Results: The study was stopped after enrollment of 125 patients, 59 in the DEB group and 66 in the DES group, due to excess of Target Lesion Revascularization (TLR) in the PEB group (14% in the PEB vs 2% in DES group; p=0.001). No significant differences in terms of clinical or angiographic characteristics were observed among the two study groups. No stent thrombosis occurred in both study groups.

Conclusion: In the treatment of de-novo coronary stenosis, a strategy of predi-
lration with Elutas PEB prior to bare-metal CoCr stent implantation was signif-
ically inferior to implantation of Xience stent in terms of 9-month target lesion revascularization.

Differential determinants of early stent thrombosis in drug-eluting and bare metal stents: ex vivo human autopsy study

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Background: Early stent thrombosis (ST) in patients with acute coronary syn-
drome (ACS) remains an ongoing problem for both drug-eluting stents (DES) and bare metal stents (BMS) where potential mechanisms associated with stent placement relative to underlying lesion histology are not well ad-

dressed.

Methods and Results: Stented lesions (n=62) from 59 patients presenting with ACS and dying within 30 days were eligible for the histological assessment. His-
tologic cross-sections prepared at 3 mm intervals were evaluated for stent throb-
mas, strut malapposition, media disruption, and necrotic core prolapse in addition to other potential indicators of early ST such as the underlying plaque morphology and vessel/lesion area. Early thrombosis was identified in 17 of 45 drug-eluting and 20 of 37 bare stents. There were no significant differences in the stented artery or relative location within the vessel with usage of DES versus bare BMS. In a “per section” analysis, 58 of 293 sections from DES showed evidence of luminal thrombosis compared with 62 of 287 section from BMS. Stut malapposition was similarly seen for DES with or without early ST, respectively (29% vs. 26%, p=0.60) while the incidence for BMS was significantly greater in those with early ST (37% vs. 19%, p=0.04). On the contrary, media disruption was more likely associated with thrombosis for DES (39% vs. 18%, p<0.002) while difference among BMS was of borderline signif-
icance (19% vs. 11%, p=0.08). Necrotic core prolapse was significantly higher for DES exhibiting thrombosis (26% vs. 13%, p=0.018) while no significant differ-
ce was noted for DES (16% vs. 10%, p=0.25).

In morphological analysis, the percentage of struts with underlying medial disrup-
tion (18% (thrombus) vs. 25.4% (no thrombus), p=0.001) was the fore-
most predictor of early ST for DES while for BMS strut malapposition (31:16 (thrombosis) vs. 21:10 (no thrombosis), p=0.006) and strut penetration into the necrotic core (28.13% (thrombosis) vs.16.10% (no thrombosis), p=0.002) were more likely correlated with early ST.

Conclusions: Autopsy data indicate divergent mechanisms of early ST between DES and BMS in ACS patients. The results suggest that further modification(s) of stent design may overcome the problem of early ST associated with current devices, which should improve early clinical outcomes of ACS patients treated by interventional means.

Thin-strut stent is favorable for severe calcified lesion needing rotational atherectomy in real world

Percutaneous Coronary Intervention


Background: Percutaneous coronary intervention (PCI) on severe calcified le-
sion is still challenging. There are a few studies about outcomes after PCI with drug-eluting stents (DES) on severe calcified lesion. The aim of this study is to clin-
ically prove if feasible thin- or thick-strut stents to calcified lesion after rotational atherectomy including hemodialysis patients and long lesion.

Methods: Sixty-six consecutive patients (115 stents) with DESs for severe calc-
fied lesions which needed rotational atherectomy before stent implantation were enrolled. We divided them into the following two groups according to strut-thickness: thin-strut group (strut-thickness: ≤100μm) and thin-strut group (>100μm). Follow-up angiography was performed at 6 to 10 months after PCI. We compared late lumen loss by quantitative coronary angiography and target vessel revascularization (TVR) rate, in addition to incidence of hemodialysis, di-
abetes mellitus, hypertension and dyslipidemia, and stent size, lesion length and num-
er of stents, between the two groups.

Results: TVR rate was significantly lower in thin-strut group than in thick-strut group while there were no differences of the other parameters between two groups.

Conclusions: Angiographic outcomes of EES and SES were similar. However, restenotic pattern and detrimental findings such as stent fracture and PSS were different between the 2 groups.

Stent maximal expansion capacity with current DES Results: A platform critical factor for left main stent selection?

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Coronary stents are usually manufactured in only 2 or 3 different “Workhorse"
Is there an advantage in using second vs. first generation drug eluting stents in acute coronary syndromes?

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Purpose: Registry series and RCTs show that DES have an overall better performance than BMS in patients treated in the clinical context of an acute coronary syndrome (ACS), both STEMI and NSTEMI/UA, mainly by reducing TLR. Whether or not the use of 1st generation DES (DES1g) versus 2nd generation DES (DES2g) differs in this particular setting is largely unknown.

Methods and analysis: In a single center prospective registry, 3266 patients were submitted to PCI with at least 1 DES from January 2003 to December 2009. Of these, 1423 (43.6%) were treated in the setting of an ACS with either DES1g only (paclitaxel or sirolimus; n=903 [64.9%]) or DES2g only (n=520 [35.1%]). The primary outcome measure was the occurrence of death, myocardial infarction (MI) or target vessel failure (TVF), whichever came first; repeat revascularization of the index stented lesion (TLR) and the occurrence of definite stent thrombosis (ac- cording to the ARC definition) were assessed as secondary outcomes. At a median follow-up of 598 days (IQR range 453; 1206), the incidence of death was 8.8% (286), 220 pts (6.7%) had MI and TVF events occurred in 349 (10.7%). Disparity of follow-up duration was accounted for by considering only one year outcome as compared with T-stenting. (single stenting with final “kissing balloon”-dilatation) is associated with similar 1 year outcomes as compared with T-stenting.

Conclusions: Our results suggest that in patients submitted to PCI with DES implantation in the setting of acute coronary syndromes, both 1st and 2nd generation devices seem to be similarly effective, despite a statistically higher incidence of ARC-defined stent thrombosis with 1st generation DES.

One-year outcome after PCI for distal left main stenosis treated with single stenting or with T-stenting


Background: Percutaneous treatment (PCI) of distal left main bifurcation may in-volve stenting of the main branch including final kissing balloon of the side branch or single stenting of both branches. There is only limited data comparing single stenting including final kissing-dilatation versus T-stenting regarding the long term clinical follow-up.

Hypothesis: We tested the hypothesis that the lesions that were treated with the single stent have a lower target lesion revascularisation (TLR) 1 year after PCI than lesions treated with T-stenting.

Methods: We established a bifurcation registry of 394 consecutive patients undergoing percutaneous catheter intervention (PCI) for distal left main stenosis in our institution between January 2002 and December 2009. One stent approach was performed in 229 patients and T-stenting in 165 patients. The need for double stenting to achieve best angiographic result was 42%. Complete 1 year clinical follow-up of all patients is available for the analysis.

Results: Baseline clinical characteristics were well matched between 2 groups. Target lesion revascularisation (TLR) 1 year of EC and SMG was non-inferior. In a per-patient analysis, at one year, ARC-defined stent thrombosis was documented in 1% of DES2g vs 2.8% of DES1g pts (corrected HR 0.37; 95% CI 0.14-0.97; p=0.042), owing mostly to a higher difference in non-acute ST.

Conclusions: PCI of de-novo distal left main stenosis using simple approach (single stenting with final “kissing balloon”-dilatation) is associated with similar 1 year outcome as compared with T-stenting.
Drug eluting stents with microporous polymeric covering as a scaffold for acquisition of extremely thin neointimal lying without disturbing branching vascular flow

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Objective: As new generation of drug eluting stents, we developed microporous polymeric-covered stents, whose design concept was utilization of covering for a scaffold for extremely thin neointimal lying. The effectiveness was demonstrated in this study for long-term animal experiments.

Methods and Results: Two types of covered stents based on different stent platforms of self-expandable stents (Luminexx from Bard Co.; 5 mm x 20 mm) and balloon-expandable stents (Momo from Japan Stent Technology Co.; 3 mm x 20 mm) were prepared in three steps, that is 1) dip-coating of polyurethane for covering, 2) laser-induced microporizing, and 3) drug coating with argatroban. The stents had structural advantage with flat luminal surface impregnating strut completely into the cover film. The stents were placed at carotid or subclavian arteries of beagle dogs or rabbits. Even at 1 month of implantation (n=3) the luminal surface was fully endothelialized. Extremely thin neointima (n=19; thickness: 187±39 nm) was observed at 1 year of implantation, which was about half of that in non-covered bare stents. The thin and stable neointima continued up to 3 year of implantation (n=15). The covered stents could maintain the branching microvascular flow perfectly due to microporing of cover film. Argatroban had strong anti-thrombogenic and anti-inflammation potentials.

Conclusion: Argatroban-loaded microporous covered stents developed here were effective for in short-term lying of extremely thin neointima with long-term highly reliability.

Comparison of 3-year clinical outcomes between classic crush and modified mini-crush technique in coronary bifurcation lesions

H.M. Yang, S.J. Tahk, S.Y. Choi, H.S. Lim, M.H. Yoon, B.J. Choi, J.W. Seo, J.W. Kim, G.S. Hwang, X. Jie. Ajou University Medical Center, Suwon, Korea, Republic of

Purpose: We aimed to compare long-term outcomes of modified mini-crush (modi-MC) technique with classic crush (Crush) technique for treating coronary bifurcation lesions. Modi-MC technique showed excellent procedural success immediately and good 9-months clinical outcomes. We compared 3-year clinical outcomes between 2 techniques.

Methods: From Jan 2000 to Nov 2009, we enrolled de novo bifurcation lesions treated with modi-MC (n=112 lesions in 111 patients) and crush technique (n=69 lesions in 67 patients). Primary end-point was major adverse cardiac events (MACE), composite of all-cause death, myocardial infarction (MI), target lesion revascularization (TLR) and stent thrombosis at 3 years.

Results: There were no significant differences in baseline characteristics. After 3 years, MACE was significantly lower in modi-MC group (25.4 vs 13.5%, p=0.046). The incidence of all-cause death was 7.5% vs. 2.7% (p=0.16), MI was 4.5% vs. 0.9% (p=0.15), TLR was 17.4% vs. 8.9% (p=0.09) and stent thrombosis was 3% vs. 1.8% (p=0.63) in Crush and modi-MC group, respectively. However, MACE of left main (LM) lesion was significantly higher than non-LM bifurcation (32.7% vs. 12.9%, p=0.001) in entire cohort. Cox regression analysis showed LM location (p=0.002, odds ratio: OR) 3.031, 95% confidence interval [CI] 1.528-6.021, and crush technique (p=0.044, OR 2.035, 95% CI:1.018-4.069) were independent predictors for MACE.

Conclusions: Modified mini-crush technique was more effective 3-year clinical outcomes comparing with classic crush technique. However, both classic crush and modified mini-crush techniques are cautiously applied in LM bifurcation lesion.
PERCUTANEOUS CORONARY INTERVENTION OUTCOMES

**P4780**

Impact of circadian variations on long-term clinical outcomes in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

J.B. Choi, K.S. Cha, M.J. Park, E.Y. Yun, H.W. Lee, J.H. Oh, J.H. Choi, H.G. Lee, T.J. Hong, S.G. An on behalf of the Korea Acute Myocardial Infarction Registry. Pusan National University Hospital, Busan, Korea, Republic of

**Purpose:** The circadian rhythm influences a number of cardiovascular physiological processes including the incidence of acute myocardial infarction. A circadian variation in infant size has recently been shown in rodents, but there is no clinical evidence of its influence on long-term outcomes. The aim of this study is to investigate whether circadian rhythm could cause differences in long-term clinical outcomes in patients with STEMI.

**Methods:** A total of 3,581 STEMI patients with less than 12 hours of symptom onset were obtained from the Korea Acute Myocardial Infarction Registry and divided into 4 time groups based on time of symptom onset (period I: 00:00-05:59, period II: 06:00-11:59, period III: 12:00-17:59, and period IV: 18:00-23:59). The primary outcome was the composite of major adverse clinical events (MACE), defined as death, non-fatal myocardial infarction, and revascularization, at one-year follow-up.

**Results:** There was no difference between groups regarding baseline patient characteristics, angiographic findings, and procedural results. There was significant difference between groups regarding symptom-to-door time and door-to-balloon time with highest levels in patients with symptom onset of period I (251.7±182.1 min, p<0.001; 107.4±62.6 min, p=0.001, respectively). However, there was no significant difference between groups regarding maximum CK-MB and left ventricular ejection fraction. Total death and MACE were not different between groups during hospitalization (period I: 4.9%, period II: 5.1%, period III: 5.1%, period IV: 5.8%, p=0.410; period I: 5.9%, period II: 5.4%, period III: 4.4%, period IV: 5.2%, p=0.062, respectively) and at one-year (period I: 8.0%, period II: 8.6%, period III: 5.8%, period IV: 7.7%, p=0.103; period I: 5.9%, period II: 5.4%, period III: 4.4%, period IV: 5.1%, p=0.410). There was no significant difference in the incidences of death or MI, target lesion revascularization between two groups. The incidence of revascularizations for new lesions was significantly higher in patients with MIA than those without MIA (13.6% vs 38.5%, p<0.0019). Independent predictor of cardiac events identified by Cox proportional hazard model was MIA (hazard ratio 2.54; 95% CI: 1.20-3.53; p=0.014) after adjusted for age, gender, and conventional risk factors.

**Conclusions:** Event-free survival was significantly higher in patients without MIA as compared to patients with MIA (74.1% vs 51.3%, p=0.012, log-rank test, Figure). There was no significant difference in the incidences of death or MI, target lesion revascularization between two groups. The incidence of revascularizations for new lesions was significantly higher in patients with MIA than those without MIA (13.6% vs 38.5%, p<0.0019). Independent predictor of cardiac events identified by Cox proportional hazard model was MIA (hazard ratio 2.54; 95% CI: 1.20-3.53; p=0.014) after adjusted for age, gender, and conventional risk factors.

**Methods:** The elevated urinary albumin excretion rate is an independent predictor of adverse cardiovascular outcomes in patients with mild renal dysfunction who underwent PCI.

**Results:** Median adiponectin level was 17±4 g/ml (25-75th percentile: 13-21 g/ml). The primary endpoint occurred in 76 patients (15.9%). TLR was undertaken in 25 patients (9.2%). Female gender, higher body mass index (BMI), and BMI less than 25 kg/m² were independent predictors of adverse outcomes (BMI: OR=2.67 [95% CI: 1.07-6.61], p=0.038). Median adiponectin level was associated with in-hospital and long-term outcomes in patients with STEMI. Adiponectin is considered to possess antiatherogenic and cardio-protective properties. In patients undergoing percutaneous coronary intervention (PCI), the prognostic value of pre-procedural total adiponectin is unknown. The present study was designed to address this issue.

**Methods:** From March 2006 to September 2007, pre-procedural total adiponectin levels were measured in 477 consecutive patients who underwent PCI for primary percutaneous coronary intervention (PCI) with a median follow-up of 3.7 years. Patients presenting with acute STElevation myocardial infarction (STEMI) were excluded. The primary endpoint was the composite of death, non-fatal MI or stroke. Target lesion revascularization (TLR) was also examined.

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Comparison on 1-Year MACE of everolimus-eluting stent Xience vs sirolimus-eluting stent cypher in diabetic patients

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Background: To expand the paucity of data on the efficacy of sirolimus-eluting stents (Cypher, Cordis, Bridgewater, NJ) vs everolimus-eluting stent (Xience, Abbott Vascular, Redwood City, CA) in diabetic patients.

Methods: Due to Tuscany Regional Medical Authority, Cypher stent was no more available after December 2008 and replaced by Xience stent. We collected the data of all-comers type 2 diabetic patients presenting with de novo or in-stent restenosis lesions in native coronary arteries treated in our institution from January 2003 to November 2008 (Cypher period) and from December 2008 to May 2010 (Xience period). The primary end point was the 1-year composite of major adverse cardiac events (MACE), including cardiac death, myocardial infarction (MI), and clinically driven target vessel revascularization (TLR).

Results: During the study periods, 440 lesions in 256 patients were treated with Cypher stent and 420 lesions in 212 patients with Xience stent (p=0.5). There were no significant differences among the two study groups except for previous myocardial surgical revascularization (8.6% in Cypher group vs 4% in Xience group, p=0.03) and stent length (22.4±8.7 vs 20.3±8.7 respectively, p=0.004). MACE-free survival was 89% in the Cypher group and 88% in the Xience group (p=0.7). Cardiac death occurred in 3 (1.2%) Cypher vs 4 (1.9%) Xience patients (p=0.7). MI in 4 (1.9%) vs 4 (1.9%) respectively, TLR in 27/440 (8%) Cypher vs 25/420 (6%) Xience lesions (p=0.2). Stent Thrombosis (ST) confirmed by angiography occurred in 2 (0.8%) Cypher vs 1 (0.5%) Xience patients (p=0.7).

Conclusion: The present study suggests that in diabetic patients, the Cypher stent is associated with a similar 1-year MACE rate when compared with Xience stent. Longer follow-up will evaluate the impact of the two stent in the occurrence of ST.

EPC capture stent and CD34+ mobilization in acute myocardial infarction

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Background: Percutaneous revascularization is the gold standard for the treatment of acute myocardial infarction (AMI), with the main limitation of in-stent restenosis for BMS and late stent thrombosis (ST) for both BMS and DES. Endothelial progenitor cells (EPC) CD34+ capture stents, promoting vascular healing, may be advantageous in preventing ST. The role of EPC on restenosis and atheromasic disease progression is unclear. The aim of the study is to evaluate the outcomes of AMI patients treated with EPC CD34+ capture stent and describe the mobilization kinetics of CD34+ and their clinical correlation.

Methods: 50 AMI patients underwent primary PCI with EPC CD34+ capture stent. Serial assays of CD34+ were performed by flow-cytometric analysis. Primary outcome was occurrence of death, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), stent thrombosis, and major adverse cardiac events (MACE).

Results: Procedural success rate was 100%. At six months follow-up cardiac death, MI, TLR and TVR occurred respectively in 2%, 4%, 10% and 12% of patients. No case of ST was observed. The MACE-free survival was 82%. The mean peak value of plasmatic CD34+ was 4.69±3.76 cells/l. A positive correlation was found between CD34+ concentration, age and infarct area. No correlation was detected between CD34+ concentration and occurrence of TVR, TLR and MACE.

Conclusions: EPC capture stent implantation seems to be safe and effective in the clinical setting of AMI, representing a possible alternative to BMS and DES. CD34+ cells plasmatic concentration seems not to correlate to coronary restenosis and atheromasonic disease progression.

Developments in the last ten years - LHC and PCI

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Conclusion: More patients were diagnosed and treated in 2010, who were older and in worse condition (ACS). The stent rate has increased and most of the procedures are performed ad hoc, there has been a trend in decision making from heart surgery to PCI.

Multivessel versus culprit lesion percutaneous coronary intervention in ST-elevation myocardial infarction: is more worse?

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Introduction: Existing data on the benefits of multivessel versus culprit lesion PCI during acute STEMI elevation myocardial infarction (STEMI) are conflicting.

Methods: We compared outcomes between STEMI patients with multivessel disease treated with multivessel PCI versus those treated with culprit lesion only PCI who were enrolled in the national AMIS Plus registry of Switzerland from 2005 to 2011. Baseline characteristics of these groups were assessed using Student t-tests and chi-squared tests while multivariable logistic regression models were used to evaluate differences in in-hospital outcomes.

Results: From 11,099 STEMI patients who presented during this study period, we identified 4559 patients (41%) with multivessel disease (including 5.6% with main stem) who underwent PCI. Among these, 3541 patients (78%) were treated with culprit lesion PCI only while 1018 patients (4.7% p=0.001) received ≥2 vessels treated with multivessel PCI during their STEMI. Patients who underwent multivessel PCI had higher rates of cardiopulmonary resuscitation prior to admission (3.8% vs 5.8%; p=0.007) and Killip class >2 (12.0% versus 5.9%; p<0.001). Immediate drugs, such as glycoprotein IIb/IIIa inhibitors, beta-blockers, ACE inhibitors or angiotensin receptor blockers, and statins were used less frequently in this group. Unadjusted rates of in-hospital events were higher among patients treated with multivessel PCI with nearly double the rate of cardiogenic shock (7.5% versus 4.7%; p=0.001) and in-hospital mortality (7.4% versus 4.4% p<0.001) compared to the patients treated with culprit lesion PCI only. However, after adjusting for age, gender, Killip class and co-morbidities, the risk of in-hospital mortality after multivessel PCI was similar in both groups (adjusted odds ratio 1.28: 95%CI 0.92-1.79; p=0.14).

Conclusion: STEMI patients with multivessel disease who undergo multivessel PCI are sicker than those who undergo culprit lesion PCI only. After multivariable adjustment, multivessel PCI was not independently associated with worse in-hospital mortality.
Impact of successful thrombus retrieval during primary percutaneous coronary intervention with thrombus aspiration on the infarct size and microvascular obstruction: a magnetic resonance imaging study


Background: Thromboaspiration (TA) during primary percutaneous intervention (PCI) is effective in opening the infarct-related artery in patients with ST-segment elevation myocardial infarction (STEMI), leading to better reperfusion and improved outcome. However, the effect of positive macroscopic efficiency of TA remains unknown. We aimed to evaluate the impact of positive thrombus retrieval during PCI with manual TA on infarct size (IS) and microvascular obstruction (MVO) as assessed by contrast-enhanced magnetic resonance imaging (CE-MRI) in a subset of patients with STEMI.

Methods: Inclusion criteria were patients aged <75 years, with first STEMI referred for PCI within 12 hours of onset of symptoms, infarct-related artery ≥2.5 mm in diameter, thrombus score ≥3 and no prior history of coronary disease. All patients underwent TA before stenting and were categorized according to positive or negative TA. Clinical and procedural characteristics of the study population and CE-MRI were performed at 5 days and 6-months to evaluate MVO and IS.

Results: 88 patients were enrolled, mean age 55±10 years; 43% in the positive TA group. Main results are presented in the table. Clinical and procedural characteristics (90-min total ischemic time, STE-segment resolution, post-procedural TIMI flow grade and post-stenting microvascular blush grade, and peak troponin) did not differ significantly between groups. Independent predictors of final IS were: positive TA (OR 0.34, 95%CI 0.30-0.71), MVO (OR 1.75, 95%CI 1.28-2.71) and IS at 5 days (OR 2.06, 95%CI 1.87-3.32).

Conclusion: Positive thrombus retrieval during primary PCI with manual TA in STEMI reduces MVO and IS at 5 days and 6 months and represents a powerful predictor of final infarct size.
Lack of gender difference and improved in-hospital mortality rates in patients with cardiac shock following primary percutaneous coronary intervention: a UK tertiary cardiac centre registry study

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Background: Despite substantial recent improvement in mortality from cardiovascular disease due primarily to success of primary and secondary prevention strategies, it remains the leading cause of death in the developed world. Among those patients hospitalized with acute myocardial infarction (AMI), cardiogenic shock (CS) is the foremost cause of death complicating up to 10% of admissions. Introduction of early revascularisation strategies and mechanical ventricular support have seen short-term mortality due to CS fall from 70-80% in the 1970s to around 50-60% in the 1990s. Previous studies suggest that women experience more CS than men (11.6% vs. 8.3%) in the setting of ST elevation MI. Whether primary percutaneous coronary intervention (PCI) for AMI has resulted in further reduction in in-hospital mortality and whether there are gender differences in outcomes due to CS is not known.

Aims: The aim of this study is to determine the rate of in-hospital mortality following primary PCI in the setting of CS and examine the gender differences in the incidence of CS and the rate of in-hospital mortality.

Methods: Data were collected prospectively among all patients presenting with AMI to a large UK tertiary cardiac centre and undergoing PCI between April 2008 and October 2011.

Results: In total 2866 patients (male: 2023 [70.6%] vs. female: 843 [29.4%]) underwent PCI. In total, 141,286 (4.9%) had percutaneous coronary procedures (balloon angioplasty only or stenting) in the setting of cardiogenic shock. There were 81/2023 (4%) male patients and 60/843 (7.1%) female patients with CS undergoing PCI. There were no significant differences in the baseline characteristics between male and female patients except female patients were older than men (male: mean age 64.1 years vs. female 69.5 years, p=0.004). The overall unadjusted in-hospital mortality rate was 35.4% with no difference in the genders (male: 35.8% vs. female: 35%, p=0.730).

Conclusion: The present analysis demonstrates that in the PCI era, there is reduction in the incidence of cardiogenic shock with reduced unadjusted in-hospital mortality rates following primary PCI. The unadjusted in-hospital mortality rates did not differ between the genders despite the fact that there were more women that had presented with cardiogenic shock.

In hospital clinical outcome of patients with definite stent thrombosis

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Background: The outcome of patients with angiographically proven stent thrombosis is only insufficiently known. We sought to evaluate presentation and outcome of patients with angiographically proven stent thrombosis.

Methods: 76 consecutive patients (mean age 69.12 years: 58 male with 81 angiographically proven stent thrombosis between 2003 and 2010 were included in the analysis. The time interval between initial stent implantation, rate of dual antiplatelet therapy at presentation with stent thrombosis, frequency of death during hospitalisation, predictors of death as well as frequency of recurrent stent thrombosis were evaluated.

Results: Of the 46 subjects 34 were male and 12 were female subjects with a mean age of 63.5±9.7 years ranging from 42 to 80 years. Hyperlipidaemia (89%), hypertension (67%) and history of myocardial infarction (33%) were the major medical risk factors. Type A (25.5%), Type B1 (61.5%) and Type B2 (8.5%) lesions were treated with a 3.25/16 mm (49.8%) or a 3.5/16 mm (51.5%) DREAMS. The lesion failure rate at 12-month was 7.0% with no cardiac death, one periprocedural target vessel coronary and two clinically driven target lesion revascularizations (TLR). There was no scaffold thrombosis. The angiographic results of 33 patients consenting for the 12-month follow-up will be available upon presentation.

Conclusion: DREAMS showed an excellent safety profile and a low TLF rate up to one year follow-up.

Twelve-month safety and performance results of the paclitaxel-eluting bioabsorbable magnesium scaffold in the prospective, multicenter first-in-man trial - BIOSOLVE-I

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Purpose: Absorbable metal scaffolds (AMS) are developed to overcome limitations of current permanent bare or drug-eluting coronary stents like stent thrombosis despite prolonged dual antiplatelet therapy (DAPT), caged vessel segment not allowing vasomotion and remodeling or chronic vessel wall inflammation. Magnesium is an essential element of the human body, thus Magnesium is considered as a potential alloy for absorption. To overcome the limitations associated with the first generation of a bare AMS a Drug (Paclitaxel) Eluting Absorbable Magnesium Scaffold was developed (DREAMS).

Methods: Between July and December 2010, 46 subjects were enrolled in the first-in-man BIOSOLVE-I study, and assigned to two different cohorts with different follow-up schedules. Clinical follow-up for both cohorts is scheduled at 1, 6, 12, 24 and 36 months. angiographic follow-up cohort at 1 months and for cohort 2 at 12 months. Angiographic assessment was performed by an independent, core laboratory. The primary endpoint is Target Lesion Failure (TLF), defined as the composite of cardiac death, target vessel myocardial infarction and clinically driven target lesion failure for cohort 1 and at 12 months follow-up cohort 2.

Results: Of the 46 subjects 34 were male and 12 were female subjects with a mean age of 63.5±9.7 years ranging from 42 to 80 years. Hyperlipidaemia (89%), hypertension (67%) and history of myocardial infarction (33%) were the major medical risk factors. Type A (25.5%), Type B1 (61.5%) and Type B2 (8.5%) lesions were treated with a 3.25/16 mm (49.8%) or a 3.5/16 mm (51.5%) DREAMS. The lesion failure rate at 12-month was 7.0% with no cardiac death, one per-procedural target vessel coronary and two clinically driven target lesion revascularizations (TLR). There was no scaffold thrombosis. The angiographic results of 33 patients consenting for the 12-month follow-up will be available upon presentation.

Conclusion: DREAMS showed an excellent safety profile and a low TLF rate up to one year follow-up.

Cost-effectiveness of drug-coated balloon angioplasty and drug-eluting stent implantation for treatment of coronary in-stent restenosis

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Purpose: In-stent restenosis (ISR) is a persistent problem limiting the long-term success of percutaneous coronary intervention. Recent studies have demonstrated safety and efficacy of drug-coated balloon (DCB) angioplasty for the treatment of coronary ISR. The cost-effectiveness of this practice is unknown.

Methods: A Markov state-transition decision analytic model was used to assess the comparative cost-effectiveness of two common treatment strategies for BMS-ISR: stenting with paclitaxel-eluting DES versus paclitaxel-coated balloon angioplasty (SeQuent Please, B. Braun Melsungen AG, Berlin, Germany). The model accounted for varying procedural efficacy rates, complication rates, and cost estimations. Data on procedural outcomes associated with both treatment strategies were derived from the literature, and the cost analysis was conducted from a health care payer perspective. Effectiveness was expressed as life-years gained. Cost-effectiveness was calculated by dividing the difference in mean costs (costs of the comparator strategy – costs for DES implantation) by the difference in effectiveness (life expectancy in the DCB arm – life expectancy in the DES arm). All simulations were performed using Monte Carlo simulations with 100,000 random trials. Results: In the base-case analysis, initial procedural costs amounted to €3,604.14 for DCB angioplasty and to €3,309.66 for DES implantation. Over a 12-month time horizon, the DCB strategy was found to be less costly (€430.38 versus €5,305.30), and slightly more effective in terms of life expectancy (0.983 versus 0.976) than the DES strategy. Extensive sensitivity analyses indicated that, in comparison with DES implantation, the cost advantage of the DCB strategy was robust to clinically plausible variations in the values of key input parameters. The variables with the greatest impact on base case results were the duration of dual antiplatelet therapy with acetylsalicylic acid and clopidogrel after DCB angioplasty, the use of generic clopidogrel, and variations in the costs associated with the DCB device.

Conclusion: DCB angioplasty is a cost-effective treatment option for coronary BMS-ISR. The higher initial costs of DCB are more than offset by later cost savings, predominantly as a result of reduced medication costs. Health care payers
would benefit from a wider adoption of this technology, as DCB angioplasty can be regarded as one of the rare innovative medical interventions that are cost-saving at equal or even increased effectiveness.

**P4796**

**Difference of vascular response between everolimus- and paclitaxel-eluting stents for small coronary artery diseases: optical coherence tomography analysis**

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1) Syothashi Heart Center, Toyohashi, Japan; 2) The Cardiovascular Institute Hospital, Tokyo, Japan; 3) Kokura Memorial Hospital, Kitakyushu, Japan; 4) Aoyama Heart Hospital, Adachi-ku, Japan; 5) Kasukabe Chuo General Hospital, Kasukabe, Japan; 6) Kokagawa East City Hospital, Kagawa, Japan; 7) Matsumoto Kyoritsu Hospital, Matsumoto, Japan; 8) Rinku General Medical Center, Osaka, Japan; 9) JR Tokyo General Hospital, Tokyo, Japan; 10) Saiseikai Fukuoka Hospital, Fukuoka, Japan

**Background:** The aim of this study is to evaluate the differences of chronic vascular response following small coronary stenting between everolimus-eluting stent (EES) and paclitaxel-eluting stent (PES) evaluated by optical coherence tomography (OCT).

**Methods:** SACRA and PLUM registries are prospective, multicenter registry to assess the efficacy of single paclitaxel (PES) or everolimus-eluting stents (EES) in patients with small coronary artery diseases. Inclusion criteria of both registries were: (1) significant stenosis in vessels ≤2.5mm in reference diameter, (2) lesion length <20mm. From these two registries (506 patients with 533 lesions), non-restenotic 50 EESs and 50 PESs were imaged with OCT at 9-month follow-up and analyzed at interval of 1 mm.

**Results:** Average intimal hyperplasia thickness was not different between the two groups. Exposed struts and layered intima were observed more frequently in PES group than EES group.

**OCT results**

<table>
<thead>
<tr>
<th></th>
<th>EES</th>
<th>PES</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>No.of.stent</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>No.of.observed cross-sections</td>
<td>859</td>
<td>625</td>
<td></td>
</tr>
<tr>
<td>Homogenous intima</td>
<td>809 (99.9%)</td>
<td>737 (99%)</td>
<td>0.0003</td>
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<tr>
<td>Heterogenous intima</td>
<td>38 (4.4%)</td>
<td>28 (3.4%)</td>
<td>0.31</td>
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<tr>
<td>Layered intima</td>
<td>18 (2.1%)</td>
<td>60 (7.3%)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Perí-stent ulcer</td>
<td>30 (3.5%)</td>
<td>100 (12.5%)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Perístent ulcer like appearance</td>
<td>53 (6.2%)</td>
<td>105 (12.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No.of.analysed strut</td>
<td>3906</td>
<td>7606</td>
<td></td>
</tr>
<tr>
<td>Exposed strut</td>
<td>26 (0.27%)</td>
<td>130 (1.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Malapposed strut</td>
<td>9 (10.9%)</td>
<td>22 (0.017)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Percent neointimal hyperplasia area, %</td>
<td>20.4±1.6</td>
<td>22.0±1.6</td>
<td>0.51</td>
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<tr>
<td>Average NIT, μm</td>
<td>0.14±0.06</td>
<td>0.15±0.08</td>
<td>0.64</td>
</tr>
<tr>
<td>Maximum NIT, μm</td>
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<td>0.28±0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>Minimum NIT, μm</td>
<td>0.07±0.04</td>
<td>0.07±0.05</td>
<td>0.75</td>
</tr>
<tr>
<td>Maximum NIT/minimum NIT, μm</td>
<td>0.15±0.04</td>
<td>0.21±0.09</td>
<td>0.001</td>
</tr>
</tbody>
</table>


**Conclusions:** This study suggested that characteristics of neointimal hyperplasia after EES implantation were more stable compared with PES although neointimal growth was similar between the two groups.

**P4799**

**Impact of adjunctive post-dilatation after drug-eluting stent implantation on the clinical outcomes in patients with acute myocardial infarction: Sub-study of EVER-ZOTA multicenter trial**

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**Backgrounds:** Although drug-eluting stents (DES) are more effective than bare-metal stents (BMS) in preventing coronary restenosis, stent underexpansion was known to be an important predictor of early stent thrombosis and restenosis in the DES era. Recently, a large retrospective study demonstrated that post-dilatation after DES implantation reduced the restenosis rate. However, the population of the study did not include patients with acute myocardial infarction (AMI). The aim of present sub-study of EVER-ZOTA multicenter trial was to evaluate the impact of an adjunctive post-dilatation after DES implantation on the clinical outcomes in patients with AMI.

**Methods:** We studied 474 (343 men, 65±12 years old) patients who underwent DES implantation for AMI including 368 with postdilatation (253 male, 66±12 years old) and 116 with un-postdilatation (90 male, 63±12 years old). Rate of cumulative 12-month events, such as cardiac death, target-vessel related MI, revascularization, or stent thrombosis were compared between groups.

**Results:** Compared with the postdilatation group, the un-postdilatation group had younger, less calcified lesion, and obtained postprocedural TIMI-3 flow. They also had significant benefit on composite events in 12 months (5.6% vs. 0.9%, p < 0.045) (Figure). However, Cox regression survival analysis showed the Killip Class ≥ 3 (odds ratio 17.271, 95% CI 5.439-54.906, p < 0.001) and age (odds ratio 1.061, 95% CI 1.005-1.119, p = 0.031) to be independent predictors of 12-month composite events rather than postdilatation itself.

**Conclusion:** Postdilatation after DES implantation in patients with AMI does not seem to have a benefit on the 12-month clinical outcomes. Age and Killip Class rather than postdilatation itself would be more predictive of 12-month clinical outcomes.

**P4800**

**Bare-nitinol stent versus paclitaxel-coated balloon for femoro-popliteal revascularization. An adjusted indirect comparison meta-analysis of randomized trials**

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**Aims:** In femoro-popliteal artery (FPA) disease, Bare-Nitinol Stent (BNS) and Paclitaxel-coated balloon (PCB) improved outcomes as compared to Uncoated Balloons (UCB). Angioplasty Nevertheless, the relative efficacy of BNS vs. PCB remains unknown, due to the lack of head-to-head comparisons. We performed an adjusted indirect comparison meta-analysis of randomized trials to evaluate outcomes of BNS versus PCB in FPA disease.
P4801 Bivalirudin Vs Unfractionated Heparin during Percutaneous Coronary Intervention in High Risk Patients for Bleeding. AntiCoagulant Regimen in High risk Patients for Bleeding - ACRIPAB Trial

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Introduction: In low to medium risk population undergoing PCI Bivalirudin (BIV) exhibited significantly lower rate of bleeding compared to unfractionated heparin (UFH). However, clinical outcome and bleeding complications in high risk population was not established yet.

Aim: Randomized double blinded prospective trial comparing efficacy and safety of BIV vs. UFH on top of dual antiplatelet therapy during PCI among patients with NSTEMI or angiographically critical lesions and with high risk for bleeding.

Methods: There were 100 consecutive patients (66.6±12.3 years old, 69% males) enrolled in our study with 1:1 distribution between BIV and UFH groups. With starting of PCI BIV or UFH were administrated in acceptable doses. The study end points were: major, minor bleeding, port of entry complications, MACE in-hospital and after 30 days follow up.

Baseline characteristics: There were 87% patients with diabetes mellitus, 98% with hypertension, 22% with chronic renal failure, 30% older than 75 years, 21% males) enrolled in our study with 1:1 distribution between BIV and UFH groups. Median FU was 11.5 months.

Angioplasty with BNS was found inferior to PCB with respect to TLR (OR= 2.60 [1.27–5.32], z= 2.63, p=0.008), with a trend toward higher binary restenosis (OR= 2.03 [0.99–4.18], z=1.93, p=0.052). No significance in mortality was evident among study groups (OR= 1.79 [0.79–3.75], z=0.73, p=0.46; BNS vs. PCB comparison).

Conclusions: In diseases of femoro-popliteal artery, PCB offers superior free-domin from repeat revascularization as compared to BNS. Both revascularization strategies appeared safe. Adequately powered, randomized, head-to-head comparisons are needed.

P4803 Why is the posterior myocardial infarction the most frequent cause of acute mechanical complications?

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Background: The prevalence of ramus circumflexus (LCX) and its branches as an infarct related artery (IRA) in STEMI patient population is low, around 10-15%. LCX is the most frequent IRA among patients with mechanical complications of AMI.

Objective: To estimate the reason for high involvement of LCX as IRA in patients with mechanical complication of AMI.

Methods: Registry of patients with acute coronary syndromes treated in the tertiary cardiac centre.

Results: In the group of 809 STEMI patients treated in period 2008-2011, the LCX, LAD, and RCA were detected as IRA in 133 (16%), 347 (43%) and 308 (38%) patients respectively. In the parallel period of 709 NSTEMI-ACS patients the LCX, LAD and RCA were detected as IRA in 63 (11%), 209 (33%) and 209 (29.5%) respectively. The difference of LCX involvement in STEMI (16%) compared to NSTEMI-ACS patients (31%) was highly significant (p<0.001).

Conclusions: It seems that the LCX is the posterior myocardial artery, which is the most frequent cause of acute mechanical complications of AMI.
of papillary muscle the LCX was identified as IRA in 6 (86%) patients. The hospital mortality was 29%. In the group of 5 patients hospitalized with the rupture of free left ventricle wall post AMI, the LCX was culprit in 3 (60%) patients. The hospital mortality was 40%. None of the 9 patients received immediate reperfusion therapy for acute LCX occlusion as they all were initially identified and treated as NSTE-ACS.

Conclusions: In the present era of catheter based reperfusion therapy, the posterior AMI due to LCX occlusion is the most frequent cause of serious mechanical complication of AIM because of improper reperfusion treatment. The incorrect evaluation of patients with posterior AMI as being NSTE-AMI is also the cause of low prevalence of LCX as culprit in the groups of STEMI patients treated with immediate reperfusion therapy. We showed that about 30% of patients with acute LCX occlusion are not receiving needed timely reperfusion therapy.

P4805 Effect of high dose statin pretreatment on endothelial progenitor cells after percutaneous coronary intervention (Hipocrates study)

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Purpose: In prospective cohort study 481 pts (mean age 59 yrs) with stable CAD on OMT (beta-blockers, statins, antiplatelets, ACE inhibitors) were included. In history (>2 months ago): acute coronary syndrome (ACS)–80.9%, PCI-14.9%, coronary bypass-12.7%, stroke-9.6%, diabetes-18.5%. 302 of pts underwent PCI (PCI group) and 179 of pts continued on conservative therapy (medical-therapy group). The mean follow-up period in PCI and medical-therapy groups was 3.5±1.6 yrs and 5.4±1.3 yrs respectively. The primary outcome was the occurrence of major adverse cardiac and cerebrovascular events (MACE)=vascular death, ACS, stroke/transient ischemic attack. The composite endpoint included MACE and revascularization in any affected arterial area.

Background: Pretreatment with high-dose statins given prior to percutaneous coronary intervention (PCI) has been shown to have beneficial effects. The mechanism of these lipid-independent statin effects is unclear. Circulating endothelial progenitor cells (EPCs) have an important role in the process of vascular repair, by promoting re-endothelialization following injury. We hypothesized that statins can limit the extent of endothelial injury induced by PCI and promote re-endothelialization by a positive effect on EPCs.

Methods: Included were patients, either statin naive or treated chronically with low-dose statins, with stable or unstable angina who underwent PCI. Patients were randomized to receive either high-dose atorvastatin (80 mg the day before PCI and 40mg 4 hours before PCI) or placebo. EPCs profile was examined before PCI and 24 hours after it. Circulating EPC levels were assessed by flow cytometry as the proportion of peripheral mononuclear cells co-expressing VEGFR2, CD133

Results: Sixteen patients (mean age 61.8±7.9 years, 14 men) were included in our preliminary data, of which 8 received high-dose atorvastatin (80 mg the day before PCI and 40mg 4 hours before PCI) or placebo. EPCs profile was examined before PCI and 24 hours after it. Circulating EPC levels were assessed by flow cytometry as the proportion of peripheral mononuclear cells co-expressing VEGFR2, CD133 and CD34. The capacity of the cells to form colony forming units (CFUs) was quantified after 1 week of culture.

Conclusions: In these preliminary results, there is a trend towards higher EPC CFU levels in patients treated with high-dose atorvastatin, both before and after PCI. This could account for the beneficial effects of statins given prior to PCI.

P4806 Elective percutaneous coronary intervention does not improve outcomes in patients with coronary artery disease (a prospective cohort study)

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2Institute of Preventive Medicine, Moscow, Russian Federation

Purpose: Previous studies have not shown benefits of percutaneous coronary intervention (PCI) involving bare-metal stents in pts with stable coronary artery disease (CAD). Our study compared drug-eluting stents (DES) PCI with optimal medical therapy (OMT) in pts with non-acute CAD.

Methods: In prospective cohort study 481 pts (mean age 59 yrs) with stable CAD on OMT (beta-blockers, statins, antiplatelets, ACE inhibitors) were included. In history (>2 months ago): acute coronary syndrome (ACS)-80.9%, PCI-14.9%, coronary bypass-12.7%, stroke-9.6%, diabetes-18.5%. 302 of pts underwent PCI (PCI group) and 179 of pts continued on conservative therapy (medical-therapy group). The mean follow-up period in PCI and medical-therapy groups was 3.5±1.6 yrs and 5.4±1.3 yrs respectively. The primary outcome was the occurrence of major adverse cardiac and cerebrovascular events (MACE)=vascular death, ACS, stroke/transient ischemic attack. The composite endpoint included MACE and revascularization in any affected arterial area.

Results: Most of the demographic and clinical characteristics were similar in the two groups. PCI was performed for 1-, 2- and multivessel diseases in 57.3%, 30.5% and 9.3% respectively, 98% of PCI group received DES (Cypher and/or second generation of DES), the double antiplatelet therapy (DAPT) was ≥ 12 months in all pts. The total frequency of MACE in the PCI group was 4.8/100 pts/ys and 5.3/100 pts/ys in the medical-therapy group (RR for the PCI group 0.96[95% CI 0.61-1.5]). The frequency of composite endpoint was 7.3/100 pts/ys and 7.1/100 pts/ys respectively (RR for the PCI group 1.02[95%CI 0.71-1.31]).

Conclusion: Elective PCI with DES and optimal duration of DAPT doesn’t have advantages over optimal medical therapy in pts with CAD.

P4807 Onset-to-needle times in patients with ST-segment elevation myocardial infarction: shortest referral route to a primary coronary intervention facility

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Introduction: Primary percutaneous coronary intervention (PCI) is the preferred therapeutic strategy for patients with acute STElevation myocardial infarction (STEMI). However, several referral routes between onset of symptoms and PCI exist namely: Pre-hospital diagnosis and direct transfer to PCI, emergency room visit and on-site transfer to PCI, or emergency room visit and secondary transfer to PCI. We compared the delays between onset and PCI associated with each referral route.

Methods: Data was obtained in a retrospective analysis of randomly selected STEMI patients from 64 hospitals in France. For each patient, the referral route and onset-to-needle time was obtained. Onset-to-needle time was defined as time from onset of symptoms to time of arterial puncture for PCI. We used a Cox proportional-hazards model to compare delays between referral routes.

Results: In total, 1217 patients were included in the analysis. Median onset-to-needle time was 186 min (Q1:133; Q3:292) for the pre-hospital diagnosis route, 237 min (Q1:165; Q3:368) for the onsite transfer route and 305 min (Q1:230; Q3:610) for the secondary transfer route. There was no difference in median onset-to-needle times between hospital types or volume of activity. After adjusting for age, year of admission and history of cardiovascular disease, pre-hospital diagnosis was associated with the shortest delay as compared to onsite-transfer (Hazard ratio (HR) 0.71 [0.59 - 0.86]) and secondary transfer (HR 0.67 [0.52 - 0.86]).

Conclusion: Pre-hospital diagnosis with direct transfer to PCI leads to shorter delays in patient care. In France, this management pathway requires the presence of an emergency physician at first medical contact.
myocardial infarction (AMI). Implementation of national quality improvement program may have the potential to obliterate the "weekend-effect" in patients with AMI.

Methods: Between November 2005 and December 2010, 25,233 patients (18.025 men; mean age = 63.3±12.8 year-old) were included from Korea AMI Registry. Exposure was defined as admission on a Saturday, Sunday, or a holiday. The study population was stratified according to three time-periods: 2005.11.1 – 2006.12.31 (KAMIR I; n=7,077), 2007.11.1 – 2008.1.31 (KAMIR II; n=4,605), and 2008.2.1 – 2010.12.31 (Kamri; n=13,722).

Results: Proportions of weekend-admissions were 27.4%, 27.9% and 28.2%, respectively. Patients admitted on weekend were younger and had more typical chest pain, inferior MI, ST-segment elevation MI, higher Killip class, and higher serum glucose, CK-MB, and triglyceride levels. Current smokers were more frequently observed in patients admitted on weekend. Cardiopulmonary re-usculation were more frequently performed in patients admitted on weekend. From KAMIR I 6.5% of patients admitted on weekends compared to 5.2% of those admitted on weekdays (p=0.037). During the two following periods the apparent difference between weekends and weekdays decreased: KAMIR II (7.1% versus 7.8%, p=0.436) and Kamri (6.2% versus 5.8%, p=0.367). Accordingly, in the adjusted multivariate analysis an increased all-cause mortality in patients admitted on weekends was only observed in KAMIR I with a weekend-weekday hazard ratio (HR) of 1.320 (95%CI: 1.001-1.741, p=0.049) but was not found in KAMIR II (HR=0.945, 95%CI 0.688-1.298, p=0.728) and Kamri (HR=0.904, 95%CI0.744-1.198, p=0.307).

Conclusions: We showed that a weekend-effect on mortality in patients with AMI has previously been present, but it has decreased over the past five years.

P4809 Syntax score predicts major bleeding after drug-eluting stent implantation


Purpose: The bleeding complication has been one of frequent complications in the drug-eluting stent (DES) era. Previous study reported that percutaneous coronary intervention (PCI) in complex lesion is an independent correlate of major bleeding. This finding may be explained by more complicated procedure and longitudinally higher platelet activity. The SYNTAX score is a current angiographic tool grading the complexity of coronary artery disease. The aim of this study was to assess the ability of the SYNTAX score to predict major bleeding after DES implantation.

Methods: We analyzed a consecutive 560 patients treated with DES in the all-comers population between January 2007 and January 2009. Endpoints were analyzed for major bleeding (defined according to the REPLACE-2 trial) and late stent thrombosis during 3 years. The SYNTAX score was assessed with angiogram before PCI by 2 cardiologists. Patients were stratified according to tertiles of the SYNTAX score: low score (0-12, n=170), intermediate score (13-24, n=202), and high score (>25, n=188).

Results: Incidence of the major bleeding was seen in 49 patients (8.6%) during 3 years. There were 15 stent thrombosis (2.7%). The median SYNTAX score was 17 (range 0 to 75.5). Among patients in the low, intermediate, and high scores, the 3-year rate of major bleeding were 4.7%, 5.0%, and 16.5%, respectively and for composite endpoints is 0.736 (P = 0.121), respectively and for in-hospital and 30-day mortality and major adverse cardiovascular and cerebrovascular events (MACCE) following PCI.

Predictive factors of Major Bleeding

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNTAX score (10-unit increase)</td>
<td>1.5</td>
<td>1.0-2.1</td>
<td>&lt;0.0501</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>3.62</td>
<td>1.9-6.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>1.68</td>
<td>1.0-2.57</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Multivariable logistic regression model.

Conclusions: In the all-comers population undergoing DES implantation, the SYNTAX score has a predictive ability for patients at risk of major bleeding. The score may be useful for clinical decision making regarding optimal duration of dual anti-platelet therapy after DES.

P4810 Clinical risk scores for the prediction of CIN before primary PCI

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Background: Several scores for risk stratification have been developed in candidates to percutaneous or surgical myocardial revascularization. These scores have been recently validated even in different settings than the ones where they were originally developed. We retrospectively analyzed the relative accuracy of AGERF score, EuroSCORE and Mehran Risk Score (MRS) for the prediction of Contrast-Induced Nephropathy (CIN) in 481 consecutive patients undergoing primary PCI for STEMI.

Methods: CIN was defined as an absolute increase in serum creatinine ≥0.5 mg/dl, or an increase ≥25% from baseline within 72 hours after the administration of contrast medium. AGERF score was calculated by adding 1 point to the Age/EF(%) ratio if the eGFR was <60 mL/min per 1.73 m². Logistic regression analysis, receiver-operating characteristic (ROC) curve analysis and Hosmer-Lemeshow <2 statistic were performed to assess accuracy and calibration of AGERF score, EuroSCORE and MRS as predictors of CIN, with the AUC as a measurement of accuracy. The best cutoff value for each score was identified according to the Youden index.

Results: Overall, the incidence of CIN was 5.2%. AGERF score was an accurate (OR 5.19, 95% CI 3.13-8.62, p<0.001, AUC 0.88) and calibrated (Hosmer-Lemeshow <2=6.24, p=0.62) predictor of CIN with a 100% sensitivity for AGERF score >1.5 points; all patients developing CIN were in the highest tertile of AGERF score (p<0.001). When considered linear, continuous variables MRS (OR1.27, 95% CI 1.17-1.39, p=0.001, Hosmer-Lemeshow <2=3.18, p=0.53) and EuroSCORE (OR1.61, 95% CI 1.36-1.91, p<0.0001, Hosmer-Lemeshow <2=5.39, p=0.50) predicted the risk of CIN as well. Both MRS (AUC 0.80, p<0.15 Vs AGERF score) and EuroSCORE (AUC 0.82, p<0.14 Vs AGERF score) were less accurate, though not significantly, than AGERF score. The cutoff for MRS was 5, with 72% sensitivity and 73.5% specificity, and coincided with the upper boundary of the lowest risk category in the original Mehran study. The cutoff for EuroSCORE was 6, with 92% sensitivity and 92% specificity, and coincided with the lower boundary of the high risk category.

Conclusion: In patients undergoing primary PCI for STEMI, a linear risk score based on age, ejection fraction and eGFR can predict the risk of CIN as well as more accurately as more complex non-linear risk scores. Simple models based on pre-procedural, readily obtainable objective variables, such as the AGERF score, are well suited to the acute settings. Complex risk models may be over fitted, at least in populations with a low rate of events.

P4811 Comparison of the new Mayo Clinic risk scores and clinical SYNTAX Score in predicting adverse cardiovascular outcomes following percutaneous coronary intervention at our heart center

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Purpose: Risk stratification of patients who will undergo percutaneous coronary intervention (PCI) can help physicians and patients and their families understand the risks of the procedure, thus providing an objective basis for decision-making.

Objectives: To compare the prognostic value of the Clinical SYNTAX Score (CSS) and New Mayo Clinic Risk Scores (NMCRS) for in-hospital and 30-day mortality and major adverse cardiovascular and cerebrovascular events (MACCE) following PCI.

Design: Prospective Cohort Study

Methods and Results: The NMCRS for Predicting Mortality, NMCRS for Predicting MACE and CSS of all patients who underwent PCI from April 1, 2011 to September 30, 2011 were computed. Of the 482 patients included in the study, 22.4 (46%) died while 37.7% had the composite endpoint (mortality, MI, emergency CABG, CVA) during hospitalization. 30 days after PCI, 9 (2.0%) died while 19 (3.9%) had the composite endpoint. The prognostic value of the NMCRS for Predicting Mortality, NMCRS for Predicting MACE and CSS for in-hospital mortality, as measured by the c-statistic, is 0.827, 0.813, and 0.816 (P < 0.05 for all), respectively and for in-hospital composite endpoints is 0.791, 0.751, and 0.755 (P < 0.05 for all), respectively and for composite endpoints is 0.746 < 0.05, 0.763 < 0.05, and 0.651 < 0.121, respectively.

Conclusion: The NMCRS for Predicting Mortality has better prognostic utility for in-hospital mortality and composite end-points while the NMCRS for Predicting MACE better predicts 30-day mortality and composite end-points as compared to the CSS.

P4812 Protamine usage following implantation drug-eluting stents: is it safe?

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Background: Prompt reversal of heparin anticoagulation by protamine is a common therapeutic option. It could help the treatment of serious procedural complications such as vessel rupture or perforation or to allow immediate femoral artery sheath removal to avoid puncture site complications and decrease patient discomfort. However, this approach is rarely used after coronary drug eluting stent(DES) implantation because of the possible increased risk of stent thrombosis. ST is a rare event, so in order to be deleted a large sample study is required.

Methods: We retrospectively analyzed the incidence of acute and subacute stent thrombosis in 6023 patients submitted to percutaneous coronary intervention who received 2465 drug eluting stent divided in 2 groups: GI with 2509 DES who
received protamine after procedure and GII with 436 DES who do not received this drug.

Results: Six patients (0.24%) had subacute stent thrombosis in the group receiving protamine (259 DES) and only one patient (0.02%) in the group who do not received this drug (436 DES) (p-value = 0.96; odds ratio: 0.96; 95% confidence limits).

Conclusion: Immediate reversal of heparin anticoagulation by protamine after coronary drug eluting stent implantation in our study was safe and did not predispose to stent thrombosis. This finding has important clinical consequences.

Does over-aggressive stent expansion without IVUS guidance predispose to restenosis?

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Purpose: Aggressive stent expansion and strut apposition are required for optimum stent deployment, but there is concern that resultant stent distortion and strut fracture may predispose to late adverse events including restenosis. The risk is potentially greater when stents are over-aggressively expanded during non-complex percutaneous coronary intervention (PCI) without intra-vascular ultrasound (IVUS) guidance. We therefore investigated how frequently stents are “over-expanded” in contemporary practice at our high-volume centre and whether this correlates with the degree of restenosis.

Methods: We studied 243 consecutive patients undergoing single-vessel stenting for the patients in whom 277 lesions. Exclusion criteria were bifurcational dissection: 3 related to stents over-expanded by less than 20% and only 1 was smaller (2.87 v 3.19 mm, P = 0.0004), longer (24 v 19 mm, P = 0.014) and rated burst pressure in 52%. The final stent size was difference between nominal and final stent size.

Conclusion: Compared to stents over-expanded by more than 20%, those over-expanded by less than 20% had higher rates of diabetes (38.1% versus 94.1% p = 0.0001), patients with cardiogenic shock (7.17% versus 1.11% p = 0.001), the presence of stent thrombosis. The group that received no Protamine presented a greater percentage of diabetic patients (38.1% versus 27.4% p < 0.0001), patients with cardiogenic shock (7.17% versus 1.11% p < 0.0001), the presence of stent thrombosis (p = 0.013 RR 2.9 CI 95% 1.25-6.7). We found that the use of Protamine significantly reduced the risk of coronary angioplasty and intracoronary thrombus independent were made. Only the clinical sign of acute infarction at ST segment elevation was identified as independent predictors for stent thrombosis (p = 0.013 RR 3.9 CI 95% 1.25-6.7). We found that the use of Protamine in patients undergoing PCI is safe and improves early and intermediate outcomes, but the European consensus on how to use Protamine in patients undergoing PCI is not associated with increased occurrence of acute and subacute thrombosis.

Impact of Mehran Risk Score for the prediction of Contrast-Induced Nephropathy in the Japanese patients who undergoing Percutaneous Coronary Intervention

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Background: Contrast-induced nephropathy (CIN) is associated with the increase of the risk of the cardiovascular event. We sought to investigate the association with Mehran risk score (MRS) and the incidence of CIN in the Japanese patients undergoing PCI.

Methods: Study subjects consisted of 2198 consecutive patients who were treated with PCI for stable angina, unstable angina or myocardial infarction, except for the patients who were receiving heparin and died within seven days after intervention (n=34). We categorized them into 4 groups according to MRS (low risk group: 1-5, medium risk group: 6-10, high risk group: 11-16 and very high risk group: 16-5). In the analysis, we calculated the odds ratio for CIN and the 95% confidence interval in the category of the MRS. The risk factors for the development of CIN were estimated by a multiple logistic regression analysis.

Conclusion: In this real-world population undergoing non-complex PCI without IVUS guidance at a high-volume centre, any tendency to over-aggressive stent expansion did not predispose at all to restenosis.

Comparison of additional versus no additional heparin during therapeutic oral anticoagulation in patients undergoing Percutaneous Coronary Intervention

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Background: Uninterrupted oral anticoagulation (OAC) therapy is increasingly used in patients with atrial fibrillation at moderate to high risk of thromboembolism undergoing percutaneous coronary intervention (PCI).

Methods: To evaluate the need for additional heparins on top of therapeutic percutaneous coronary intervention (PCI), we assessed bleeding complications and major adverse cardiac and cerebrovascular events (MACCE) in 414 consecutive patients undergoing PCI during therapeutic (International Normalized Ratio 2.5-3.5) periprocedural OAC. Patients were divided into those with no (N=196) and with (N=218) additional use of periprocedural heparin.

Results: No differences in MACCE (4.1% vs. 3.2%, p=0.79) or major bleeding (1.0% vs. 3.7%, p=0.11) were detected, but access site complications (5.1% vs. 6.6% p=0.42) were increased in patients who underwent PCI with additional heparin (p=0.032).
Functional syntax score improves stratification of risk in patients with left main coronary artery disease

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The Functional Syntax Score (FSS) is obtained including in the computation of the Syntax Score (SS) only FFR positive lesions (i.e. FFR > 0.80). FSS has demonstrated better prognostic value as compared with SS in patients with multivessel disease (lesions of left main excluded) treated with DES implantation. The purpose of the present analysis is to assess whether FSS is able to better discriminate the potential PCI-related risk in patients with left main (LM) lesions compared with SS.

Methods and results: Patients (pts) with angiographically equivocal LM stenosis (n=209) undergoing FFR measurement were enrolled. Pts with (n=138) LM FFR > 0.80 were further divided to optimal medical treatment or to PCI of other significantly stenotic vessels. Pts (n=75) with LM FFR < 0.80 underwent bypass surgery. SS was calculated on all angiographies. FSS was calculated by excluding from the computation LM stenosis with FFR > 0.80. Based on the SS, patients were classified in the following tertiles: 68 pts in the low (<14 SS), 69 pts in the intermediate (15-21 SS), and 72 pts in the high (<22 SS). After calculation of FSS, 67 out of 209 patients (32%) were reclassified to lower SS tertile. More specifically, out of 69 patients with intermediate SS (15-21), 37 (54%) were reclassified to low tertile (<14). While out of 72 patients with high SS (22-42), 13 (18%) pts were reclassified to the intermediate tertile and 17 (24%) to the low tertile.

Conclusion: The present study demonstrates that FSS is particularly useful in the risk stratification of patients with equivocal LM stenosis, allowing to down-grade or up-grade coronary artery disease severity in up to one third of the cases. Further studies assessing the prognostic significance of FSS in LM disease are warranted.

Impact of real time 3D-echocardiography in the assessment of right ventricular volumes and function in patients with pulmonary hypertension

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Background: Right ventricular (RV) function is tracking last years a higher relevance as a clinical and prognostic marker in many physiological conditions. The aim of the study is to point out the incremental value of real time three dimensional echocardiography (RT3DE) and Tissue Doppler imaging (TDI) in the evaluation of patients affected by pulmonary hypertension (PH).

Methods: Enrolled 42 subjects affected by PH who underwent 2D and Doppler echocardiography, RT 3D Echocardiography and TDI evaluation of RV, and an healthy control group. PH can induce itself severe functional and structural abnormalities of RV, such as RV hypertrophy, RV dilatation, RV systolic and diastolic dysfunction.

Results: RV fractional area contraction (RV FAC) and tricuspid annular plane systolic excursion (TAPSE) showed marked alterations in patients with PH compared to control group (C); RV FAC: (PH) 0.30 ± 0.08 vs (C) 0.50 ± 0.05%, p < 0.001; TAPSE (PH)15.4 ± 3.1 vs (C) 21.0 ± 2.5 mm, p < 0.0001. 3D RV End Diastolic Volume was significantly higher in PH than in C (PH) 138.5 ± 25.1 vs (C): 83.1 ± 12.6 ml, p < 0.0001. As well as 3D RV End Systolic Volume (PH) 97.7 ± 21.4 vs (C) 39.4 ± 9.6 ml, p < 0.0001. 3D RV EF was significantly lower in pulmonary hypertension than in healthy subjects (31.6 ± 6.8 vs (C) 52 ± 4.6%, p < 0.0001).

Discussion: RV diastolic, systolic volume and ejection fraction evaluated by RT3DE showed a higher discriminating power in comparison respectively with 2D RV diastolic area and the relative fractional area changes in patients with pulmonary hypertension compared with controls.

Right ventricular dp/dt in normal subjects: feasibility and normal values

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Recently published guidelines for the Echocardigraphic Assessment of the Right Heart in Adults, point out that because of the limited data in both normal subjects and pathologic conditions, RV dp/dt cannot be recommended for routine uses. Our aim was to assess the feasibility of obtaining the dp/dt value in normal subjects with mild tricuspid regurgitation and to determine the normal values in this specific population.

Methods: Four hundred and thirty nine consecutive patients were enrolled. Patients were eligible if they were 18 years or older and their echocardiograms were performed as normal with the presence of mild tricuspid regurgitation. The highest tricuspid regurgitation (TR) velocity obtained from a sinus beat was measured to obtain the peak systolic RV-riatral gradient. TR velocity-time integral (VTI) was manually traced in order to obtain a high quality border to define the exact position of the pointer at 0.5 s, 1 m/s and 2 m/s. dp/dt measurements were repeated in 20 patients by the same investigator and by a second investigator. The right chamber’s echo-Doppler variables are shown in the table below.

Conclusions: RV dp/dt measurement is feasible in a small proportion of normal subjects with mild tricuspid regurgitation (44.9%). Mean value from 0.5 to 2 m/s was 352.7 mmHg/s with a minimum of 0.75 mmHg/s. The methodology used offers only a poor intra and inter-observer agreement.

Purpose: Right Ventricular (RV) diastolic functional assessment is often limited and underreported in comparison to the LV. RV diastolic function has shown changes with age similar to that of the LV. However the routine reporting of RV diastolic function is hampered by a lack of concise measurements. Strain Rate (SR), calculated via speckle tracking, is an angle and load independent measure of myocardial deformation. Analysis of one-to-one propensity matching pairs showed a significantly higher risk of access site complication in patients receiving additional antiocoagulation (13.1% vs 5.7%, p = 0.049).

Method: 140 volunteers consisting of five age groups (<30, 30-39, 40-49, 50-59 & 60+) Mean age 44 ± 10 years were pre-assessed and underwent a full LV and RV echocardiogram. Early and late diastolic strain rate measurements were calculated on both a global (GSRe & GSRa) and segmental scale (SRe & SRa) using EchoPAC software. Statistical analysis was conducted using SPSS 19.0 using Pearson Correlation, ANOVA testing and Tukeys post hoc testing.

Results: 840 segments were successfully tracked creating a six segment model for the RV. Global strain rate results showed that with increasing age there existed a significant correlation for GSRe (r = 0.45 p = 0.001) but only a weak negative correlation with GSRa (r = -0.19 p = 0.02). Tukeys testing revealed this difference existed between the remaining age groups when compared to the <30 group, with the trend displaying an increase in SRe with age. The results were then analysed based on a six segment model. This suggested that the significant increase in SRA existed within the Apical (p = 0.0001) Mid (p = 0.001) and Basal (p = 0.001) septal segments only.

Discussion: Significant changes in RV late diastolic strain rate were found when specified by age. Typically these enrolled those found throughout the LV, with a trend towards an increase in the late diastolic phase. However these differences were located within the three septal segments of the RV only. The potential resistance that the RV lateral wall displays to the typical diastolic aging process could be due to the variation in fibre types found within the RV. Primarily consisting of longitudinal fibres compared to the multiple fibre types found in the LV, these fibres may maintain their contractile function for longer.

RV speckle tracking has the potential for diastolic assessment in conjunction with other more traditional measurements. Further work needs to clarify the effects of aging has on different myocardial fibre types. These results suggest that diastolic relaxation may not occur in the same way as found in the LV.
Impact of untreated obstructive sleep apnea on left and right ventricular myocardial function and effects of CPAP therapy

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Background: Obstructive sleep apnea (OSA) has deteriorating effect on LV function, whereas its impact on RV function is controversial. We aimed to determine the effect of OSA and continuous positive airway pressure (CPAP) treatment on left and right ventricular (LV, RV) function using transesophageal echocardiography (TEE) and 2 dimensional speckle tracking (2D ST) analysis of RV deformation capability.

Methods and results: 82 patients with OSA and need for CPAP therapy were prospectively enrolled and underwent TTE at study inclusion and after 6 months of follow up (FU). Multivariate regression analysis revealed an independent association between baseline apical RV-SI, BMI and the severity of OSA (apical RV-SI: P<0.0002, BMI: P=0.02). After CPAP therapy, LV functional parameters were improved, nevertheless due to the cross-sectional analysis we cannot determine if CPAP therapy was effective. RV strain and strain rate parameters were not related with any RV echocardiographic parameters.

Conclusions: OSA seems to have deteriorating effect on LV and RV function. We found a beneficial effect of CPAP on LV and RV functional parameters predominantly in patients with severe OSA. 2D speckle tracking might be of value to determine early changes in global and regional right ventricular function.

P4834 Biomarkers and imaging in early diagnosis of right ventricular dysfunction

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Background: While left ventricular dysfunction has been intensely studied, knowledge regarding the right ventricular dysfunction in diabetic patients is still incomplete.

Aims: To evaluate inflammatory biomarkers: high sensitivity C-reactive protein (hsCRP), tumor necrosis factor-alpha (TNF-alfa), lipoprotein associated phospholipase A2 (Lp-PLA2) and their correlation with right ventricle strain and strain rate parameters in patients with diabetes mellitus type II.

Methods: We studied 51 patients with type 2 diabetes mellitus (DM), divided into two groups; group 1 DM with coexisting cardiovascular complications (coronary artery disease) and high blood pressure (29 patients) and group 2 DM and controlled high blood pressure only, with no coexisting cardiovascular complications (22 patients).

We conducted the analysis of right ventricular (RV) function through Vector Velocity Imaging and determined the inflammatory profile (hsCRP, TNF-alfa, Lp-PLA2) in predicting RV function in patients with DM.

Results: In group 1, patients with type 2 diabetes and cardiovascular disease, the Lp-PLA2 activities were significantly higher, with mean value 419.46 UI compared to group 2, where Lp-PLA2 activity mean value was 307.22 UI. In addition, we identified significant differences between groups for hsCRP and HDL cholesterol (p<0.01). A higher impairment of right ventricular longitudinal systolic function was noticed within group 1, compared with group 2, being statistical significant for Spea1RV, SmidRV and SRmidRV (p<0.01). Lp-PLA2 activity was statistically positive correlated with RV strain and strain rate (p<0.01), TNF-alfa and hsCRP did not correlate with any RV echocardiographic parameters.

Conclusion: By assessing the inflammatory profile of diabetic patients, it has been revealed that, even those asymptomatic for cardiovascular diseases, have a continuous inflammatory state, together with a decrease in RV systolic function, it should be screened as well in each diabetic patient. Lp-PLA2 was the best correlated marker with RV parameters, nevertheless due to the cross-sectional design, data collected could not provide prognostic value for the investigated inflammatory markers and it is necessary to extend the study with a follow-up period.

P4845 Echo derived tricuspid dp/dt as a marker of right ventricular function

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Purpose: Right ventricular (RV) systolic function appears prognostic significance in various disease states. RV geometry is not readily amenable to volumetric assessment by 2-dimensional echocardiography. Intraventricular pressure rate of rise (dp/dt) predicts myocardial contractility and adjusting dp/dt for the maximal regurgitant velocity (Vmax) eliminates the effect of preload. We ex-
amined the relationship of echo-derived tricuspid dP/dt and dP/dt/Vmax with RV ejection fraction (EF) by cardiac magnetic resonance imaging (MRI) as a measure of RV systolic function.

Methods: Fifty cardiac MRI and echocardiograms performed within 30 days were included in the study cohort. The tricuspid regurgitation (TR) spectral doppler trace was analyzed offline. TR dP/dt calculated using simplified Bernoulli (dP/dt corrected for TR jet velocity and m/s, dP/dt/Vmax was calculated as a ratio of dP/dt and TR Vmax. RV end diastolic and end systolic volumes obtained from contouring of steady state free precession axial stack MRI images; RVEF was calculated as [(RV end diastolic volume - RV end systolic volume)] / RV end diastolic volume x 100. RV EF = 44% was considered normal.

Results: A majority (78%) of studies were adequate for measurement of dP/dt and included in the final analysis. Median age of the study population was 48 years (IQR: 36-63); 56.4% were female (n=22/39). There was moderate correlation between dP/dt and RVEF (r = 0.51, p < 0.01) which improved with dP/dt/Vmax (r = 0.59, p < 0.01). Using 400mmHg/s as the lower limit of normal for RV function, TR dP/dt had a positive predictive value of 91% and a sensitivity and specificity of 74% and 84% respectively. Interobserver agreement and repeatability analysis of dP/dt by Pitman’s variance ratio test showed no significant difference (ratio of standard deviation = 0.95, 95% CI 0.90-0.99, t = 1.9, p = 0.06).

Conclusion: Tricuspid dP/dt is a reproducible measure of RV function and correlates significantly with MRI RV EF. A dP/dt of more than 400mmHg strongly predicts normal RV EF. Adjusting for preload (dP/dt/Vmax) further improves this correlation.

Tricuspid annular plane systolic excursion obtained in the right ventricle modified apical four chamber view shows strong correlation with right ventricular fractional area change

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Purpose: Analysis of right ventricular (RV) function is considered to be difficult because of the complex structure. Tricuspid annular plane systolic excursion (TAPSE) is a simple, easy-to-obtain parameter. The aim of this study was to assess TAPSE in the right ventricular (RV) function.

Methods: In total, 150 patients (80% males; 58.5 ± 10.7 years) with acute myocardial infarction were included in the study cohort. The tricuspid regurgitation (TR) spectral doppler trace was analyzed offline. TR dP/dt calculated using simplified Bernoulli (dP/dt corrected for TR jet velocity and m/s, dP/dt/Vmax was calculated as a ratio of dP/dt and TR Vmax. RV end diastolic and end systolic volumes obtained from contouring of steady state free precession axial stack MRI images; RVEF was calculated as [(RV end diastolic volume - RV end systolic volume)] / RV end diastolic volume x 100. RV EF = 44% was considered normal.

Results: A majority (78%) of studies were adequate for measurement of dP/dt and included in the final analysis. Median age of the study population was 48 years (IQR: 36-63); 56.4% were female (n=22/39). There was moderate correlation between dP/dt and RVEF (r = 0.51, p < 0.01) which improved with dP/dt/Vmax (r = 0.59, p < 0.01). Using 400mmHg/s as the lower limit of normal for RV function, TR dP/dt had a positive predictive value of 91% and a sensitivity and specificity of 74% and 84% respectively. Interobserver agreement and repeatability analysis of dP/dt by Pitman’s variance ratio test showed no significant difference (ratio of standard deviation = 0.95, 95% CI 0.90-0.99, t = 1.9, p = 0.06).

Conclusion: Tricuspid dP/dt is a reproducible measure of RV function and correlates significantly with MRI RV EF. A dP/dt of more than 400mmHg strongly predicts normal RV EF. Adjusting for preload (dP/dt/Vmax) further improves this correlation.

Right ventricular systolic function is highly dependent on left ventricular dysfunction in patients with previous myocardial infarction and high plasma brain natriuretic peptide levels

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Background: Although right ventricular (RV) dysfunction often coexists with left ventricular (LV) dysfunction after myocardial infarction (MI), the underlying mechanisms responsible for RV dysfunction have remained unclear in the clinical setting.

Methods: We analyzed 82 patients with previous MI with no history of RV infarction (LV ejection fraction 45±17%) and 28 age-matched normal controls (LV ejection fraction 65±5%). All patients underwent complete echocardiography including speckle-tracking strain measurements both in the LV and RV. Global RV longitudinal peak systolic strain (RV-strain) was assessed from apical 4-chamber view by using speckle-tracking strain imaging. Global left ventricular longitudinal peak strain (LV-strain) was assessed from apical 2-, 3-, and 4-chamber views and was calculated by averaging three strain values by using speckle-tracking strain imaging. Plasma BNP level was also assessed in patients without (versus) in patients with MI.

Results: RV-strain and LV-strain were significantly reduced in patients with MI compared to normal controls (RV-strain: -16.6 ± 25.4%; LV-strain: -12.6 ± 17.2%; p < 0.05 vs. normal controls). Multivariable linear regression analysis indicated that only LV-strain (standardized coefficients of 0.44) were independent determinants of RV-strain. When patients were divided into 3 groups according to plasma BNP levels (group A: BNP > 100 pg/ml; n = 32, group B: BNP 100 < BNP ≤ 500 pg/ml; n = 31, and group C: BNP ≤ 500 pg/ml n = 18), only group C had a strong correlation between RV-strain and LV-strain (r = 0.63, p < 0.05).

Conclusion: Longitudinal RV systolic function highly depends on longitudinal LV systolic function after MI especially in patients having high plasma BNP levels. These results may indicate that RV dysfunction can progress as remote remodeling which regulated in response to the increase in loading conditions after MI.

Clinical and echocardiographic predictors of right ventricular functional changes after acute myocardial infarction

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Purpose: Right ventricular (RV) function is a well-known prognostic factor after acute myocardial infarction (AMI). However, only a few studies so far explored which parameters are associated with RV function after AMI. Accordingly, the aim of this study was to identify potential predictors of RV improvement after AMI, including the assessment of RV strain and left ventricular (LV) perfusion indices.

Methods: A total of 150 patients (80% males; 58.5 ± 10.7 years) with AMI and treated with primary percutaneous coronary intervention underwent echocardiography within 48 hours of admission, in order to evaluate conventional parameters of RV systolic function. RV function (including tricuspid annular plane systolic excursion –TAPSE) and valvular function. In addition, RV strain was assessed by speckle-tracking analysis, and myocardial contrast echocardiography was performed to evaluate LV segmental and global perfusion. At 6-month follow-up, echocardiography was repeated for LV and RV function reassessment. Improvement in RV function was defined as an improvement of TAPSE>10%

Results: Patients with RV functional improvement at follow-up (66, 57%) had a significantly higher baseline LV ejection fraction as compared to patients without RV function improvement (49.2±8.6% versus 44.2±10.2%, p<0.005). Furthermore, they also showed lower baseline wall motion score index (1.6±0.3 versus 1.8±0.3, p<0.003), global myocardial perfusion index (1.3±0.3 versus 1.5±0.3, p<0.001), and myocardial perfusion index in the right coronary artery territory (1.3±0.4 versus 1.7±0.4, p<0.001). Baseline RV (but not RV fractional area change) was also significantly lower in patients with RV function improvement (18.8±4.9% versus 23.4±4.7%, p<0.001). At multivariate logistic regression analysis, baseline RV strain (odds ratio=0.84; 95% CI 0.760-0.937; p=0.001), myocardial perfusion index in the right coronary artery territory (odds ratio=0.198, 95% CI 0.064-0.616; p=0.005) and peak troponin T (odds ratio=0.872; 95% CI 0.785-0.969; p=0.011) were the only independent determinants of RV function improvement at follow-up. In particular, RV strain provided significant incremental predictive value over clinical and conventional echocardiographic variables, and myocardial perfusion index in the right coronary artery territory (C-statistic improved from 0.728 to 0.738 to 0.850 to 0.832, p<0.001).

Conclusions: Baseline RV strain and myocardial perfusion index in the right coronary artery territory are important predictors for RV function improvement after AMI.
Comparison of strain measurements with speckle tracking echocardiography and velocity vector imaging in detection of RV dysfunction in patients with ischemic cardiomyopathy: a validation study
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Background: Though strain measurement has been introduced and used to measure LV function, it has been used to estimate RV function. However, variations in strain measurement by different vendors have limited the application of these techniques for assessment of RV dysfunction. We sought to compare two methods for the assessment of RV function, compared with cardiac magnetic resonance imaging (CMR).
Methods: We studied 25 patients (21 men. 66±12y) with ischemic cardiomyopathy who underwent both echocardiography and CMR. Global longitudinal strain of RV was measured with speckle tracking echocardiography (GLS-VII; Siemens Medical Systems) and with GLS with speckle tracking echocardiography (GLS-STE; GE Medical Systems). RV fractional area change (RVFAC) was measured in all the subjects (r=0.24 ∼0.58, P<0.05). When compared with controls, EF-inflow changed in severe PH, while the other parameters changed in moderate and severe PH (P<0.05). EF-body was 52±9% (area under the curve = 0.70, P<0.10), sensitivity 75% and specificity 68%.
Comparison of correlations between GLS-V
Parameter GLS-VII GLS-STE
Correlation Coefficient (r) P-value Correlation Coefficient (r) P-value
CMR RVEF -0.748<0.001 -0.555<0.004
RVFAC -0.701<0.001 -0.619<0.001
TAPSE -0.675<0.001 -0.574<0.004
RV Telindex 0.605 0.002 0.491<0.017
Conclusion: Although GLS-VII and GLS-STE show significant correlations with CMR RVEF and other conventional echocardiographic parameters of RV function, GLS-VII appears superior to GLS-STE in the detection of RV dysfunction.

Right ventricular regional systolic function and dysynchrony in patients with pulmonary hypertension evaluated by three-dimensional echocardiography
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Objective: Right ventricular (RV) function is of diagnostic and prognostic importance in patients with pulmonary hypertension (PH). The purpose of the present study was to evaluate RV regional systolic function and dysynchrony in patients with PH using real-time three-dimensional echocardiography (RT3DE).
Methods: A total of 70 patients with PH and 26 age-matched controls were enrolled. RT3DE images were acquired and analyzed to obtain RV (flow, body, outflow) function (EF) and to measure systolic volumetric (Tmssv). The dysynchrony index was calculated as the standard deviation of Tmssv in three RV segments corrected by heart rate (Tmssv-SD2). Conventional echocardiographic parameters including RV fractional area change (FAC), tricuspid annular peak systolic velocity (S), RV myocardial performance index (MPI) as well as echocardiography-estimated pulmonary artery systolic pressure (PASP) and pulmonary vascular resistance (PVR) were recorded. The patients with PH were divided into 3 groups as mild PH (PASP: 40mmHg–49mmHg), moderate PH (PASP: 50mmHg–69mmHg) and severe PH (PASP≥70mmHg) Results: Average RT3DE acquisition and analyze time was less than 10 minutes. RT3DE image quality was adequate to analyze in more than 95% of all the subjects. RV local and regional EF measured by RT3DE correlated with FAC, S and MPI in all the subjects (r=0.24 ∼0.58, P<0.05). When compared with controls, RV EF-inflow and EF-global was lower in all patients with PH (P<0.05), while EF-body was decreased in moderate and severe PH (P<0.05) and EF-outflow changed in severe PH (P<0.001). Tmssv-SD2% in healthy moderate PH was similar to that in the control group and was significantly lowered in severe PH (P<0.05). EF-inflow and EF-global correlated with PASP (r=0.731, 0.769, P<0.001) and PASP (r=0.789, 0.801, P<0.001) negatively. The relationship between other systolic parameters with PASP or PVR was weaker or not significant. The optimal cut-off value in determining PASP: 70 mmHg and PVR: 3 wood was 40.5% for EF-inflow (sensitivity and specificity was 97% and 55%, 93%, and 61%, respectively), and 42.2% for EF-global (sensitivity and specificity was 97% and 76%, 90% and 85% respectively).
Conclusions: In patients with PH, RV inflow and global systolic function was impaired in inverse relationship with PASP and PVR. RV systolic synchronicity was impaired in severe PH. Evaluation of RV regional systolic function using RT3DE method may play a potential role in the non-invasive assessment of the severity of PH.
Assessment of the valvuloarterial impedance

Gender difference in regression of myocardial

Transthoracic echocardiography to study the

Incremental accuracy of transoesophageal

Figure 1. 3D morphological types of plaques

In conclusion, 3D TEE is a feasible method and provides a new morphological and quantitative approach of AAP

Assessment of the valvuloarterial impedance calculated with the use of 3-dimensional transesophageal echocardiography

Methods: We analyzed 74 patients (62±10 years) with moderate to severe AS. Ellipticity of the left ventricular outflow tract (LVOT) and the sino-tubular junction (STJ) were calculated as the short axis dimension divided by the long axis one. The areas of LVOT and STJ were evaluated using circular formula (π×[dimension/2]2) by 2-dimensional transthoracic echocardiography (2D-TTE) and using direct measurement by 3-dimensional transesophageal echocardiography (3D-TEE). Zva was calculated as the estimated left ventricular systolic pressure (systolic arterial pressure + the net mean pressure gradient taken into account post-stenotic pressure recovery) divided by the stroke volume index.

Results: Systolic blood pressure was 123±17 mmHg; peak EF, 56±15% and; mean pressure gradient, 41±14 mmHg. The ellipticity of LVOT and STJ was 0.77±0.10 and 0.95±0.05, LVOT and STJ areas using 2D-TTE (3.6±1.1, 5.0±1.4 cm², respectively) was smaller than those using 3D-TEE (4.4±1.0, 5.4±1.3, respectively, p < 0.001); subsequently, energy loss index using 2D-TDE was smaller than that using 3D-TEE; consequently, Zva using 2D-TEE (4.2 mm Hg/ml/m², 1.2±1.4, 3.1-5.5, median with inter-quartile ranges) was larger than that using 3D-TEE (3.4, 2.6-4.2, p < 0.01).

Conclusions: Two D-TTE overestimated the value of ELI relative to 3D-TEE due to the elliptical shape of the aortic root. It is desirable to use 3D TEE in the evaluation of Zva for risk stratification in patients with AS

Transthoracic echocardiography to study the ascending aorta: in search of the best approach

Methods: 80 patients with a severe aortic valvular disease (stenosis or regurgitation) were evaluated with a transthoracic echocardiography and MSCT to measure the thoracic aorta at different levels: sinuses of Valalsma, sino-tubular junction and ascending aorta. Three different echocardiographic methods were used: leading edge to leading edge, inner to inner and outer to outer and then compared to the ones obtained from MSCT. The interobserver and intraobserver variability was also performed.

Results: Transthoracic echocardiographic diameters were obtained in all patients but 3 (4%) because of poor acoustic window. The three methods showed an excellent interobserver and intraobserver variability, however, the inner to inner method presented the best reproducibility. Also, the inner to inner method showed the best correlation with MSCT for the assessment of thoracic aorta diameters (intraclass correlation coefficient): sinuses of Valalsma 0.83, sino-tubular junction: 0.87, and ascending aorta: 0.88. Mean difference between TTE and MSCT in measuring the ascending aorta were: by inner to inner 0.25±0.6 mm, leading to leading -0.77±0.43, and outer to outer -3.2±1.23.

Conclusions: Transthoracic echocardiography is an accurate technique for the assessment and follow-up of thoracic aortic diameters in valvular patients. The inner to inner approach is the method that shows the best agreement with MSCT measurements of aortic root dimensions.

Incremental accuracy of transoesophageal echocardiography over transthoracic approach for description of functional anatomy of aortic regurgitation

Background: Preoperative description of mechanisms of Aor Regurgitation (AoR) is essential for planning valve sparing surgery (VSS). Either tran-oesophageal (TEE) or transthoracic echocardiography (TTE) provide detailed anatomic view of aortic valve and ascending Aorta (AA) and information about dimensions and dynamic function of its components. Objective. To establish diagnostic value of multiplane TEE in comparison with TTE for definition of functional anatomy of AoR.

Methods: Using surgical observations as a reference, overall accuracy of TEE and TTE were calculated for both functional and anatomic classification of AoR in 51 patients operated on for AoR. Incremental accuracy of TEE over TTE was calculated as the ratio of the difference between their accurate diagnoses to the total number of cases examined and tested using McNemar’s test.

Results: Overall accuracy of TTE for functional classification was high (82%), but accuracy of TEE was higher (86%). Percentage of errors and information about mechanisms (20.5%). Agreement between both modalities in AoR jet direction was good (kappa = 0.85): eccentric jet in 12/15 cases of AWP in TEE (p<0.0001) and in 11/15 in TTE (p=0.002).

Conclusions: Both TEE and TTE provide high degree of accuracy. Incremental value of TEE for AVP and mechanism to define mechanisms (20.5%). Agreement between both modalities in AoR jet direction was good (kappa = 0.85): eccentric jet in 12/15 cases of AWP in TEE (p<0.0001) and in 11/15 in TTE (p=0.002).

Transthoracic echocardiography to study the ascending aorta: in search of the best approach

Methods: Transthoracic echocardiography (TTE) is used for a quantitative evaluation of the extent and severity of ascending aortic (AA) dilatation. The leading edge to leading edge has been recommended as the standard method to measure AA diameters, however other approaches have been proposed (inner to inner or outer to outer). Our aim was to analyze the accuracy of TTE by different methods in the evaluation of aortic dimensions in comparison with multidetector gated computed tomography (MSCT).

Results: Transthoracic echocardiographic diameters were obtained in all patients but 3 (4%) because of poor acoustic window. The three methods showed an excellent interobserver and intraobserver variability, however, the inner to inner method presented the best reproducibility. Also, the inner to inner method showed the best correlation with MSCT for the assessment of thoracic aorta diameters (intraclass correlation coefficient): sinuses of Valasalva 0.83, sino-tubular junction: 0.87, and ascending aorta: 0.88. Mean difference between TTE and MSCT in measuring the ascending aorta were: by inner to inner 0.25±0.6 mm, leading to leading -0.77±0.43, and outer to outer -3.2±1.23.

Conclusions: Transthoracic echocardiography is an accurate technique for the assessment and follow-up of thoracic aortic diameters in valvular patients. The inner to inner approach is the method that shows the best agreement with MSCT measurements of aortic root dimensions.

Gender difference in regression of myocardial hypertrophy after aortic valve replacement

Background: In patients with aortic stenosis, pressure overload induces cardiac hypertrophy and fibrosis. Female sex influences cardiac remodeling and fibrosis in animal models. However, sex differences in hypertrophy regression after aortic valve replacement have not yet been studied.

Methods: We prospectively performed echocardiography before and 2 weeks, 3
and 6 months after operation in 47 patients, 28 women and 19 men, undergoing aortic valve replacement for isolated aortic stenosis.

Results: Preoperatively, women and men had similar ejection fraction (56 and 59%) and left ventricular mass (142 and 148 g/m²). Postoperatively, there was no difference in effective valvular orifice area index, mean transvalvular pressure gradient between men and women. Two weeks after operation, increased LV mass persisted in men (131 g/m²), although LV hypertrophy in women (119 g/m²) regressed to the similar level of 6 months (121 g/m²). LV mass in men was similar to those in women in 6 months after operation.

Figure 1

Conclusion: Women adapt to pressure overload quickly than men, while men caught up to women in 6 months after operation.

Aorta and aortic valve 851

and 6 months after operation in 47 patients, 28 women and 19 men, undergoing aortic valve replacement for isolated aortic stenosis.

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without CAP (n=118, 63±13 years). Vs and Vd were compared between groups and with conventional vessel parameters including carotid-ankle vascular index (CAVI, calculated from blood pressure and pulse wave velocity), ankle brachial pressure index (ABPI), and carotid plaque score (PS, a composite index based on carotid artery plaque thicknesses).

**Results:** Comparing patients with vs. without CAP, Vs and ABPI were significantly decreased (2.9±1.2 vs. 3.8±1.3 cm/sec, p<0.001; 1.6±0.5 vs. 2.0±0.8 cm/sec, p<0.001, 0.88±0.23 vs. 1.10±0.12, p<0.001, respectively), and Aoji and PS were significantly increased (17.4±12.5 vs. 12.3±8.6, p<0.01; 9.0±5.0 vs. 5.3±4.8, p<0.001, respectively). Furthermore, Vs and Vd were significantly correlated with Aoji (r=0.381, p<0.001 and r=0.348, p<0.001, respectively), CAVI (r=0.328, p<0.001 and r=0.396, p<0.001, respectively), ABI (r=-0.219, p<0.01 and r=-0.269, p<0.001, respectively) and PS (r=-0.228, p<0.01 and r=-0.358, p<0.001, respectively), although there were no significant correlations with blood pressure, or heart rate.

**Conclusions:** Evaluation of Vs and Vd using PW-TDI in the aortic arch wall may be a novel and easily acquired indicator of aortic arch stiffness, and also correlates with several conventional vessel parameters.

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**ATRIAL FIBRILLATION AND ATRIAL FUNCTION**

**P4843** The relation between the CHADS2, CHA2DS2-Vasc score and echocardiographic parameters of thromboembolism in patients with atrial fibrillation

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**Background:** CHADS2 score has been revised as CHA2DS2-Vasc score for better embolic risk stratification in patients with AF. The aim of this study was to evaluate the relation between 2 clinical risk scores and echocardiographic parameters of embolism in AF patients.

**Methods:** 365 (M=305, mean age=55±10.4) patients with non-valvular AF who had trans-oesophageal echocardiography and trans-oesophageal echocardiography were enrolled. CHADS2 and CHA2DS2-Vasc scores were calculated and correlated to echocardiographic findings. LA volume, LA emptying fraction(EF), LA enoding velocity, LAA EF, the presence of dense SEC and thrombus, septal hypertension(UHV) (defined as >115 mmHg in men, >95 mmHg in women) were evaluated.

**Results:** Increased LAV(LAVi≥35ml/m2) was found in 143 patients, impaired LAAE(LAEF<30%) in 130 patients, decreased LAA emptying velocity(≤20cm/s) in 46 patients, decreased LAA EF(≤30%) in 136 patients, SEG in 102 patients and LAA thrombus in 2 patients. The patients with higher than 2 CHADS2 score were 65 and 182 respectively. Higher than 2 CHADS2 and CHA2DS2-Vasc score was 65 and 182 respectively. The presence of SEC was related with increased LAV, low LAEF, the presence of UHV. But low LAEF and low LAA emptying velocity was related with higher than 2 CHADS2-vasc score only. The presence of SEC and thrombus was associated with higher than 2 CHADS2-vasc score only.

**Conclusion:** CHADS2 and CHA2DS2-vasc scores were correlated with echocardiographic markers of LA dysfunction. But LA dysfunction was associated with higher than 2 CHADS2-vasc score only. CHADS2-vasc score appears to be more sensitive than CHADS2 score in detecting high risk patients.
Assessment of left atrial deformation and dysynchrony by three-dimensional speckle tracking imaging: comparative studies in healthy subjects and patients with atrial fibrillation


Background: Here we examined whether left atrial (LA) strains and synchrony are assessable by three-dimensional speckle tracking (3DS) and how the 3DS parameters are modified by atrial fibrillation (AF).

Methods: LA peak longitudinal, circumferential and area strains in systole (LSs, CSs, ASs) and those in late diastole (LSa, CSA, ASa) were determined by 3DS, and standard deviations (SD) of times to peaks of regional LA strains were calculated as indices of LA dysynchrony. LA strain and synchrony in AF patients were compared with those in age-matched healthy subjects (controls).

Results: 3DS could measure LA strains in 75 (97%) of 77 healthy subjects and all 30 patients with AF (20 with paroxysmal AF (PAF) and 10 with permanent AF). The mean time of analysis was 3.3±1.9 min for 3DS analysis, which was 18% shorter than for two-dimensional speckle tracking (2DS) analysis (4.0±2.3 min, P<0.05). In 3DS, inter-observer and intra-observer variabilities of LA strain were less than 10% and 12%, respectively. LSs (15.8±6.9 vs 25.7±7.2%, P<0.05), CSs (19.2±11.9 vs 17.1±10.2%, P<0.05), ASs (30.2±23.0 vs 74.2±26.2%, P<0.05), and 2DS-LSs (22.3±9.2 vs 32.6±6.5%, P<0.05) were significantly reduced in PAF than in age-matched controls (n=15), and further reduction of all of the parameters was observed in permanent AF. SDs of LSs, CSs, ASs were similarly larger in PAF and permanent AF than in controls. LSs (6.2±4.1 vs 12.0±4.1%, P<0.05), CSs (10.0±8.0 vs 22.8±8.1%, P<0.05), and ASs (18.6±10.2 vs 31.4±14.4%, P<0.05) were also reduced in PAF than in controls. SDs of CSs and ASs were larger in PAF than in controls. In multivariate analysis, CSs (odds ratio (OR) 0.77, P<0.043), ASs (OR 0.90, P=0.011), SD of ASs (OR 1.15, P=0.039) and 2DS-LSs (OR 0.71, P=0.045) were independent factors for identifying PAF patients. ROC analysis indicated that optimal threshold to predict PAF was <32% for CSs, <57% for ASs, >22% for SD of ASs and <26% for 2DS-LSs. Using these thresholds, sensitivity and specificity of prediction of PAF were 80% and 95%, respectively, for CSs, 97% and 85% for ASs, 75% and 86% of SD of ASs and 100% and 75% for 2DS-LSs.

Conclusions: 3DS is feasible for measurement of both LA strain and synchrony in both PAF and permanent AF patients. 3D LA strain appears to be comparable to the 2D LA strain for identifying PAF patients.

Measurement of left and right atrial volume in patients undergoing ablation for atrial arrhythmias: comparison of different algorithms of real-time 3D echocardiography


Methods: A total of 88 patients were studied by real-time 3DE. Atrial volume was measured using a muliplane interpolation method algorithm (Cardio-View v1.3, Tomtec) with manual planimetry of 8 equidistant slices. These volumes were compared with atrial volume determined by the QLAB 7.1 software (Philips) using a semiautomated border detection method.

Results: Linear regression showed that both LA and RA an excellent correlation between values determined by Tomtec and QLAB software (r^2=0.99 and 0.89 respectively, p<0.001). Bland-Altman analysis of Tomtec versus QLAB volume determination showed rather narrow 95% limits of agreement (-12 to +16 cc for LA volume and -12 to +14cc for RA volume) with a minimal slight bias of -1.9±7 cc and +0.8±6.5 cc respectively by the Tomtec method.

Conclusions: The QLAB 7.1 semiautomated border detection method shows excellent correlation for left and right atrial volume determination compared to the older more time consuming multipane interpolation method by the Tomtec software, with only slight underestimation. The results indicate that values of left and right atrial volume obtained by either algorithm can be compared, for example during follow-up examinations.

Left atrial dysynchrony in patients with paroxysmal atrial fibrillation - three-dimensional speckle tracking analysis


Background: Left atrial (LA) enlargement is commonly known to be associated with the presence of atrial fibrillation and we have already reported about decreased LA compliance in patients with paroxysmal atrial fibrillation (PAF) using the parameter of the peak global strain and LA emptying fraction (LAEF) assessed with three-dimensional (3D) speckle tracking imaging. The purpose of this study was to investigate LA wall mechanical synchrony in patients with PAF.

Methods: A total of 150 subjects (96 males; mean age 61±14 years) including 50 PAF patients, 50 hypertension (HT) patients and 50 control were enrolled. All the subjects were in sinus rhythm during examination. LA volume, LAEF and LA wall strain were analyzed by 3D area tracking imaging and the maximal value of global area strain curve was defined as peak global strain. Time-to-peak standard deviation (TP-SD) was calculated as the standard deviation of the time from R-wave on electrocardiogram to peak positive value of the segmental strain curve in six mid LA segments to assess LA dysynchrony.

Results: 84% of PAF patients had hypertension. Early diastolic mitral annular velocity (Ea) was lower in HT (P=0.0001) and PAF (P<0.0001) than in control and the ratio of early diastolic transmural flow velocity to Ea (Ea/Ea) was higher in HT (P=0.0002) and in PAF (P<0.0001) than in control. The maximal LA volume index was larger in HT than in control (P=0.0003) and was larger in PAF than in HT (P=0.0007). LAEF and peak global strain was lower in PAF than in HT (P<0.0001 and P<0.0001, respectively) and in control (P<0.0001 and P<0.0001, respectively). TP-SD was higher in PAF than in HT (P=0.006) and in control (P<0.001). Conclusion: LA dysynchrony is developed in patients with PAF and it may have a potential to predict the incidence of PAF.

Echocardiographic assessments of left atrial function in patients with chronic primary mitral regurgitation by two-dimensional speckle tracking


Background: In conjunction with left atrial (LA) volume, the evaluation of LA performance, including reservoir, conduit, and booster pump function, provides incremental information pertaining to LA function. The aim of this study was assess the hypothesis that global LA function is altered in patients with chronic primary mitral regurgitation (MR).

Methods: Two-dimensional speckle tracking of the left atrial was acquired from the apical 4-chamber view in 49 normals and 72 subjects with chronic MR. Maximum LA volume and minimal LA volume and the LA volume before atrial contraction were measured. Similarly, global atrial longitudinal strain was measured by averaging all atrial segments. Reservoir (S-LAs), conduit (S-LAe), and contractile (S-LAa) phase strain were obtained.

Results: To explore the effects of MR severity on LA function, subjects were divided into two groups: mild MR group (n=52) and moderate/severe MR group (n=20). Reservoir (total LA emptying fraction), and booster pump function (active LA emptying fraction) were impaired in the moderate/severe MR. S-LAs was significantly reduced in the moderate/severe MR group than in the mild MR group and the controls. Similarly, S-LAa was significantly reduced in the moder-
Atrial fibrillation and atrial function

Reference values of right atrial area and volume in healthy adults by two-dimensional echocardiography

Methods: In this prospective study 880 healthy adult subjects (mean age 28±5.9 years, 38% female, 395 top-level endurance athletes, 225 strength athletes and 230 non-athletes) were examined by echocardiography. For comparison we performed a meta-analysis of 9 previously published studies (1979-2010) describing RA area in healthy subjects (n=624). Statistical analysis included the calculation of 95% quantiles (for defining cut-off values) and the identification of possible confounding factors.

Results: Mean RA area was significantly larger in endurance athletes as in strength- and non-athletes (15.4±2.0 cm² vs. 12.8±1.6 cm² and 12.3±2.0 cm², p<0.001). RA area correlated significantly with age, gender, body surface area and endurance exercise training and was similar in previously described 624 healthy adults (12.6±3.8 cm²). 95% quantiles for RA-area of all investigated groups separately.

Conclusions: Right atrial RA size is important in several indications as for screening, diagnosis and follow-up assessment in patients with pulmonary hypertension. The objective of this paper was to define normal-cut off values for RA area by echocardiography in healthy subjects.

<table>
<thead>
<tr>
<th>Controls (n=27)</th>
<th>Mild MR (n=47)</th>
<th>Moderate/severe MR (n=25)</th>
<th>Overall (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA total emptying fraction</td>
<td>42.6±9.4</td>
<td>41.3±7.5</td>
<td>34.7±11.1</td>
</tr>
<tr>
<td>S-LA (%)</td>
<td>20.3±5.6</td>
<td>19.9±4.3</td>
<td>15.3±6.4</td>
</tr>
<tr>
<td>Conduit function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA passive emptying fraction</td>
<td>22.9±8.8</td>
<td>20.8±8.6</td>
<td>20.6±8.9</td>
</tr>
<tr>
<td>S-LA (%)</td>
<td>10.5±5.4</td>
<td>9.8±4.0</td>
<td>8.7±4.1</td>
</tr>
<tr>
<td>Booster pump function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA active emptying fraction</td>
<td>15.7±7.3</td>
<td>25.7±7.4</td>
<td>17.6±10.1</td>
</tr>
<tr>
<td>S-LA (%)</td>
<td>9.7±3.5</td>
<td>10.1±3.3</td>
<td>6.1±4.2</td>
</tr>
</tbody>
</table>

P-value 1: controls vs. moderate/severe MR; P-value 2: mild MR vs. moderate/severe MR.

P4850 Evaluation of left atrial appendage dysfunction by strain imaging using transthoracic echocardiography

Y. Lee, M. Nishino, M. Tanike, N. Makino, H. Kato, Y. Egami, R. Shutt, T. Tanouichi, Y. Yamada, Osaka Rosai Hospital, Osaka, Japan

Background: Left atrial appendage (LAA) thrombus is common cause of cardioembolic stroke. LAA dysfunction, which can induce thrombus formation, is usually evaluated by LAA peak flow velocity measured by transesophageal echocardiography (TEE), but it is a semi-invasive procedure. Therefore, we investigated whether LAA dysfunction can be evaluated by recently developed speckle tracking strain imaging using noninvasive transthoracic echocardiography (TTE).

Methods: Consecutive 55 patients, who underwent TEE to rule out thrombus or evaluate valvular disease, were enrolled. Immediately before TEE, we observed LAA by parasternal short-axis view using TTE. A following TTE parameter was evaluated as LAA dysfunction in this study: LAA shortening fraction which was defined as the difference between maximum and minimum longitudinal strain of LAA. We compared LAA shortening fraction with classical TEE parameter, LAA peak flow velocity and also analyzed the parameter in sinus or atrial fibrillation group separately.

Results: LAA shortening fraction was significantly correlated with LAA peak flow velocity measured by TEE (r=0.641, P<0.001). In addition, LAA shortening fraction was significantly higher in sinus rhythm group (n=22) than atrial fibrillation group (35.6±15.3% vs. 25.3±15.7%, P<0.001). LAA thrombi were found in three patients, whose rhythm were all atrial fibrillation and they were all on adequate anticoagulant therapy. LAA shortening fraction of these three patients showed significantly worse value than the other patients in atrial fibrillation group (10.5±3.92% vs 26.7±15.7%, P<0.001).

Conclusion: LAA dysfunction including possible thrombus formation can be evaluated noninvasively by strain imaging using transthoracic echocardiography.

P4851 Comparison between two-dimensional and real-time three-dimensional speckle tracking echocardiography in the assessment of left atrial structure and function

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Purpose: Two-dimensional speckle tracking echocardiography (2-DSTE) using Simpson’s method has been recently used to assess left atrial (LA) volume (LAV) and function. To evaluate the accuracy of 2-DSTE, we compared 2-DSTE with 3-DSTE as a reference standard because major advantage of 3-DSTE is the improvement of accuracy in the evaluation of cardiac chamber volume without any geometrical assumption.

Conclusions: Fabry disease is associated with reduced atrial compliance and reservoir function, irrespective of the presence of LVH, suggesting a coexistent atrial myopathy. The reduction in E-Sr with LVH reflects the associated reduction in left atrial conduit function. These results suggest that Fabry cardiomyopathy involves not only the ventricle but also the atrium. Consequently, measurements of left atrial reservoir function and compliance may be useful in subclinical diagnosis of Fabry disease.

Table 1

<table>
<thead>
<tr>
<th>Atrial strain and strain rate</th>
<th>Controls (n=50)</th>
<th>Fabry: no LAH (n=10)</th>
<th>Fabry: with LAH (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass (g/m²)</td>
<td>70±18</td>
<td>79±16</td>
<td>127±23†</td>
</tr>
<tr>
<td>Left atrial volume (m³/m²)</td>
<td>23±4</td>
<td>25±7</td>
<td>28±6†</td>
</tr>
<tr>
<td>Systolic SI (%)</td>
<td>69±16</td>
<td>66±11</td>
<td>64±12</td>
</tr>
<tr>
<td>Diastolic SI (%)</td>
<td>42±7</td>
<td>42±8</td>
<td>39±11</td>
</tr>
<tr>
<td>S-ur [cm/s]</td>
<td>3.0±0.8</td>
<td>2.4±0.5†</td>
<td>2.3±1.0†</td>
</tr>
<tr>
<td>E-ur [cm/s]</td>
<td>3.3±1.2</td>
<td>2.9±0.8</td>
<td>2.3±1.0†</td>
</tr>
<tr>
<td>A-ur [cm/s]</td>
<td>3.0±0.7</td>
<td>3.0±0.8</td>
<td>2.9±0.6</td>
</tr>
</tbody>
</table>

§p<0.05 compared to Normal.
Methods: We measured phasic LAV (max., min. and pre-atrial contraction (AC) volume) and emptying function (EF) (total, passive and active EF) and LA peak strain by 3-DSTE (Atria) which can provide time-LA volume curve with volume rates at 25-60fps and by 2-DSTE from apical 2, 3 and 4-chamber views in 61 subjects. Parameters were compared between 2-DSTE and 3-DSTE.

Results: LAV and function were easily and rapidly obtained by 3-DSTE. There was a good correlation between LAV by 3-DSTE and LAV in 2, 3, 4-chamber views and the average of these three views by 2-DSTE (=0.76, 0.80, 0.78 and 0.84, p<0.001, respectively). LA total and passive EF in 4-chamber view by 2-DSTE were increased compared to 3-DSTE despite no difference in LA peak strain. Phasic LAV in 3-chamber view by 2-DSTE was decreased and LA phasic function was increased compared to 3-DSTE (table).

Table 1. LA function and structure assessed by 3-D and 2-D speckle tracking

<table>
<thead>
<tr>
<th>3-DSTE</th>
<th>2-DSTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. LAV, ml</td>
<td>52.2±13.4</td>
</tr>
<tr>
<td>Min. LAV, ml</td>
<td>28.0±9.4</td>
</tr>
<tr>
<td>Passive EF, %</td>
<td>31.6±9.1</td>
</tr>
<tr>
<td>Active EF, %</td>
<td>19.5±5.1</td>
</tr>
<tr>
<td>LA strain</td>
<td>17.9±5.7</td>
</tr>
</tbody>
</table>

*p<0.05 vs. 3-DSTE.

Conclusion: Although LA volume and function assessed in 3 and 4-chamber view by 2-DSTE and tendency to be over-estimated compared to 3-DSTE, those by 2-chamber view and the average of 3 views were comparable to 3-DSTE and revealed more reliable for the accurate diagnosis. This study demonstrated that 3-DSTE will be more promising method in assessing of LA structure and function than 2-DSTE.

P4855 Evaluation of right atrial function using 3D echocardiography in patients with pulmonary artery hypertension


Purpose: In patients with pulmonary artery hypertension (PAH), right ventricular pressure overload causes right heart failure (RHF). In these patients, right atrial pressure (RAP) increased, and cardiac index (CI) decreased. RAP CI, and serum brain natriuretic peptide (BNP) were independent predictors to evaluate the prognosis. We sought to investigate the degree of right atrial (RA) overload and the severity of RHF using 3-dimensional (3D) right atrial volume index by 3D echocardiography.

Methods: We performed 3D echocardiography and right heart catheterization in 53 PAH patients (age:41±15 years). We measured right atrial end-diastolic volume index (3DRAEDVI), right atrial end-systolic volume index (3DRAESVI), and right atrial ejection fraction (3DRAEF) by 3D-echocardiography. Mean right atrial pressure (mRAP) and cardiac index (CI) by right heart catheterization, and serum BNP were measured.

Results: mRAP was 8.7±6.0 mmHg (range 2 to 30 mmHg), 3DRAEDVI was 21.4±20.1 ml, 3DRAESVI was 37.2±26.8 ml, and 3DRAEF was 55.2±15.3%.

Conclusions: The degree of right atrial overload and the severity of RHF using 3D echocardiography.
There were significant positive correlations between mRAP and 3DRAEDV (r=0.66, p<0.01), 3DRAESV (r=0.70, p<0.01). There were significant negative correlations between mRAP and 3DRAEF (r=0.60, p<0.01). There were significant positive correlations between CI and 3DRAEDV (r=0.39, p<0.01), 3DRAESV (r=0.35, p=0.02). There were significant positive correlations between CI and 3DRAEF (r=0.39, p<0.01). There were significant positive correlations between BNP and 3DRAEDV (r=0.58, p<0.01), 3DRAESV (r=0.64, p<0.01). There were significant negative correlations between BNP and 3DRAEF (r=0.70, p<0.01).

Conclusions: 3D echocardiography was useful for noninvasive evaluation of RA overload and severity of RVH in patients with PAH.

### P4856

**Supranormal diastolic function in elite endurance-athletes is related to left atrial geometry and function**

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Endurance-training is associated with specific structural and functional cardiac changes. "Supranormal" diastolic function in athletes was demonstrated previously, but data on left atrial (LA) geometry and function are lacking. Our aim was to investigate complex changes in LA structure and deformation assessed by 2D speckle tracking echocardiography (STE), and their relation with left ventricular (LV) diastolic properties in elite endurance-athletes.

**Methods:** 64 subjects (21±4 years, 44 male) were enrolled: 40 endurance athletes and control group of 24 age- and sex-matched sedentary subjects. LA geometry was assessed by volumes at the MVO (MVOV), MVC (MVCV), and at the beginning of the P wave (PV), while LA function by passive EF (aEF) as PV-MVCV/PV. LA deformation was measure by STI: contraction from MVOV-PV/MVOV, expansion index (EIx) as MVOV-MVCV/MVOV, and active EF at the beginning of the P wave (PV), while LA function by passive EF (pEF) as PV-MVCV/PV-MVCV/MVCV. Global geometry was assessed by volumes at the MVO (MVOV), MVC (MVCV), and at the beginning of the P wave (PV), while LA function by passive EF (aEF) as PV-MVCV/PV-MVCV. LA deformation was measure by STI: contraction from peak negative strain (PNS) and strain rate (PNSR); relaxation from peak positive strain (PPS) and strain rate (PPSR), and global strain (GS). LV diastolic function was assessed by E/A ratio, flow propagation velocity (FPV), E/FPV, S/D (from pulmonary vein flow), long-axis early diastolic velocity (E), and E/E'.

**Results:** Athletes had 'supranormal' LV diastolic function (E/A=2±3.0 vs 1.5±0.2; P=4.7±1.4 vs 37±5.0 cm/s; EFPV=3±1.07 vs 1.8±1.1; S/D=0.7±0.2 vs 1.3±0.1; E=4.8±1.2 vs 5.9±2.1; p<0.05). There were changes in LA geometry and optimized LA deformation in athletes (see table). Univariate analysis showed that GS was correlated with E, E/FPV (r=0.71, p<0.02; and r<0.5, p<0.05) and with E/E' and S/D (r=0.64 and r=0.68, p<0.01). By multiple stepwise regression analysis, best independent determinant of GS was E/E' ratio (p=0.62, r=0.48, p<0.01).

**Conclusion:** Elite endurance-athletes had a "supranormal" LV diastolic function, related to LA deformation. Assessment of complex changes in LA geometry and function may help to understand the role of LA in the cardiac changes induced by endurance training.

### P4857

**Dependence of atrial strain and strain rate on ventricular function - implications for the assessment of left atrial function**


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**Background:** Speckle tracking echocardiography (STE) has been used to determine left atrial (LA) strain (S) and strain rate (SR) in order to measure intrinsic LA function (booster, reservoir, conduit). However, LA deformation is influenced by LV function since both chambers are connected through the mitral annulus. Our aim was to estimate how much of the variability of LA S and SR can be accounted for by LV S and SR in subjects without cardiovascular symptoms.

**Methods:** Global longitudinal S and SR were determined by STE from 3 apical planes in 50 asymptomatic subjects aged 31±7 yrs. In LA and LV, using the same cardiac cycle and the P-wave onset as reference, we measured peak amplitude and timings of S and SR during LA contraction (Sa, SrS, and SR during LV contraction (Sa, SrS), and SR during LV early diastolic relaxation (SrE). By conventional echo, we also measured LA and LV volumes at P-wave onset, end-diastolic and end-systolic, estimated arterial elastance (Ea). LV stroke work – SW, and diastolic function (E, A, ETD, Vp, E).

**Results:** Peak SrSa occurred on average 9 ms earlier in the LA compared with LV (p=0.02); all other events occurred at the same time in both chambers. LA S and SR had higher absolute values compared with corresponding LV S and SR values (p=0.001 for all). Sa correlated with changes in LA length (r=0.59, p=0.006) and volume (r=0.30, p=0.035) during LA contraction. LA Sa correlated with changes in LA length (r=0.63, p=0.001) and volume (r=0.44, p=0.001) during LV contraction. Multiple stepwise regression analysis revealed that the single most important independent predictor of LA S and SR was the corresponding LV S and SR. This was consistent during LA contraction (r=0.39, p<0.05) when compared with the events during LV contraction and LV early relaxation (r=0.5, r=0.27). Additionally, LA Sa, SrS and SrE were also predicted by LA end-diastolic volume. There was no significant correlation between LA Sa and LA wave, and LV wave and LA volume at P-wave onset, and LA and LV EDV; between LA SaS and A wave, and LA and LV volume at P-wave onset; between LA SrS and E wave, ETDT, Vp, E; LV ESVV and LV EDV; and between LA SrSs and LV SW and Ea.

**Conclusions:** There is substantial interaction of LA S and SR on the corresponding LV S and SR through the shared mitral annulus, most pronounced when the LV is the driving chamber. Thus, STE may be useful to assess only the LA booster function, rather than assessing intrinsic LA reservoir and conduit function, because of its less dependence on corresponding LV S and SR during LA contraction.

### P4858

**Detection of pulmonary congestion using the newly-developed pocket-sized transthoracic echocardiographic imaging device in patients with suspected heart failure**

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**Background:** Ultrasound lung comets (ULCs) assessment is simple, fast and clinically useful for the evaluation of pulmonary congestion in patients with heart failure (HF). Recently-developed pocket-sized transthoracic echocardiographic (pTTE) imaging device has allowed performing screening study in a variety of clinical settings. The aim of this study is to investigate the feasibility and usefulness of pTTE for the evaluation of ULCs in patients with HF.

**Methods:** This prospective study consisted of 51 consecutive patients (25 female, 66±15 years) with known or suspected HF who underwent the standard TTE (sTTE) and pTTE. Exclusion criteria included the following: patients with hemodialysis, recent cardiac surgery, known pulmonary diseases. The examination of pTTE was performed with the VSCAN (GE Medical Systems). Immediately after the pTTE study including the assessment of ULCS, all patients underwent sTTE and ULCS assessment by another sonographer blinded to the results of pTTE study. We defined ULC score according to the number of ULCs observed in each 4 segments (right upper & lower, left upper & lower) of chest wall as follows; None: 0, Mild (the number of ULCs; 0-5): 1, Moderate (6-10): 2, Severe (11-): 3. The sum of these scores in each 4 segments is defined as total ULC score (0-12 points). Clinical diagnosis of congestive HF was based on the Framingham criteria, with all corroborative information reviewed by 2 cardiologists blinded to the information of ULCs and other corroborative signs. The ULCs examinations by pTTE were successfully completed in all cases (feasibility 100%), the time needed for the ULCs assessment is about 5 min-utes. ULCs were observed on pTTE in 44 patients (67%). There was a highly significant correlation between the total ULC score evaluated by pTTE and sTTE (p=0.93; Spearman, p<0.0001). The patients with ULCs had lower left ventricular (LV) ejection fraction and larger IVC diameter, left atrial volume index. BNP values were also well correlated with ULC score evaluated by pTTE (p=0.60; Spearman, p<0.0001). Receiver Operating Characteristic (ROC) curve analysis revealed the relationship between ULC score evaluated by pTTE and the diagnosis of HF (AUC: 0.93). The ULC score of 2 was maximum to diagnose pulmonary congestion with a sensitivity of 88% and a specificity of 83%. The ULC score of 4 had a sensitivity of 60% and a specificity of 100%.

**Conclusion:** Detection of pulmonary congestion using the newly-developed pTTE imaging device in patients with HF is feasible and accurate.

### P4859

**Test accuracy of hand-held echocardiographic imaging**

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**Aims:** To investigate intra- and inter-rater variability of expert-users interpreting hand-held echocardiographic studies (HAND).

**Methods:** We scanned 320 consecutively enrolled patients both with HAND and high-end scanners (HIGH). Imaging studies were interpreted independently by two blinded level III echocardiographers. HIGH readings served as gold-standard. Segmental endocardial-border delineation was scored to describe image quality. Assessment
of LV dimensions, regional/global LV-function and grading of valve disease were compared.

Results: We found correlations of \( r = -0.8 \) (\( p < 0.01 \)) for intra-rater variability for both expert-readers analysing HAND and HGH studies for image quality, wall-motion abnormalities and left ventricular measurements. For intra-rater variability of LV-EF assessment correlations were at least moderate (\( r = -0.6 \), \( p < 0.01 \)). Inter-rater variability for HGH studies was \( r = -0.9 \) (\( p < 0.01 \)) for all parameters. Inter-rater variability for all parameters assessed by HAND was less favourable, but still at least moderate for all parameters (\( r = -0.6 \), \( p < 0.01 \)).

Conclusions: The test accuracy for hand-held echocardiographic study interpretation focusing on basic assessment of cardiac morphology and function as compared to standard echocardiography is moderate to very good for experienced echocardiographers. However, training in interpreting hand-held echocardiographic findings is desirable.

Effect of through plane motion for the accuracy of two-dimensional circumferential strain analysis

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Purpose: Measurements of 2D circumferential strain (CS) is affected by loss of speckles due to through plane motion, raising the doubt regarding its accuracy. 3D speckle tracking echocardiography (STE) may eliminate this limitation. If through-plane motion affects 2D speckle tracking analysis, we hypothesized worst correlation and largest mean difference of CS were observed at basal level, and best correlation and least difference of CS were noted in the apical level between 2DSTE and 3DSTE measurements.

Methods: We obtained 2D basal, middle and apical short-axis images, and 3D full-volume datasets (GE, Vivid E9) in 44 patients with various cardiovascular diseases (mean age 62.1 ± 19 years, 23 men). Using 2D/3D speckle tracking software, segmental CS at end-systole was measured. Global CS and average CS at each of 3 LV short-axis levels were calculated in both modalities. Using anatomical M-mode, we measured mitral annular displacement (MAD) on apical 4-chamber view, and patients were divided into two groups according to the median value of MAD (9.4mm) for investigating the effect of through plane motion.

Results: Although a good correlation of global CS was noted between the two methods (\( r = 0.80 \), \( p < 0.01 \)), mean values were significantly higher in 3DSTE compared to 2DSTE (\( -18.4 \pm 6.3 \) vs. \( -14.7 \pm 5.0 \), \( p < 0.001 \)). Correlation of averaged CS and their mean bias between the two methods were 0.664±0.61 at basal level, 0.784±0.17 at middle level and 0.60±0.23 at apical level, respectively. Correlation of global CS between the two methods was higher in group of patients who showed MAD less than 9.4mm (\( r = 0.81 \)) compared to group of patients with MAD > 9.4mm (\( r = 0.61 \)).

Conclusions: Our results suggest that through plane motion affects CS measurements using 2DSTE, especially in subjects with normal longitudinal function.
Results: A total of 104 patients were studied. There was excellent agreement between the Vscan and the high-end echocardiograph for left ventricular systolic function and pericardial effusion (Kappa 0.89 and 0.81 respectively), and agreement was good or moderate for evaluating aortic, mitral and tricuspid valve function and left ventricular size (Kappa 0.55-0.66). Visualization of the Vscan images in full-screen format on a PC did not in general confer added value.

Conclusions: The Vscan used by a trained cardiologist has good diagnostic accuracy in the emergency setting compared to a high-end echocardiograph, despite small screen size and lack of pulse-wave and continuous Doppler.

### P4863

**Inter-vendor variability for measurements of left ventricular strain using two-dimensional speckle tracking analysis: a study of Japanese Ultrasound Speckle Tracking of the Left Ventricle (JUSTICE)**

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Purpose: Two-dimensional speckle tracking analysis of the left ventricular (LV) strain has been widely used for the evaluation of the LV mechanics. However, controversy exists regarding the inter-vendor agreement of LV 2D strain in healthy subjects. Methods: Among 817 healthy subjects enrolled in JUSTICE, inter-vendor variability was determined by acquiring echocardiographic images from 2 of 3 different vendors (V1 vs. V2, n=47; V1 vs. V3, n=96; V2 vs. V3, n=50). The acquired images included 3 short axis views and 4 apical views. With the 2D speckle tracking software from each vendor, radial, circumferential and longitudinal strain were measured using an 8-segment model, and global 2D strain values were determined. Agreement was assessed by intraclass correlation coefficient (ICC) with its limit of agreement (LOA) and Bland-Altman analysis. Results: Global 2D strains were significantly different between the two vendors in majority of comparisons. In two-vendor comparison, the ICCs of global strain were poor to fair (Table). The ICC was the worst for the global radial strain, and the best for the global longitudinal strain.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>V1 vs. V2</th>
<th>V1 vs. V3</th>
<th>V2 vs. V3</th>
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<tbody>
<tr>
<td>GRS</td>
<td>0.53 ± 0.17</td>
<td>0.37 ± 0.11</td>
<td>0.13 ± 0.07</td>
</tr>
<tr>
<td>GLS</td>
<td>0.21 ± 0.23</td>
<td>0.19 ± 0.27</td>
<td>0.15 ± 0.11</td>
</tr>
</tbody>
</table>

Table 1. Inter-vendor variabilities

Conclusions: 2DSTE-derived LV strain measurements are highly vendor-dependent. Due to a low inter-vendor agreement, 2D strain data are not interchangeable when conducting a longitudinal follow-up or across-sectional assessment of the LV myocardial deformation.

### P4864

**Usefulness of automated function imaging to detect myocardial ischemia during dipyridamole stress echocardiography**

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Purpose: Dipyridamole stress echo (DSE) is currently used as an alternative to dobutamine stress echo in detecting coronary artery disease (CAD). However, the lower sensitivity, especially in single-vessel disease and the high inter-observer variability of wall motion (WM) analysis are two major drawbacks of DSE. We aimed in this study to investigate the usefulness of global longitudinal strain (GLS) by automated function imaging (AFI, Echopac GE Horten, Norway) to improve diagnostic accuracy and reproducibility of DSE in detecting myocardial ischemia. Methods: 37 patients (18 men, 67±9 years), with intermediate/high-pre-test CAD probability underwent DSE followed by coronary angiography within one week. Diagnostic accuracy in the identification of CAD, evaluated through sensitivity, specificity and positive/negative predictive values (PPV/NPV), was analyzed for wall motion score index (WMSI) and GLS. Optimal cutoff value to define normal GLS was 20%. Concordance between each diagnostic method and the reference standard, represented by coronary angiography, was evaluated by kappa score and Kendall’s tau coefficient. Furthermore, the agreement between two observers with different experience in DSE was assessed by using Cohen’s k coefficient. Results: Prevalence of significant CAD (more than 50% of luminal narrowing) was 70% and prevalence of single vessel disease was 60%. Mean GLS significantly decreased from rest (+17.4±4.9% to peak DSE (+15.4±4.9, p<0.001); Sensitivity, specificity, PPV and NPV for WMSI were respectively: 50%, 67%, 83% and 29%. However, combination GLS and WMSI had the highest sensitivity (70%), specificity (70%), PPV (87.5%) and NPV (40%). Furthermore, GLS showed higher concordance with coronary angiography (k = 0.75; Kendall’s tau = 0.78) than WMSI (k = 0.11; Kendall’s tau = 0.14). In addition, there was a good agreement between a trainee and an expert observer by using GLS in comparison with WM analysis for images interpretation at rest (k = 0.61 for WM, k = 0.57 for GLS). However, the agreement significantly improved for images interpretation at peak stress (k = 0.50 for WM, k = 0.50 for GLS). Conclusions: Combination of GLS and WMSI resulted in significant increase in the accuracy of DSE to detect myocardial ischemia, especially with regard to the test sensitivity. Besides, GLS analysis provides an increase of the agreement for images interpretations between experienced and non-experienced observer, especially at peak stress. Hence, adding routinely GLS analysis during DSE could probably be helpful for more accurate patient risk stratification.

### P4865

**Changes in left ventricular strain during exercise stress echocardiography in healthy subjects: a speckle tracking echocardiography study**

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Background: Stress echocardiography is widely used but its major limitation is the subjective interpretation of wall motion changes. Speckle tracking echocardiography (STE) offers a quantitative method with the semiautomatic evaluation of the different components of myocardial deformation. The aim of our study was to evaluate changes in left ventricular (LV) systolic performance during the different steps of exercise stress echocardiography (ESE) in a population of healthy subjects. Methods: ESE was performed in 25 healthy subjects (mean age 26±3.1) in the semi-supine position on a lifting cycleergometer: the workload was increased every 2 minutes by 25W, up to the achievement of 100W. Echo was performed at each stage of the physical exercise and during the recovery phase. LV global longitudinal strain was calculated averaging values of all myocardial segments in apical 2-, 3- and 4-chamber views; radial, circumferential strain and LV twisting were obtained from the parasternal short-axis views at basal and apical levels. Results: Mean heart rate of 164±21 bpm was reached. All LV parameters explored increased significantly, reaching the maximum value at peak exercise. Subjects showed a relative increase of strain values respect to baseline of 48±14.1% for LV global radial strain (baseline: 23±8.8, peak value: 35±4.10.1, 43±12.2% for LV twisting baseline: 10.5±3.6, peak value: 15.5±7.4%), 34.9±8.6% for global circumferential strain (baseline: 24±3.6; peak value: 32.8±9.6%) and 13.4±4.9% for global longitudinal strain (baseline: 20.1±2.9; peak value: 22.8±2.8%).

Conclusions: This is the first study that reported the normal range values and the percentages of increment of LV strain that physiologically occurs during ESE, fixing a reference point to better interpret pathological studies.
Hypertrophic cardiomyopathy in Iceland: MYBPC3 founder mutation?

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The aim of this study was to investigate Hypertrophic Cardiomyopathy (HCM) in Iceland, identify sarcomeric mutations causing HCM and understand the phenotype-specific consequences of these mutations. Iceland, an island with the population of 300,000 offers a great opportunity to investigate this heterogeneous disease in a whole population.

Methods: The study cohort consisted of all patients having clinical diagnosis of HCM in Iceland in the period from 1997-2010. Patients were searched through medical records and echocardiographic database at the main hospitals and cardiologists private clinics. All HCM patients were invited to have genetic testing and an interview. Samples were screened for the MYBPC3 c.927-2A-G mutation previously described in two Icelandic families. If negative, targeted sequencing of 8 HCM genes and the GLA gene was performed. Information on phenotype and clinical history was obtained from patient medical records and interviews.

Results: 177 patients with HCM diagnosis were identified, 156 were still alive. 12 had already been genotyped and 119 accepted to participate in the study. 72 (55%) had the c.927-2A-G mutation in MYBPC3. Additionally, 4 had other variants in MYBPC3, one was diagnosed with a variant in MYH7. 5 were diagnosed with variants in the GLA gene. Fabry disease has been confirmed in three of these.

Clinical data on patients with c.927-2A-G mutation in MYBPC3 are shown in the table 1.

Table 1

<table>
<thead>
<tr>
<th>Age at diagnosis (mean, range)</th>
<th>40.4 (9-72)</th>
</tr>
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<tbody>
<tr>
<td>Adverse cardiac event</td>
<td>21 (9.5%)</td>
</tr>
<tr>
<td>Age at first adverse event</td>
<td>51 (17-72)</td>
</tr>
<tr>
<td>Adrenal Function</td>
<td>12 (16.7%)</td>
</tr>
</tbody>
</table>

*Sudden cardiac death (SCD), ICD implant, myectomy, alcohol septal ablation.

Conclusions: The c.927-2A-G mutation in MYBPC3 is the leading cause of HCM in Iceland, accounting for 55% of cases. The c.927-2A-G mutation causes serious disease with an average age of onset of 40 yrs. We hypothesize that all 72 individuals with the c.927-2A-G mutation are offspring of a common ancestor. At present, we cannot estimate when this common ancestor lived in Iceland, but we expect from inheritance studies, that he/she lived more than 5 generations ago.

Hypertrophic cardiomyopathy in muscular dystrophy: genetically caused structural weakness vs. acquired myocarditis? Answers based on a siblings study


Background: Muscular dystrophy type Duchenne (DMD) and type Becker (BMD) represent the most common X-linked genetic diseases. Apart from progressive proximal skeletal muscle weakness, DMD and BMD are characterised by cardiac muscle involvement with a characteristic pattern of myocardial damage affecting the subepicardium of the left ventricular (LV) free wall. The molecular pathomechanism leading to cardiomyopathy is still unclear: the fragility of the cell membrane caused by deficient sarcocellular dystrophin may predispose cardiomyocytes to cell death in response to mechanical stress. However, it is also argued that DMD/BMD patients are more susceptible to myocarditis which in turn may also cause subepicardial damage in the LV free wall. In order to further elucidate the molecular pathomechanism of muscular dystrophy, we evaluated subepicardial magnetic resonance (CMR) studies of DMD/BMD siblings of the same age group.

Methods: Since 2007, we have performed cardiac examinations comprising (amongst others) comprehensive CMR studies in more than 120 patients with DMD and BMD. The CMR studies comprised (amongst others) cine-CMR and T1-weighted late-gadolinium-enhancement (LGE) imaging in order to assess functional and structural parameters. In order to enable a meaningful comparison of CMR study results, we selected only those DMD/BMD siblings who were at least 12 yrs (DMD) or 20yrs (BMD) old and in whom the difference of age was less than 10yrs.

Results: Four pairs of siblings were identified (with each sibling having the same dystrophin gene mutation) fulfilling the inclusion criteria. The age of sibling pair no.1 (BMD) was 21yrs and 24yrs, left ventricular ejection fraction (LVEF) was 42% and 40%, and the extent of LGE was 2.8% and 2.6%, respectively. The age of sibling pair no.2 (BMD) was 36yrs and 38yrs, LVEF was 36% and 42%, and the extent of LGE was 4.1% and 3.3%, respectively. The age of sibling pair no.3 (BMD) was 29yrs for both (monozygous siblings), LVEF was 65% and 66%, and the extent of LGE was 0.5% and 1.1%, respectively. The age of sibling pair no.4 (BMD) was 40yrs and 43yrs, LVEF was 58% and 63%, and the extent of LGE was 3.7% and 5.1%, respectively. All siblings demonstrated the same localization of LGE in the subepicardium of LV free wall (-/+ septal wall).

Conclusions: The similar results in LVEF, extent of LGE and localization of LGE in siblings with the same dystrophin gene mutation clearly suggest that the fragility of the cell membrane caused by genetically deficient dystrophin – but not by acquired myocarditis – is the cause of the characteristic cardiomyopathy in DMD/BMD patients.

Phenotype-genotype correlation in patients with mutations in the beta-myosin converter domain


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Purpose: Our main purpose was to evaluate the genotype-phenotype correlation of mutations located in the beta-myosin converter domain. This region, located between amino acids 797 and 799, is responsible for the elasticity of the protein which allows strain to develop within the motor before the cargo is actually moved. Several mutations affecting this important and highly conserved domain have been recently described.

Methods: Identification of mutations in the converter domain on MYH7 was performed in a cohort of more than 800 cases diagnosed either with Hypertrophic Cardiomyopathy (HCM) or Dilated Cardiomyopathy (DCM). Additionally, a single family with a mutation in MYOM2 was also studied.

Results: In our centre, mutations were identified in 11 families comprising 59 relatives and 30 carriers, all diagnosed with HCM except 1 family (LVNC and DCM). These mutations were G716R (2 families), G741R (1 family), G768R (1 family), 1730N (1 family, novel mutation), 17367 (5 families) and R1790Q (1 family).

Conclusions: Identification of mutations in the converter domain on MYH7 was performed in a cohort of more than 800 cases diagnosed either with Hypertrophic Cardiomyopathy (HCM) or Dilated Cardiomyopathy (DCM). These mutations were G716R (2 families), G741R (1 family), G768R (1 family), 1730N (1 family, novel mutation), 17367 (5 families) and R1790Q (1 family).

Is the gene MYOM2 encoding myosin 2 involved in the pathogenesis of hypertrophic cardiomyopathy?

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Background: Hypertrophic cardiomyopathy (HCM) is the most frequent genetic myocardial disease with a prevalence 1/500. Although twenty mostly sarcomeric genes have been shown to cause HCM, it is anticipated that additional so far unknown disease genes exist. In a candidate gene approach, we did a genetic screening of myosin 2 (MYOM2), a M-band protein expressed in cardiac sarcomeres.

Methods: We clinically evaluated a cohort of fifty-eight HCM patients on the basis of medical history, physical examination, echocardiography, and 12-lead ECG, after obtaining informed consent. Using PCR and direct automated Sanger sequencing, the thirty-six coding exons of MYOM2 were analyzed. The study was approved by the institutional review board of the Charité.

Results: As expected, a number of known single nucleotide polymorphisms (SNPs) were detected. Interestingly, we identified three novel mutations (M269T, S466R, R1079X) in three unrelated HCM patients. All mutations were G716R (2 families), G741R (1 family), G768R (1 family), 1730N (1 family, novel mutation), 17367 (5 families) and R1790Q (1 family).

Taking into account our data and data from literature, a total of 21 pathogenetic mutations have been identified within this domain. They were distributed in 143 families comprising 470 relatives (in half of those families more than 1 member was described). Of these relatives, 342 were affected or possibly affected (11 of them diagnosed with DCM and the rest with HCM) and 382 were mutation carriers. We observed an early onset of disease with a mean age at the diagnosis of 27±18 years (range 1 to 77, 56% males). Thirteen of 21 mutations were associated with a severe adverse event affecting at least one member in 52/143 families (36%). These serious events occurred in 151 affected or possible affected relatives (36%), distributed as follow: sudden death occurred in 96 patients (22% and at least 54 of them were younger than 45 years old, heart failure death in 35 (8,2%), cardiac transplantation in 18 (4,2%) and fatal stroke in 6 (1,4%). Finally, 61 patients (16%) presented an impairment in the left ventricular systolic function.

Conclusion: Data from our families and from the extensively reviewed publications indicated that mutations located within the beta-myosin converter domain presented an early onset of disease. A significant proportion of mutations was associated with the occurrence of a severe adverse event and also left ventricular dysfunction, in a high proportion of families.

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well as a number of other disease genes (MYL2, MYL3, ACTG, TNNT2, TNN3, TPM1, TNNC1, CSRPR3) showed no mutation in this HCM cohort. Notably, the phenotype of the three identified patients was characterized by left ventricular outflow tract obstruction and arrhythmias which lead in one of them to an ICD implantation. The examination of the families is underway.

Results:

Unraveling mutation effects from secondary adaptations in cardiomyocytes of Familial Hypertrophic Cardiomyopathy patients

T. Kraft1, K. E. Paalberendsz2, N. M. Boot3, S. Tripathi4, J. Montag1, A. Francino5, F. Nava-Lopez6, B. Bremer7, G. J. M. Steinen2, J. van Der Velden8, Medical School, Hannover, Germany; 2VU University Medical Center, Amsterdam, Netherlands; 3Hospital Clinic Provincial, Barcelona, Spain

Purpose:

About 1/3 of genotyped FHC patients carry missense mutations in the β-cardiac myosin heavy chain (β-MHC). Yet, at the sarcolemma level of cardiomyocytes, secondary functional effects of these mutations are still largely unknown. We aimed to characterize the effects of the highly malignant β-myosin heavy chain (β-MHC) missense mutation R722G in myocardial tissue and to compare the data with previous findings in M. soleus fibers with the same mutation. This allows to differentiate (1) the primary functional effects of the mutation and (2) adaptation processes in the myocardium.

Methods:

In left ventricular cardiomyocytes from explanted hearts of patients with the β-mutation R722G and in donor cardiomyocytes we determined force generation, force-calcium relations, and cross-bridge kinetics. We also determined the relative expression of mutated vs. wildtype β-MHC at the mRNA- and protein level and analyzed the phosphorylation of sarcomeric proteins. To assess cardiomyocyte structural properties, histology and electron microscopy was also performed.

Results:

Measurements revealed reduced maximum force generation but unchanged calcium-sensitivity of the myocytes. Yet, previous studies on slow skeletal muscle fibers with the same mutation showed reduced calcium-sensitivity and increased maximum force. The expression of mutated β-MHC-mRNA and β-myosin in LV tissue was found to be 68% and 64% of total β-MHC-mRNA and β-myosin, respectively, which is the same fraction as in M. soleus. Get electrophoresis of the HCM cardic tissue showed reduced phosphorylation of troponins I and T, myosin binding protein C, and myosin light chain 2 compared to donor tissue, which is similar to previous findings for failing human heart. Treatment with protein kinase A (PKA) to adjust phosphorylation of Tnl and MyBP-C in donor and HCM myocytes, however, uncovered reduced calcium-sensitivity, similar to what was observed previously in M. soleus, while maximum force was not affected by PKA.

Electron microscopy showed lower myofibrillar density and disorganization of myofilaments in the cardiac tissue samples which most likely accounts for the reduced force.

Conclusions:

(1) The primary effects of HCM related mutations might obscure typical adaptations commonly seen in end stage heart failure since increased calcium-sensitivity due to changes in protein phosphorylation. (2) To identify primary functional effects of a mutation in myocardial tissue at an advanced stage of the disease, posttranslational modifications like protein phosphorylation and ultrastructural alterations must be taken into account.

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Lamin A/C mutation is independently associated with an increased risk of arterial and venous thromboembolic complications

I.A.W. van Rijssingen1, A.L. van der Kooi1, J.P. Van Tinteren2, M.P. van Den Berg2, I.A.W. Van Rijsingen1, A.J. van der Kooi1, J.P. Van Tintelen2, M.P. van der Velden2, I. Christiaans1, A.A.M. Wilde1, J.C.M. Meijers1, Academic Medical Center, Amsterdam, Netherlands; 2UCL Genomics, London, United Kingdom; 3UCL Genetics Institute, London, United Kingdom; 4University College London, London, United Kingdom

Introduction:

Mutations in sarcomere proteins expressed in the heart have been reported to cause dilated cardiomyopathy (DCM). Recently, missense mutations in the giant protein titin and its associated cytoskeletal proteins have been linked to LV hypertrophy in DCM patients. In a heterogeneous study population of 255 independent cases we reported that 49% of missense mutations, 9153 exonic and splice-site calls (976 distinct SVs) were selected and further filtered by frequency, resulting in 462 unique SV candidates. In total, 204 patients (92%) carried at least one candidate SV and 164 (74%) carried multiple. Excluding the highly variable titin gene, 112 distinct rare sarcomeric and 35 rare 2-disc and cardiac-handling SVs were present in 141 patients (64%), including 60 known pathogenic mutations and 22 novel nonsense, frameshift, insertion-deletion or splice-site SVs predicted to cause loss-of-function. Eighty-six SVs (64 novel) in 91 patients (41%) were present in genes implicated in arrhythmogenic cardiomyopathy and channelopathies.

Methods:

We analyzed the clinical application of NGS in a large cohort of unrelated HCM patients. A majority of patients carried multiple rare variants, questioning our understanding of the genetic basis of HCM and suggesting a role for extra-sarcomere variants as possible modifiers.

Lamin A/C mutation is independently associated with an increased risk of arterial and venous thromboembolic complications

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these mutations were found in healthy subjects. Immunohistochemical analysis of endomyocardial biopsies demonstrated an abnormal distribution of myofilaments in cardiac myocytes from the p.P961L mutation carrier, while the periodic localization of myofilaments in sarcosomes was unchanged in the p.R955W carrier and four other DCM patients used as controls. Interestingly, in cardiac myocytes from the p.P961L patient we also observed a disturbed localization of u-actinin, which is a known binding partner for myofilaments. In the ANKRD1 gene we identified only one novel synonymous mutation in a DCM patient, which was a mononucleotide substitution in exon 2 (c.106C>T), but failed to detect non-synonymous mutations.

Conclusions: Taken together, we have identified novel point mutations in the third immunoglobulin-like domain of myofibrilin. One of these missense mutations, a substitution of a highly conserved prolyl residue in position 961, was associated with structural alterations in the sarcomere organization. These findings point to the role of myofibrilin in myofibrillarlogenesis with impact on the pathogenesis of dilated cardiomyopathy.

Figure 1. NT-proBNP increases with age in men and women

Results:

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>124.84 ± 24.80</td>
<td>100.00 ± 16.00</td>
</tr>
</tbody>
</table>

NT-proBNP concentrations were significantly higher in the Fabry patients (124.84 ± 24.80 pg/mL) compared to controls (100.00 ± 16.00 pg/mL).

Discussion:

NT-proBNP has an established role in the diagnostic and prognostic assessment of heart failure. Cardiac involvement in Fabry disease is common, however detection of early disease is challenging. The aim of this study was to determine the relation between serum NT-proBNP concentration and cardiac abnormalities in patients with Anderson Fabry disease (AFD).

Methods:

- NT-proBNP was measured using a Randox kit in 117 patients with AFD (48±15 years old, 46.2% male). All patients underwent clinical evaluation including ECG and echocardiogram.
- Results: NT-proBNP concentrations ranged from 5.5 pg/mL to 605 pg/mL. Eighty-six (74%) patients had cardiac involvement (defined as an abnormal ECG or echocardiogram). A cut-off of 20 pg/mL had a 69% sensitivity and 94% specificity for detecting cardiac involvement in AFD with area under a receiver operator characteristics curve of 0.85 (95% CI 0.79-0.92). In multiple regression analysis the following were independently associated with logNT-proBNP levels: age, creatinine, LVEF and the presence of an abnormal ECG (R² = 0.67, p < 0.05).

Conclusions:

NT-proBNP concentrations are raised in patients with Anderson-Fabry disease and cardiac involvement and correlate with non-invasive markers of diastolic dysfunction. These findings suggest that measurement of NT-proBNP may assist in decisions on the timing of enzyme replacement therapy.

Advanced left heart disease in cystic fibrosis: a distinct form of cardiomyopathy

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During decades, occasional cases of cardiomyopathy (CMP) have been described in patients with cystic fibrosis (CF). Necropsies of children with CF who died of sudden death showed dilated left ventricles with patchy fibrosis. Currently, patients with CF usually reach adulthood, and the incidence and features of CMP in them are unknown.

Methods: We describe cardiology findings of 9 adult patients with CF and left ventricular (LV) systolic dysfunction, 3 of them referred to our centre for cardiac pulmonary transplantation and 6 found in a study of 120 CF patients without known cardiac involvement.

Results: The mean age of the 9 CMP patients was 31±7 years and 6 were male. Four of them had desferrioxamine and 2 had a rare mutation of other CF-related genes. Their mean LV ejection fraction was 36% (vs 66±8% in controls, p<0.01) and 55% had also diastolic dysfunction (vs 5% in controls, p<0.01). Four patients (44%) showed moderate mitral regurgitation. Right ventricle was affected in 1 patient (11%) and was normal in all controls. Mean NT-proBNP in CF patients with CMP was 1498±3219 pg/mL (vs 58±45 pg/mL in controls, p<0.001). MRI showed a patchy delayed myocardial gadolinium uptake in 43% of CMP patients, vs 0.04 among controls, p<0.05. Pathology of the 3 hearts explanted at transplantation showed patchy myocardial fibrosis in all cases, a finding similar to the autopsies of Keshan syndrome (CMP due to selenium deficiency). Eight patients (89%) with CMP had pancreatic exocrine deficiency, needing high-dose pancreatic enzyme supplements (vs 30% in the control group, p<0.05), and 6/9 (67%) had a body mass index < 20 kg/m² (vs 53 among controls, p=0.07). From the pulmonary standpoint, the mean FEV1 for the 9 patients was 45±16% (vs 60±20% for controls, p=0.08). All of them had a permanent airway colonization by Pseudomonas (vs 58% among controls, p=0.04). In fact, 4/9 (44%) patients with cardiac involvement required lung transplantation (vs 1% in controls, p<0.05).

Conclusions: A small percentage of adult CF patients show a distinct CMP with a characteristic patchy myocardial fibrosis, a finding similar to the autopsies of children with CF and other malnourishment syndromes. CMP should be suspected in CF patients with significant malnutrition and more severe pulmonary involvement. ProBNP levels could serve as a screening tool for this form of CMP.

Role of serum NT-proBNP measurement in the diagnosis of early cardiac involvement in patients with Anderson-Fabry disease

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Purpose: NT-proBNP has an established role in the diagnostic and prognostic assessment of heart failure. Cardiac involvement in AFD is common, however detection of early disease is challenging. The aim of this study was to determine the relation between serum NT-proBNP concentration and cardiac abnormalities in patients with Anderson Fabry disease (AFD).

Methods: NT-proBNP was measured using resting conditions in 117 patients with AFD (48±15 years old, 46.2% male). All patients underwent clinical evaluation including ECG and echocardiogram.

Results: NT-proBNP concentrations ranged from 5.5 pg/mL to 605 pg/mL. Eighty-six (74%) patients had cardiac involvement (defined as an abnormal ECG or echocardiogram). A cut-off of 20 pg/mL had a 69% sensitivity and 94% specificity for detecting cardiac involvement in AFD with area under a receiver operator characteristics curve of 0.85 (95% CI 0.79-0.92). In multiple regression analysis the following were independently associated with logNT-proBNP levels: age, creatinine, LVEF and the presence of an abnormal ECG (R² = 0.67, p < 0.05).

Conclusions: NT-proBNP concentrations are raised in patients with Anderson-Fabry disease and cardiac involvement and correlate with non-invasive markers of diastolic dysfunction. These findings suggest that measurement of NT-proBNP may assist in decisions on the timing of enzyme replacement therapy.

Cardiac autonomic nervous system dysfunction in a cardiomyopathy mouse experimental model

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Purpose: Desmin is the major muscle specific intermediate filament protein.
Desmin null mice (des−/−) develop dilated cardiomyopathy with myocardial de-generation, extensive calcification and fibrosis which leads to arrhythmias and sudden cardiac death. Our aim was to investigate the cardiac autonomic nervous system function in the des−/− mouse by measuring heart rate variability (HRV) indices.

Methods: We generated des−/− mice by gene targeting via homologous recombination in ESV genetic background. Twenty four hours EG2 recordings were obtained from 6m old des−/− and wild type (WT) mice, using a telemetry system (DSI) and all RR intervals were recorded. The following linear and non-linear HRV indices were calculated: Approximate Entropy (ApEn) modified to avoid self-occurrences, Detrended Fluctuation Analysis (DFA) and the beta-Spectro Explos. Poincare map measures were used to extract 3D measures of spread and maximum and the 2D distances axis s1 and s2. Time domain (SDNN, SDNNi, RMSSD, pNN50) and frequency domain (LV, HF) indices were also calculated.

Results: Results are presented in Table 1. ApEn < 0.10, ApEn < 0.08, DFA˛ < 0.08, DFT < 0.08, DFA˛ < 0.01, DFT < 0.01, DFA˛ < 0.006, DFA˛ < 0.002, DFA˛ < 0.001, DFA˛ < 0.0001, DFA˛ < 0.016, DFA˛ < 0.011, DFA˛ < 0.004, DFA˛ < 0.0001.

Conclusion: Desmin null mice show a global autonomic nervous system dysfunction which affects both the sympathetic and the parasympathetic components. This may explain the presence of arrhythmias and sudden cardiac death in these mice. Further investigation is needed so as to clarify whether this dysfunction is a result of the extended myocardial fibrosis and calcification caused by the absence of desmin.

MYOCARDITIS

Left ventricular mechanics in acute myocarditis

Correlation of 2D speckle tracking deformation and rotation imaging with troponin release and cardiac magnetic resonance findings

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Background: Acute myocarditis with normal ejection fraction (EF) represents a diagnostic challenge for conventional echocardiography. Cardiac magnetic resonance imaging (CMRI) is the current non-invasive reference standard for diagnosis. Speckle tracking imaging (STI) allows measurement of left ventricular (LV) torsion and deformation. Abnormalities of these parameters may contribute to earlier diagnosis of myocardial inflammation.

Aim: The purpose of this study was to explore the longitudinal, circumferential, and torsional mechanics of the LV in patients with acute myocarditis.

Methods: Longitudinal, circumferential and torsional mechanics of the LV were quantified by STI in 50 patients with potential diagnosis of myocarditis based on clinical, laboratory and CMRI findings and 50 healthy age-matched controls. All patients had chest pain, abnormal ECGs and preserved EF (>45%) whereas coronary artery disease was angiographically excluded.

Results: In comparison with controls, global longitudinal strain values in myocarditis group (-17.35 ± 3.08% vs. -20.08 ± 2.63%, p > NS) were not statistically different, reflecting the preserved longitudinal contractility. On the contrary, myocarditis patients showed decreased LV torsion (10.30 ± 4.92 degrees, p < 0.001), apical rotation values (4.74 ± 3.77 vs 8.7372 ± 3.85 degrees, respectively, p < 0.003) and circumferential strain in the mid posterior (-7.5 ± 4.9% vs -16.5 ± 7.4%, p < 0.001), mid lateral (-17.1 ± 7.3% vs -16.5 ± 11.1%, p < 0.001) and mid inferior wall (-11.5 ± 6.9% vs -20.5 ± 4.7%, p < 0.001) compared to controls. Tropinin elevation was found in 25 patients (50%), with mean values 14.84 ± 23.79 ng/ml and was correlated with both LV torsion (r = -0.584, p < 0.001) and the number of affected segments in CMRI (r = 0.57, p < 0.0001) compared to controls. In accordance, LV mass index (R = 0.44, p < 0.001), LGE (R = 0.57, p < 0.0001), and the number of affected segments in CMRI (R = 0.57, p < 0.0001) were significantly correlated with both LV torsion (r = -0.584, p < 0.001) and the number of affected segments in CMRI (r = 0.57, p < 0.0001).

Conclusions: The purpose of this study was to explore the longitudinal, circumferential, and torsional mechanics of the LV in patients with acute myocarditis. Longitudinal, circumferential and torsional mechanics of the LV were quantified by STI in 50 patients with potential diagnosis of myocarditis based on clinical, laboratory and CMRI findings and 50 healthy age-matched controls. All patients had chest pain, abnormal ECGs and preserved EF (>45%) whereas coronary artery disease was angiographically excluded.

Clinical presenting patterns and CMR features of acute myocarditis predicting outcome

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Background: Acute myocarditis (AM) clinical onset can span from subclinical disease to acute heart failure (AHF) ventricular fibrillation (VF) or sudden cardiac death in young adults. Myocarditis may cause arrhythmias both in the acute phase and through remodeling and the chronic phase of disease. Here we analyzed the clinical and structural remodeling aspects of myocarditis based on cardiac magnetic resonance imaging (CMR).

Methods: Seventy-three consecutive patients (pts) referred for suspected myocarditis from 2007 to 2010 were analyzed. Symptoms, ECG changes, reduced regional and/or global myocardial function, elevated creatine kinase, positive troponin T, suggested AM. Coronary artery disease was excluded. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR. The diagnosis was confirmed by CMR (Siemens Avanto 1.5 Tesla) performed within 2 weeks after the onset of symptoms, according to the presence of signal hyperintensity at STIR at CMR.

Results: According to the initial clinical picture pts were divided into two groups: group 1 (G1,n = 62), presenting with chest pain; group 2 (G2, n = 11); presenting with AHF or VF. Age, LV volumes and functional parameters were similar in the 2 groups. In G2 LVEF was slightly lower. G2 showed a larger percentage of edema (50%) with mean values 14.84 ± 23.79 ng/ml and was correlated with both LV torsion (r = -0.584, p < 0.001) and the number of affected segments in CMRI (r = 0.57, p < 0.0001). In all CMRI LVEF was significantly inversely correlated to edema (R = 0.49 ± 0.001, p < 0.001). LVEF (R = 0.49 ± 0.001) and LV mass index (R = 0.49 ± 0.001). At FU LV volumes and function did not change. edema (G1 p < 0.0001, G2p < 0.004) and LVEF (G1p < 0.002,G2p < 0.006) were significantly reduced in both groups. In G2 pts had refractory ventricular arrhythmias (VT) and an ICD implanted.

Conclusions: Pts with AM presenting with AHF or VF at admission showed significantly larger percentage of edema and LGE directly correlated to global con-
**P4881** In vivo delivery of adenoaviral vector containing interleukin-17 receptor A reduces cardiac remodeling and improves myocardial function in CVB3-induced chronic myocarditis

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**Purpose:** Th17 cells have been implicated in the pathogenesis of myocarditis. Interleukin (IL)-17A produced by Th17 is dispensable for viral myocarditis but essential for the progression to dilated cardiomyopathy (DCM). This study investigated whether adenoviral transfer of IL-17 receptor A would reduce myocardial remodeling and dysfunction in chronic viral myocarditis.

**Methods and Results:** In a mouse model of Coxsackievirus B3 (CVB3)-induced chronic myocarditis, delivery of adenovirus containing IL-17 receptor A (Ad-IL17R:Fc) reduced IL-17A production and decreased the mortality compared with a control adenovirus null (Ad-null) 3 months after first CVB3 infection (56% versus 76%). Cardiac function was significantly improved in Ad-IL17R:Fc compared with Ad-null treated mice. Th17 cells were detected in the heart, suggesting an important role of IL-17A in fibrosis. These effects of Ad-IL17R:Fc correlated with a decrease of Th17 cells in the spleen and heart, and a reduction of systemic TNF-α and IL-6 productions. In cultured cardiac fibroblasts, IL-17A induced expressions of ADAMTS-1, MMP-2, collagen subtypes I and III, and a reduction in fibroblasts in the heart, suggesting a key role of IL-17A in fibrosis. Furthermore, myocardial collagen deposition was attenuated in Ad-IL17R:Fc treated mice, which was accompanied by down-regulation of ADAMTS-1, MMP-2, collagen subtypes I and III, and a reduction in fibroblasts in the heart, supporting the pivotal role of IL-17A in fibrosis.

**Conclusion:** Th17 cell and IL-17A induces cardiac fibrosis through mediating extracellular matrix remodeling and fibroblast proliferation in chronic viral myocarditis and DCM. Thus, blockade of IL-17A by adenoviral transfer of IL-17 receptor A may represent an alternative therapy for chronic viral myocarditis and its progression to DCM.

**P4882** Relationship between cardiac magnetic resonance criteria for acute myocarditis and biomarkers of inflammation and myocardial damage

G. Nucifora1, A. Di Chiara1, D. Miani1, G. Piccoli2, M. Puppato3, G. Slavich1, D. Gasparini1, A. Proclemer1. 1Cardiothoracic Department, University Hospital “Santa Maria della Misericordia”, Udine, A.S.S. n.3 Alto Friuli, Department of Cardiology, Tolmezzo, 2Division of Interventional Radiology, University Hospital “Santa Maria della Misericordia”, Udine, Italy.

**Purpose:** Diagnostic cardiac magnetic resonance (CMR) criteria for acute myocarditis (“Lake Louise” criteria) have been recently proposed. In the setting of clinically suspected myocarditis, CMR findings are consistent with myocardial inflammation, at least 2 of the following features are present: 1) regional or global myocardial thickening; 2) hyperemia and 3) ≥1 focal lesion of myocardial necrosis with non-ischemic regional distribution. Scarce data are however available regarding the relation between these criteria and biochemical markers of inflammatory activity and myocardial injury.

**Methods:** A total of 26 consecutive patients (20 males, mean age 38±14 years) with diagnosis of acute myocarditis on the basis of clinical presentation (chest pain, dyspnea or palpitations, associated with recent gastrointestinal or respiratory infection) and CMR “Lake Louise” criteria were included. For each patient, peak values of C-reactive protein (CRP) and cardiac troponin I (cTnI) were determined. In addition, the following CMR features were determined: 1) global myocardial signal intensity (SI) in T2W images, quantified by a SI ratio of myocardium over skeletal muscle (expression of myocardial oedema); 2) global myocardial early gadolinium enhancement (EGE) ratio between myocardium and skeletal muscle (expression of myocardial hyperaemia) and 3) extent of late gadolinium enhancement (LGE) in inversion recovery-prepared gadolinium-enhanced T1-weighted images (expression of myocardial fibrosis). The extent of LGE was expressed as percentage of the left ventricular (LV) mass (%LV LGE). Univariate and multivariate linear regression analysis was performed to investigate the relationship between biochemical markers of inflammatory activity and myocardial injury (i.e. CRP and cTnI) and the following CMR features: T2 ratio, EGE ratio and %LV LGE.

**Results:**
- Peak values of CRP and cTnI were 78±69 mg/l and 9±7 ng/ml, respectively.
- Myocardial T2 ratio, EGE ratio and %LV LGE were 1.94±0.29, 6.40±2.0 and 8.8±7.2, respectively. At multivariate analysis, peak value of CRP was significantly and independently related only to T2 ratio (β=0.64, p<0.001) and EGE ratio (β=0.33, p=0.030).
- Conversely, peak value of cTnI was significantly and independently related only to %LV LGE (β=9.03, p<0.001).

**Conclusions:** In patients with acute myocarditis, T2 ratio and EGE ratio are expression of inflammatory activity, while LV LGE is expression of irreversible myocardial injury.

**P4884** Injectable collagen implant improves survival and early cardiac remodeling after fulminant myocarditis in rats

R. Rekiewicz-Shig1, N. Landa-Rouben1, R. Holbova1, F.H. Epstein2, T. Ben Mordechai1, M.S. Feinberg1, O. Golten1, T. Kushnir1, E. Koen1, J. Loe1. 1Cardiovascular Research Institute, Tel-Aviv University, Sheba Medical Center, Tel Hashomer, Israel; 2Departments of Radiology and Biomedical Engineering, University of Virginia, USA; 3Diagnostic Imaging Department, Sheba Medical Center, Tel Hashomer, Israel.

**Purpose:** Acute myocarditis can lead to massive cell death, destruction of extracellular matrix, left ventricle (LV) dilatation, dysfunction and death. We sought to test the hypothesis that injection of collagen-based implant into the inflamed myocardium would stabilize LV and prevent adverse remodeling and dysfunction.

**Methods and Results:** Autoimmune myocarditis was induced in 42 male Lewis rats. Fourteen days after immunization, sick animals were randomized into either injectable-collagen implant or saline injection, into anterior inflamed myocardium. LV remodeling and function were assessed by serial echocardiography and cardiac magnetic resonance (CMR) scans; before immunization, before collagen implantation and 17 days after immunization. Thirty days after collagen implantation, all animals were euthanized and subsequently underwent histopathological examination. Notably, 30 day survival rate was significantly higher in collagen-treated group compared with control (87.5% vs. 50%; p<0.003). CMR imaging of control animals showed epicardial late gadolinium enhancement, as marker of fibrosis, LV wall motion abnormalities, and in some cases pericardial effusion. The injectable collagen implant increased systolic and diastolic wall thickness, 10 days after treatment, compared with control (p=0.07, p=0.05). Furthermore, while injectable collagen implant attenuated the LV systolic and diastolic dilatation and preserved LV function, control animals developed significant LV dilatation (p=0.02, p=0.04) and dysfunction (p=0.01). However, these favorable effects disappeared within 17 days after treatment.

**Conclusions:** Injectable collagen implant improves survival in a rat model of fulminant myocarditis. However, while the effect on survival was sustained, the early protective effect on LV remodeling was limited to the early period after treatment.

**P4885** Matrix Metalloproteinase-13 is beneficial in viral myocarditis not only by preventing cardiac inflammation but also reducing cardiac inflammation due to regulating chemokinles

D. Westermann, D. Lindner, H.P. Schultzke, G. Tischoepe. Chante - University Medicine, Campus Benjamin Franklin, Berlin, Germany.

**Purpose:** Myocarditis is an important cause for cardiac failure especially in younger patients followed by the development of cardiac dysfunction and death. The present study investigated whether gene deletion of matrix metalloproteinase-13, an important collagenase in the heart, influences cardiac inflammation and remodeling in murine coxsackievirus-B3 (CVB3) induced myocarditis.

**Methods and Results:** MMP-13 knockout mice (MMP-13(-/-)) and their controls (WT) were infected with CVB3 to induce myocarditis and 7 days later LV function was analyzed invasively. CVB3 induced a significant cardiac enhancement (increased CD3 (+18 fold) and CD68+ (+25 fold) cells) as well as cardiac dysfunction (decreased cardiac output (-24%) in WT CVB3 animals. Interestingly, deletion of MMP-13 increased the protein level of the chemokine MCP-1 (4 fold). This incre-
ment of a potent chemokine due to MMP13 KO aggravated cardiac inflammation (3 fold) as well as cytokine levels (increased TNF-alpha 6 fold and IL1 beta 3 fold) compared to infected WT animals. Moreover, this excessive cardiac inflammation resulted in an increased transdifferentiation of fibroblasts to pathological activated myofibroblasts (10 fold), which are known to be induced by inflammatory cells. This was associated with detrimental cardiac remodeling leading to severe cardiac dysfunction when MMP-13−/− were compared to WT animals after CVB3 infection. Interestingly, also viral load was increased in MMP-13−/− mice with significantly more cardiac apoptosis being present in the infected myocardium.

Conclusions: Loss of MMP-13 increased the inflammatory response and CAV3 infection, which impaired cardiac remodeling, apoptosis and function during CVB3 induced myocarditis due to an increment of the chemokine MCP-1. MMP-13, similar to other MMPs like MMP-2 might be more than just a degradation system for cardiac collagen but may modulate inflammation by processing chemokines as MCP-1 and therefore being one negative feedback loop in cardiac inflammation.

Table 1. Characteristics of different subgroups

<table>
<thead>
<tr>
<th></th>
<th>Myocarditis</th>
<th>AMI</th>
<th>Apical ballooning</th>
<th>Inconclusive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (%)</td>
<td>25 (75%)</td>
<td>10 (30%)</td>
<td>3 (75%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>ST segment</td>
<td>24 (75%)</td>
<td>6 (20%)</td>
<td>2 (50%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Troponin (mean ± SD)</td>
<td>18.3 ± 3.1</td>
<td>31 ± 1</td>
<td>11 ± 1.7</td>
<td>0.3 ± 0.4</td>
</tr>
<tr>
<td>Wall motion index (mean ± SD)</td>
<td>18.6 ± 3.1</td>
<td>20.2 ± 2.0</td>
<td>21.2 ± 7.5</td>
<td>16.6 ± 1.2</td>
</tr>
</tbody>
</table>

CVM is necessary to establish a definite diagnosis in each patient. Apical ballooning can be generally ruled out by clinical and echocardiographic information.

**P4884**

No evidence of adenoviral genome in endomyocardial biopsy specimens in patients with new-onset unexplained dilated cardiomyopathy

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Background and aim of the study: Dilated cardiomyopathy (DCM) may represent a sequela of acute or chronic myocarditis, either due to persistence of infectious agent (mostly virus) or to a secondary autoimmune myocardial injury. Several studies reported adenovirus as an important causative agent in the pathogenesis of myocarditis and DCM in children and adults. Therefore, we aimed to prospectively evaluate the presence of genomes of several cardiotropic pathogens including adenovirus and Borrelia burgdorferi (Bb) in myocardium of patients with new-onset unexplained DCM.

Methods: In 58 consecutive patients (53±11 years, 42 men) with new-onset unexplained DCM (left ventricular ejection fraction 30±8%), endomyocardial biopsy (EMB) specimens were studied by immunohistochemistry (HLA expression) and polymerase chain reaction (PCR) techniques.

Results: The genome of cardiotropic infectious agent was found in EMB specimens in 35 (59%) patients. Namely, Bb genome was present in 13 subjects and adenovirus parovirus B19 in 6 (10%), enterovirus in 5 (9%), human herpes virus 6 in 5 (9%), cytomegalovirus in 3 (5%) and Epstein-Barr virus in 2 (3%) patients. Adenovirus and herpes simplex virus 1 genomes were not detected in any subjects. Myocardial inflammation was found in 18 patients (31%), of whom in 7 subjects (12%) the presence of viral or Bb genome was also revealed.

Conclusions: The genome of cardiotropic infectious agent, viral or Bb, is present in the myocardium of more than half of the patients with new-onset unexplained DCM. Notably, Bb genome can be detected in almost one quarter of these subgroups in the myocardium of more than half of the patients with new-onset unexplained DCM.

**P4887**

Clinical, ECG and echocardiographic criteria are insufficient to reach a definite diagnosis in patients with myocardial injury and normal coronary angiogram: insights from magnetic resonance-based secretome


Purpose: Some patients (p) with troponin-positive chest pain have no coronary obstruction on angiography, leading to diagnostic uncertainty. Cardiac magnetic resonance (CMR) is able to determine causative aetiology in most p. The aim of this study was to analyse whether clinical, ECG or echocardiographic criteria could be useful for diagnostic assessment using CMR as gold standard.

Method: 59 consecutive p referred for CMR after admission in our institution for a troponin-positive chest pain and normal coronary arteries or non-low-flow limiting CAD in coronary angiography were analysed. CMR studies were performed with a 1.5 T Philips Intera and included SSFP sequences, T2-weighted black-blood, first pass perfusion and late enhancement. P were classified as AMI, myocarditis, apical ballooning or unclusive study. Clinical data including age, sex, type of chest pain, troponin levels, ECG recordings, echocardiography and coronary angiogram were reviewed and compared between different groups defined by CMR.

Results: Mean age was 45±15 years and 43 p (72%) were male. P with myocarditis showed a non-significant trend towards more frequent non-significant stenosis in coronary arteries (3 p) compared to myocarditis (2 p, 9%) or apical ballooning (0 p). A p with apical ballooning recalled a previous stress event and showed a typical distribution of wall motion abnormalities. 17 p (50%) with myocarditis had evidence of a recent infection, whereas no p from the other groups had (p=0.001). Characteristics of different subgroups are displayed in table 1.

Conclusions: In p admitted for troponin-positive chest and no coronary obstruction on angiography which do not recall a recent infection, clinical, ECG and echocardiographic data are unreliable to differentiate between AMI and myocarditis.

**P4888**

Olimesartan, an angiotensin II type 1 receptor antagonist, suppresses cytotoxic myocardial injury in autoimmune heart failure

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Background: Some angiotensin II receptor type 1 (AT1) antagonists are reported to inhibit proinflammatory cytokine production. However, the effects of the drugs on autoimmune diseases are unknown.

Methods and Results: We tested the hypothesis that olimesartan, an AT1 antagonist, ameliorated experimental autoimmune myocarditis (EAM) in rats attributed to the suppression of inflammatory cytokines.

Results: In 58 consecutive patients (53±11 years, 42 men) with new-onset unexplained dilated cardiomyopathy (DCM), we investigated the presence of genomes of several cardiotropic pathogens including adenovirus and Borrelia burgdorferi (Bb) in myocardium of patients with new-onset unexplained DCM.

Methods: In 58 consecutive patients (53±11 years, 42 men) with new-onset unexplained DCM (left ventricular ejection fraction 30±8%), endomyocardial biopsy (EMB) specimens were studied by immunohistochemistry (HLA expression) and polymerase chain reaction (PCR) techniques.

Results: The genome of cardiotropic infectious agent was found in EMB specimens in 35 (59%) patients. Namely, Bb genome was present in 13 subjects and adenovirus parovirus B19 in 6 (10%), enterovirus in 5 (9%), human herpes virus 6 in 5 (9%), cytomegalovirus in 3 (5%) and Epstein-Barr virus in 2 (3%) patients. Adenovirus and herpes simplex virus 1 genomes were not detected in any subjects. Myocardial inflammation was found in 18 patients (31%), of whom in 7 subjects (12%) the presence of viral or Bb genome was also revealed.

Conclusions: The genome of cardiotropic infectious agent, viral or Bb, is present in the myocardium of more than half of the patients with new-onset unexplained DCM. Notably, Bb genome can be detected in almost one quarter of these subgroups in the myocardium of more than half of the patients with new-onset unexplained DCM.

Therefore, it is not necessary to perform adenovirus PCR assay of EMB specimens in patients with new-onset unexplained DCM.

**P4889**

Secretome from mononuclear cells confers immunosuppression in a murine autoimmune myocarditis model

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Although auto-immunity is thought to play a major role in the pathogenesis of myocarditis, “classical” immunosuppression has not been effective in treating patients suffering a post-infectious viral myocarditis. However, a modification of the autoimmune response could possibly lead to better results. We have recently shown that a high dose application of parasite factors obtained from mononuclear cells (MNC) modulates the inflammatory response following myocardial ischemia. In this subsequent study, we sought to determine immunosuppressive features of MNC secretome in a CD4+ cell dependent model of murine myocarditis (EAM model).

Cell culture supernatants derived from murine MNC were injected intraperitoneally after induction of autoimmune myocarditis with a cardiac myosin peptide homologue. The inflammatory response was determined by histopathological evaluations and by ELISA. Impact of MNC secretome on proliferation and cell viability of T-cells was measured by FACS and histone release assays. Treatment of EAM mice with a single high dose of MNC secretome resulted in an attenuation of myocardial infiltrate (myocarditis score 2.7±0.4 vs 0.0±0.1; p<0.002). We further enpacted the effect of MNC secretome on JURKAT cell line and purified human CD4+ cells. Coinubation of MNC secretome with T-cells led to a caspase-9 dependent induction of apoptosis.

Our data first provide that secretome obtained from MNC possess immunosuppressive features in an autoimmune myocarditis model.
Eтанретепт treatment improves acute chagas disease and alters cardiac conduction and repolarization parameters

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Background: Chagas disease affects 8 million people in Latin America. Even some decrease in transmission has been achieved, recently acute cases especially by oral transmission has been reported. The Tumoral Necrosis Factor (TNF-α) is a key role in the immune response against the Trypanosoma cruzi, but is not clear their beneficial or deleterious effects on disease outcome. In this sense, the aim of this work is to determine the effects of the TNF blocker etanrcept on inflammation parameters, ECG recordings and survival in an acute infection with a wild T. cruzi virulent strain.

Methods: NMRI male mice (30 g) were infected with 1000 tripanosomes per gram and treated subcutaneously with 0.38 mg/kg of etanrcept at 7 day post infection(dpi). Levels of TNF and C reactive protein (CRP) were determined in blood by semiquantitative RT-PCR and ELISA respectively at day 0, 7, 14 and 21 dpi. Vertical, Horizontal motility and mechanical allodynia were recorded with an accelerometer and a dynamic plantar aesthesiometer during the last and second week post-infection. ECG was taken weekly with surface electrodes coupled to a Bio amplifier.

Results: The survival of treated animals was increased significantly with respect to infected untreated animals (20 vs 24 days, p = 0.0048). The peak of CRP was at 7 dpi and decreased until 21 dpi in all groups, but the levels were significantly lower in treated animals. TNF relative levels peak occurred at 7dpi and there was no differences between treated and untreated animals. Vertical and Horizontal motility reduction and hyperalgesia in infected animals was reversed by etanrcept treatment. Finally, the infected animals showed Teawave height and repolarization slope reduction. However, was observed an alteration of ECG parameters that could be associated with arrhythmogenesis and progression to chronic cardiomyopathy, which suggest an role ofTNF-α in cardiac regional response.

Conclusions: Acute and viral myocarditis is characterized by elevated concentrations of hs-TNT. However, these biomarkers do not replace EMB for diagnosis of myocardial inflammation.

MYOCARDIAL INVOLVEMENT IN SYSTEMIC DISEASES

Measurement of interatrial dysynchrony using tissue doppler imaging predicts functional capacity and cardiac involvement in systemic sclerosis

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Background: Heart involvement in systemic sclerosis (SSc) is associated with poor prognosis, and early detection is crucial. SSc may affect all heart structures, including conduction pathways: interatrial block is considered common and may reflect atrial involvement, but has been so far poorly evaluated. Echocardiography may detect interatrial dysynchrony, using either M-mode or strain modalities.

Methods: Patients with SSc were selected if there were in sinus rhythm and were able to walk. The following data were collected: NYHA functional class and distance walked in 6 minutes (6'WD); P wave duration on ECG, serum creatinine and Nt proBNP levels. Echo-Doppler study comprised: left ventricular (LV) mass, LV systolic and diastolic function, right ventricular (RV) function, pulmonary artery pressure (PAP), left atrial (LA) volumes and function. IAMD was assessed using colour TDI study, by measuring the delay between annular tricuspid and mitral a' waves. A cut off value of 35 ms was chosen to define the presence of IAMD.

Results: Forty patients were studied. Forty% of patients were found to have IAMD. These patients were significantly older. Using age-adjusted analysis, patients with IAMD had more severe symptoms, lower 6'WD, higher Nt proBNP and creatinine levels, and longer P wave duration than patients without IAMD. No difference was found regarding LV dimension and LVEDV. LV mass was higher, E/A and E/E' ratio were significantly different, LA volume was significantly higher, TAPSE was lower, and PAP was higher. Most importantly, IAMD correlated well with 6'WD (r = 0.72, p = 0.0001). During a 1-year follow-up, 5 patients died or had severe events: all of them were in the dysynchrony group.

Discussion: The prevalence of interatrial dysynchrony among SSc patients is high (40%). IAMD was found to be associated with lower exercise capacities, altered LV diastolic function, decreased LA and RV function, increased pulmonary pressure, and increased natriuretic peptides. This finding suggests that IAMD may represent a marker of myocardial involvement and may indicate a poorly compliant left atrium.

Conclusion: IAMD is a simple parameter showing good correlations with all other usual indices of heart involvement. We believe that it should be added to the routine echocardiographic evaluation of SSC patients, and that its prognostic value should be evaluated.

Myocardial mechanics for the early detection of cardiac sarcoidosis

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Purpose: Speckle tracking has emerged as valuable tool for a more comprehensive assessment of regional myocardial function, providing angle-independent measurements of strain. The aim of this study was to evaluate left ventricular (LV) function in patients with newly diagnosed sarcoidosis, utilizing the novel method of 2D speckle tracking.

Methods: 67 patients with newly-diagnosed sarcoidosis and with unremarkable medical history of cardiovascular disease, as well as 29 healthy age- and gender-matched controls underwent echocardiographic study. Apical 4-, 2-, 3-chamber as well as short axis acquisitions were made. In addition to conventional 2D, Doppler and TDI measurements, speckle tracking echocardiography was applied and LV global longitudinal strain was derived from the obtained images. Moreover, LV base and apex rotation angles were assessed from which LV twist was derived.

Results: The mean age of patients (26 men) was 43±6.1 years old. Compared with controls, patients had similar conventional 2D and Doppler measurements. TDI revealed increased E/E' in the patient group vs control group (8.9±1.45 vs. 4.7±1.29, p<0.05). Strain analysis demonstrated reduced global longitudinal strain values in the patient vs control group (19.86±1.89% vs 22.92±2.82%, p<0.05). Furthermore, twist was increased in the patient group as compared to the healthy individuals (13.1±2.3° vs 10.7±1.7°, p<0.05).

Conclusions: Speckle tracking echocardiography revealed alterations in strain and rotational indices, implying elevated filling pressures of the left ventricle. This could represent an early sign of myocardial involvement in patients with newly-
Echocardiographic abnormalities and their relation to exercise capacity in young unselected survivors of Hodgkin's lymphoma late after mediastinal irradiation

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Purpose: To assess the prevalence of cardiac abnormalities and their relation to exercise capacity in young unselected survivors of Hodgkin’s lymphoma late after mediastinal irradiation.

Methods: We performed echocardiography, multispiral CT and cardiopulmonary exercise test (CPET) in 60 patients without known cardiac disease (38 male and 22 female, mean age 28.8 ± 6.5 years) 5-16 years after mediastinal irradiation for Hodgkin’s disease. Mean age at the time of treatment was 19.6 ± 6.0 years, mean mediastinal irradiation dose =36.5 ± 5.9Gy, anthracyclines in 83.3% patients. Echocardiographic measurements above or below ≤2SD age specific normal mean were considered abnormal.

Results: 26 patients were asymptomatic, 34 had mild nonspecific symptoms (cardiac aneurysms). Any cardiac abnormality was found in 53 (83.3%) patients. 2 had mitral regurgitation grade 2, 3- aortic regurgitation grade 1, 1- tricuspid regurgitation grade 2. Pericardial impairment was found in 6 cases (1 effusion and 5 thickening). 14 patients had increased right VT and 15 (25%) patients. Mild and moderate diastolic dysfunction was present in 12 (20%), severe - in 15 (25%) patients. All - increased right VT. Late- wall end diastolic volume (EDV) =45.7 ± 6.0 ml/m² and RVLS = 10.7 ± 2.6 ml/m² vs 20 ± 3.1 ml/m² and 5.3 ± 0.7 ml/m², respectively, at <0.05 for all cases).

Conclusion: Echocardiography with tissue Doppler annuli measurements detected the abnormalities in 83.3% of young asymptomatic or oligosymptomatic survivors of Hodgkin’s lymphoma ≥5 years after mediastinal irradiation. Early signs of restrictive/constrictive impairment were prevalent and correlated with exercise limitations.

Cystic fibrosis (CF) is characterized by an obstructive pulmonary pattern and a pancreatic exocrine deficiency, frequently associated with malabsorption and malnutrition. Cardiac involvement in CF has been described in children with CF since the 1950's, with histologic features similar to those seen in malnourishment-related CMF, such as Keshan's disease. Our aim in this study was to describe the prevalence and features of CMP in a population of unselected adult CF patients.

Methods: As part of an investigation of the prevalence and causes of CMP in CF, we studied a series of unselected adult CF patients without known cardiac disease. After obtaining clinical and genetic information, we performed a blood test, a proBNP, and an echocardiographic study. We defined systolic dysfunction as left ventricular ejection fraction less than 55% (Simpson's method). Diastolic dysfunction was defined by pathological patterns in mitral flow as classically obtained by doppler ultrasound. Patients with data of CMP were also studied with magnetic resonance (MR).

Results: Study population included 120 adult CF patients recruited from 4 specialized CF centers in Italy. Mean age was 31 ± 8 years. Pancreatic disease was present in 80% of them, and low levels of vitamins and trace elements were common in spite of receiving dietary supplements. Left heart disease was found in 12 patients, with a prevalence of 10%; systolic dysfunction was evident in 6 patients (5%), and diastolic dysfunction in 9 patients (7.5%). There was a 2.5% that had both systolic and diastolic dysfunctions. Systolic dysfunction was significantly associated with a patchy myocardial enhancement pattern on MR (P < 0.05), as well as with a higher frequency of Pseudomonas aeruginosa airway colonization (p < 0.04) and a trend to having a lower body fat tracer (22.6 ± 9.3 kg/m² vs 20.9 ± 8.2 kg/m²; p = 0.07). Median value for proBNP in systolic dysfunction was 53 pg/ml (range 22 - 800 pg/ml).

Conclusions: The prevalence of CMP in an unselected group of adults with CF was 10%. The subgroup with left ventricular systolic dysfunction showed patchy fibrosis, similar to that described in malnourishment-related CMP. This form of heart disease should be included in the spectrum of organic involvement in CF patients and should be ruled out, especially in those with severe malabsorption or under evaluation for pulmonary transplant.
arteries in PXE patients independently of the presence of cardiovascular risk fac-
tors. In heterogeneous carriers, diastolic ventricular function is also abnormal, in-
dicating cardiovascular involvement and the need for cardiovascular assessment in
this specific group.

**Results:** Naïve patients had lower values of PWV compared to patients on
ART (6.68 m/sec vs. 7.45 m/sec, P=0.05). Regarding drug regimens, those on
NRTI/PIs had higher levels of PWV compared to those on NRTI/NNRTIs and to
ART (6.68 m/sec vs. 7.45 m/sec, P=0.037 for overall ANOVA) (Figure).

**Conclusions:** HIV patients on ART have higher levels of aortic stiffness com-
pared to naïve patients. Moreover, NRTI/PIs leads to heightened levels of PWV
compared to NRTI/NNRTIs. These findings suggest that the detrimental effect of
PIs on cardiovascular outcomes may be mediated through mechanisms of aortic
dysfunction. Measurements of aortic stiffness in the setting of HIV infection can
aid in risk stratification.

**Conclusion:** RV performance as measured by S significantly improves during
follow-up in PH patients who are under PV treatment. Further investigation is
needed to find out whether this improvement is secondary to a functional recovery
of the RV or to a decrease in RV afterload. We suggest routine measurement of
RV S to follow up the disease progression.

**Purpose:** The aim of the study was to assess the interplay of ART and
atherosclerosis in the setting of HIV infection. Measurements of aortic stiffness in
the setting of HIV infection can aid in risk stratification.

**Conclusions:** In patients with pulmonary hypertension (PH), progression of the disease and
survival are related to the capability of the right ventricle (RV) to adapt to the
cronically elevated pulmonary artery pressure (sPAP). Recent studies have suc-
cessfully applied speckle-tracking derived strain (S) to quantify RV dysfunction in
PH. Little is known about RV deformation evolution under pulmonary vasodilator
(PV) treatment.

**Methods:** We performed echocardiographic follow-up of 17 patients with PH
(Groups I and IV of the Dana Point classification) during 13.2±5.8 months and
measured RV longitudinal systolic S from 6 RV segments. All cases were under
PV treatment according to their physician’s criterion.

**Results:** We found a significant improvement in most conventional echocardi-
ographic measurements as well as global and regional S during follow-up (table 1,
figure 1).

<table>
<thead>
<tr>
<th>Table 1. Echo-parameters evolution</th>
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<tr>
<td>TAPSE</td>
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<td>------</td>
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<tr>
<td>Echo 1</td>
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<td>Echo 2</td>
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**PAC:** Fractional Area Change. **TAPSE:** Tri-cuspid Annular Plane Systolic Excursion. **sPAP:** Systolic Pulmonary Artery Pressure. **S:** Strain.

**Conclusion:** Our patients compared to 2.3% mortality in other studies which might be due to
adequate treatment or incomplete patient follow up.

**PULMONARY HYPERTENSION IMAGING**

**Methods:** Thirty consecutive newly diagnosed patients with IPAH were exam-
ined with 3DE and CMR during a follow up of 2 years and we associated RV volumetry with clinical
deterioration.

**Purpose:** In the present study we assessed the RV remodeling with 3DE and
CMR during a follow up of 2 years and we associated RV volumetry with clinical
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ined with 3DE and CMR during a follow up of 2 years and we associated RV volumetry with clinical
deterioration.
Echocardiographic prognostic factors for mortality in pulmonary hypertension: way beyond tricuspid annular displacement


Right ventricular (RV) function is the main determinant of morbidity and mortality in pulmonary hypertension (PH) and echo-derived tricuspid annular plane systolic excursion (TAPSE) has a well-recognized prognostic importance in this setting. Recently, RV deformation parameters have shown to accurately quantify RV function in PH. The aim of our study was to find out whether RV speckle-derived strain (S) may have an additional prognostic role for PH patients when added to classic RV function measurements such as TAPSE.

Methods: We prospectively studied 55 patients with PH of varied etiology and 22 healthy controls. RV longitudinal systolic S was evaluated by echocardiography for 6 RV segments (from the 4-chamber apical view).

Results: We found a significant reduction of global and regional S in PH patients when compared to controls: -15.5±5.9 vs -25.9±3.9 (p<0.005). During a mean follow-up of 9.2±7.1 months, 8 cardiovascular (CV) events (death and cardiac or pulmonary transplant) occurred. We identified two variables significantly associated with CV events: TAPSE (<0.005) and S (p=0.002). Global S was found to improve the Area Under the ROC Curve (AUC) for the prediction of adverse CV events when added to TAPSE (from 0.841 (p=0.005) to 0.907 (p<0.05), figure 1a). Kaplan-Meier survival analysis showed that the subgroup of patients with low TAPSE and low S has an additional prognostic role to clinical deterioration and death when compared to the groups with either low TAPSE or low S alone (figure 1b).

Conclusion: In our study global S has shown an additional value for the prediction of CV events when added to TAPSE. Therefore we suggest the routine assessment of deformation parameters for the follow-up of PH patients.

P4902

Echocardiography of pulmonary vascular function in asymptomatic carriers of the bone morphogenetic protein receptor type 2 mutation

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Purpose: Relatives of patients with idiopathic pulmonary arterial hypertension (IPAH) tend to present with enhanced pulmonary vascular responses to exercise or hypoxia as measured by the maximum velocity of tricuspid regurgitation (TRV), this may be driven by carriers of a mutation of the bone morphogenetic protein receptor type 2 (BMPR-2). We wondered if this potentially important risk factor might better defined by more extensive study of pulmonary vascular function.

Methods: Echocardiographic measurements were performed during an incremental exercise test and during 2 hours of hypoxic breathing in 35 relatives (of whom 5 were carriers of a BMPR-2 gene mutation) of IPAH patients, and in 38 healthy controls. Pulmonary artery pressures (PAP) were estimated from TRV, total pulmonary vascular resistance (PVR) was calculated from the right ventricular outflow time-velocity integral and TRV, and cardiac output (Q) from left ventricular outflow tract velocity. Multipoint PAP-Q relationships and a distensibility coefficient, alpha were also derived.

Results: In BMPR-2 carriers, non carrier relatives and controls, PAP at an average workload of 100 watts and after 120 min of hypoxia, and the PAP-Q slopes were not different. However, alpha was markedly decreased in BMPR-2 carriers, at rest (0.018±0.005 vs 0.034±0.004 vs 0.029±0.004 mmHg, p<0.05) and exercise (0.012±0.004 vs 0.021±0.002 vs 0.015±0.009 mmHg, p<0.05). The hypoxia induced increase in PVR was greater in the relatives with BMPR-2 compared to relatives without mutations.

Conclusion: Asymptomatic carriers of the BMPR-2 mutation present with decreased pulmonary vascular distensibility and increased hypoxic pulmonary vasconstriction which are identifiable at echocardiographic examination.

P4904

Survival in pre-capillary pulmonary hypertension: does echocardiography make the difference?

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Purpose: The aim of this study was to assess pulmonary arterial hypertensive (PAH) and chronic thromboembolic pulmonary hypertensive (CTEPH) patients’ survival in relation to a prospective, protocol-based collection of echocardiographic data in pre-capillary pulmonary hypertensive patients, referred to the National Pulmonary Hypertension Centre in London. All patients received the guideline-indicated best medical therapy.

Methods: All patients referred to the National Pulmonary Hypertension Service from 2002 until 2010 were included in the study. The patient cohort was solely focused in all pre-capillary pulmonary hypertensive patients and consisted of 777 consecutive patients. The data was analyzed using a univariate and multivariable time-dependent Cox model. The survival outcome was determined by death. Of 777 patients, 195 (25.1%) died. Median follow up of patients was 4.75±2.1 years. Echocardiographic indices were inserted into univariate and multivariable analysis according to the cause (pulmonary arterial hypertension vs. chronic thromboembolic pulmonary hypertension) and Youden cut-off values were used for the overall population as well as for the establishment of a prognostic index. Hugely time-dependent ROC curves were employed for the predictive value of each parameter.

Results: The overall survival was best determined by the severity of tricuspid regurgitation (p=0.005, HR=10.98), the presence of pericardial effusion (p=0.0003, HR=1.714) and the composite score of RV systolic function (p=0.0002, HR=1.37), followed by left atrial diameter (p=0.0349, HR=1.04), the diameter of inferior vena cava (p=0.001, HR=0.896) and the echocardiographic measurement of pulmonary vascular resistance (p=0.0002, HR=0.822) that were the strongest predictors of mortality.

Conclusions: In a large group of consecutive pre-capillary pulmonary hypertensive patients, the severity of tricuspid regurgitation, RV systolic function and the presence of pericardial effusion may indicate poor survival. Inoperable CTEPH patients had worse survival when compared to patients with pulmonary arterial hypertension.
P4905 Improving echocardiography estimation of right atrial pressure: comparison among several models and a new one based on right atrial evaluation

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Purpose: The estimation of right atrial pressure (RAP) has a great impact on the non-invasive evaluation of pulmonary hemodynamics. Several models have been developed to estimate RAP based on the inferior vena cava (IVC) diameter and collapsibility. However, IVC evaluation is not reliable for intermediate RAP values, young athletes, patients on ventilators or bad subcostal window. The aim of this study was to compare several known models of RAP estimation against the invasive RAP (iRAP) and develop a new one to overcome the limitations of IVC analysis.

Methods: Echocardiography was performed on 75 patients within 60 minutes from cardiac catheterization. IVC was evaluated in long and short-axis view. Images of right chambers, tricuspid Pulsed and Tissue Doppler, and hepatic vein flow were acquired. RAP was estimated using 5 different known models based on IVC evaluation and a new one based on right atrium analysis. All RAP models were compared to iRAP by Bland-Altman analysis.

Results: A population of 75 patients was evaluated (age: 62±14 years; iRAP: 9.5 mmHg [7-12]; range 1 - 22 mmHg). IVC measured by M-mode in long-axis view showed better correlation with iRAP. Among the 5 models based on IVC, the most recent one performed better (r = 0.29; p=0.04), but had a wide confidence interval (13.0 ± 11.6 mmHg). Right atrial total ejection fraction (TeEF) and systolic volume (v0L) showed a strong positive (r=0.29) and inverse (ToTEF) linear association with iRAP (p = 0.0001). Our model based on these parameters performed significantly better (r = 0.48; p = 0.001) and had a narrower confidence interval (8.9 ± 8.4 mmHg) (see figure).

Conclusion: RHC remains the gold standard for the diagnosis of PH. Nevertheless, an easy and integrated echo score allows pathophysiologic insight along a hemodynamic spere evaluated in a mixed cohort providing a good pre-test probability of having a pre-capillary rather than post-capillary PH.

Figure 1. Comparison of RAP models

Conclusions: The adoption of a new model based on RA morphology and function can provide a better estimation of RAP helping to improve non-invasive pulmonary pressure estimations.

P4908 Pulmonary artery trunk dilation in symptomatic subjects referred for coronary artery calcium scoring by means of a 64-row cardiac computed tomography

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Non-contrast cardiac computed tomography is as established method for coronary artery calcification determination in symptomatic and asymptomatic subjects. We aimed at assessment of the prevalence of ancillary findings, including pulmonary artery dilation.

1075 females and 484 males examined between March 2010 and January 2012 were examined for CAC scoring by means of cardiac MDCT (64-row Aquilion). A retrospective analysis of the data for evaluation of pulmonary artery trunk diameter (PAD, mm) was performed. Gender-dependent upper normal limits were established in 74 women and 50 men with normal CT scanning, zero CAC score, who were never smokers, non-obese, non-diabetic and non-hypertensive. Proportion of subjects with abnormal PAD was determined separately in women and men. Abnormal PAD was detected in 209 women (19%), while increased PAD:AAD ratio in 57 women (5%). In total, the PA dilation was found in 219 women (20.3%) including 172 with one measure abnormal, and 47 with both measures abnormal. Among men, abnormal PAD was detected in 89 subjects (18%), while abnormal PAD:AAD ratio in 9 men (2%). In total, any PAD increase was found in 82 men (17%) and both measure abnormal was found in 8 subjects (2%). Logistic regression analysis revealed that independent predictors of PAD increase in females were a positive CACS (OR 2.78) and obesity (1.83). Similar determinants were recognized in men (a positive CAC OR 3.31 and obesity 1.98). The PAD:AAD ratio in 9 men (2%). In total, any PAD increase was found in 82 men (17%) and both measure abnormal was found in 8 subjects (2%).

Conclusions: Pulmonary artery trunk dilation is relatively frequently observed in subjects referred for coronary artery calcium determination. Presence of coronary atherosclerosis and obesity were found as independent predictors of PAD enlargement. Detection of PAD abnormality might help to optimize diagnostic and therapeutic approaches in symptomatic subjects referred for CAC scoring.
Egr-1 expression is specific for neointimal development in both human and experimental PAH

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Objectives: In Pulmonary Arterial Hypertension (PAH) due to congenital heart disease, increased pulmonary blood flow is an essential trigger for neointimal formation. Using micro-array analysis, we recently identified that transcription factor Egr-1 is upregulated in experimental flow-associated end-stage PAH. Its role in neointimal development in PAH is unknown. Here, we aimed to assess in both human and rats spatiotemporal expression of Egr-1 in neointimal (flow-associated) PAH compared to non-neointimal Pulmonary Hypertension (PH).

Methods: In rats, flow-associated PAH was created by combining monocrotaline with an aortocaval shunt (MCT+Flow); and compared with a non-neointimal PH model (MCT-only). Animals were sacrificed 1 day before increased flow and at multiple time points after flow addition (1 day, 1 week, 4 weeks). Egr-1 expression was assessed using laser-dissection, qRT-PCR and immunohistochemistry. In humans, vascular Egr-1 expression was studied in lung samples of 27 end stage PAH patients (associated with congenital shunt (flow) PAH, n=12; IPAH, n=15) and compared with non-neointimal PH (hypoxic PH; n=4) and healthy controls (n=11).

Results: In rats, MCT+Flow rats developed, within 4-5 weeks, severe PAH (pSRVP 64±12 mmHg, Fulton index 0.57±0.08) and complex neointimal lesions (vessel occlusion 46±3%; compared to MCT-only (pSRVP 50±14 mmHg; Fulton index 0.32±0.03, no neointimal lesions) and control (pSRVP 25±4 mmHg Fulton index; 0.26±0.04)). In MCT-flow rats Egr-1 mRNA expression was upregulated 1 day after flow addition and in end-stage PAH. Increased flow directly induced Egr-1 expression in pulmonary endothelial cells; during disease development, Egr-1 expression migrated throughout the vascular medial layer. In contrast, Egr-1 mRNA was not upregulated in MCT-only rats and Egr-1 expression was observed only sporadically in the non-neointimal vessel remodeling. In both flow PAH and IPAH patients, Egr-1 expression was upregulated compared to hypoxic PH (P<0.001) and controls (P>0.001). The strongest expression was seen in the intra-acinar vessels of flow-PAH (P≤0.05 vs IPAH; P≤0.001 vs hypoxic PH and control) and in plexis flows. In flow-PAH, endothelial Egr-1 expression in the intra-acinar vessels correlated with increase in pulmonary artery pressure (mPAP).

Conclusions: We show that in both experimental and human PAH, not in non-neointimal PH, Egr-1 is upregulated and associated with neointimal development. This suggests that Egr-1 is an important regulator in the development of pulmonary neointimal lesions in PAH.

A female model of severe neointimal pulmonary hypertension: evidence for increased susceptibility in a female rat following pneumolocrotaline

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Pulmonary arterial hypertension (PAH) is an enigmatic, fatal disease with few treatment options. Decades of important animal studies in pulmonary hypertension have utilized male rats, exposed either to chronic hypoxia or monocrotaline (MCT), to define disease mechanisms and test novel treatment strategies. However, females represent 70-80% of the afflicted human population, and a female rat model with the key features of pulmonary hypoxia (pulmonary arterial hypertension; PAH) has been lacking.

Methods: Young female rats treated with relatively low dose MCT following left pneumonectomy developed severe, neointimal pulmonary vasculopathy with vascular pruning and RV failure. This model offers a unique opportunity to explore hormonal or sex chromosomal influences on the susceptibility to PAH. It also affords the opportunity to examine sex-specific differences in the response to an experimental PH therapy and the potential to analyze sex-specific PH adaptation to increased afterload.

Results: In Sprague-Dawley rats by combining monocrotaline (MCT) with an aortocaval shunt (MCT+Flow) and; Rats that received monocrotaline MCT Only (non-flow, non-neointimal Pulmonary Hypertension) and sham operated rats (Con) served as control. After invasive hemodynamic measurements, animals were sacrificed 1 day before flow addition and 1 day, 1 week, 4-5 weeks after flow addition for biomolecular analysis.

Conclusions: Results: MCT+Flow rats developed neointimal lesions with perivascular proliferation and severe PAH (pSRVP 64±12 mmHg; Fulton index 0.46±0.03) compared to MCT-only (pSRVP 50±14 mmHg) and control (pSRVP 25±4 mmHg). Neointimal lesions were not seen in MCT-only rats or Con. Perivascular macrophage (CD163+) accumulation was highly increased in MCT+Flow rats to Con (P<0.005) and was specific for increased pulmonary blood flow (monocrotaline only; P<0.05 vs MCT-only). In MCT+Flow rats strong perivascular macrophage infiltration was seen around neointimal lesions. In MCT+Flow rats mRNA expression of the pro-inflammatory cytokine MCP-1 increased during disease development.

Conclusions: We show that in experimental flow-associated PH, perivascular macrophage infiltration is increased due to increased pulmonary blood flow. These data add to the consensus that inflammation plays an important role in neointimal development in PAH associated with congenital heart disease.
main only incompletely understood. Besides the increase in afterload, inflammation and oxidative stress have been identified as important cofounders for induction of right heart dilatation and failure. Nitrated fatty acids (NO2-FA) represent endogenously generated biomolecules, which convey potent anti-inflammatory and anti-oxidative effects. We have shown recently that these molecules are strongly cardioprotective. Whether NO2-FA modulate the development of right heart failure in PAH however remains unknown.

Methods and Results: Wild-type C57BL/6J mice were housed under hypoxic conditions (10% oxygen concentration) and treated for 4 weeks with vehicle or nitro-oleic acid (OA-NO2, 6 mg/kg bodyweight, n=8) via subcutaneous minipumps. Animals treated with OA-NO2 displayed a reduced right ventricular pressure as assessed by in vivo-right heart catheterization (RVPP: 48.67±2.05 vs. 54.0±1.30 mmHg, p<0.001) and relative right ventricular hypertrophy (RV/LV weight: 0.25±0.01 vs. 0.37±0.02 sec, p<0.01) as compared to vehicle-treated animals. This translated in significantly reduced right heart failure as determined by BNP (p<0.05). Leukocyte infiltration as well as oxidative stress supraoxide bioavailability in the right ventricle were significantly reduced following OA-NO2 treatment. In addition, picrocumarol red staining revealed attenuated ventricular fibrosis in response to OA-NO2 (1.23±0.43 vs. 2.33±0.31 in vehicle treatedanimals, p<0.05).

Conclusions: The current findings not only underscore the significance of inflammation and oxidative stress in the pathophysiology of right ventricular dysfunction in pulmonary hypertension, but reveal that nitrated fatty acids may provide a novel therapeutic option in pulmonary arterial hypertension.

Right ventricular hypertrophy and failure abolish cardioprotection by ischemic preconditioning

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Purpose: To investigate whether hypertrophy and failure of the right ventricle changes the response to ischemia and ischemic preconditioning.

Materials and Methods: Male Wistar rats were subjected to moderate pulmonary trunk banding (mPTB), severe PTB (sPTB) or SHAM operation. The degree of right ventricular hypertrophy and failure (RVHF) where evaluated by right ventricular weight and murine alanine minipump. Animals treated with OA-NO2 displayed a reduced right ventricular pressure as assessed by in vivo-right heart catheterization (RVPP: 48.67±2.05 vs. 54.0±1.30 mmHg, p<0.001) and relative right ventricular hypertrophy (RV/LV weight: 0.25±0.01 vs. 0.37±0.02 sec, p<0.01) as compared to vehicle-treated animals. This translated in significantly reduced right heart failure as determined by BNP (p<0.05). Leukocyte infiltration as well as oxidative stress supraoxide bioavailability in the right ventricle were significantly reduced following OA-NO2 treatment. In addition, picrocumarol red staining revealed attenuated ventricular fibrosis in response to OA-NO2 (1.23±0.43 vs. 2.33±0.31 in vehicle treatedanimals, p<0.05).

Conclusions: The current findings not only underscore the significance of inflammation and oxidative stress in the pathophysiology of right ventricular dysfunction in pulmonary hypertension, but reveal that nitrated fatty acids may provide a novel therapeutic option in pulmonary arterial hypertension.

Pulmonary hypertension: mechanisms / Populations genetics

P4914 New single nucleotide polymorphisms associated with altered platelet response to acetylsalicylic acid in diabetic population: genome-wide association approach and pooled DNA strategy

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Patients with type 2 diabetes mellitus (T2DM) are characterized by hypercoagulable state and decreased platelet response to acetylsalicylic acid (ASA) treatment. The objective of this research was to use genome wide association study (GWAS) and pooled DNA strategy to look for the new loci associated with the abnormal platelet reactivity in diabetic patients treated with ASA.

Methods and Results: Study cohort consisted of 295 Caucasians with T2DM who had been taking ASA at the dose of 75 mg per day for at least 3 months. We tested association of approximately 2.5 million single nucleotide polymorphisms (SNPs) with platelet reactivity using VeriFyNowAspirin and PFA-100 as asays. We identified associations of several new loci with platelet reactivity. The highest statistical significance (p value between 0.0001– 0.008) was observed for RGS7 gene (rs2502448) using recessive genetic model and carries of both minor alleles of RGS7 were characterized by increased odds ratio (OR) (3.45-3.75 depending on the cut-off times) when compared with wild type allele in type on ASA platelet activity. The statistical significance using logistic regression statistics was also observed for DPP6 (rs1387180) and GRS (rs3779647). Moreover several other SNPs displayed nominal statistical significance in this model including FOSL1, CACNA1A, PLAG246E, AK5, KNC21, AKMP16, EBRB4 and HS6ST1.

Conclusions: The untargeted GWAS approach provides an opportunity to identify novel biologic pathways related to platelet activation and to direct future studies of candidate genes that hold the most promise for relevance to platelet activation and aggregation.

P4915 Impact of clinical and genetic factors on acenocoumarol dose requirements in Polish patients - dose calculation algorithm

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Purpose: Widespread use of warfarin in Western Europe allowed extensive studies of warfarin dose determining factors. We present the first large Eastern European study looking at another oral anticoagulant from the vitamin K antagonist group - acenocoumarol (AC). Our aim was to establish the prevalence of CYP2C9 and VKORC1 polymorphisms in Polish population and factors determining dose requirements of AC.

Methods: We included 321 patients attending our outpatient cardiology clinic: 207 receiving long-term AC for atrial fibrillation (65.7%) and artificial valve replacement (34.3%), aged 36-89 (mean 71), 54.5% women, and 114 control patients matched by demographic characteristics not receiving AC.

Results: Prevalence of CYP2C9 polymorphisms is shown in the table. Dose requirements in patients carrying CYP2*2 and *3 polymorphic alleles were significantly lower compared to wild-type homozygotes CYP2*1/*1, 2.3±1.17 mg/day and 2.9±1.1 mg/day respectively (P<0.006). Dose requirements in patients carrying VKORC1 haplotypes A/A* and G/A were significantly lower compared to wild-type homozygotes G/G*, 1.7±0.6 mg/day, 2.3±0.7 mg/day and 3.5±1.2 mg/day respectively (P<0.001). Additional determinants identified were age (negative correlation) P<0.001 and body mass P<0.004. Genetic and clinical factors explained 48% of the variance of dose. Using multivariate regression analysis we created an algorithm for calculation of dose of AC (mg/day): 3.268 + Prevalence of gene polymorphisms

<table>
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<th>Gene</th>
<th>CYP2C9</th>
<th>VKORC1 A/A*</th>
<th>VKORC1 G/A</th>
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<td>1.17 mg/day</td>
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<td>2.5 mg/day</td>
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<tr>
<td>*2/*2</td>
<td>1.6 mg/day</td>
<td>3.1 mg/day</td>
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Conclusions: This study confirmed the hypothesis that the dose requirements of AC are influenced by genetic and clinical factors, particularly the presence of certain VKORC1 and CYP2C9 gene variants. The use of these genetic markers can potentially improve the accuracy of dose estimation and reduce the risk of adverse drug reactions.
Conclusions: Prevalence of VKORC1 and CYP2C9 polymorphisms in Polish population is similar to that of other Caucasians. Genotype, age and body mass are independent determinants of dose requirements for Acenocoumarol.

Conclusions: We conclude that low frequency intermediate penetrance variants in the ROCK1 gene predispose to congenital heart disease.

Conclusions: The variant rs2957717, near the ADM gene, was associated with both lower levels of MRproADM and left ventricular mass index in the general population. The effect on left ventricular mass index was independent of MRproADM levels and cardiovascular risk factors. Such finding supports the hypothesis of a possible causal relationship between the variant and left ventricular mass warranting further investigation.

Conclusions: The association between a genetic variant near adrenomedullin gene with left ventricular mass index was significant for both genders. The advantage of our study is the high degree of phenotype homogeneity (inertial exercise testing) and the fact that it was performed on a population-based sample. The major limitation of our study is the small sample size.
restenosis, p=0.041. Subsequent analyses of the individual genes demonstrated that the observed association of the complete set was determined by 7 of the 36 genes. Removing these 7 genes from the complete set and subsequent analysis of the subset of the other 29 genes did not demonstrate a remaining jointed effect, p=1.0 (subset1).

Conclusion: Despite the overt inconsistencies of individual candidate gene studies, this study demonstrates that the joint effect of all these genes together, indeed is associated with clinical restenosis.

Table 1

<table>
<thead>
<tr>
<th>Set</th>
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<th>Significant SNPs</th>
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P4920

Chromosome 9p21.3 effect on CDKN2A/2B expression in human coronary atherosclerosis

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Purpose: Coronary artery disease is significantly influenced by genetic background. Genome-wide association studies showed that common genetic variants in vascular regulatory sequences and be required for the correct vascular expression of CDKN2A/B. This current understanding of the pathophysiology of early onset CAD.

Methods: Human atherosclerotic plaques were obtained from a cohort of 30 patients with ischemic heart disease. Coronary artery stenosis was isolated from 20 patients who underwent heart transplantation for post-ischemic dilated cardiomyopathy.

Genetic analysis was performed on atherothrombotic material and vascular smooth muscle cell (VSMC) (isolated from coronary arteries. Total RNA and gDNA were extracted using the semi-automated platform Maxwell 16 and total RNA were reverse transcribed using a high-capacity cDNA Archive Kit. SNP rs1333040 was investigated by means of the Assay on Demand platform and expression level of CDKN2A/B in human coronary atherosclerotic plaques.

Results: Genotype distribution of rs1333040 in atherosclerotic plaques was as follows: 5 had no risk allele (CC), 10 had one (CT) and 15 had two (TT). The expression of CDKN2A/B expression was significantly lower in the TT plaques than in the plaques without the risk allele (CC), whereas their expression in the CT plaques was intermediate (p=0.0012). Genotype distribution of rs1333040 in coronary arteries was the following: 4 had no risk allele (CC), 2 had one (CT) and 14 had two (TT). Expression analysis on VSMCs showed that expression of CDKN2A/B in coronary arteries was not affected by genotype as expressed according to the rs1333040 genotype (p=0.001 for both genes).

Conclusion: Our findings show a link between 9p21.3 genotype and CDKN2A/B gene expression in diseased human coronary arteries, which support the hypothesis that sequence variations in the 9p21.3 risk interval on chromosome 9p21.3 are associated with ischemic heart disease. However, the mechanistic basis for this association is still obscure. This study demonstrates that the joint effect of all these genes together, indeed is associated with clinical restenosis.

P4921

Gene expression profiling in patients with myocardial infarction at young age

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Myocardial infarction (MI) is one of the main causes of mortality. It usually is a disease of the middle-aged and elderly and MI in young adults is a rare phenomenon. Experiments show that sequence variations in the 9p21.3 risk interval on chromosome 9p21.3 are associated with ischemic heart disease. However, the mechanistic basis for this association is still obscure. This study demonstrates that the joint effect of all these genes together, indeed is associated with clinical restenosis.

Methods: Human coronary atherosclerotic plaques were obtained from a cohort of 30 patients with ischemic heart disease. Coronary artery stenosis was isolated from 20 patients who underwent heart transplantation for post-ischemic dilated cardiomyopathy.

Genetic analysis was performed on atherothrombotic material and vascular smooth muscle cell (VSMC) (isolated from coronary arteries. Total RNA and gDNA were extracted using the semi-automated platform Maxwell 16 and total RNA were reverse transcribed using a high-capacity cDNA Archive Kit. SNP rs1333040 was investigated by means of the Assay on Demand platform and expression level of CDKN2A/B in human coronary atherosclerotic plaques.

Results: Genotype distribution of rs1333040 in atherosclerotic plaques was as follows: 5 had no risk allele (CC), 10 had one (CT) and 15 had two (TT). The expression of CDKN2A/B expression was significantly lower in the TT plaques than in the plaques without the risk allele (CC), whereas their expression in the CT plaques was intermediate (p=0.0012). Genotype distribution of rs1333040 in coronary arteries was the following: 4 had no risk allele (CC), 2 had one (CT) and 14 had two (TT). Expression analysis on VSMCs showed that expression of CDKN2A/B in coronary arteries was not affected by genotype as expressed according to the rs1333040 genotype (p=0.001 for both genes).

Conclusion: Our findings show a link between 9p21.3 genotype and CDKN2A/B gene expression in diseased human coronary arteries, which support the hypothesis that sequence variations in the 9p21.3 risk interval on chromosome 9p21.3 are associated with ischemic heart disease. However, the mechanistic basis for this association is still obscure. This study demonstrates that the joint effect of all these genes together, indeed is associated with clinical restenosis.

P4922

Synergistic effects of genetic variants of the apolipoprotein-A V gene and the butyrophilin subfamily 2, member A1 gene on dyslipidemia in East Asian populations

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Purpose: The genes underlie genetic susceptibility to dyslipidemia in Asian populations remain to be identified definitively. This study shows that the association of the rs662799 of the apolipoprotein A-V gene (APOA5) and the C-G polymorphism (rs6929846) of the butyrophilin, subfamily 2, member A1 gene (BTN2A1) are significantly associated with increased serum concentrations of triglycerides (TG) and a decreased serum concentration of HDL-cholesterol in Japanese individuals. The purpose of this study was to examine whether these polymorphisms synergistically affect serum lipid profiles and the prevalence of dyslipidemia in East Asian populations.

Methods: The current study is based on a cohort of 7471 Japanese and 3529 Korean individuals. Genotype association was assessed in a population of 5000 East Asian ancestry adults from Japan, Korea, and China. Genotypes were determined using Affymetrix SNP array 6.0.

Results: Genotype of APOA5 and the CC genotype of BTN2A1 (rs662799) were significantly associated with serum concentrations of TG and HDL-cholesterol, but not LDL-cholesterol, in Japanese and Korean individuals, whereas the rs6929846 of BTN2A1 was significantly associated with serum concentrations of TG and HDL-cholesterol, but not LDL-cholesterol, in Japanese individuals. There was no relation between rs6929846 of BTN2A1 and serum concentrations of TG, HDL-cholesterol, or LDL-cholesterol in Korean individuals. Multivariate logistic regression analysis with adjustment for age, gender, hypertension, diabetes, smoking, BMI, and the C-G polymorphism revealed that the genotype of APOA5 and the CC genotype of BTN2A1 were significantly associated with serum concentrations of TG and HDL-cholesterol, but not LDL-cholesterol, in Japanese and Korean individuals. There was no relation between rs6929846 of BTN2A1 and serum concentrations of TG, HDL-cholesterol, or LDL-cholesterol in Korean individuals. Multivariate logistic regression analysis with adjustment for age, gender, hypertension, diabetes, smoking, BMI, the rs662799 of APOA5 and the CC genotype of BTN2A1 was significantly associated with serum concentrations of TG and HDL-cholesterol, but not LDL-cholesterol, in Japanese and Korean individuals. The purpose of this study was to examine whether these polymorphisms synergistically affect serum lipid profiles and the prevalence of dyslipidemia in East Asian populations.

Conclusions: This study provides novel insights in the genetic basis and pathways involved in myocardial infarction and expand our current understanding of the pathophysiology of early onset CAD.
Results: After conditional analysis, among 34 variants exceeding significance threshold and located all near the adenomodulin gene, GWAS identified 2 variants, rs9267692 (p = 5.10e-13) and rs2957717 (p = 4.20e-10) independently associated with PRU. Interaction terms between the 2 SNPs of the epithelial sodium channel protein 1 (SCNN1G) gene for the variability before and after 4.5% [3.2-5.8] after adjusting for non-genetic correlates.

Age (p = 1.6111), female gender (p = 2.9e-17), body mass index (p = 8e-150), smoking (p = 3e-6), Plasma levels of creatinin (1e-60), CRP (1e-11), NTproBNP (p = 2e-52), Interleukine-18 (p = 1e-04), Interleukine-1 receptor antagonist (p = 2e-10) and CYP2C19*1/*1 (p = 1e-240) were identified as independent non-genetic correlates of mPRaD levels accounting together for 70% [69-72] of its variance. CYP2C19*1/*1 was the most important source of variance accounting alone for 43% [40-45].

All genetic and non-genetic variables remained independently associated to mPRaD levels in the multivariable model (table) accounting for 72%[70-73] of its variance.

Conclusions: mPRaD levels increase in association with endothelial ag- gression, cardiovascular risk factors, hemodynamic status and inflammatory processes. Although mPRaD levels’ variance is dominantly related to non-genetic factors, genetic variants near the ADN gene also affect such levels.

P4924
Genetic polymorphisms of CYP2C19 and effect of clopidogrel therapy in healthy Malay workers.

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Purpose: CYP2C19*2 allele may be associated with reduced antiplatelet effect of clopidogrel and potentially worsened clinical outcomes. We assessed the prevalence of CYP2C19 polymorphisms, namely CYP2C19*2 and CYP2C19*3 alleles in healthy Malay volunteers and we linked the CYP2C19*2 allele with platelet reactivity after administration of 300-mg oral dose of clopidogrel.

Methods: 90 volunteers (34 Malays, 49 Chinese, 7 Indians) were genotyped for CYP2C19*2 and CYP2C19*3 alleles using polymerase chain amplification followed by Automated Sequencer. The CYP2C19*1 allele was assigned when none of the other said alleles were present. Subsequently, 45 of these volunteers (18 Malays, 25 Chinese, 2 Indians) were given 300 mg clopidogrel and their platelet reactivity was assessed at 4 hours post dosing using VerifyNow-P2Y12 assay. They were classified into 3 genotypes, namely CYP2C19*1/*1 (n=17 [8 Malay, 8 Chinese, 1 Indian]), CYP2C19*1/*2 (n=21 [7 Malays, 14 Chinese]) and CYP2C19*2/*2 (n=7 [3 Malays, 3 Chinese, 1 Indian]). The data were reported in P2Y12 Reaction Units (PRU). Nonresponder status was prespecified at 230 PRU or greater.

Results: Of the 90 volunteers genotyped, 53 (59.8%) had at least 1 CYP2C19*2 allele [38 CYP2C19*1/*2 (42.2%), 15 CYP2C19*2/*2 (16.7%) and 34 (37.8%) assigned CYP2C19*1/*1. CYP2C19*1/*3 was detected in 2 volunteers and CYP2C19*2/*3 in 1 volunteer. No CYP2C19*3/*3 was found in this study population. CYP2C19*2 allele was detected in all 3 ethnic groups. The prevalence of CYP2C19*2 allele appeared to be high in Chinese volunteers (67.3%). Mean pre dosing platelet reactivity in CYP2C19*1/*1 (n=17), CYP2C19*1/*2 (n=21) and CYP2C19*2/*2 (n=7) carriers were essentially similar (303.9 ± 81.4 vs. 325.6 ± 87.2 PRU, P=0.01). After clopidogrel administration, CYP2C19*2/*2 carriers had significantly higher mean PRU than CYP2C19*1/*2 and CYP2C19*1/*1 (291.0±62.1 vs. 232.5±81.4 vs. 147.4±87.2 PRU, P<0.01). Of 62 volunteers given clopidogrel, 21 (46.7%) were found to be non-responders with PRU >230 (3 were CYP2C19*1/*1, 11 were CYP2C19*1/*2 and 7 were CYP2C19*2/*2).

Conclusions: CYP2C19*2/*2 allele is commonly found in Malaysian population and is associated with marked decrease in platelet responsiveness to clopidogrel. A high proportion of Chinese volunteers appeared to carry this allele. The results of this study show that genotyping or phenotyping may be useful in clopidogrel therapy.

P4925
Matrix metalloproteinase: investigation from gene to protein expression using immunoblotting and zymography analysis; and mRNA expression by quantitative reverse transcription polymerase chain reaction.

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Background: Matrix metalloproteinase (MMP) has a role in early atherosclerosis, plaque rupture and myocardial infarction. We investigated the relation between A-173G polymorphism in MMP1 in longitudinal observation in general population.

Methods: The study group included 237 subjects, members of two-generation families, recruited from the general population. At baseline and after on average 6.8±1.4 years of follow-up, we used the same methods for phenotyping. To obtain information about coronary artery disease, participants were programmed to measure BP each 15 min daytime (8.00 – 22.00) and each 30 min nightime (22.00-06.00). Venous blood samples were drawn for measurement of serum creatinin and for further genotyping. Estimated glomerular filtration rate (eGFR) was calculated using MDRD formula. The analyses of genotype-phenotype relations were adjusted for covariables and relatedness of study participants.

Results: The study group included 108 men and 129 women. Mean age at base- line was 50.6 years in 113 parents and 24.1 years in 124 offspring. The genotype frequencies were: AA – 16.1%, GA – 48.5%, GG – 34.6%, and did not deviate from Hardy-Weinberg equilibrium (P=0.98). The active form of MMPs was measured by enzyme linked immunosorbent assay (ELISA); MMP proteins presence and expression by immunoblotting and zymography analysis; and mRNA expres- sion by quantitative reverse transcription polymerase chain reaction.

Results: Plasma concentrations of MMPs were significantly increased in pa- tients compared to control subjects (MMP-1, 7.0±1.84 vs. 1.1±0.17; MMP-2, 2.9±4.11 vs. 1.3±2.0±3.13; MMP-3, 4.18±1.03 vs. 1.00±0.17; MMP-5, 15.45±3.19 vs. 16.6±0.55 respectively). Gel zymography revealed 43, 66, 45, and 83 kDa molecular weight bands which consistent with active MMP-1, -2, -3, and -9 respectively exhibiting gelatin-degrading activity in both patient and control subjects. Comparison of the patients with AMI and control subjects demonstrated that in patient subjects, MMP-9, -1, -3, and -2 activity were 13-fold, 6-fold, 4-fold, and 3.5-fold higher respectively than in control samples. No up-regulation of mRNA expression was found.

Conclusions: To our knowledge, it is the first monitoring of MMP gene and pro- tein expression and also circulating active MMPs in Iranian patients with AMI and normal subjects. Up-regulation of MMPs activity is common in the failing my- ocardium and missing up-regulation of transcription indicates that protein levels of MMPs were regulated at the post transcriptional level.
Influence of rs5065 atrial natriuretic peptide gene variant on Coronary Artery Disease

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Either modified ANP plasma levels or peptide structural alterations have been involved in development of cardiovascular events. To investigate the impact of rs5065 atrial natriuretic peptide (ANP) gene variant on coronary artery disease (CAD) and its outcomes and to gain potential mechanistic insights on the association with CAD.

Methods: 104 patients undergoing coronary angiography for suspected CAD [432 stable angina (SA), 572 acute coronary syndrome (ACS)] were genotyped for rs5065 ANP gene variant. Data in SA and ACS groups were replicated in an independent population of 482 SA patients (rSA) and of 675 ACS patients (rACS), respectively. Clinical follow-up was available for both SA and rSA patients. Plasma NT-proANP myeloperoxidase (MPO), lipoprotein-associated phospholipase A2 (Lp-PLA2), oxidized low density lipoprotein (oxLDL), were assessed in a subgroup of rSA patients.

Results: rs5065 minor allele (MA) was an independent predictor of ACS (OR=1.90; 95% CI: 1.40-2.58; p=0.001). At follow-up, rs5065 MA was independently associated with significantly higher rate of major adverse cardiovascular events (MACE) in SA group, p<0.001. Data were replicated in rSA group at follow-up (p=0.008). Cox proportional hazard analysis tested by 4 models confirmed the association of the rs5065 variant on Coronary Artery Disease (CAD). Sensitivity analysis which is of Eastern European ancestry. We focused on six loci: 1p13.3, 2q36.3, 6q25.1, 9p21, 10q11.21 and 15q22.33 characterized by SNPs rs599839, rs2943634, rs692269, rs1333049, rs501120 and rs17728212 respectively.

Methods: All six SNPs were genotyped in a case-control study consisting of 1100 clinically confirmed CAD cases and 452 population controls with no history of cardiac manifestations. Written informed consent was obtained from all participants of this study. Genomic DNA was extracted from white blood cells by chloroform-phenol method and genotyped using fluorescently labeled hydrolysis probes by real-time PCR system.

Results: Two of the investigated polymorphisms rs2943634 and rs1333049 were significantly associated with CAD. Allele C of the rs1333049 had frequency 0.522 and 0.437 in cases and controls respectively (CAD OR=1.40; 95% CI: 1.20-1.64; P=2.12e-5). None of other four SNPs reached significance level of P=0.05 even before correction of results.

Conclusion: Our findings suggest that rs1333049 is strongly associated with CAD risk in population with stable and that rs2943634 also increases risk of CAD. Further we found evidence that MAF difference of SNPs among regions within Europe is significant, therefore making interpretations based on other population samples challenging.

GENETICS AND GENE THERAPY

Cost-effectiveness of genetic studies in inherited cardiomyopathies

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Introduction: Genetic diagnosis in inherited cardiomyopathies is still limited and reimbursement policies are lacking. There is a need to evidence the cost of genetic testing and know their profitability in order to establish criteria for prioritizing access to genetic testing for these diseases.

Methods: We determined the cost per positive genotyping (PG) in 234 index cases with diagnosis of HCM, ARVC, and Brugada Sdr (BS). The genetic test of the most prevalent genes in this panel was included (MYH7 and MYBPC3 for HCM; PKP2, DSP, DSC2, DSQ2, PKG for ARVC; KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2 for LQTS; and SCN5A for BS). Genetic studies expenses were HCM 1500 €, ARVC 2050 €, BS 725 €, LQTS 1755 €. Estimation of the cost of periodical screening in wildtype relatives (WT) were calculated from 10-60 yrs (ECG 20 €, echocardiogram 60 €, cardiac consultation 40 €). Frequency of the clinical screening of relatives was based on previous studies (HCM 10/31 (22):2715-26; i.e: HCM annually from 10-20 yrs, every 3 yrs for 20-60 yrs).

Results: Mutations in HCM-related genes were identified in 92 of 115 patients (80%); leading to a PG cost of 1650 € in HCM group. Mutations in ARVC-related genes were identified in 14 of 17 (84%). The cost of genetic testing of 40 WT from ARVC was 28,650 €. A high pick up rate of HCM and ARVC was probably due to bias towards the high risk (sudden death) or high penetrance cases, and a founder effect of some of the mutations. A total of 738 individuals from 234 probands (917 HCM (293 carriers of mutation (CM)), 76 ARVC (36 CM), 71 LQTS (35 CM) and 74 BS (33 CM)) were genotyped. The cost of clinical periodical screening in the 224 WT from HCM compared with the cost of estimated test of probability of HCM was 1500 € (51,860 € - (51,150 €) €). The cost of genetic testing of 40 WT from ARVC was 28,650 € vs 36,900 € (-8,250 €) of the expenses of genotyping. Similarly, for LQTS the estimated figure of 14,220€ was 38,775 € of the expenses of genotyping (-24,555 €). Balance in BS was 12,220 € for tests saved in 33 WT vs 60,900 € (49,680 €).

Conclusion: Our data suggests that individuals with conclusive clinical diagnostic of HCM should have a priority to access genetic testing. The benefits from periodical tests saved in WT that can be discharged exceed the expenses of genetic testing. The yield of genotyping is substantially high in ARVC and LOTS patients suggesting these two groups should be genetically studied too, although less cost-effective.

Secretoneurin gene therapy reverses the impairment of hindlimb post-ischemic recovery in Apo E-/- mice

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Introduction: Hypercholesterolemia (HC) is a major risk factor for peripheral arterial disease (PAD) and has been shown to impair the angiogenic response in the unilateral mouse hind limb ischemia (HLI) model. The impairment of up-regulation of angiogenic factors seems to be one of the underlying mechanisms for reduced vessel formation. Since previous studies revealed an angiogenic potential of secretoneurin (SN) we tested the hypothesis if SN-gene therapy might also improve neovascularization in a mouse model associated with impaired vascular response.

Results: To simulate HC in-vitro, endothelial cells were treated with 50 μg/ml oxidized low-density-lipoprotein (oxLDL). Under these experimental conditions the induced proliferation was impaired but a beneficial effect still remained (rel. proliferation SN vs. ctr: no oxLDL: 1.59±0.032; n=5; P<0.001; with oxLDL: SN 1.36±0.024; n=5; P<0.01). Similarly, in the matrigel assay the effect of SN in promoting capillary tube formation was reduced but couldn’t be abolished by addition...
oxLDL (rel. tube formation SN vs. ctr.: no oxLDL 1.71±0.02; n=5; P<0.01; with oxLDL 1.44±0.03; n=5; P<0.05). Moreover, the SN-induced activation of signal transduction pathways like ERK 1/2 wasn’t abrogated by addition of oxLDL. SN induced effects were similar to vascular endothelial growth factor.

To evaluate the therapeutic effect of SN in vivo we performed the HLI model in Apo E-/- mice set on western diet for 12 weeks. HLI was induced by ligation of femoral artery and 50 ug of SN-plasmid (p-SN)/control plasmid (p-ctr) was injected. The groups showed no significant difference regarding body weight and levels of cholesterol. Blood flow recovery (BFR) was assessed using a laser Doppler perfusion-imaging (LDPI) machine. Interestingly, p-SN injection increased capillaries/high power field 200x: p-SN 35.64±1.4 vs. p-ctr 204.87±8.6; n=10; P<0.01) and arterioles (arterioles/high power field 200x: p-SN 5.69±0.52 vs. p-ctr 3.16±0.24; n=10; P<0.001) density in ischemic muscles and ameliorated BFR (rel. LDPI ratio ischemic/non ischemic limb after 4 weeks: p-SN 0.78±0.04 vs. p-ctr 0.64±0.02; n=10; P<0.019). Moreover, SN-treatment resulted in a significant necrosis reduction (necrosis score: p-SN 1.55±0.2 vs. p-ctr 2.5±0.3; n=10; P=0.03).

Conclusion: Our data suggest therapeutic potential of SN under hypercholesterolic conditions and open up new therapeutic options for the treatment of PAD.

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**P4932** Early AAV9-mediated over-expression of S100A1 ameliorates myocardial hypertrophy in dystrophin-deficient mice

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Mutations of dystrophin leading to a complete loss of the protein cause x-chromosomal Duchenne muscular dystrophy (DMD), frequently associated to severe cardiomyopathy (CMP). However, although cardiac complications increase in severity and contribute to premature death of these patients, strategies to efficiently treat the CMP are not well established. It has been suggested that the loss of cardiomyocyte Calcium (Ca²⁺) cycling integrity plays a key role in the development and progression of CMPs, although so far its role in dystrophin-associated CMPs is unclear. In this context, the cardiomyocyte EF-hand Ca²⁺-sensor protein S100A1 plays a critical role in regulating Ca²⁺-cycling integrity and has been considered to be a promising candidate for gene therapy approaches to treat CMP. We have investigated the efficacy of Adeno-associated virus serotype 9 (AAV9) -mediated cardiac over-expression of S100A1 to prevent the development of CMP in dystrophin-deficient (mdx) mice. Therefore, AAV-9 vectors containing S100A1 CDNA under transcriptional control of a CMV-MLC promoter (AAV9/S100A1) were created. 1012 AAV9/S100A1 vector particles were intravenously injected into 8 week-old mdx mice before the onset of CMP. AAV9 harboring an enhanced green fluorescent protein reporter (AAV9/Egfp) was used as a control vector. At the age of 1 year histological examinations, echocardiography and PW-loops were performed to assess myocardial morphology and contractile function (cardiomyocyte cross-sectional areas (cm²), cm²eldiastolic posterior wall thickness (PWTd; mm), fractional shortening (FS; %) and left ventricular maximum rate of pressure change (dp/dtmx; mmHg/sec).

Uninjected and AAV/Egfp-treated mdx mice showed distinct myocardial hypertrophy and reduced contractility (systolic pressure (mmHg) 181±10, 167±10 and 155±10 mmHg in control, S100A1-treated and Egfp-treated mdx mice, respectively). AAV9/S100A1-treated mdx mice showed significant improvement of myocardial hypertrophy (PWTd 21±5 vs 20±3 mm; P<0.01) as well as fractional shortening (50±5% vs 48±2%; P<0.05). Our data suggest that AAV-mediated cardiac overexpression of S100A1 attenuates myocardial hypertrophy in mdx mice thereby representing a valuable tool to limit cardiac dysfunction in dystrophin-deficient cardiomyopathy.

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**P4934** Post-infarct treatment with microRNA145 reduces myocardial infarct size and improves cardiac remodeling and function in rabbits

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Background: It has been reported that micro RNA145 (miRNA145) inhibits proliferation of vascular smooth muscle and progression of atherosclerosis. However, it is still unclear whether miRNA145 is involved in ischemia-reperfusion injury. Objective: We investigated the involvement of miRNA145 in ischemia reperfusion injury and investigated whether post-infarct treatment with miRNA145 has a cardioprotective effect in a rabbit model of myocardial ischemia and reperfusion. Methods: Male Japanese white rabbits underwent 30 min of coronary occlusion followed by 6 hours and 14 days of reperfusion. Rabbits were then sacrificed with overdose of pentobarbital and the hearts were removed. From the myocardial tissues, miRNA145 expression levels relative to RNU6B were obtained at 6 hours and 14 days after myocardial infarction. In another series of experiments, rabbits underwent 30 min of coronary occlusion and 14 days of reperfusion. Rabbits then received intravenous injection of saline (control group, n=5) or 0.035 mg/kg of miRNA145, respectively, compared to the infarction and non-infarction areas of the myocardium at 6 hours after myocardial infarction. However, the expression of miRNA145 in control group was significantly increased in the border area compared with the infarction and non-infarction areas of the myocardium at 6 hours after myocardial infarction. Moreover, the decrease in miRNA145 expression in the border area was significantly attenuated at 14 days after myocardial infarction. Post-infarction treatment with miRNA145 significantly reduced the myocardial infarct size (16.7±3.7%) as compared to the control (31.8±2.7%) at 14 days after myocardial infarction. The miRNA145 also improved LV dimensions and improved dp/dtmx/sec.

Conclusions: It is suggested that miRNA145 is involved in the regulation of ischemia-reperfusion injury and post-infarction treatment with miRNA145 is protective against ischemia-reperfusion injury.
omponent of an in vitro model to facilitate development of vectors for cardiac gene transfer in large animals and for future clinical trials.

Methods: To identify the most suitable in vitro model, luciferase reporter constructs driven by the CMV-promoter have been crosspackaged into the capsids of AAV serotypes 1-6, 8 and 9. These constructs have been tested for their gene transfer efficiency in isolated cardiomyocytes and/or 300 μm organotypic myocardial slices of mice, rats and pigs. After the models had been validated for rodents, we analyzed gene transfer efficiency into the porcine heart with the two most promising vectors from the porcine in vitro study and AAV9, the most efficient serotype in mice. In order to facilitate cardiac gene transfer, vectors were applied via retroinfusion into the coronary venous system of pigs.

Results: Both isolated cardiomyocytes as well as organotypic slices revealed strong transgene expression after transduction with certain serotypes, while others failed almost completely to mediate transgene expression. Isolated cells and organotypic slices led to similar results, with AAV6 being most efficient for rat and pig. Comparison between the mouse, rat and porcine in vitro models showed that species differences are evident in vitro. Furthermore, comparison of reporter activities in the pig in vivo revealed that AAV6 enables the most efficient cardiac gene transfer followed by AAV5, while AAV9 was 300-fold less efficient than AAV6, confirming the predictions of the in vitro model.

Conclusion: We have developed in vitro models that show valuable prediction power for the efficiency of cardiac gene delivery of AAV vectors, allowing us to predict transgene delivery to the porcine heart 300-fold compared to AAV9. The correlation with published rodent in vivo data and our porcine in vivo data in this study underlines the feasibility of both models (primary cardiomyocytes and organotypic slices) for in vitro vector assessment. The predictive power of our models unveiled two AAV serotypes much more suited for cardiac gene transfer in the pig than AAV9, the most efficient vector for cardiac gene transfer in mice.

R14Del, a Dutch phospholamban mutation in Spanish family. Genotype-phenotype aspects

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Introduction: The sarcoplastic reticulum Ca(2+)-cytolyzing proteins are key regulators of cardiac contractility, and alterations in sarcoplastic reticulum Ca(2+)-cytolyzing properties have been shown to be causal of familial cardiomyopathies. Through genetic screening of dilated cardiomyopathy patients, we identified a previously described deletion of arginine 14 (PLN-R14Del) in the coding region of the phospholamban (PLN) gene known to cause dilated, arrhythmogenic right ventricular and non-contraction cardiomyopathy. The mutation is located in a conserved domain of phospholamban and consists of a loss of 3 nucleotides (AGA) leading to loss of the R14 residue but not a change in reading frame.

Methods: The index case was a 29 year old woman presented with syncopal rapid ventricular tachycardia and was diagnosed with dilated cardiomyopathy (EF 40%). A family study of first degree relatives included examination, ECG and echocardiogram. DNA samples from 9 individuals were evaluated using dhPLS and bidirectional sequencing of the exon and intron regions flanking the PLN gene through the ABI3130 analyzer and Seq Scape and Sequencing Analysis softwares.

Results: Seven of the 9 patients studied were mutation carriers although only 2 of them met diagnostic criteria of dilated cardiomyopathy: the proband and her asymptomatic 78 year old maternal grandmother. Five of the 7 carriers showed strikingly low voltage QRS complexes, despite no echocardiographic abnormalities in 3 (mother and 2 maternal aunts). Apart from proband all carriers were asymptomatic with no history of arrhythmia evidenced. Of note, proband's father showed strikingly low voltage QRS complex, despite no echocardiographic abnormalities, and did not carry the mutation. Index patients with mutations had more frequently spontaneous type I Brugada pattern (87.5% vs 52.9%, p = 0.06) and evidence of familial disease (62.5%, vs 23.5%, p = 0.03). Symptoms and risk profile of the proband carriers (146 patients) did not differ from the patients without mutation.

Discussion: The penetrance of type I ECG varied according to sex in carriers, with 8 cases among 18 men (44.4%) and no cases among 9 female (p=0.2). However, all 27 probands and 8 род non-carriers, the rate of type I ECG was 62.5% and 5% respectively (66.7% vs 62.5%, p=0.9). Flecainide test unmasked a higher proportion of females (66.7% vs 25.0%, p = 0.4).

Conclusions: The penetrance of spontaneous type I ECG in carriers was 29.6%, and rise to 63.2% after drug challenge test. Percentage of carriers who expressed type I ECG varied among different mutations (figure 1). A 36.8% of carriers who underwent a complete study, had normal ECG despite the drug challenge test.

Penetent study in SCNSA-mutations in brugada syndrome

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Introduction: Brugada syndrome (BS) is an inherited channelopathy associated with mutations in SCNSA gene and up to 7 genes more. The disease is inherited in autosomal dominant manner, although with variable penetrance.

Aim: To evaluate the penetrance of the disease in a unselected population.

Material and Methods: Seventy six non-related patients with BS were studied. Clinical characteristics and family risk profile were recorded. Direct sequencing of the SCNSA gene for identification of mutations and familial genetic study of parents was performed.

Results: Eight patients (10.5%) had point mutations (R27H, E901K, G1743R, E1356Q, N1443S, E1152X), and 19 additional carriers (10 male and 9 female) could be identified. Index patients with mutations had more frequently spontaneous type I Brugada pattern (87.5% vs 52.9%, p = 0.06) and evidence of familial disease (62.5%, vs 23.5%, p = 0.03). Symptoms and risk profile of the proband carriers (146 patients) did not differ from the patients without mutation.

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Conclusions: The penetrance of spontaneous type I ECG in carriers was 29.6%, and rise to 63.2% after drug challenge test. Percentage of carriers who expressed type I ECG varied among different mutations (figure 1). A 36.8% of carriers who underwent a complete study, had normal ECG despite the drug challenge test.
Association of a matrix metallopeptidase 1 gene polymorphism with long-term outcome of thoracic aortic aneurysm

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Objective: Although genetic variants are thought to contribute to the development of thoracic aortic aneurysm including dissection (TAA), it remains unclear whether gene polymorphisms are associated with the long-term outcome of TAA. The identification of genetic variants related to the long-term outcome of medically treated TAA may lead to a better understanding of the factors relevant to the progression or rupture of TAA, and consequently may better inform the selection of patients as candidates for surgical therapy because of a higher risk of rupture. The purpose of the present study was to identify genetic variants associated with the long-term outcome of medically treated patients with TAA.

Methods: A total of 103 medically treated patients with TAA (age, 63.3 ± 11.9 years; 13 aneurysms and 90 dissections) were retrospectively studied for their outcomes (mean follow-up period, 24 months). An unfavorable outcome was defined as: (1) death from cardiovascular causes or aneurysm rupture, (2) reoperation, (3) operation to repair surgical repair, or (4) the occurrence of cardiovascular events after initial hospitalization. The genotypes for 95 polymorphisms of 89 candidate genes were determined by a method that combines polymerase chain reaction and sequence-specific oligonucleotide probes with suspension array technology.

Results: The prevalence of Stanford A, hypertension, prior cardiac surgery, shock, and a maximum aneurysm diameter were greater in subjects with the unfavorable outcomes than in those with the favorable outcomes of this condition. Evaluation of genotype distributions by the chi-square test and subsequent multivariable logistic regression analysis with adjustment for covariates revealed that the −340A→G polymorphism (rs154821) of the matrix metallopeptidase 1 gene (MMP1) was significantly (P = 0.0288) associated with the outcome of TAA, with the minor G allele being related to a favorable outcome. The aneurysm diameter was significantly larger (P = 0.0167) smaller in the combined group of the AG and GG genotypes for this polymorphism (42.3 ± 14.0 mm) than in subjects with the AA genotype (48.6 ± 11.2 mm). Kaplan-Meier survival curves constructed according to MMP1 genotypes showed a more favorable outcome of TAA (log-rank P = 0.0146) in subjects with the AG or GG genotypes.

Conclusion: The G allele of rs154921 in MMP1 is associated with favorable long-term outcome of TAA. Determination of genotypes for this polymorphism may prove informative for assessment of the long-term outcome of TAA.

The onset of type 2 diabetes and related complications

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Purpose: To investigate whether sensitivity towards ischaemia-reperfusion (IR) injury in the type 2 diabetic heart is dependent on the stage of the disease. Inhibition of mitochondrial metabolism during ischaemia and initial reperfusion confers protection against IR-injury. We hypothesized that the acute metabolic alterations present at onset of T2DM entail cardioprotection by metabolic shutdown during IR, and that chronic alterations seen in late T2DM cause increased IR-injury.

Methods: Isolated perfused hearts from 6 (prediabetic), 12 (onset of T2DM) and 24 (late T2DM) weeks old Zucker diabetic fatty rats (ZDF) and their age-matched heterozygote controls were subjected to 40 min ischaemia/120 min reperfusion. IR-injury was assessed by TTC-staining. Myocardial glucose metabolism was evaluated by glucose tracer kinetics (glucose uptake, glycolysis and glucose oxidation rates), myocardial microdialysis (metabolomics), coronary effluent measurements and tissue metabolite measurements.

Results: At onset of T2DM ZDF hearts had a significant decrease in infarct size (A) and a significant reduction of endogenous glucose oxidation during initial reperfusion (B). Correlation analyses showed that the protection at onset coincided with the emergence of hyperglycemia (C). At late T2DM ZDF hearts suffered significantly larger IR-injury. Metabolomics, effluent measurements and tissue metabolite concentrations supported the role of metabolic shutdown during IR in the presence of cardioprotection at onset of T2DM.

Conclusion: The acute metabolic alterations at onset of T2DM induce protection towards IR-injury due to a shutdown of mitochondrial metabolism during ischaemia and initial reperfusion - alterations that become detrimental in late diabetes. These findings explain previous conflicting results on IR-injury in T2DM.

NO from neuronal NO synthase increases after beta-adrenergic stimulation but does not control mitochondrial respiration

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Background: During beta-adrenergic stimulation, the amplitude and frequency of myocadial [Ca2+]t transients and contraction increase as does the demand for ATP supply. The latter is matched by an increase in mitochondrial Ca2+ uptake which stimulates Krebs cycle dehydrogenases to accelerate the regeneration of mitochondrial NADH and FADH2, the electron donors for the respiratory chain. Because NO can compete with O2 at the respiratory chain, it was proposed that NO may regulate mitochondrial respiration. Myocardial NO is constitutively produced by a neuronal NO synthase (nNOS), located to the sarcoplasmic reticulum and an endothelial NOS (eNOS), located to the sarcolemmal caveolae, while the existence of a mitochondrial NOS (mtNOS) remains controversial. Since constitutive NOS activity is stimulated by increases in [Ca2+]t, we speculated that NO may control mitochondrial NO production during beta-adrenergic stimulation.

Methods and Results: Experiments were performed in isolated mitochondria and field-stimulated left ventricular (LV) myocytes from mice and guinea-pigs. In mitochondria, the NO donor spermine-NONOate induced ADP-activated O2 consumption and NADH oxidation. In LV myocytes, isoproterenol (30 nM) and an increase in stimulation frequency from 0.5 to 5 Hz augmented intracellular NO production by ~12% within 3 minutes (as evaluated by the L-NAME-inhibitable DAF-AM fluorescence). eNOS inhibition (with L-NIO, 1 μM) or genetic ablation (KO) did not reduce NO production in response to increased pacing frequency (p = 0.0002). In contrast, nNOS inhibition (7-NI; 2 μM) or genetic ablation (KO) did not reduce NO production in response to increased pacing frequency (p = 0.0002). Compared to SHR-lean and Ctr, SHR-ob were obese (638.3 ± 400.7 g) and field-stimulated LV myocytes from SHR-ob had increased mitochondrial NO production (p = 0.0002). At onset of beta-adrenergic stimulation, the amplitude and frequency of LV-ejection fraction was impaired vs. Ctr (46.2 ± 5.9 vs. 59.6 ± 5.1). LV-enddiastolic pressure (21.5 ± 1.1 vs. 19.5 ± 0.5). The amplitude and frequency of LV-remote NO production was increased in SHR-ob (p = 0.0007). Compared to SHR-lean and Ctr, SHR-ob were obese (638.3 ± 400.7 g) and field-stimulated LV myocytes from SHR-ob had increased mitochondrial NO production (p = 0.0002). At onset of beta-adrenergic stimulation, the amplitude and frequency of LV-ejection fraction was impaired vs. Ctr (46.2 ± 5.9 vs. 59.6 ± 5.1). LV-enddiastolic pressure (21.5 ± 1.1 vs. 19.5 ± 0.5). The amplitude and frequency of LV-remote NO production was increased in SHR-ob (p = 0.0007).

Conclusion: These findings explain previous conflicting results on IR-injury in T2DM.

Obesity and metabolic syndrome: implications for the type 2 diabetic heart

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Purpose: The additive effects of obesity and metabolic syndrome on left ventricular (LV) maladaptive remodeling and function in hypertension are not characterized. We compared an obese spontaneously hypertensive rat model (SHR-ob) with lean spontaneously hypertensive rats (SHR-lean) and normotensive controls (Ctr).

Methods: LV-function was investigated by cardiac magnetic resonance imaging and invasive LV-pressure measurements. LV-territorial fibrosis was quantified and protein levels of phospholamban (PLB), Serca2a and glucose transporters (GLUT1) were determined immunohistochemically.

Results: Blood pressure was similar in SHR-lean and SHR-ob (252.7 ± 24.1 vs. 254.2 ± 7.7 mmHg, p = 0.03) but increased when compared to Ctr (155.2 ± 2.4 mmHg, p = 0.002). Compared to SHR-lean and Ctr, SHR-ob were obese (638.3 ± 400.7 ± 1.1 vs. 400.7 ± 3.7 g and 465.5 ± 17.4 g (p = 0.001, respectively) and showed impaired glucose tolerance. In SHR-ob, LV-ejection fraction was impaired vs. Ctr (46.2 ± 1.1 vs. 59.6 ± 1.9). LV-enddiastolic pressure (21.5 ± 1.1 vs. 19.5 ± 0.5 mmHg, p = 0.0002) and Tau (18.6 ± 1.6 vs. 12.7 ± 1.1 ms, p = 0.002) were more increased
Subclinical hyperthyroidism and cardiovascular mortality


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Background: It is still uncertain if subclinical hyperthyroidism and "high-normal" thyroid function is a risk-factor for cardiovascular mortality.

Objectives: To examine the risk of cardiovascular mortality in relation to subclinical hyperthyroidism.

Methods: Patients consulting their general practitioner from 2000–2009 in Copenhagen, Denmark, who underwent thyroid blood tests, were identified by individual-level linkage of nationwide registries. Patients with a history of thyroid disease or related medication were excluded. Risk of cardiovascular mortality was analyzed using Kaplan-Meier curves and Poisson regression models to estimate Incidence Rate Ratios (IRR).

Results: Of 525,100 individuals in the study population (mean age 51.7 years ±18.0; 39.5% males) 204,113 (96.0%) were euthyroid, 1,474 (0.3%) had clinical hypothyroidism, 10,679 (2.0%) subclinical hypothyroidism, 3,421 (0.7%) clinical hyperthyroidism, and 1,101 (0.2%) subclinical hyperthyroidism. The prevalence of subclinical hyperthyroidism was higher in women. The prevalence of clinical hyperthyroidism was lowest in both genders. The risk of cardiovascular mortality was found to be increased in subclinical hyperthyroidism (8.8 ±0.62ms, respectively, p<0.0001 for all). Increased LV-fibrosis, collagen1 and TGF-β-axis. Serca2a protein levels were decreased in SHR-lean but not altered in SHR-ob suggestive for an upregulation of the GLUT1/ANF- and GLUT1/TGF-β-axis may link metabolic disarranges to structural cardiac remodeling in the state of insulin resistance and obesity on the background of hypertension.

Conclusion: Subclinical hyperthyroidism and "high-normal" thyroid function is a significant risk-factor for cardiovascular mortality.

Endothelial Microparticles derived under high Glucose concentrations increase monocyte adhesion on endothelial cells through upregulation of adhesion proteins in a p38 dependent way

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Background: Circulating endothelial microparticles (EMP) are increased in diabetic patients, but their role in the progression of atherosclerosis is unclear. We tested the hypothesis if EMP isolated from glucose treated human coronary endothelial cells (HCAEC) influence adhesion protein expression in target endothelial cells and thereby increase adhesion of monocytes to the endothelium, an important step in the development of atherosclerosis.

Methods and results: We created a hyperglycemic condition by treating HCAEC for 72h with 30mM glucose and generated EMP after 24h starvation. These modified EMP were defined as "injured" EMP (IEMP). Confocal microscopy, flow cytometry and electron microscope were used to characterize size (~1um) and cellular origin of IEMP. The effects of IEMP were compared with EMP generated from untreated HCAEC. IEMP, but not EMP, induced upregulation of ICAM-1 and VCAM-1 in target HCAEC demonstrated by Western Blot and real-time RT-PCR.

Moreover, Western Blot experiments revealed that IEMP treated HCAEC expressed higher levels of ICAM-1 and VCAM-1 in a time- and dose-dependent way. Following experiments showed increased monocyte adhesion on IEMP treated HCAEC compared to EMP-treatment and control (47.3% vs. 26.9% vs. 8.4%, p<0.05). We next investigated how IEMP activate endothelial cells and found pro-inflammatory cytokines IL-8, IL-6, TGF-β and MCP-1 were detectable in EMP. IEMP contain higher level of TGF-β (807 ng/l vs. 1647 ng/l, p<0.05) and IL-8 (115 pg/ml vs. 33 pg/ml, p<0.05) than EMP. As cytokines mentioned above activate p38 into phosphorylated p38 (phospho-p38), expression of p38 activity was analyzed in HCAEC after IEMP stimulation. Time dependent experiments revealed that EMP induced activation of p38 into phospho-p38 in HCAEC within 30 min. Inhibition of p38 by p38 independent induction of adhesion proteins on HCAEC and promotion of monocyte adhesion on target cells.

Conclusion: Endothelial Microparticles from glucose treated cells increase monocyte adhesion by altering adhesion protein expression in endothelial cells. Activation of p38 through proinflammatory cytokines containing MP might be a possible pathway.

Effects of combined genotypes for polymorphisms of the apolipoprotein A-V gene and the butyrophilin, subfamily 2, member A1 gene on metabolic syndrome in East Asian populations

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Purpose: Although recent genome-wide association studies have implicated several loci and genes in predisposition to metabolic syndrome (MetS) in Caucasian populations, the genes that confer susceptibility to this condition in Asian populations remain to be identified definitively. We previously showed that the −1131T→C polymorphism (rs662799) of the apolipoprotein A-V gene (APOA5) and the C→T polymorphism (rs6928464) of the butyrophilin, subfamily 2, member A1 gene (BTN2A1) were significantly associated with an increased serum concentration of triglycerides, a decreased serum concentration of HDL-cholesterol, and the prevalence of MetS in Japanese individuals. The purpose of this study was to examine whether these polymorphisms synergistically affect the prevalence of MetS in East Asian populations.

Methods: The study population comprised 3474 Japanese (2744 subjects with MetS, 730 controls) and 1671 Korean (1294 subjects with MetS, 377 controls) individuals. Subjects with MetS had three or more of the five components of criteria for MetS, whereas control individuals had none of the five components. Bonferroni's correction was applied for statistical significance of association.

Results: Comparison of allele frequencies by the chi-square test revealed that rs662799 of APOA5 was significantly (P = 0.025) associated with MetS in Japanese and Korean individuals, whereas rs6928464 of BTN2A1 was significantly associated with MetS in Japanese individuals, but not in Korean individuals. Multiple logistic regression analysis revealed that the TT genotype of BTN2A1 was associated with an increased prevalence of MetS in Japanese individuals (P = 0.0056) and in increased in Japanese individuals with the C allele of APOA5 and any genotypes of BTN2A1 compared to those with the TT genotype of APOA5 and the CC genotype of BTN2A1. There was no relation detected between combined genotypes and MetS in Korean individuals. Multivariable logistic regression analysis with adjustment for age and sex revealed that rs662799 of APOA5 and rs6928464 of BTN2A1 were significantly (P < 0.01) associated with MetS in Korean individuals, but not in Korean individuals. Similar analysis of combined genotypes with adjustment for age and sex revealed that individuals with the C allele of APOA5 and the T allele of BTN2A1 had a 2.87-fold increased risk for MetS compared to those with the TT genotype of APOA5 and the CC genotype of BTN2A1 in Japanese individuals. There was no relation between combined genotypes and MetS in Korean individuals.

Conclusions: Genetic variants of APOA5 and BTN2A1 may synergistically affect the prevalence of MetS in Japanese individuals.

Clinical and prognostical implication of advanced glycation in acute coronary syndromes

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Aims: Advanced glycation end products (AGEs) are molecules with important
Acute cardiac ryanodine receptor loss-of-function leads to bradycardia, arrhythmia, heart failure and transcriptional metabolic reprogramming

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Rationale: The cardiac ryanodine receptor Ca\(^{2+}\) channel (Ryr2) plays a central role in excitation-contraction coupling. Ryr2-mediated Ca\(^{2+}\) flux into mitochondria also controls metabolism, stimulates TCA cycle flux and aerobic metabolism, and atypical cell death in other cell types. Cardiac Ryr2 levels can be reduced up to 50\%, with age and in disease states such as heart failure, ischemia and diabetes. Objective: We tested whether a similar, controlled depletion of cardiac Ryr2 proteins sufficient to recapitulate the pleiotropic events associated with heart failure.

Methods and Results: We report that conditional Ryr2 knockout mice (cRyr2KO) rapidly exhibit functional, structural and molecular hallmarks of heart failure, as well as bradycardia and arrhythmia at a time point when they exhibit a 50\% reduction in Ryr2 protein. Cardiomyocytes from cRyr2KO mice lacked caveolae and showed axial tubulure-organization, hypertrophy and fibrosis within days of Ryr2 knockout. Cell death was associated with increased calpain-10, but not caspase-3 activation or ER-stress. Insulin receptor expression and cardioprotective pathways were reduced. Consistent with a state of cellular energy starvation and stress, hypoxia-inducible factors and autophagy were activated, while energy-consuming uncoupling proteins were reduced. Ryr2 controlled master transcriptional regulators of cardiomyocyte metabolism, differentiation, and survival, including Akt3, Klf15, and Sirt1/foxo1/pcg1a. Ryr2 was also genetically upstream of a network of Ca\(^{2+}\) signaling genes.

Conclusions: Our data show that Ry2loss is sufficient to rapidly induce a complex heart failure-like phenotype, placing Ryr2 and its associated energy-stimulating Ca\(^{2+}\) fluxes above hierarchical cascade of core transcription factors controlling cardiomyocyte metabolism, function and survival.

Conclusion: We conclude that elevated values of sRAGE are associated with worse in-hospital prognosis, whereas high AGE levels are associated with more follow up events.

CD40L deficiency ameliorates diet-induced adipose tissue inflammation, but does not protect from insulin resistance and hepatic steatosis in mice

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Background: Adipose tissue inflammation fuels the metabolic syndrome. We recently reported that CD40L – an established marker and mediator of cardiovascular disease – induces inflammatory cytokine production in adipose cells in vitro. Here, we tested the hypothesis that CD40L deficiency modulates adipose tissue inflammation in vivo.

Methods and Results: WT or CD40L\(^{-/-}\) mice consumed a high fat diet (HFD) for 20 weeks (n=15 per group). Inflammatory cell recruitment was impaired in mice lacking CD40L as shown by a decrease of adipose tissue macrophages, B-cells, and an increase in protective Tregulatory cells. Mechanistically, CD40L-deficient mice expressed significantly lower levels of the pro-inflammatory chemokine MCP-1 both, locally in adipose tissue and systemically in plasma. Moreover, levels of pro-inflammatory IgG2a antibodies against oxidized lipids were reduced in CD40L\(^{-/-}\) mice. Accordingly, CD40L deficiency partially protected from weight gain and fat deposition in the early stages of diet-induced obesity (DIO). Also, circulating low-density lipoproteins and insulin levels were lower in CD40L\(^{-/-}\) mice. However, CD40L\(^{-/-}\) mice consuming HFD were not protected from the onset of insulin resistance and hepatic steatosis, suggesting that CD40L selectively limits the inflammatory features of diet-induced obesity rather than its metabolic phenotype. Interestingly, CD40L\(^{-/-}\) mice consuming a low fat diet (LFD) showed both, a favorable inflammatory and metabolic phenotype characterized by diminished weight gain, improved insulin tolerance, and attenuated plasma adipokine levels.

Conclusion: We present the novel finding that CD40L deficiency limits adipose tissue inflammation in vivo. These findings identify CD40L as a potential mediator at the interface of cardiovascular and the metabolic disease.
Stress-induced adipose inflammation promotes a procoagulant state and impairs insulin sensitivity by adipocyte-derived monocyte chemoattractant protein-1

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Objective: Stressors contribute to thrombosis and perturbation in glucose metabolism. Since adipose inflammation is also involved in obesity-induced insulin resistance and thrombotic disease, we tested the hypothesis that stress correlates with adipose inflammation.

Research Design and Methods: Male mice were subjected to daily restraint stress for 2 weeks. Inguinal white adipose tissue (WAT) was collected from control and stressed mice to examine CD11b-positive cells and expression of macrophage markers (CD68 and F4/80), proinflammatory cytokines (MCP-1, TNF-α, and IL-6), adiponectin, and coagulation factors (PAI-1 and tissue factor (TF)) using immunohistochemistry and RT-PCR, respectively. Glucose metabolism was assessed by glucose (GTT) and insulin tolerance tests, and expression of IRS-1 and GLUT4 in WAT. To examine the effects of MCP-1 blockade, animals were intraperitoneally transplanted with control- or TNF-α-overexpressing adipose-derived stromal cells (ADSCs). Plasma fatty free acid (FFA), mouse MCP-1, TNF-α, and IL-6 levels were measured.

Results: Stress increased accumulation of CD11b-positive cells and expression of CD68 and F4/80 in WAT. The stressed mice also showed a higher frequency of smaller adipocytes in the inguinal adipose tissue compared to the control mice. Chronic stress also induced proinflammatory cytokine expression including MCP-1, TNF-α, and IL-6 and reduced adiponectin. Furthermore, stressed mice showed increase in FFA, MCP-1, TNF-α, and IL-6 concentration. The stress-induced adipose inflammation worsened the prothrombotic state through induction of PAI-1 and TF. Without any changes in GTT, stress worsened insulin sensitivity and decreased IRS-1 and GLUT4 in WAT. 7ND-ADSCs reversed the stress-induced adipose inflammation with reduction of CD11b-positive cells, macrophage markers, and proinflammatory cytokines. Moreover, 7ND-ADSC treatment rescues the stress-induced decline in insulin sensitivity and the prothrombotic state.

Conclusions: Restraint stress over a 2-week period evoked the expression of MCP-1 and other inflammatory adipokines in adipose tissue and a low-grade chronic state of adipose inflammation that exacerbated insulin resistance and induced the procoagulant factors through the expression of MCP-1. MCP-1 inhibition with 7ND-ADSCs reversed adipose inflammation and these pathological consequences. Increased lipolysis and FFA would be also involved in stress-induced adipose inflammation.

Chronic consumption of reheatred vegetable oils increases cardiometabolic risk factors


Purpose: To establish whether the chronic ingestion of re-used vegetable oil contributes to the development of cardiovascular risk.

Methods: A canola commercial vegetable oil was used to fry corn flour dough in a proportion of 1g per 10 mL. Cooking temperature was kept between 190°C and 200°C. The oil (1 cycle oil, 1CO) was stored up to one week under nitrogen atmosphere until utilisation. The same heating protocol (1CO) repeated up to 10 times using fresh dough at each cycle. The reheated oil (10cycles oil, 10CO) was kept under the same conditions. Chow diet for rats was supplemented with raw oil (RO), 1CO or 10CO at a mass ratio of 2%. Groups of 10 rats received the different diets: control group received only chow diet. Food consumption was monitored daily whereas systolic blood pressure (SBP) and bodyweight weekly. When SBP reached a stable plateau, blood samples were drawn from abdominal aorta and animals were euthanized and organs were euthanized and organs were collected for histological analysis.

Results: After 10 weeks of follow-up, mean body weight was about 10% higher in both groups receiving heated oil than those receiving raw oil or chow diet (P < 0.05 for both). SBP was about 20% higher in 1CO and 10CO groups as compared to controls or to RO (P < 0.05 for both). A significantly reduced acetycholine-induced vasculatu relaxation was observed in the three groups receiving oil-supplemented diet compared to control diet. Similarly, hemin reduced the pro-inflammatory macrophage-M1 phenotype, but increased the M2-phenotype that dampens inflammation in the heart, and improved cardiac hemodynamics by enhancing ejection fraction, stroke volume, cardiac output, while reducing left ventricular end diastolic pressure (LVEDP). Hemin improved glucose metabolism by potentiating insulin-signaling agents like the insulin-receptor substrate-1 (IRS-1), phosphatidylinositol-3-kinase (PI3K), protein-kinase-B (PKB). The hemin effects were accompanied by increased HO-activity, whereas the HO-blocker, stannous-mesoporphyrin (SnMP) nullified the effects. Interestingly, the hemin effects were less-pronounced in Zucker-lean controls with high-insulin status, suggesting greater selectivity in ZDF with disease.

Conclusion: The vitamin D metabolism gene CYP27A1 rs4674344 is significantly associated with both cholesterol and adipokine homeostasis and may contribute to the development of MetS.

The heme oxygenase system reduces pericardial adiposity and improves diabetic cardiomyopathy in Zucker diabetic fatty rats

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Visceral adiposity adversely affects many vital organs including the heart. We investigated the effects of the heme oxygenase (HO) inducer, hemin on pericardial adiposity and diabetic cardiopathy in Zucker diabetic fatty rats (ZDF), and age-sex-matched Zucker-lean controls.

Hemin administration normalised glyceric levels in ZDF rats and suppressed pericardial adiposity with the reduction of pro-inflammatory/oxidative mediators including, NF-κB, c-Jun-N-terminal kinase (c-JNK), endothelin (ET-1), TNF-α, interleukin (IL)-6, IL-1β and β-isoprostane. Similarly, hemin reduced the pro-inflammatory macrophage-M1 phenotype, but increased the M2-phenotype that dampens inflammation in the heart, and improved cardiac hemodynamics by enhancing ejection fraction, stroke volume, cardiac output, while reducing left ventricular end diastolic pressure (LVEDP). Hemin improved glucose metabolism by potentiating insulin-signaling agents like the insulin-receptor substrate-1 (IRS-1), phosphatidylinositol-3-kinase (PI3K), protein-transporter-2 (GLUT2) and protein-kinase-B (PKB). The hemin effects were accompanied by increased HO-activity, whereas the HO-blocker, stannous-mesoporphyrin (SnMP) nullified the effects. Interestingly, the hemin effects were less-pronounced in Zucker-lean controls with high-insulin status, suggesting greater selectivity in ZDF with disease.

Conclusion: The vitamin D metabolism gene CYP27A1 rs4674344 is significantly associated with both cholesterol and adipokine homeostasis and may contribute to the development of MetS.

Synergistic effect of human immunodeficiency virus and the metabolic syndrome on arterial stiffness

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Purpose: With Human Immunodeficiency Virus (HIV) on combination antiretroviral therapy have a high incidence of the metabolic syndrome (MS) and cardiovascular (CV) disease. To determine the contribution of HIV infection and the MS to vascular disease, we investigated aortic stiffness using aortic pulse wave velocity (PWV) in HIV patients with and without the MS.

Results: The presence of both conditions significantly increased PWV and aortic stiffness compared to patients with either condition alone. Furthermore, PWV was negatively correlated with body mass index (BMI) and waist circumference (WC) and positively correlated with higher fasting glucose levels. The conclusions are based on a strong correlation between PWV and the metabolic syndrome (MS) in the HIV-infected group. The metabolic syndrome is a strong predictor of aortic stiffness in HIV-infected patients. The findings suggest that the metabolic syndrome is an independent risk factor for increased arterial stiffness in HIV-infected patients.
The metabolic syndrome significantly affects the association between resting heart rate and all cause as well as cardiovascular mortality.

Methods: Subjects were divided into: 1) HIV-ve/MS-ve (n=64), 2) HIV-ve/MS-ve (n=35), 3) HIV+ve/MS-ve (n=73) and 4) HIV+ve/MS+ve (n=17) according to the National Cholesterol Education Program-Adult Treatment Panel III guidelines. Magnetic resonance imaging was used to assess aortic PWV between the ascending aorta at the level of the pulmonary artery (PA) and descending aorta 11 cm below the PA. PWV was calculated as Δx/Δt (distance between the 2 imaging levels)/Δt (time delay between the arrival of the pulse wave between these imaging levels). To compare PWV in groups 1-4, one-way ANOVA analysis was performed with post hoc Bonferroni correction.

Results: PWV was 16% higher in HIV-ve/MS-ve and 14% higher in HIV+ve/MS-ve compared to HIV-ve/MS+ve subjects (6.26±1.73 vs 5.38±1.00 m/s, p=0.042 and 6.14±1.91 vs 5.38±1.00, p=0.032 respectively, Figure 1). HIV+ve/MS-ve subjects had 21% higher PWV compared to HIV-ve/MS-ve subjects (7.43±2.43 vs 6.14±1.93, p=0.028). PWV was 16% higher in HIV+ve/MS+ve and 14% higher in HIV+ve/MS+ve subjects with similar PWV to HIV+ve/MS-ve subjects (6.26±1.73 vs 5.38±1.00 m/s, p=0.042 and 6.14±1.91 vs 5.38±1.00, p=0.032 respectively, Figure 1). HIV+ve/MS-ve subjects had similar PWV to HIV+ve/MS+ve subjects (p=0.99). HIV+ve/MS+ve subjects had 21% higher PWV compared to HIV-ve/MS-ve subjects (7.43±2.43 vs 6.14±1.93, p=0.028).

Conclusion: HIV patients without the MS have increased PWV compared to controls. The increase in PWV observed with HIV alone is similar to that seen with the MS alone. The detrimental impact of HIV and the MS on PWV appears to be synergistic. Given the increased prevalence of the MS in HIV patients, therapeutic interventions aimed at controlling this increased risk may reduce HIV-related vascular disease.

Exercise affects insulin sensitivity in HCR and LCR-rats differentially

Methods: We applied aerobic interval training to male HCR and LCR rats for 4 weeks. We performed echocardiograms to assess cardiac function. We studied insulin response in exercised and sedentary HCR and LCR-rats (28 generation, weeks of age average 36 and 41) with hyperinsulinemic-euglycemic clamp. We assessed changes in glucose infusion rate and gluconeogenesis in the whole body and glucose uptake in individual organs and tissues in response to insulin.

Results: After 28 generations of selective breeding, LCR and HCR differed in their exercise capacity (LCR vs. HCR 194±26m vs. 171±37, p<0.001), body weight (523±16g vs. 379±19, p<0.001) and tibia length (44.0±3.03mm vs. 41.6±0.4, p<0.001). Echocardiography did not reveal changes in cardiac function or morphology after exercise. Body weight decreased in both LCR and HCR (17.4% vs. 15.7%, p<0.01) and heart to body weight increased (12.6% vs. 11.4%, p<0.05). Epididymal fat pads and liver weight were significantly reduced after exercise (31.7% vs. 51.6%, p<0.01) and (53.3%, p<0.001) in LCR but not in HCR. In HCR, exercise decreased glucose uptake in liver (40.4%, p<0.01) and brain (21.4%) and increased glucose uptake in gastrocnemius (31.9%, p<0.05). In both strains, glucose uptake in lung (45.0% vs. 48.8%, p<0.01) decreased and in epididymal fat pads (29.0% vs. 51.5%, p<0.05) increased after exercise.

Conclusion: The selective breeding of HCR and LCR results in genotypic differences which induce differences in glucose tolerance, and also cause different response pattern upon exercise. In contrast to HCR, LCR rats showed reduced cardiac glucose uptake with exercise.
Multi compartment body composition analysis in chronic heart failure: air displacement plethysmography, body impedance analysis, dual-energy X-ray-absorptiometry, and 3D-white light scan analysis


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Purpose: Chronic Heart Failure (CHF) is characterized by impaired body fluid distribution and associated with obesity and cachexia. Early recognition of changes in body composition is vital for optimal adjusted medical therapy and has high prognostic relevance for patients suffering from CHF. Prospective data on body composition in CHF is sparse. We investigated whether Body composition can be as adequately assessed by Air-Displacement Plethysmography (ADP) and Bio-electrical Impedance Analysis (BIA) as by the current gold-standard Dual-X-Ray Absorptiometry (DXA).

Methods: In this single centre, prospective, observational study we included 52 consecutive symptomatic NYHA II, outpatients who presented with HFREF and left ventricular ejection fraction (LVEF) ≤ 40%. Exclusion criteria were: BMI > 40 kg/m², prior CABG, atrial fibrillation, inotropes or inotropic therapy. Body composition was assessed by 3D-Body-surfacescanner LightScan (DSBS). The mean percentage of extracellular fluid measured by BIA was 45.0% (CI 43.7–46.3; mean BMI 26.7 ± 4.5; mean age was 70.4 ± 4.6; mean BMI was 30.0 ± 5.5; mean FM was 34% ± 8.6; p < 0.05). Lin’s Concordance Correlation Coefficient (CCC) for FM in DEXA vs ADP was 0.76 (95% CI 0.64–0.89) and vs BIA was 0.69 (95% CI 0.54–0.85). The mean percentage of extracellular fluid measured by BIA was 45.0% (CI 45.0%–44.4%) and BIA in HFREF vs 46.1% (CI 95.0%–45.1%–47.1%) in HFREF, which differed significantly (p = 0.039); consequently percentage of intracellular body fluid was 55% (CI 54.6–56.4) in HFREF and 54% in HFREF (p = 0.6); percentage of extracellular fluid in patients with CHF was significantly higher as compared to patients with healthy controls. In summary, percentage of extracellular fluid was significantly higher in patients suffering from CHF as compared to healthy controls.

Results: Concordance Correlation Coefficient (CCC) for FM in DEXA vs ADP was 0.76 (95% CI 0.64–0.89) and vs BIA was 0.69 (95% CI 0.54–0.85). The mean percentage of extracellular fluid measured by BIA was 45.0% (CI 45.0%–44.4%) and BIA in HFREF vs 46.1% (CI 95.0%–45.1%–47.1%) in HFREF, which differed significantly (p = 0.039); consequently percentage of intracellular body fluid was 55% (CI 54.6–56.4) in HFREF and 54% in HFREF (p = 0.6); percentage of extracellular fluid in patients with CHF was significantly higher as compared to patients with healthy controls. In summary, percentage of extracellular fluid was significantly higher in patients suffering from CHF as compared to healthy controls.

Conclusion: Body composition can be accurately assessed by ADP and BIA in heart failure with reduced preserved ejection fraction and healthy volunteers. Further studies reveal body composition differences in HFREF vs HFREF with respect to FM, FFM and body fluid distribution, independent of the prevalence of oedema or body fluid status.

Early-induced overweight causes rapid changes in heart gene expression and long-term cardiovascular, metabolic and oxidative alteration

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Several studies in rodents have shown that postnatal overfeeding (OF) induces permanent moderate increase of body weight in the adult; however, cardiovascular and oxidative repercussions of postnatal OF are less known. Immediately after birth, litters of C57BL/6 mice were either maintained at 10 (normal-fed group, NF), or reduced to 3 in order to induce an OF situation. At weaning, mice of both groups received a standard diet. Measurements of phe-notypic characteristics and of plasma metabolic parameters were performed at 7 weeks of age, in the normoglycemic state. The hypothesis dynamics of OF was assessed by echocardiography and susceptibility to myocardial global ischemia and reperfusion was measured ex vivo in isolated perfused heart. Determination of cardiac gene expression profile was performed in illiconeutrate chips at early and late stages of development. AGE plasma levels were higher in diabetic patients (male, female) mean age 65.60 years ± 6.39 (SD) all in sinus rhythm undergoing coronary artery bypass grafting surgery (CABG surgery) with a mean BMI of 26.7 ± 4.5 kg/m² as assessed by enzyme-linked immunosorbent assay (ELISA). AGE plasma levels were higher in diabetic patients pre- (64.1 ± 26.2 vs 64.7 ± 21.1 g/mL, p < 0.05) and post- (33.1 ± 12.6 vs 14.7 ± 5.1 μg/mL, p < 0.05) CABG. Taking into account gender differences, non diabetic women vs males had increased AGE plasma levels pre- (108 ± 70.8 vs 39.5 ± 12.4 μg/mL, p < 0.05) and post- (75.7 ± 39.8 vs 21.9 ± 6.3 μg/mL, p < 0.05) whereas, diabetic males had higher AGE plasma levels pre- (54.6 ± 27.4 vs 22.4 ± 21.6) and post- (16.6 ± 6.5 vs 10.1 ± 4.8 μg/mL, p < 0.05). CABG induced a drop in AGE plasma levels independent of diabetes or gender. Non diabetic and diabetic pts on stabilization therapy had no higher AGE levels pre- and post- CABG. Female diabetics experienced a significant drop in plasma AGE levels. Similar significant drop happens after CABG in female patients not treated with statins. In pts not under stabilization therapy the post CABG drop in AGE plasma concentrations was significantly higher in non diabetics vs diabetic patients, a reduction 3- to 4-fold higher than the significant reduction for pts treated with statins (diabetic and non-diabetic). AGE plasma levels significant reduction post-CABG in patients with diabetes was on average almost 50-fold the post-CABG reduction in patients not submitted to stabilization treatment. The significant mean reduction of post-CABG AGE plasma levels was not different in magnitude between diabetic and non diabetic pts. Statin treatment and diabetes may contribute to gender differences in AGE plasma levels pre- and post- CABG and may have a similar effect in limiting the post-CABG drop of AGE plasma levels in female patients.
**Detection of subclinical left ventricular dysfunction in asymptomatic young adults with type-2 diabetes: a cardiac magnetic resonance study**


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**Introduction:** There is an epidemic of obesity and Type 2 diabetes (T2DM) in the developed world. Although diabetic cardiomyopathy is well documented in older adults with T2DM, there is very little data on younger adults and no published CMR data.

**Objective:** To use CMR to assess whether asymptomatic young adults with T2DM have evidence of subclinical left ventricular (LV) dysfunction compared to healthy lean and obese controls.

**Methods:** 40 asymptomatic subjects (20 T2DM, 10 obese non-diabetic controls, 10 lean non-diabetic controls) underwent CMR assessment of the LV on a Siemens Avanto 1.5T system. LV function and volumes were assessed using SSFP. Circumferential strain was assessed using a multi-breakhold CSPAMM tagging sequence at 3 slices (basal, mid-cavity, apical). Perfusion was assessed on first-pass contrast imaging during adenosine stress.

**Results:** Subjects were matched for age, height and blood pressure. Global peak early diastolic strain rate (PES) was significantly lower in T2DM, compared to lean and obese controls (Table 1). There was no evidence of coronary artery disease on perfusion testing.

**Conclusions:** This is the first CMR study demonstrating subclinical diastolic dysfunction in young adults with T2DM. The significant difference between the T2DM and obese groups suggest that T2DM in early adulthood has detrimental effects on cardiac function, additional to those associated with obesity.

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**National cardiovascular risk assessment in type 2 diabetes in China**


1Peking University People's Hospital, Beijing, China, People's Republic of; 2Beijing Anzhen Hospital affiliated to Capital University of Medical Sciences, Beijing, China, People's Republic of; 3China PLA General Hospital, Beijing, China, People's Republic of; 4Fudan University, Shanghai, China, People's Republic of; 5Fudan University, Shanghai, China, People's Republic of; 6VitalStrategic Research Institute, Shanghai, China, People's Republic of; 7Fudan University, Shanghai, China, People's Republic of;

**Objectives:** The China Cardiometabolic Registries (CCMR), is designed to assess the level of CVD risk control in patients with type 2 diabetes (T2D).

**Methods:** Patients were recruited from cardiology, endocrinology, nephrology, and internal medicine clinics across China. Patients' demographics, socioeconomic status, health behaviors, medical history, current medication, physical characteristics, and recent laboratory tests were collected.

**Results:** A total of 25,454 patients with the mean age of 62.6 years were enrolled from 104 hospitals; 53% were females, 72.1% had HTN and/or DLYP. Patients with T2D+HTN+DLYP had the highest proportion of CVD compared to T2D+HTN, T2D+DLYP, and T2D only (27.6% vs. 13.8%, 9.0% and 4.1%) and the highest proportion of BMI≥24 kg/m² (Figure 1). While 47.7%, 28.4%, and 36.1% of the population achieved the appropriate targets of blood glucose (HbA1c <7%), blood pressure (SBP/DBP = 130/80 mmHg), and total cholesterol (<4.5 mmol/L), respectively; only 5.6% achieved all three targets. Older age (<65 years), male sex, BMI≥24 kg/m², no smoking or drinking, higher education, and less than 5 years of diabetes were independent predictors of better achieving the CVD risk control.

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**Heart rate variability, postprandial responses of glucose and insulin and beta-cell function: the NEO study**


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**Introduction:** Low heart rate variability (HRV) is associated with diabetes mellitus (DM). We hypothesize a negative association of HRV with insulin resistance in fasting state (IR) and postprandial responses of glucose and insulin and a positive association with beta-cell function.

**Methods:** Baseline analysis of the Netherlands Epidemiology of Obesity (NEO) study, including 6000 individuals aged 45-65y with a BMI≥27kg/m². HRV was calculated as SDNN (ms), RMSSD (ms), LF (ms²) and HF (ms²). Blood was sampled fasting, 30min and 150min after a mixed meal (400 ml, 600 kcal). We calculated Homeostasis Model Assessment of insulin resistance (HOMA2-IR) as a measure IR. Area under the curve (AUC) for glucose and insulin were used as measures of the postprandial responses. Beta-cell function was calculated with the insulogenic index (IGI)=:insulin(30-150)/glucose(30-150) and AUC/IACU. Linear regression analysis was used to assess the association of HRV with IR, postprandial responses and beta-cell function, stratified by day/night and adjusted for sex, age, BMI, waist circumference, ethnicity, education, smoking, medication, hypertension, beans per minute and episode of physical activity.

**Results:** Of 4562 included participants, 639 had HRV measurements. Participants with recordings <27h (n=742), CVD (n=43) or DM (n=47) were excluded, resulting in 489 participants (46% men, mean age (SD): 56 (6) years, BMI: 31 (4) kg/m², fasting glucose: 5.6 (0.78) mmol/L. We found no association of InSDNN (ms) during daytime with InHOMA2-IR (r=0.15, 95%CI: -0.32, 0.03), InLF (ms²) with lnHOMA2-IR (r=0.32, 95%CI: 0.006 -0.62), InHF (ms²) with lnHOMA2-IR (r=0.34, 95%CI: 0.006 -0.62) and InAUC (mg/L) with lnHOMA2-IR (r=0.46, 95%CI: 0.006 -0.62).

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**Abstract P4963 – Table 1. CMR results**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lean control (LC)</th>
<th>Obese control (OC)</th>
<th>Type 2 diabetes (T2DM)</th>
<th>T2DM v LC (pg)*</th>
<th>T2DM v OC (pg)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30±0.6±6</td>
<td>30±0.5±6</td>
<td>31.8±6.6</td>
<td>0.871</td>
<td>0.862</td>
</tr>
<tr>
<td>Sex (no. M/F)</td>
<td>6.4</td>
<td>11.1</td>
<td>5.5</td>
<td>0.834</td>
<td>0.406</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.9±1.7</td>
<td>33.2±2.55</td>
<td>33.8±5.80</td>
<td>-0.001</td>
<td>0.240</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>131±10.13.74</td>
<td>130±3.14.92</td>
<td>136±5.14.74</td>
<td>0.239</td>
<td>0.255</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>79.8±12.31</td>
<td>84.3±8.66</td>
<td>90.7±9.88</td>
<td>0.417</td>
<td>0.816</td>
</tr>
<tr>
<td>LVEDD/kv (cm)</td>
<td>0.45±0.5</td>
<td>0.54±0.48</td>
<td>0.54±0.45</td>
<td>0.052</td>
<td>0.816</td>
</tr>
<tr>
<td>LVNC (%)</td>
<td>55.0±3.53</td>
<td>53.6±4.46</td>
<td>54.8±5.95</td>
<td>0.727</td>
<td>0.481</td>
</tr>
<tr>
<td>FS (%) (n for analysis)</td>
<td>-20.35±4.23</td>
<td>-20.50±2.89</td>
<td>-18.41±1.69</td>
<td>0.028</td>
<td>0.054</td>
</tr>
<tr>
<td>PESD (μS/ct) (n for analysis)</td>
<td>1.80±0.47</td>
<td>1.59±0.32</td>
<td>1.27±0.24</td>
<td>0.006</td>
<td>0.026</td>
</tr>
</tbody>
</table>

*Mean±SD, or median (IQR) where non-parametric data (normalised using log10). Data corrected for sex and ethnicity (ANCEOM).
Diabetes is related to higher central blood pressure

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Background: Central blood pressure (BP) is directly related to LV overload as well as blood supply to the heart and brain. It may also directly damage coronary and carotid artery walls being one of the most important causes of atherosclerosis. Several studies have shown closer correlation between end-organ damage and central than peripheral BP. Central BP was also shown to better predict cardiovascular (CV) risk. Diabetes is related to at least two-fold increased in CV risk. The influence of diabetes on central BP values is unknown.

Aim: To assess the independent influence of diabetes on the ascending aortic CVR values.

Methods: BP in the aorta was measured using fluid-filled filter in 400 patients (200 with type 2 DM and 200 without DM matched for age and gender) undergoing non-emergency coronary angiography. Brachial BP was measured using a sphygmomanometer. Both groups did not differ in respect of age and sex. General regression model (age, sex, mean BP, risk factors, LVEF, creatinine level, and drugs were included into the model) was used to assess the independent influence of diabetes on BP.

Results: Systolic, diastolic, and mean brachial BP did not differ between the study groups (138.6±21.3 vs 133.7±20.3 mmHg; p=0.06; 83.4±12.0 vs 82.6±10.7 mmHg; p=0.08; 40.1±15.0 vs 39.9±13.0 mmHg; p=0.27 in diabetics and non-diabetics resp.), but brachial pulse pressure was higher in diabetics (55.4±15.3 vs 51.1±14.2; p=0.02). Central BP values are shown in the Table. In multivariable analysis diabetes was related to higher ascending aortic systolic BP by 2.7% (95% confidence intervals: 1.7-3.8 mmHg) and pulse pressure by 4.1% (2.5-7.7 mmHg) as well as higher brachial pulse pressure by 1.8% (0.2-3.3 mmHg). The differences in mean and diastolic (both brachial and central) BP as well as brachial systolic BP were not significant in multivariable analysis.

Central BP - diabetes and non-diabetes

<table>
<thead>
<tr>
<th></th>
<th>Non-diabetics (N=200)</th>
<th>Diabetics (N=200)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>136.0±20.2</td>
<td>143.5±23.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>73.4±12.3</td>
<td>72.3±11.3</td>
<td>0.543</td>
</tr>
<tr>
<td>Mean BP</td>
<td>94.0±14.3</td>
<td>96.0±14.2</td>
<td>0.204</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>62.5±18.0</td>
<td>71.2±19.6</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: Diabetes is independently related to higher values of systolic and pulse pressure in the ascending aorta. This may partly explain the higher CV risk in diabetics.

Diabetes is independently related to higher values of systolic and pulse pressure in the ascending aorta. This may partly explain the higher CV risk in diabetics.


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Background: Obesity has reached pandemic proportions and is an established risk factor for insulin resistance, type 2 diabetes (T2D) and cardiovascular disease. It causes a plethora of adverse health outcomes, including increased risk of diabetes. Our study aimed to determine the glycemic profile of non-diabetic hypertensive patients according to the presence of diabetes family history.

Purpose: To determine the glycemic profile of non-diabetic hypertensive patients according to the presence of diabetes family history.

Materials and Methods: Nested case-control study was conducted in a population-based cohort: the Electricity Generating Authority of Thailand study, 1998-2008. The baseline demographic, anthropometric and clinical data were collected in 1998. The resurvey was done 10 years later in the same participants. One hundred and sixty eight individuals with newly diogenosed diabetes and 168 age-, sex-matched control were enrolled to the study. baseline serum omentin-1 concentrations were measured by ELISA.

Results: Baseline socioeconomic status, educational background BMI, and waist circumference were significantly higher in incident cases compared with control. omentin-1 concentrations were significantly negatively correlated with BMI (r=-0.196, p<0.0001) and waist circumference (r=-0.168, p=0.002), newly diagnosted diabetes group had significantly lower omentin-1 concentrations compared with control group (437.4±148.4 vs. 465.0±172.1 mg/mL, p=0.007) even after further adjusting for family income, educational background, smoking, drinking, family history of diabetes, and waist circumference (p=0.019). Hazard ratios (95%CI) for developing diabetes for those in the highest tertile vs. lowest tertile of omentin-1 concentrations were 0.29 (0.098-0.86) and 0.528 (0.298-0.935) in unadjusted and multivariate adjusted model, respectively.

Conclusions: Omentin-1 was found to be associated with a substantially reduced risk for incident diabetes over 10 years follow up in a cohort of initially healthy middle-aged Thais and the observed association was independent of obesity.

Impaired glucose homeostasis in non-diabetic hypertensives with family history of diabetes

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Purpose: Arterial hypertension (AH) and diabetes mellitus (DM) are established cardiovascular risk factors. Impaired glucose homeostasis (IGH, i.e. impaired fasting glucose and impaired glucose tolerance), obesity and family history of diabetes identify individuals at risk for DM in whom preventive interventions should be required. The aim of this study was to determine the glycemic profile of non-diabetic hypertensive patients according to the presence of diabetes family history.

Materials and Methods: Diabetes family history, obesity markers (waist to hip circumference ratio - WHR, body mass index - BMI), glycemic parameters (fasting glucose, glycated haemoglobin - HbA1c, insulin resistance indices (homeostasis model assessment - HOMA), quantitative insulin sensitivity check index - QUICKI, McAuley) and the prevalence of IGH were all determined in a large cohort of 11540 hypertensives (mean age 56.8 years, 57.7% males, mean office blood pressure 164.0/98.8 mmHg) who were referred to the hypertensive units of our institutions.

Results: Positive DM family history was associated with elevated glucose (9.7±13.1 vs 9.4±12.3 mg/dl), HA1c (5.58±0.49 vs 5.05±0.46%), insulin (9.74±4.20 vs 9.21±3.63 μIU/ml) and HOMA values (2.43±1.19 vs 2.24±1.01), lower QUICKI (0.342±0.025 vs 0.345±0.023), and McAuley values (6.73±3.43 vs 9.95±3.44) and higher IGH prevalence (45.3 vs 38.7%), P<0.01 for all comparisons. The difference in the prevalence of IGH according to DM family history was significant (P<0.01) in each subgroup of WHR and BMI (Figure).

Conclusions: Non-diabetic hypertensives with positive diabetes family history present with higher prevalence of impaired glucose homeostasis and worse glycomic indices levels compared to those with negative family history.
Results: Of 857 participants, 231 (27%) had prediabetes. Compared to normoglycemic subjects, prediabetics were significantly older (40 vs 38 years, p<0.0002), more often male (57 vs 43%, p<0.001), and they had a higher body mass index (24.9 ± 3.9 kg/m², p<0.0001). The prevalence of active smoking among prediabetic and normoglycemic subjects was 29% and 19%, respectively (p=0.0003), with a median (interquartile range) number of pack years among current smokers of 11.5 (5.8-18.8) and 5.9 (3.8-13.5), respectively (p=0.003). In age- and sex-adjusted logistic regression models using prediabetes as the outcome variable, current smoking was significantly associated with prediabetes (Odds ratio (OR) 1.79 (95% confidence interval 1.24-2.59), p=0.004). Former smoking was not significantly related to prediabetes (OR 0.76 (95% CI 0.51-1.13), p=0.18). Compared to never and past smokers, current smokers with <5, 5 to 10 and >10 pack years had an OR (95% CI) of 1.07 (0.53-2.13), p=0.86; 2.09 (1.08-4.07), p=0.03; and 2.22 (1.34-3.68), p=0.002, respectively.

Conclusion: Accumulating as few as 5-10 pack years of smoking carries a more than 2-fold increased risk of having prediabetes in healthy young adults. Thus, our data reinforce the importance of smoking cessation in the general population.

P4970 Membrane type 1-matrix metalloproteinase correlates with the coronary plaque stability in patients with postprandial hyperglycemia

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Background: We reported pericellularly localized membrane-type matrix metalloproteinases (MT-MMPs), which are main activator of secreted latent type MMPs, were highly expressed on circulating peripheral blood mononuclear cells (PBMCs) from patients with acute myocardial infarction (AMI). Although, postprandial hyperglycemia (PPH) is an independent risk for development of cardiovascular disease, there are few knowledge about predictor of coronary plaque in type 2 diabetic patients with PPH.

Methods: Fifty eight outpatients with type 2 diabetes whose glycated hemoglobin (HbA1c) ranged between 5.5 and 8.0 (±0.3), and 1.5-2.0 mmol/L as a short-term marker for PPH did not exceed 14 mg/L, were enrolled. Subjects underwent 64-detector computed tomography to analyze the plaque. Vulnerable plaque was defined as positive remodeling (remodeling index > 1.05), low-attenuation plaque (< 39 Hounsfield Units), and/or adjacent spotty calcification. PBMCs were examined for the frequencies of CD14 positive cells expressing MT-1-MMP using flow cytometry. Serum levels of MMPs, pentraxin-3 were measured by using ELISA methods.

Results: The prevalence of vulnerable plaque was 19 patients (33%), MT-1-MMP expression on PBMCs in all patients with PPH was significantly elevated in cases compared to normal subjects without PPH. In patients with vulnerable plaque, MT-1-MMP expression was higher than that in without plaque (36±6.3('/)-4% vs 27±7.9, p=0.012), but no differences in HbA1c, serum MMP-2, 9, and plasma pentraxin-3 levels.

Conclusion: The elevated MT-1-MMP expression on PBMCs is associated the existence of vulnerable plaque in type 2 diabetic patients with PPH. These finding suggested that the measurement of MT-1-MMP on PBMCs may become a new predictor of vulnerable plaque in postprandial hyperglycemia patients.

P4971 Prognostic impact of concurrence of metabolic syndrome and chronic kidney disease in patients undergoing coronary intervention; involvement of coronary plaque morphology

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Background: Both metabolic syndrome (MetS) and chronic kidney disease (CKD) have been reported to be risk factors of cardiovascular events. Objectives: The aim of this study was to assess the synergistic effect of MetS and CKD on atherosclerotic plaque and cardiovascular outcomes. Methods: The Risk of Invasive procedures associated with Cardiovascular disease (RISC) registry data was used to evaluate the concurrence of MetS and CKD. The independence of the association of MetS and CKD with cardiovascular outcomes was assessed using a multivariable Cox regression model. Results: Of 2,017 patients undergoing coronary intervention, 1,014 patients (50%) had MetS, 952 (47.3%) had CKD, and 647 (32.1%) had both conditions. In univariate analysis, the presence of both conditions was associated with a higher risk of major adverse cardiovascular events (MACE) including postoperative death, nonfatal myocardial infarction, target lesion revascularization, and revascularization for new lesion as well as coronary plaque characteristics using integrated backscatter intravascular ultrasound (IB-USVs). The incidence of major adverse cardiovascular events was significantly increased in patients with both MetS and CKD (46.2%) as compared to the other three groups during follow-up period (log rank p=0.029). In the IB-USV analyses, patients with both MetS and CKD showed a greater plaque burden (p<0.001) with larger lipid contents (p<0.008) as compared to the other three groups. In cox analyses, patients with both MetS and CKD proved to be an independent predictor of MACE even after adjustment of confounding factors (hazard ratio 1.739, 95% confidence interval 1.011-2.991, p=0.046).

Conclusion: Administration of alogliptin significantly improved postprandial endothelial dysfunction and increase in triglyceride, suggesting alogliptin that may be a promising anti-atherogenic agent.
has been suggested to be the mediating mechanism. We tested if change in maximum heart rate (ΔMHR) through seven years predicts NOD over 28 years. Methods: Exercise MHR was measured among 1,387 healthy men at two separate examinations, in 1972 and in 1979. The men were divided into quartiles (Q1–Q4) by ΔMHR. NOD events were registered in a nationwide survey of all participants’ hospital charts through 2008. Relative risk of NOD in the quartiles was calculated using Cox proportional hazard regression adjusting for baseline MHR, maternal diabetes, smoking status, systolic blood pressure, fasting triglycerides, fasting blood glucose, age, BMI, physical fitness and change in physical fitness. Results: A total of 124 NOD events were registered. Median MHR at baseline was 165 and 160 seven years later. The incidence of NOD was the highest among the men who decreased their MHR the most (Q1) and lowest among those who increased their MHR (Q4). Q1 was associated with an 82% increased NOD-risk compared with Q4.

Conclusions: These findings indicate that a reduction of MHR of more than 15 BPM over seven years is independently associated with a significantly increased long-term risk of new onset diabetes. We suggest that a marked fall in maximum heart rate could be associated with autonomic nervous system dysfuction. This observation could be helpful when identifying individuals at high risk of developing diabetes.

P4974
Metabolic syndrome in the Czech population. Current status and trends
J. Brhatins, R. Cikova, Z. Slodova, Z. Adamkova, M. Jozifova, P. Wohlfarth, M. Galovcova, V. Lanska. Institute for Clinical and Experimental Medicine, Prague, Czech Republic
Purpose: The prevalence of the metabolic syndrome is perceived as high and increasing among Czech adults. Our objective was to determine its exact prevalence and trends of its components, lifetime trends since 1997/8 and to evaluate the control and treatment of the metabolic syndrome in the Czech population.
Methods: A total of 3196, 3249 and 3537 men and women aged 25-64 years from 1997/8, 2000/1 and 2006-9 Czech post MONICA cross-sectional population surveys (1% random representative population sample of nine districts of the Czech Republic) were included in the analyses. We used the definition of the metabolic syndrome developed by the Joint Interim Statement of several major scientific organizations (Circulation 2009;120:1640-1645).
Results: The prevalence of the metabolic syndrome was 37.1% in 1997/8 and 32% in 2006-9 among women (P=0.002, a significant decrease) and 50.5 and 48.2% among men (P=0.216). The prevalence of the metabolic syndrome increased with the age in all surveys. In 2006-9 survey in men 25-34 years old the prevalence was 20.1%, in 35-44 years old 33.4%, 45-54 years old 56.1% and 55-64 years old 67.1%; among women the prevalence was 5.8%, 18%, 36.5% and 58% respectively. The prevalence decreased with the level of achieved education. In both genders, prevalence of central obesity and of raised blood pressure in 55-64 years old 67.1%; among women the prevalence was 5.8%, 18%, 36.5% and 58% respectively. The prevalence decreased with the level of achieved education. In both genders, prevalence of central obesity and of raised blood pressure in 55-64 years old 67.1%; among women the prevalence was 5.8%, 18%, 36.5% and 58% respectively.
Conclusions: In the Czech population the metabolic syndrome is prevalent as high and increasing among both genders and age groups.

P4975
Autonomic neuropathy is independently associated with new heart failure and atrial fibrillation in diabetic patients with preserved ejection fraction: prognostic significance of heart rate recovery
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Purpose: Atrial fibrillation (AF) and heart failure (HF) are important and interacting complications of type 2 diabetes mellitus (T2DM), and may be predicted by left atrial volume index (LAVI). Diabetic autonomic neuropathy may be an important contributor to AF, and may be evidenced by attenuated heart rate recovery (HRR). We sought whether HRR had an association with HF and AF in T2DM, independent of LA size. Methods: We enrolled 814 consecutive uncomplicated patients with T2DM (56±11 yrs, 508 men) who had negative stress echocardiography from 2004 to 2007. Patients with prior cardiac surgery, AF, +/− mild valvular disease, HF, ejection fraction <50% or any cancer at enrollment were excluded. Demographics, clinical assessment, standards of diabetes care, co-morbidities, and treatment with insulin, diuretics, beta-blockers, statins, ace-inhibitors and aspirin were collected prospectively. Atrial fibrillation, Associations of echo indices and HRR with a composite of new onset HF and AF were sought using a Cox proportional hazard model. Results: There were 47 events (22 HF and 25 AF) during 7.8 yrs follow up. HbA1c with patients with and without outcome were 7.6±1.5 and 7.4±1.7 (p<NS). The composite endpoint showed univariate associations with age, exercise capacity (maximal metabolic equivalent [MaxMets]), HRR and LAVI, but not with left ventricular mass index, diastolic functional stage, E/A ratio or deceleration time. HRR and LAVI were independently associated with outcomes (Table).

P4976
Tight glycemic control after cardiac surgery reduces the incidence of post-surgical atrial fibrillation regardless of existence of diabetes mellitus
Purpose: Atrial fibrillation is a common occurrence after cardiac surgery. However, there remains some uncertainty surrounding the relationship between onset of atrial fibrillation and pre-existing diabetes mellitus as well as the role of tight glycemic control after cardiac surgery. The purpose of this study was to clarify the relationship between incidence of atrial fibrillation after cardiac surgery and diabetes mellitus, and the effect of tight glycemic control.
Methods: Consecutive 60 subjects after cardiac surgery were divided into two groups, tight glycemic control group (Group T, n=30) and usual control group (Group C, n=30, 62±13 yrs). In Group T, tight glycemic control was aimed to be between 80-150 mg/dL. Incidence of atrial fibrillation was compared between two groups, as well the effect of diabetes status on occurrence of atrial fibrillation was investigated.
Results: Atrial fibrillation occurred in 24 patients. There was no significant difference in the occurrence of atrial fibrillation between patients with and without previously diagnosed diabetes mellitus and those who were not diagnosed (p=0.90). Incidence of atrial fibrillation was greater in Group C (50.0%) than in Group T (30.0%).

Conclusions: It is revealed that tight glycemic control after cardiac surgery reduces the incidence of post-surgical atrial fibrillation regardless of the diabetic status.
Chemerin is associated with the metabolic syndrome as well as elevated triglycerides were independent. The aim of the present study was therefore to elucidate a possible association between chemerin anti-PC measured in hospital and undiagnosed abnormal glucose regulation in patients with acute ST-elevation myocardial infarction (STEMI).

Methods: 92 patients (n=200, median age 58 (50, 68) years) with a primary percutaneous coronary intervention (PCI) treated STEMI without known diabetes were included. Serum levels of IgM anti-PC were measured in-hospital and a standardized 75g OGTT (venous plasma glucose measurements at 0 and 120 min) was performed at three-month follow-up. Based on the OGTT results, the patients were categorised according to the WHO criteria, and the term abnormal glucose regulation was defined as the sum of impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes.

Results: A total of 50 patients were classified with abnormal glucose regulation at three-month follow-up. Median (25th, 75th percentiles) levels of IgM anti-PC in patients with abnormal vs. normal glucose regulation were 32.9 (23.7, 51.7) U/ml vs. 41.5 (24.7, 59.7) U/ml (p=0.05). Low levels of IgM anti-PC (<24.6 U/ml) were not associated with abnormal glucose regulation (OR 1.2 (95% CI: 1.0, 2.56), p=0.07).

No significant correlations were found between IgM anti-PC and different glucose parameters (admission glucose, HbA1c, fasting glucose and 2-h glucose).

Conclusions: Low levels of IgM anti-PC were not associated with newly detected abnormal glucose regulation in patients with acute STEMI without previously known diabetes. The previously reported association between low levels of IgM anti-PC and myocardial infarction seems to be independent of glucometabolic disturbances.

P4981
Copeinop and adrenomedullin in a large cohort of catheterisation laboratory patients with newly diagnosed diabetes or impaired glucose tolerance: the Silent Diabetes Study

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Purpose: Copeinop and adrenomedullin (ADM) play an important role in the development of cardiovascular diseases and diabetes.

Introduction: Scientific investigations have shown that caffeine can temporarily have a regulatory impact on cardiovascular risk factors. On the other hand, several prospective studies demonstrate a protective effect of coffee on the development of type 2 diabetes (DM) as coffee consumption can reduce glucose uptake. The aim of this study was to evaluate the impact of Greek type coffee consumption on the development of DM in elderly population.

Methods: From June to October of 2009, we studied 343 men and 330 women (mean age 75.5±6.5 years old), permanent inhabitants of Ikaria island. Among several socio-demographic, bioclinical, lifestyle and dietary characteristics, cardiovascular risk factors like hypertension, diabetes, hypercholesterolemia, obesity, anthropometric indices, physical activity status and biochemical parameters related to cardiovascular risk and daily coffee consumption were evaluated. According to the classification 29% were defined as diabetic, 17% (32%) individuals reported rare coffee consumption (3.5 cups per week); 271 (51%) individuals reported moderate consumption (10.5 cups per week); 78 (17%) more than 28 cups per week. Those with moderate consumption (11-25 cups per day) had lower prevalence of DM (22% vs. 34%, p=0.02), lower prevalence of hyperlipidaemia (41% vs. 55%, p=0.001), lower body mass index (28.5 ± 9.25 vs. 29.5 ± 0.04), higher creatinine clearance (120.7 ± 25.1 vs. 111.0 ± 0.04), lower prevalence of cardiovascular disease (19% vs. 26%, p=0.04) and higher values of arterial distensibility (p<0.05); while no differences were observed according to dietary habits, systolic and diastolic blood pressure levels. Coffee consumption in ml per week was found to be inversely correlated with the prevalence of DM (OR=0.98 ± 0.01, 95% CI: 0.98-1.00) and waist circumference (OR=1.048, 95% CI: 1.022-1.074), after adjustment was made for age, gender, body mass index and physical activity status. When we stratified our analysis according to gender, coffee consumption was inversely significant associated with DM in males (OR=0.99 95% CI: 0.98-1.00) but not in females after the same adjustments. Additionally, when we stratified our analysis according to the quantity of weekly consumption, moderate consumption showed beneficial effect on the prevalence of DM (OR=0.554, 95% CI: 0.281-1.00), compared with rare coffee consumers; while high coffee consumption showed no benefit. (OR=0.99 ± 0.05, 95% CI: 0.99-1.00).

Conclusion: Moderate coffee consumption seems to have beneficial effect on DM prevalence even in elderly individuals. However this protective effect is lost with higher amount of coffee consumption.
Impacts of exercise training on waist circumference, glucose metabolism and endothelial function in pre-diabetic, adipose patients with severe coronary heart disease

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Purpose: Certain fat-tissue-derived adipokines are thought to contribute to impaired glucose metabolism and endothelial dysfunction, which is a predictor of future cardiovascular events. The aim of our study was to elucidate the association between obesity and endothelial function of the left internal mammary artery (LIMA) in pre-diabetic patients with severe coronary heart disease (CHD), who were scheduled for elective coronary bypass grafting (CABG), and to investigate the influence of 4 weeks of regular physical exercise training (ET) in these patients.

Methods: 29 patients with CHD (age ≤ 75 years), obesity (BMI > 26 kg/m²) and impaired glucose tolerance were randomized to 4 weeks of ET (in-hospital basis, 6 times a day for 20 min on a bicycle and rowing ergometer) (n=15) or sedentary lifestyle (n=14). At baseline and after 4 weeks, waist circumference, oral glucose tolerance, LDL- and HDL-cholesterol levels, maximum oxygen uptake (VO2max) and average peak velocity (APV) in response to LIMA selective intraarterial infusion of increasing doses of acetylcholine (0.072, 0.72 and 7.2 μg per minute) and nitroglycerin (200 μg as bolus) were assessed by Doppler velocimetry (Cardioclinic, USA).

Results: Compared to C exercise training was associated with a reduction in waist circumference by 4.4±0.1 cm (p<0.01), Blood glucose levels two hours after oral glucose load decreased from 10.2±2.0 to 7.7±0.5 mmol/l (p<0.01), LDL-cholesterol level declined from 2.87±0.28 to 2.36±0.17 mmol/l (p<0.05), weight loss was 4.4±0.5 kg to 3.0±0.4 kg (p<0.05). VO2max during cardiodiaphramatic exercise testing improved from 20.2±1.0 to 23.9±1.4 ml/min/kg body weight (p<0.01). Additionally, four weeks of ET resulted in an increase in APV in response to acetylcholine compared to intraarterial saline infusion by 87%, 50% and 25%, respectively (p<0.05). In contrast, endothelium-independent alteration of APV in response to nitroglycerin remained unchanged.

Conclusions: Limited improvements in metabolic parameters were observed in patients with severe coronary heart disease, whereas significant reductions in lipid parameters were achieved. ET resulted in an improvement in VO2max during cardiodiaphramatic exercise testing and an increase in APV in response to acetylcholine compared to intraarterial saline infusion by 87%, 50% and 25%, respectively (p<0.05). In contrast, endothelium-independent alteration of APV in response to nitroglycerin remained unchanged. The treatment of metabolic syndrome in pre-diabetic patients with severe coronary heart disease can be facilitated by regular ET.

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Comparison between the effects of ibradinod and atenolol on heart rate variability in type II diabetic patients

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Purpose: Beta-blockers improve cardiac autonomic function in patients with type II diabetes mellitus. No study investigated whether ibradinod, a selective inhibitor of sinus node depolarization, may also influence cardiac autonomic function.

Methods: We enrolled 56 type II diabetic patients (age 60±3.4y) without overt cardiovascular disease. Patients were randomized to receive atenolol 25 mg b.i.d. (n=29) or ibradinod 5 mg b.i.d. (n=20) or placebo b.i.d (n=19) for 1 month. Cardiac autonomic function was assessed by measuring time-domain and frequency-domain heart rate variability (HRV) on 24-hour ECG Holter monitoring both at baseline and at 1-month follow-up.

Results: HRV results are summarized in the table. Basal clinical variables were similar in the 3 groups. Most HRV variables improved significantly at follow-up in the atenolol group, compared to placebo. Ibradinod significantly improved HF.
amplitude, and also tended to improve SDNN and VLF amplitude, compared to placebo, although the latter differences did not achieve statistical significance.

| Table 1 | Wall thickness (mm) Basal 5.4 (3.5-10.5) 6.4 (3.7-9.3) p-value |
|---------|-------------------|------------------|----------|
| RR interval (ms) Basal 746±85 504±53 759±89 p<0.001 |
| Follow-up 844±104 809±111 746±89 -0.01 |
| SDNN (ms) Basal 105±40 103±21 107±26 0.30 |
| Follow-up 107±54 112±19 103±35 0.30 |
| SDNN (ms) Basal 37±9 36±9 46±20 0.02 |
| Follow-up 43±8 39±10 41±14 0.02 |
| VLF amplitude (ms) Basal 31±4 7 31±18 8 38±17 0.04 |
| Follow-up 34±7 36±8 43±12 43±12 0.04 |
| LF amplitude (ms) Basal 16±2 5 16±5 5 21±2 7 0.04 |
| Follow-up 18±6 6 16±6 6 19±6 6 0.04 |
| HF amplitude (ms) Basal 10±8 3 9±3 4 12±2 6 0.01 |
| Follow-up 13±6 7 10±5 5 10±6 5 0.01 |

*p for changes among groups; †p for changes <0.05 vs. placebo; ‡p for changes <0.1 vs. placebo.

**Conclusions:** In type 2 diabetic patients atorvastatin, as expected, significantly improved cardiac sympathovagal balance. Interestingly, iravatradine also showed some favourable effects on HRV variables, which deserves further assessment in larger studies, due to their potential clinical implications.

**P4985**

**Hyperglycaemia-induced oxidative stress mediates monocyte dysfunction in diabetes mellitus**

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**Purpose:** Monocytes play a very vital role in the biological process which increases the diameter of the existing arterial vessels. This process, also known as arteriogenesis, is essential for maintaining vascular integrity. Circulating monocytes are recruited to the sites of collateral growth where arteriogenesis is mediated through VEGFR1 signalling pathways, among others. The impaired monocyte function in hyperglycaemia, due to the reduced ability of monocytes to respond to VEGF stimulation, has been implicated in reduced arteriogenesis in diabetes patients. Molecular mechanisms leading to this VEGF-specific signal transduction defect in monocytes is incompletely understood.

**Methods:** Human monocytes were isolated from peripheral blood through gradient centrifugation and subsequent negative immunomagnetically isolation. THP-1 was used as the model monocyctic cell line. Expression of relevant molecules was detected by RT-qPCR analysis and confirmed by Western blotting. Reactive oxygen species (ROS) was detected using Amplex Red and H2DCFDA dye. Protein tyrosine phosphatase (PTP) activity was measured using pNPP substrate. VEGF-A-induced monocyte chemotaxis was assessed in the modified Boyden chamber assay.

**Results:** The monocyte cell line THP-1 and primary monocytes isolated from healthy donors were subjected to normoglycaemia (5.5 mM glucose) or hyperglycaemia (25 mM glucose) for 7 days and 72 hours, respectively. Hyperglycaemia induced reactive oxygen species in the cells leading to a reduction in total PTP activity. Induced oxidative stress resulted in reduced VEGF-A-induced chemotaxis. RT-qPCR analysis indicated that NADPH oxidase 2 (NOX2) is upregulated in hyperglycaemia (25 mM glucose) for 7 days and 72 hours, respectively. Hyperglycaemia induced oxidative stress mediates monocyte dysfunction in diabetes mellitus (DM). The relation between main epidemiological and CAD related factors was then evaluated.

**Conclusions:** Our results reveal oxidative stress as a negative regulator of human monocyte function. Our results suggest that the hyperglycaemia-induced ROS in monocytes is mediated through NF-$\kappa$B.

**P4987**

**Can we predict the risk of glucose metabolism abnormalities in patients with previous percutaneous coronary intervention?**

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**Background:** Oral glucose tolerance test (OGTT) is recommended in all patients who underwent coronary artery disease, since glucose metabolism abnormalities (GMA) adversely impact their prognosis. However, there are no risk models developed for the assessment of GMA in CAD patients. These models would be useful to identify patients with higher risk and to obviate the need of an OGTT in lower risk patients.

**Purpose:** To identify risk related factors for GMA in patients with previous percutaneous coronary intervention (PCI).

**Methods:** 294 patients (mean age 60.9±10.9 years, 222 males), with previous PCI and without known diabetes were included. OGTT was performed according to WHO protocol and patients were classified, according to ADA criteria in normal (N), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and diabetes mellitus (DM). The relation between main epidemiological and CAD related factors was then evaluated.

**Results:** The OGTT identified 63 patients (21.4%) with IFG, 61 patients (20.7%) with IGT and 48 (16.3%) with DM, leaving only 122 (41.5%) patients with a normal test. On univariate analysis, BMI (p=0.007) was the only variable related with the presence of GMA. Although there was a trend for the presence of previous hypertension (RR=1.48, 95%CI 0.91-2.39, p=0.07), dislipidemia (RR=1.41, 95%CI 0.88-2.24, p=0.09), presence of multivessel coronary disease (RR=1.58, 95%CI 1.23-2.53, p=0.005) and LV ejection fraction <30% (RR=3.52, 95%CI 0.99-12.53, p=0.052). Other risk factors for non-CAD populations, including age, were not significantly related with the risk of GMA. On multivariate analysis, there were no variables significantly associated with the risk of GMA.

**Conclusions:** In patients previously submitted to PCI and without known DM, GMA are very frequent (58.5% of patients). Age, previous hypertension, dislipidemia and BMI (all included in most risk models for the prediction of diabetes in non-CAD populations) were not useful in this CAD population. These results suggest that all patients with CAD should have an OGTT, since it’s not possible to identify lower risk groups.

**P4988**

**Low rate of LDL-cholesterol target achievement in patients with type 2 diabetes with and without manifest vascular disease in Germany: Results of DiaRegis**

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**Background:** Patients with type 2 diabetes are at high risk for cardiovascular events. The new ESC/EAS guidelines for the management of dyslipidemias recommend LDL-cholesterol (LDL) not only <100mg/dl but even <70mg/dl. Little is known about the current lipid target achievement in diabetics in clinical practice in Germany.

**Methods:** In the DiaRegis registry, 3,740 consecutive outpatients with type 2 diabetes and insufficient glycemic control under chronic oral antidiabetic monotherapy or dual combination therapy were enrolled to document patient characteristics, medical treatment and prevalence of hypoglycemia. We examined differences between diabetics with and without vascular disease (VD), defined as known coronary artery disease (CAD) or prior stroke or peripheral artery disease (PAD) in the achievement of LDL targets.

**Results:** A total of 909 patients had known VD (17.9%, CAD, 4.7% prior stroke, 6.0% PVD). Type 2 diabetes outpatients with manifest VD were older, less often female and already had a significantly longer duration of diabetes. No difference was found in baseline HbA1c. Only 42.0% of the overall population were on statin treatment, 66.1% of diabetics with manifest VD and 34.3% of diabetics without known VD. Mean LDL was lower in diabetics with VD as compared to diabetics without known VD. The newly defined LDL target of <70mg/dl was reached in only 12.1% of diabetics with manifest VD and in only 5.2% of diabetics without VD.

**Conclusions:** Despite the high risk of subsequent cardiovascular events in type 2 diabetes less than half of the patients were treated with a statin. In very high risk diabetics with already manifest VD only 12.1% did reach the recommended target values of LDL <70mg/dl in clinical practice.

**P4989**

**The impact of diabetes mellitus according to gender difference on acetylcholine induced coronary artery spasm**

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**Background:** The gender difference is known to be a strong predictor of coronary artery spasm(CAS). Diabetes mellitus (DM) is also a well known risk factor of atherosclerosis and endothelial dysfunction. However, the impact of DM according to gender difference on CAS during acetylcholine (Ach) provocation test has not been defined.

**Methods:** A total of 2504 consecutive patients without significant coronary artery disease who underwent the Ach provocation test were enrolled between November
The influence of anemia on long-term prognosis in patients with acute myocardial infarction and concomitant glucose abnormalities

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Background: Anemia deteriorates the prognosis in patients (pts) with myocardial infarction. However, the prognostic value of anemia in subjects with different glucose abnormalities (GA) and acute myocardial infarction (AMI) treated invasively remains unclear.

Aim: To assess the incidence and impact of anemia on clinical outcomes in subjects with different GA and AMI treated with percutaneous coronary intervention (PCI).

Methods: A prospective registry of 2154 consecutive AMI subjects treated with PCI was analyzed. In all in-hospital survivors without the history of diabetes mellitus diagnosed before or during index hospitalization standard oral glucose tolerance test (OGTT) was performed during stable condition before hospital discharge and interpreted according to WHO criteria. This made it possible to divide the study population into 5 groups with different GA: diabetes mellitus (DM, n=360), new onset DM (n=298), impaired glucose tolerance (IGT , n=434), impaired fasting glycaemia (IFG, n=340), and control group (n=616). Anemia was defined using WHO criteria - hemoglobin level <13 g/dl for men and <12 g/dl for women. Cox regression was used to identify independent mortality predictors.

Results: The incidence of anemia in different glucose abnormalities was as follows: in DM (27.9%, n=99); new onset DM (23%, n=69); IGT (18.4%, n=88); IFG (16.4%, n=56); and in control group (14.7%, n=91). The long-term mortality in all AMI in-hospital survivors with anemia was significantly higher than in subjects without anemia (11.4 vs 5.6%, P<0.05). Further analysis with (15.2 vs vs. 28.8% vs. 37.3%, Log-rank P<0.001). In multivariate analysis, anemia and DM were a meaningful predictors of mid-term mortality, and the combination of the two was an even stronger predictor (hazard ratio = 1.790; 95% confidence interval = 1.313-2.442; P<0.001).

Conclusion: Acute MI patients with a history of DM or hypertension had a higher mortality in mid-term than acute MI patients without such a history. The combination of DM and hypertension appeared to be more strongly associated with mortality than DM alone or hypertension alone.

Table 1

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
</tr>
<tr>
<td>Sex</td>
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<tr>
<td>Mean Blood Glucose (mg/dl)</td>
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<tr>
<td>HbA1c (%)</td>
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<td>Serum Creatinine (mg/dl)</td>
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<td>Height (cm)</td>
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<tr>
<td>BMI</td>
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<td>Cholesterol (mg/dl)</td>
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</tr>
<tr>
<td>CRP (mg/dl)</td>
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<td>0.026</td>
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</tbody>
</table>

Boys with T1D had higher cIMT than girls; moreover cIMT correlated with weight and glycemia dependent parameters in girls but not in boys. Our pilot study suggests an important sex-dependent difference from the very beginning of atherosclerosis in patients with type 1 diabetes.

P4991

The influence of anemia on long-term prognosis in patients with acute myocardial infarction and concomitant glucose abnormalities

M. Mazurek1, J. Kowalczyk1, R. Lenarczyk1, T. Kurek1, A. Swiatkowska1, E. Jedrzejczyk-Patej1, J. Gumprecht1, K. Strojek1, L. Polonski1, Z. Kalarus1.
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Conclusion: Acute MI patients with a history of DM or hypertension had a higher mortality in mid-term than acute MI patients without such a history. The combination of DM and hypertension appeared to be more strongly associated with mortality than DM alone or hypertension alone.
Genetic variability of sCD40L reveals a novel pathophysiological role of sCD40L in insulin resistance, in advanced atherosclerosis

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Purpose: Soluble CD40 ligand (sCD40L) is an inflammatory marker released by activated platelets and inflamed adipose tissue. Recent evidence suggests that sCD40L levels are higher in patients with metabolic syndrome. We sought to examine the relationship between chronically elevated sCD40L levels and insulin resistance by using the functional single nucleotide polymorphism (SNP) A3459G of the sCD40L gene.

Methods: The study population consisted of 265 individuals. After an overnight fast, a sample of blood was collected and used for biochemical measurements and genotyping. Plasma sCD40L levels were determined by ELISA. Plasma insulin levels were used to calculate insulin resistance by means of the Homeostatic Model Assessment (HOMA-IR). DNA was extracted from whole blood by using a commercially available kit and genotyping for the A3459G SNP of the sCD40L gene was performed by restriction fragment length polymorphism PCR method.

Results: In the study population, 188 individuals were carriers of the AA genotype, 44 of the AG and 33 of the GG genotype. Subjects exhibiting the GG genotype had significantly higher sCD40L levels when compared to AA and AG individuals (AA vs. GG, p=0.001; AG vs. GG, p=0.05). A strong correlation between insulin resistance and sCD40L levels was observed (p<0.05 for all markers), and HOMA-IR (OR 2.21, p=0.001) correlated with the presence and extent of CAD only in non-DM patients.

Conclusion: Our data show that chronically increased activation of platelets and the related inflammation of the adipose tissue releasing sCD40L, are associated with increased insulin resistance. Therefore, our study shows novel links between the CD40/CD40L axis and insulin resistance, providing novel insights into the pathophysiology of diabetes mellitus.

Components of the interleukin-6 transsignalling system are associated with the metabolic syndrome, endothelial dysfunction and arterial stiffness

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Objective: The metabolic syndrome (MetS) is an increasing epidemiologic challenge and cardiovascular risk factor. The interleukin-6 (IL-6) is a cytokine that exerts its biological function via a complex orchestration of soluble and membrane bound receptors. We have investigated associations between IL-6 and its soluble receptors, soluble IL-6-receptor (sIL-6r) and soluble glycoprotein 130 (sGP130) and the metabolic syndrome. Furthermore, we have investigated possible associations with endothelial dysfunction and arterial stiffness.

Methods: A total of 563 subjects were included in this study. Adult treatment panel III criteria of the national cholesterol education program were used for the definition of MetS. We used commercially available ELISA to analyse circulating levels of the markers. Pulse wave propagation time (PWP) was determined to assess arterial stiffness.

Results: The criteria for having MetS were fulfilled by 221 subjects. sGP130, sIL-6r and IL-6 levels were elevated in subjects with MetS (p<0.05 for all markers), and were associated with increasing components of MetS. Particularly hypertriglyceridaemia, hypertension and fasting plasma glucose (FPG) seem to carry this association. sGP130 (p<0.001), IL-6 (p=0.05) and partial sIL-6r (p=0.05) correlated with markers of endothelial function (E-selectin, ICAM-1, VCAM-1) and inversely with PWP after adjustment for relevant covariates.

Conclusion: sGP130, sIL-6r and IL-6 were significantly elevated in subjects with MetS. In addition, sGP130, IL-6 and partially sIL-6r were associated with markers of endothelial function and arterial stiffness. This finding sheds new light on the role of these inflammatory cytokines in subjects with MetS and the development and progression of clinically silent atherosclerosis.
Introduction: Type 2 Diabetes mellitus (T2DM) is a public health problem associated with several complications such as hypertension, dyslipidemia and obesity. Prevalence of cardiovascular events in T2DM is twice the observed in non-diabetic subjects, even after adjustment for classic risk factors. Early detection of predictors of hard outcomes is needed to try to avert this scenario. Objectives: To identify biomarkers associated with higher rates of clinically relevant events in a prospective cohort of patients with T2DM. Materials and methods: Padro et al evaluated a cohort of 323 individuals with T2DM followed by 10 years. Blood samples were collected at baseline. We examined biomarkers with potential risk of events in this population. Troponin, homocysteine, creatinine, fasting glucose, high-sensitivity C-reactive protein (CRP), and lipid profile. Fatal and nonfatal acute coronary syndromes and stroke were evaluated. ECG and clinical information were obtained from all patients. Cumulative survival curves were analyzed by Log-rank/Mantel-Cox.

Results: The study population comprised individuals of both genders, 59% males, age 59y, with mean time of diagnosis of 8y, obese (39%), mostly with hypertension and dyslipidemia. The prevalence of prior myocardial infarction (MI) at baseline was 32%. Mean levels of CRP (mg/l) were present at 4.1 mg/l. Sub analyses of differences between higher event rates in males (HR 2.5 CI 1.6 to 4.1), with previous MI (HR 1.5 CI 1.4 to 1.6), reduced creatinine clearance (HR 1.6 CI 1.1 to 2.5) and elevated levels of serum creatinine (-1.3 mg/l for men and -1.1 mg/l for women) (HR 2.3 CI 1.1 to 4.3).

Conclusion: Male gender, previous MI and renal function impairment were associated with higher rates of cardiovascular events, thus highlighting the importance of risk factors and comorbidities in this high-risk population.

The association of the A3872G polymorphism with hs-c-reactive protein levels and peripheral arterial disease in patients with type 2 diabetes mellitus

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Purpose: The aim of this study was to examine the impact of A3872G polymorphism on C-reactive protein (CRP) gene on high sensitivity CRP (hs-CRP) levels and peripheral arterial disease (PAD) in patients with type 2 diabetes mellitus (T2DM).

Methods: The study population consisted of 431 patients with T2DM (documented for PAD or not). The A3872G polymorphism was detected by polymerase chain reaction and appropriate restriction enzyme digestion (HpyCH4III). C-reactive protein was assayed by particle-enhanced immunonephelometry. Peripheral arterial disease was evaluated based on history of intermittent claudication, reduced or absent foot pulses, interventional procedure of revascularization or amputation. hs-CRP levels were determined by nephelometry. Significance was defined as p<0.05.

Results: The genotype distribution was 52, 27.2, 20.8 for the GG, AG, AA genotypes respectively, [mean age 66.5±9.953, males n=518 (50.6), females n=212 (49.2)] with significant gender difference males/females GG (46.4%/53.6%), AG (50%/50%), AA (61.8%/38.2%), (p=0.019). Hs-CRP levels were higher in GG homozygotes (GG; 0.61±0.257) compared with carriers of “A” allele (AG+AA; 0.56±0.188), (p=0.021). The presence/absence of PAD was not significantly different among the GG (34.2%/65.8%), the AG (39.7%/60.3%) or the AA (40%/57.3%) genotypes (p=0.059). However, carriers of “A” allele (AG+AA) had higher hs-CRP levels with GG homozygotes (GG) had increased odds (odds ratio=1.622, 95% confidence intervals=1.029-2.536, p=0.037), to have PAD after adjustment for gender, age, duration of diabetes, body mass index, smoking, hypertension, lipids, haemoglobin A1c and glomerular filtration rate. Sub analyses demonstrated that there were significant interactions between the carriers of the “A” allele with coronary artery disease, carotid artery disease, retinopathy, use of insulin, use of antplatelet medications, use of clopidogrel (increased odds for PAD for all), and with use of oral antidiabetic medications, use of metformin as well as use of angiotensin receptor blockers (lower odds for PAD for all).

Conclusion: The CRP3872G polymorphism affects the hs-CRP levels and the presence of PAD in patients with T2DM. Specifically, the carriers of the “A” allele although have lower levels of hs-CRP, they have higher odds for PAD than GG homozygotes. In addition, the odds for PAD are affected significantly by interactions between the carriers of the “A” allele with other micro and macrovascular complications and the use of antidiabetic, anti-hypertensive and antplatelet treatment compared with GG homozygotes.

One-third of patients with diabetes mellitus do not have subclinical coronary atherosclerosis

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Purpose: All patients with diabetes mellitus (DM) are recommended lipid lowering treatment, although not all are at similar risk. Measuring coronary artery calcification (CAC) allows to further the cardiovascular risk, also in diabetics. The prevalence of CAC among random selected patients with DM is uncertain. For this purpose we set out to examine the occurrence of CAC in patients with DM, and compared with healthy non-diabetic subjects.

Method: A random selected cohort of 1825 men and women, 50 or 60 years old were invited to the screening study. DM was defined as the use of anti-diabetic medication or fasting plasma blood glucose level ≥7.0 mmol/l on two different days. Traditional risk factors were obtained and for the non-diabetics HeartScore was calculated. A non-contrast CT-scan was performed to assess the CAC score (Agatston score ≤400 was considered as high).

Results: A total of 1226 subjects without previous cardiovascular disease participated. Five % (59 subjects) had DM while 92% (1167 subjects) were non-diabetics. Among patients with DM the prevalence of males, 60 years old, smokers, hypertension and statin treatment were 49%, 58%, 32%, 57% and 52% respectively, while 47%, 50%, 25%, 49% and 10% for the non-diabetics. Also CAC was more frequent in diabetics (63% versus 44%; p=0.006), as well as severe calcification (9% versus 5%; p=0.022). However, adjusting for CAC in multivariate logistic regression results only in a non-significant increased risk for calcification in diabetic patients (OR=1.3; p=0.44).

Conclusion: We found that one-third of patients with DM did not have any coronary calcification and thus a better prognosis, while few had severely calcified coronaries. These data suggest that also in diabetics preventive therapy should be individualized based on CAC.
Arterial elastic wall properties are similarly impaired in first degree relatives and diabetic patients on the grounds of significant insulin resistance

Evaluation of the relationship between aortic elasticity and insulin sensitivity in healthy subjects with a normal carbohydrate metabolism

Suboptimal LDL-cholesterol control by atorvastatin therapy in high-risk patients with coronary heart disease or atherosclerotic vascular disease in the UK

Type 2 diabetes and the progression of visualized atherosclerosis to clinical cardiovascular events

Table 1

<table>
<thead>
<tr>
<th>Atorvastatin dose</th>
<th>Follow-up LDL-C (mmol/L)</th>
<th>N</th>
<th>LDL-C &lt; 1.8 mmol/L</th>
<th>LDL-C ≥ 2.0 mmol/L</th>
<th>LDL-C ≥ 2.5 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>567</td>
<td>23.1 ± 0.8</td>
<td>24%</td>
<td>37%</td>
<td>77%</td>
</tr>
<tr>
<td>20</td>
<td>655</td>
<td>2.22 ± 0.65</td>
<td>23%</td>
<td>37%</td>
<td>69%</td>
</tr>
<tr>
<td>40</td>
<td>841</td>
<td>2.15 ± 0.71</td>
<td>29%</td>
<td>42%</td>
<td>73%</td>
</tr>
<tr>
<td>80</td>
<td>340</td>
<td>1.99 ± 0.77</td>
<td>39%</td>
<td>55%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Table 1: Follow-up LDL-C (mmol/L) after 5 years of atorvastatin therapy in high-risk patients.
Preliminary observations of passive exercise using whole body periodic acceleration in patients with type-2 diabetes

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Purpose: Whole body periodic acceleration (WBPA) system is recently developed as a passive exercise device by providing increased pulsatile shear stress for improvement of peripheral and coronary endothelial function (Figure left). This study aimed to investigate the acute effects of WBPA on coronary microcirculation and glucose tolerance in patients with type 2 diabetes (T2D).

Methods: The study subjects were 8 patients with T2D who underwent transthoracic Doppler echocardiography (TTEC) for the assessment of coronary flow reserve (CFR) before and immediately after 45-min session of WBPA. The flow velocity in the distal portion of the left anterior descending coronary artery was measured at baseline and during adenosine infusion. The CFR represented the ratio of hyperemic to baseline mean diastolic flow velocity.

Results: WBPA was completed and well-tolerated in all patients, and no significant hemodynamic or mechanical complications were observed during the procedure or follow-up. WBPA increased CFR from 2.3±0.3 to 2.6±0.4 (p=0.02) (Figure right). WBPA decreased serum insulin level from 26.1±19.6 μIU/ml to 19.1±15.2 μIU/ml (p=0.01) and increased total adiponectin from 11.6±7.3 μg/ml to 12.5±8.0 μg/ml (p=0.02). High molecular weight adiponectin from 4.9±3.6 μg/ml to 5.3±0.9 μg/ml (p=0.03), whereas the serum glucose level was stable from 207±66 mg/dl to 203±56 mg/dl (p=0.8).

Conclusions: This study demonstrates that a single session of WBPA treatment simultaneously improved coronary microcirculation and glucose tolerance in patients with T2D, providing the mechanical insights into the relationship between exercise and adiponectin.

A novel anti-inflammatory adipokine, secreted frizzled-related protein 5, is associated with coronary artery disease in non-elderly population

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Background: Secreted frizzled-related protein 5 (Sfrp5) has been reported to be a novel anti-inflammatory adipokine. Sfrp5 deficient mice fed a high-calorie diet showed severe glucose intolerance and hepatic steatosis, leading to the inflammation in adipose tissue. Those evidences suggest that sfrp5 would be involved in the development of atherosclerosis; however, the clinical relevance of sfrp5 remains unknown. We investigated whether reduced serum sfrp5 level can be a novel marker of coronary artery disease.

Methods: We studied 185 patients aged <65 years (68±11 years, 79% male) who underwent coronary angiography (CAG). The subjects were divided into two groups based on the CAG findings: patients with significant coronary stenosis defined as ≥50% or greater luminal diameter narrowing (CAD) and without significant coronary stenosis (non-CAD). Serum sfrp5 levels were measured by ELISA.

Results: In all subjects, serum sfrp5 levels in CAD patients tended to be lower than those in non-CAD patients (49.8±26.9 vs. 52.4±31.5 ng/ml). Median IQR, <0.08 by Mann-Whitney test). There were no significant differences in serum sfrp5 between two groups according to gender, the presence of diabetes, hypertension, and dyslipidemia. Serum sfrp5 levels were significantly associated with body mass index (r = -0.15, p = 0.03) and HDL-cholesterol (r = 0.15, p = 0.03), but the associations of other biochemical parameters with sfrp5 levels were not significant.

Conclusions: Serum sfrp5 levels are significantly associated with coronary artery disease in subjects aged < 65 years. Low sfrp5 levels may contribute to coronary atherosclerosis.

Predictors of Hypoglycaemia in patients with Type-2 Diabetes - an Analysis of the Prospective DiaRegis Registry

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Hypoglycaemia is a serious complication of antidiabetic drug therapy, especially when treatment is intensified. We aimed to identify predictors of hypoglycaemia in a cohort of type-2 diabetic patients prospectively followed over a one year follow-up. Using logistic regression analysis with stepwise backward selection (alpha 0.05) independent predictors of hypoglycaemia were determined. A total of 3347 patients were available for the present analysis. Of these 473 (14.1%) had hypoglycaemia of any severity over a follow-up of 12 months. Patients with incident hypoglycaemia had a longer diabetes duration, a higher HbA1c and more frequent co-morbid disease conditions such as coronary artery disease (CAD), peripheral arterial disease (PAD), amputation, heart failure, peripheral neuropathy, diabetic retinopathy and clinically relevant depression at baseline. Multivariable adjusted positive predictors of incident hypoglycaemia over the 12 months follow-up were prior anamnestic hypoglycaemia (OR 4.05), retinopathy (OR 3.27), clinically relevant depression (OR 1.81) and insulin use (OR 2.99). On the contrary, glitazones (OR 0.55), DPP-4 inhibitors (OR 0.57) and GLP-1 analogues (OR 0.48) were associated with a reduced risk of hypoglycaemia. Incident vascular disease such as stroke/transitory ischemic attack, amputation, autonomous neuropathy, non-proliferative retinopathy and also clinically relevant depression were more frequent in those patients reporting hypoglycaemia during follow-up than in those without this complication. We conclude that hypoglycaemia is a frequent complication in ambulatory patients when treatment is intensified. Particular attention is warranted in patients with prior episodes of hypoglycaemia, microvascular disease such as retinopathy and in patients receiving insulin. On the other hand glitazones, DPP-4 inhibitors and GLP-1 analogues appear to be associated with a reduced risk.

Blood pressure response to exercise is exaggerated in normotensive diabetic patients

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Objective: The aim of this study was to investigate the blood pressure (BP) response to exercise in normotensive patients with type II diabetes mellitus (DM).

Methods: A cross-sectional study was carried out on 75 normotensive subjects with type 2 DM (Group 1), and 70 age-gender matched normotensive healthy volunteers (Group 2). Treadmill exercise test, 24 hours ambulatory BP monitoring (ABPM) were performed for each patients and healthy volunteers.

Results: There were 67 patients (mean age 52.9±4.2 male) in group 1 and 68 healthy volunteers (mean age 51.7±4.3% male) in group 2. Eight patients from group 1 and 2 subjects from group 2 were excluded because of high
blood pressure on ABPM. Groups were similar for SBP and DBP on office mea-
suring and on ABPM. Groups were similar for rest SBP, DBP, heart rate, exercise
duration on exercise test. Peak SBP was significantly higher in group 1 than in
group 2, but peak DBP was not (196.5±18 vs. 165.9±18, p = 0.001; 88.1±11.6 vs.
86.2±8.7, p=0.283, respectively). Hypertensive response to exercise (HRE)
was more frequent in group 1 than in group 2 (39 (58%) vs. 6 (%), p<0.001
(Figure 1). Independent predictors of peak SBP were DM, office SBP and male
gender. While independent predictors of HRE were DM, office SBP and age in
multivariate analysis.

Conclusions: SBP response to exercise is exaggerated in normotensive diabetic
patients comparing to non-diabetic subjects. DM, office SBP and male gender are
independent predictors of peak SBP. DM, office SBP and age are independent
predictors of HRE.

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**P5008**

**Serum adiponectin is a negative predictor of incident metabolic syndrome: a population-based follow-up study**

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**Objective:** Growing evidence suggests that increased adiponectin levels may play a pivotal role in the development of metabolic abnormalities, but prospective
studies of adiponectin levels and incident metabolic syndrome are lacking. We investigated whether serum adiponectin predicts of incident metabolic syn-
drome and its components in a population-based longitudinal study.

**Methods:** We analyzed data from 2,068 adults (838 men and 1,230 women) with-
out metabolic syndrome, aged 40 to 70 years, who participated in a health sur-
vey in 2005-2011. Baseline serum adiponectin concentrations were measured by
radioimmunoassay. Metabolic syndrome was defined according to the modified
National Cholesterol Education Program Adult Treatment Panel III report.

**Results:** During an average of 2.6 years of follow-up, 154 men (16.4%) and 206
women (16.6%) developed metabolic syndrome. Median baseline adiponectin
levels in subjects who developed metabolic syndrome were significantly lower
than in those who did not, both in men (7.08 vs. 8.63 μg/mL, p < 0.001) and
women (10.96 vs. 12.16 μg/mL, p < 0.001). In multivariable adjusted models, the
odds ratio (95% confidence interval) for incident metabolic syndrome comparing
the highest to the lowest quartiles of adiponectin levels was 0.28 (0.14 – 0.48) in
men and 0.43 (0.27-0.70) in women. Serum adiponectin levels were also inversely
associated with the number of metabolic syndrome components developed by
study participants over follow-up (P trend <0.001 in both men and women).

**Conclusion:** Our findings suggest that increased serum adiponectin could be a
negative predictor of incident MetS and its components.

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**P5009**

**Impact of a cardiac diabetic nurse in reducing the incidence of hypoglycemic events in cardiac patients with type 2 diabetes mellitus**


**Introduction:** Hypoglycemia is a potential lethal complication of hypoglycaemic
medications for patients with diabetes mellitus (DM), as was demonstrated in the
Diabetes Control and Complication Trial (DCCT). United Kingdom Prospective
Diabetes Study (UKPDS) reported an annual incidence of major hypoglycemic
events of 2.3% in that receiving insulin therapy.

**Objective:** To evaluate the effectiveness of the Cardiac Diabetic Nurse in Reduc-
ing the Incidence of Hypoglycemic Events in Cardiac Patients with Type 2 DM at
KACC.

**Methodology:** In this prospective study, we implemented two interventions. The
first focused on an intensive educational strategy for 140 cardiac nurses, and fa-
cilitates delivery of the latest evidence based guidelines over a six week period.
The second intervention addressed timing of patient snacks and a pre and post
audi instigated to evaluate any improvement in deficit areas.

**Results:** In September and October, 2010 in KACC, 40/1183 (3.4%) patients had
documented hypoglycemic events. A total of 27 patients (20.2%) developed hypo-
glycemic events of 2.3% in that receiving insulin therapy.

**Conclusion:** Our findings suggest that increased serum adiponectin could be a
negative predictor of incident MetS and its components.

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**P5010**

**Non-dipping heart rate and microalbuminuria in a type 2 diabetic population**

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**Purpose:** There is increasing interest in the association between non-dipping heart rate and target organ damage. However, this has not been adequately studied in diabetic patients. The aim of the study is to iden-
tify factors that are independent predictors of non-dipping heart rate in a type 2
diabetic population who is at high risk of cardiovascular disease.

**Methods:** One hundred eighty six type 2 diabetic subjects with mean diabetes
duration of 18.3 (± 9.5 years) were recruited. All participants had proliferative
retinopathy, thus enabling analysis of factors independent of glycaemic control.
All underwent 24-hour BP and heart rate monitoring, and were assessed for
markers of inflammation (erythrocyte sedimentation rate and high-sensitivity C-
protein), insulin resistance as well as albuminuria, presence of peripheral
neuropathy (as assessed using vibration perception thresholds) and peripheral
vascular disease. Data were analyzed using SPSS version 20.0. Randomized
right-time heart rate did not decrease > 10% as compared to day-time readings
were classified as non-dippers. Independent samples t-test and Mann-Whitney
U test were performed for parametric and non-parametric variables respectively,
while categorical variables were analysed using chi-squared test. Multivariate
regression analysis ensued to identify independent predictors of non-dipping heart
rate.

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**P5011**

**Cost-effectiveness of cardiac resynchronization therapy in combination with an implantable cardioverter defibrillator in mild heart failure based on Markov modeling using UK cost approach in MADIT CRT**

V. Kutytyla, V. Adelsburger, S. Schauer, B. Merkely, H. Klein, M. Kuniss, A. Klopek, T. Kayser, R. Peppa, A.J. Moss. On behalf of On Behalf of the MADIT-CRT Investigators. 1Heart Center, Budapest, Hungary; 2CAREM GmbH, Sauerlach, Germany; 3University of Rochester Medical Center, Cardiology Division, Rochester, United States of America; 4Kerckhoff Clinic, Bad Nauheim, Germany; 5Maeklinische Kliniken GmbH, Klinikum Luedenscheid, Luedenscheid, Germany; 6Boston Scientific Corp., Brussels, Belgium

**Purpose:** Aim: To evaluate the cost-effectiveness of CRT-D in mild heart failure LBBB or female patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial – Cardiac Resynchronization Therapy (MADIT-CRT).

**Methods:** A decision analytic Markov model was created to evaluate the costs,
gained life-years and quality-adjusted life years (QALYs) associated with CRT-
D compared to ICD treatment. Analysis was performed in 1281 LBBB patients
and in 453 CRT-D females enrolled in MADIT-CRT from the perspective of the
United Kingdom National Health Service. Costs and utilities were discounted at
3.5% per year. Base-case analysis and multiple one-way sensitivity analyses were
performed.

**Results:** Compared with ICD treatment, CRT-D gained 1.51 QALYs having a cost
of €19,855 in LBBB patients, resulting in an incremental cost-effectiveness ratio
(ICER) of €13.147 per QALY gained when using a lifetime horizon of 35 years.
The female population gained 3.81 QALYs at an additional cost of €30,088
resulting in an ICER of €7,898. ICER implemented for a 10-year time-period was
€14,282 for LBBB patients, €8,313 for female patients, respectively. One-way
sensitivity analyses revealed the discount rate and the utility per cycle without
heart failure events to be the most sensitive variables for cost-effectiveness.

**Conclusions:** CRT-D treatment is cost-effective in mild heart failure LBBB or
female patients with severely depressed left ventricular function and a wide
QRS when compared to ICD only, for a 10-year and 35-year time horizon.

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**P5012**

**Cost-effectiveness of the molecular autopsy in sudden unexplained death in the young**

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**Purpose:** Sudden unexplained death (SUD) accounts for 30% of young sudden cardiac deaths under the age of 35 years. The underlying cause is suspected primary arrhythmogenic disease in such cases, including long QT
syndrome (LQTS). The “molecular autopsy” (genetic testing of postmortem DNA)
can clarify both the cause of death, and the genetic status of asymptomatic fam-
ily members. This study sought to determine the incremental cost-effectiveness
of a family management strategy including the “molecular autopsy” in addition to
typical clinical screening, compared to clinical screening alone.
Economic analysis of the randomised assessment of saving benefit in predictive genetic testing of the surviving family members, particularly for those who test gene negative. The “molecular autopsy” is expected to become even more cost saving as newer genetic technologies facilitate testing more genes, at lower cost, with higher mutation detection rates.

Conclusions: The addition of the “molecular autopsy” to the conventional approach of clinical screening is a cost-saving strategy. There is significant cost-saving benefit in predictive genetic testing of the surviving family members, particularly for those who test gene negative. The “molecular autopsy” is expected to become even more cost saving as newer genetic technologies facilitate testing more genes, at lower cost, with higher mutation detection rates.

Methods: A decision tree model was developed to explore the costs and health outcomes associated with different diagnostic strategies. The model took an economic perspective of the NHS from a societal perspective, and presented in Australian dollars ($A = € 0.808). Effectiveness was measured using life-years gained (LYG). One-way sensitivity analysis was carried out to assess the impact of each input variable on the overall incremental cost-effectiveness ratio (ICER).

Results: Assuming a 35% mutation pick-up rate (cost $A3500/CT) to screen 4 genes (KCNQ1, HERG, SCN5A, RyR2) and 4 family members per decedent, the addition of the “molecular autopsy” to conventional family management was found to be cost-saving, dominating the clinical screening strategy. One-way sensitivity analysis found the key variables to be the cost of the “molecular autopsy” and the mutation detection rate. If the cost of genetic testing was more than $A3988 ($€3224), or the mutation detection rate below 28%, then it became the less cost-effective strategy.

Conclusions: The overall incremental cost-effectiveness of using highly sensitive troponin assays (at presentation alone or presentation and 90 minutes later) and new cardiac biomarkers instead of 10-12 hour troponin measurement.

Methods: A decision tree model was developed to explore the costs and health outcomes associated with different diagnostic strategies. The model took an economic perspective of the NHS in England and Wales and a lifetime horizon with mortality based on UK interim life tables and applied different testing strategies for myocardial infarction (MI) to a hypothetical cohort of patients presenting to hospital with symptoms suggestive of MI, but with no diagnostic ECG changes. The following diagnostic strategies were applied to each patient:

No testing: Discharge all patients without treatment. High sensitivity troponin at presentation: Discharge if negative or admit for troponin testing at 10-12 hours if positive. High sensitivity troponin and HFABP at presentation: Discharge if negative or admit for troponin testing at 10-12 hours if either test is positive. HFABP at presentation and 90 minutes: Discharge if both tests negative or admit to hospital for troponin testing at 10-12 hours if either test is positive. Standard troponin testing at 10-12 hours. It was assumed blood tests performed at presentation were undertaken in the emergency department (ED) and that results would be available and a decision made within two hours of sampling. Standard troponin measurement at 10-12 hours was the reference standard for MI.

Results: At the £20,000/QALY threshold, ten hours troponin testing is cost-effective compared to NO TROPO at 14 days post-discharge when immediate discharge occurs but not in any other scenario, where the ICER for ten hour troponin, compared to high sensitivity troponin T and HFABP at presentation, exceeds £20,000 per QALY, so it is unlikely to be considered cost-effective. In the other two scenarios (once daily ward and twice daily ward rounds), the analysis shows that the strategies based on high sensitivity troponin T and HFABP at presentation are likely to be considered cost-effective compared to the next most effective alternative using a £20,000/QALY threshold.

Conclusion: The results showed that, as expected, effectiveness (QALY’s) increased with increasing sensitivity and costs increased with decreasing specificity. At £30,000/QALY threshold, in all but one scenario a strategy of monitoring high sensitivity troponin T and HFABP at presentation (with admission for a ten hour troponin if positive and discharge home if negative) was the optimal strategy.
A retrospective cohort of long term all-cause mortality and recurrent cardiovascular events in patients with acute coronary syndrome in Thailand

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Objective: To assess the long-term outcome of patients presenting with acute coronary syndrome (ACS); ST-segment elevation myocardial infarction (STEMI), non-STEMI and unstable angina (UA) in Thailand.

Methods: This is a retrospective cohort study. The data of admission and the vital status were obtained from the records of ICD 10 and ICD 9CM systems of central office for healthcare information and bureau of policy and strategy of Thailand. All patients admitted to the hospitals using 2 health security services of Thailand; national health security (UC) and civil servant (CS) due to ACS, in 2005 (from January 1st- December 31st) were collected and followed through 2010. Primary outcome was 5 years all-cause mortality.

Results: A total of 31,087 patients with ACS in 2005 were collected. In-hospital death rate was 14%. A total of 26,722 patients (86%) survived at discharge (UA 51.6%, MI 48.4%). The post-discharge overall all-cause mortality was 11.3% and 14%. A total of 26,722 patients (86%) survived at discharge (UA 51.6%, MI 48.4%). The post-discharge overall all-cause mortality was 11.3% and 14%. The serotonin levels in thrombocytes are decreased in hypertensive patients. The serotonin levels in thrombocytes are decreased in hypertensive patients. The serotonin levels in thrombocytes are decreased in hypertensive patients.

Conclusions: There is a positive, significant change in the guidelines of the ESC towards the reduction of guidelines based on expert opinion (Level C) and on divergence in opinion (Class II). Despite many randomized studies published in last years, still less than 25% of current recommendations is based on the strongest evidence (Level A) and an effort should continue to obtain a significant increase in this section.

AMBULATORY BLOOD PRESSURE MONITORING: FOCUS ON NOCTURNAL BLOOD PRESSURE

Non-dipping pattern in untreated hypertensive patients is related to increased pulse wave velocity independent of raised nocturnal blood pressure

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Background: Non-dipper pattern, characterized by diminished nocturnal decline in blood pressure (BP), is associated with an increase in cardiovascular risks. In this study, we investigated the association between pulse wave velocity as the surrogate of arterial stiffness and non-dipper pattern in untreated hypertensive patients.

Methods: Eighty-four hypertensive patients, consulted for initial evaluation of hypertension, were enrolled. CF-PWV as the indicator of arterial stiffness was measured by a validated tonometry system (Sphygmocor). Patients with the history of any cardiovascular disease were excluded from study.

Conclusions: There is a positive, significant change in the guidelines of the ESC towards the reduction of guidelines based on expert opinion (Level C) and on divergence in opinion (Class II). Despite many randomized studies published in last years, still less than 25% of current recommendations is based on the strongest evidence (Level A) and an effort should continue to obtain a significant increase in this section.

RESULTS

Table 1

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>1.037</td>
<td>0.734-1.494</td>
<td>0.862</td>
</tr>
<tr>
<td>Gender (female, %)</td>
<td>5.112</td>
<td>2.928-20.398</td>
<td>0.021</td>
</tr>
<tr>
<td>Night mean BP (mmHg)</td>
<td>1.243</td>
<td>1.071-1.396</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total mean BP (mmHg)</td>
<td>1.050</td>
<td>0.986-1.115</td>
<td>0.115</td>
</tr>
<tr>
<td>Day mean BP (mmHg)</td>
<td>1.004</td>
<td>0.952-1.059</td>
<td>0.873</td>
</tr>
<tr>
<td>CF-PWV (m/sn)</td>
<td>1.992</td>
<td>1.240-3.198</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Conclusions: Our results suggest that diminished nocturnal decline in BP is independently associated with PWV and nocturnal BP rather than day-time BP. Non-dipper pattern, mainly related to increased pulse wave velocity and impaired modulation of vascular smooth muscle tone during the night, may justify an increased cardiovascular risk in these patients.

AMBULATORY BLOOD PRESSURE MONITORING AFFECTS SLEEP QUALITY AND BLOOD PRESSURE

V. Katsi, G. Souretis, S. Veiloglitis, T. Galerinos, D. Tsouolis, C. Stefanadis, I. Kallikazaros. Hippokration General Hospital, Athens, Greece

Purpose: During nocturnal non-invasive ambulatory blood pressure monitoring (ABPM), inevitably an undesirable external stimulus due to pump noise and pressure produced by cuff inflation may affect the quality of sleep, influence the physiological nocturnal blood pressure profile and lead in increased nocturnal blood pressure. We assessed the hypothesis that blood pressure monitoring provokes awakenings may affect sleep quality, thus blood pressure and/or heart rate.

Methods: The study population consisted of 108 consecutive subjects with stage I-III essential hypertension (aged 54.9±9 years, 59 male, office BP=148±97 mm Hg). Participants were divided into two groups according to whether they underwent ambulatory blood pressure monitoring (group A, n=60) or not (group B, n=48). Repeated measurements of blood pressure were registered with non-invasive automatic blood pressure monitors (SpaceLab90207, Welch Allyn 6100S devices) every 20 min. Self-reported data regarding the quality of sleep, numbers and duration of arousals were obtained via standardized questionnaire.

Results: Group A compared to group B demonstrated a small but significant increase in the number of nocturnal awakenings (2.8 vs 1.2, p=0.045), although their duration did not significantly differ from each other (p=NS). However, the two groups exhibited similar mean values of nocturnal blood pressure and heart rate (121/73 vs 119/71 mm Hg, 67 vs 65 beats/min, p=NS in both cases). The reported sleep quality did not differ between the two groups but both sleep quality and higher numbers of awakenings (-3) were associated with non-dipping status (p=0.05, in both cases).

Conclusions: Our findings indicate that even though ambulatory blood pressure monitoring induces modest sleep disturbances, it can accurately evaluate night-time blood pressure profile and heart rate, without affecting sleep efficiency and quality. Sleep evaluation may be particularly useful in essential hypertension, as poor quality of nocturnal sleep was associated with non-dipping status.

THE RELATION BETWEEN SEROTONIN LEVELS AND INSUFFICIENT BLOOD PRESSURE DECREASE DURING NIGHT-TIME IN HYPERTENSIVE PATIENTS

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Aim: The serotonin levels in thrombocytes are decreased in hypertensive patients. The aim of our study was to investigate the relationship between serotonin levels and insufficient nocturnal blood pressure (BP) decrease (non-dipper) in hypertensive patients.

Patients and methods: Fifty-six hypertensive patients and 27 healthy control subjects were included in the study. Of the hypertensive patients, 28 were classified as dippers and 28 as non-dippers based on nocturnal BP drops of <10 mmHg and <10 mmHg, respectively. Thrombocyte serotonin levels, serum uric acid, and C-reactive protein (CRP), and urinary albumin/creatinine ratios were analysed. After the serotonin levels were measured using an enzyme immunoassay.

Results: The thrombocyte serotonin level was 378.9±69.5 ng/109 platelet in the non-dipper group, 424.7±58.6 ng/109 platelet in the dipper group, and 518.1±35.9 ng/109 platelet in the control group. Serotonin levels in the non-dipper
group were significantly lower than in the dipper group. Serotonin levels negatively correlated with blood pressure (r = -0.8, p < 0.01). CRP concentration in the non-dipper group was higher than in the dipper (48.6±1.4 vs 36.5±1, p < 0.01) and control (48.8±0.6, p < 0.01) groups, and microalbuminuria was significantly higher in the non-dipper group compared with dipper (24.9±8.6 vs 13.4±8.8, p < 0.001) and control (9.6±4.8, p < 0.01) groups. Serotonin level was negatively correlated with nocturnal blood pressure decrease (p = 0.01, r = -0.3), uric acid (p = 0.01, r = -0.3), and CRP (p < 0.01, r = -0.3).

Conclusion: In non-dipper hypertensive patients, thromboocyte serotonin levels were significantly lower than in dipper and control groups. Serotonin levels may be related to insufficient nocturnal blood pressure decrease in hypertensive patients.

**P5021**
Circadian variation of blood pressure is impaired in normotensive pregnant women with gestational diabetes mellitus

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**Purpose:** Approximately 5% of all pregnancies are complicated by gestational diabetes mellitus (GDM). Gestational diabetes mellitus is accepted as longstanding hyperinsulinemia, which is a metabolic dysfunction of pregnancy. Women with GDM have an increased risk of gestational hypertension. Since GDM is a state of temporary insulin resistance, we therefore aimed to test our hypothesis that day time circadian blood pressure variation is impaired even in normotensive women with GDM. We sought to determine this hypothesis by comparing the normotensive women complicated with GDM with normal pregnant women in terms of horler monitoring derived dipper and non-dipper circadian variation of blood pressure profile.

**Methods:** Forty-two women with GDM and 33 normal uncomplicated pregnant subjects were screened and diagnosed between 24 and 28 weeks of gestation, according to the criteria of the American College of Obstetricians and Gynecologists. Twenty-four-hour non-invasive ambulatory blood pressure monitoring by using a portable compact digital recorder automatic device was carried out on a weekday. In order to obtain diurnal and nocturnal values, diurnal readings at 20-min intervals and nocturnal readings at 30-min intervals were recorded. Nondipper and dipper blood pressure definition was calculated as follows: (Awake BP – Sleep BP) x100/Awake BP. Patients with a nocturnal reduction in average daytime systolic BP (54.4±1.9 vs 102.3±1.6, p<0.001) and diastolic BP (38.1±1.6 vs 72.3±1.6, p<0.001, respectively). Night phase systolic blood pressure and night phase diastolic blood pressure were higher in GDM group. Night phase systolic and diastolic blood pressure dipping were diminished in GDM group (4.6±3.7 vs -8.9±3.6, p<0.001 and -6.9±5.1 vs -8.9±3.6, p<0.001).

**Conclusion:** Day time circadian blood pressure variation is impaired and left ventricle mass index is increased in normotensive GDM which deserves further studies in this topic.

**P5022**
Dipping status is characterized by augmented administration of benzodiazepines and elevated arterial stiffness

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**Purpose:** Blunted reduction of blood pressure (BP) fall as well as psychological stress have both been related to adverse cardiovascular prognosis and potentially harmful to pregnancy as a common pathophysiological substrate. We hypothesised that dipping status might be correlated with benzodiazepine’s administration (sympathetic action) in the setting of essential hypertension (EH). 

**Methods:** Our population consisted of 134 consecutive subjects with stage I-II untreated EH (aged 52.8±9 years, 72 male, office BP=151/97 mm Hg). They were classified according to the nocturnal BP fall on 24-hour ambulatory BP monitoring, to non-dippers (those with <10% nocturnal systolic and diastolic BP fall, n=36) and dippers (the remaining subjects, n=98). All participants underwent arterial stiffness evaluation on the basis of carotid to femoral pulse wave velocity (c-f PWV) by means of a computerized method (Complior SP). Anthropometric data were recorded and venous blood samples were drawn for estimation of high sensitivity C-reactive protein (hs-CRP) and homocysteine levels. Self-reported data on nocturnal benzodiazepines’ administration were obtained via interview.

**Results:** Non-dippers compared to dippers did not differ regarding age, gender, body mass index, office and 24-hour systolic and diastolic BP (p>NS for all cases). Non-dippers had significantly increased 24-hour pulse pressure (54.8±8 vs 49.9±9 mmHg, p<0.05). Additionally, they exhibited higher c-f PWV values (8.5 vs 7.6 mm/s, p<0.05), increased hs-CRP (2.8±1.08 vs 2.1±0.6 mg/L, p<0.05) and homocysteine levels (14.6±6.8 vs 11.9±5.4 mmol/L, p<0.05). Benzodiazepine’s administration as anxiolytic was significantly more prevalent among nondippers compared to dippers (78% vs 23%, p<0.05).

**Conclusions:** In conclusion, non-dippers compared to dippers hypertensives were characterized by increased benzodiazepine’s administration, impaired arterial elasticity and more pronounced activation of proatherogenic mechanisms.

**P5023**
Incremental effects of restless legs syndrome (RLS) on nocturnal blood pressure in relatively young untreated hypertensive patients and normotensive individuals

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**Background:** The aim of the present study was to assess the relationship between RLS and night-time blood pressure patterns in a relatively young cohort who had not been treated before.

**Methods:** This cross-sectional study included 230 consecutive patients with never-treated hypertension who presented to our institution for initial evaluation of hypertension. Restless legs syndrome was assessed by a self-administered questionnaire based on the International Restless Legs Study Group criteria.

**Results:** Of the study group, 133 patients were diagnosed as hypertensive (53.4% nondippings) and 81 patients as normotensive (54.3% nondippings). The prevalence of RLS, globally, were significantly higher in nondippings compared with dippings (34.7% vs 21.2% respectively, p=0.028). Logistic regression analysis showed that the RLS is an independent determinant for both hypertension (odds ratio=0.43 [95% confidence interval (CI)=0.21–0.83; P=0.013) and the nondipping blood pressure patterns (odds ratio=1.96 [95% confidence interval (CI)=1.05–3.67, P=0.035]).

**Table 1. Independent predictors of nondipping blood pressure profile**

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex (male)</th>
<th>Non-smoker</th>
<th>RLS</th>
<th>F value</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.052</td>
<td>0.030</td>
<td>0.07</td>
<td>0.949</td>
<td>0.896–1.006</td>
<td></td>
</tr>
<tr>
<td>(in years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.001</td>
<td>0.313</td>
<td>0.997</td>
<td>0.999</td>
<td>0.541–1.846</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>0.441</td>
<td>0.332</td>
<td>1.183</td>
<td>1.555</td>
<td>0.812–2.978</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RLS</td>
<td>0.676</td>
<td>0.320</td>
<td>0.035</td>
<td>1.965</td>
<td>1.050–3.678</td>
<td></td>
</tr>
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<td></td>
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</table>

**Figure 1**

**Conclusions:** We have showed that clinically diagnosed RLS was associated with the nondipping pattern which was shown to be a predictor of cardiovascular risk.

**P5024**
Inverse dose-response association between urinary melatonin excretion and nocturnal systolic blood pressure in the elderly

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**Purpose:** Oral melatonin administration decreases nocturnal systolic blood pressure (SBP); however, it remains unclear whether endogenous melatonin, considerably lower than pharmacological levels, is associated with nocturnal SBP. The purpose of this study was to evaluate the association between urinary melatonin excretion (UME), an index of endogenous melatonin, and nocturnal SBP.

**Methods:** In this cross-sectional study, 109 elderly individuals aged 60 years or older (50 males, 69.1±6.1 years), not taking antihypertensive medication, and completed two 48-h monitoring sessions were consecutively selected from 217 subjects (HELO-KYO cohort). We simultaneously measured overnight UME (dissulatoxymelatonin), ambulatory BP at 30-min intervals, and physical activity evaluated by actigraphy. The final model was based on 216 BP data (the average in 48 h) from 109 participants.

**Results:** The median UME was 7.6 μg (interquartile range 4.7–11.5) and mean nocturnal SBP was 114.8±17.8 mmHg. Univariate mixed linear regression analysis showed significant associations between nocturnal SBP and age, gender, current smoking status, diabetes, log-transformed UME, daytime physical activity,
nocturia, and duration in bed. In a multivariate mixed model controlling simulta-
necessarily for the former confounders, log-transformed UME was significantly asso-
ciated with nocturnal SBP (regression coefficient: -3.6, 95% confidence intervals
[CI] from -7.1 to -0.042). Moreover, to explain this association more prac-
tically, nocturnal SBP was estimated to decrease by 3.2 mmHg (95% CI from 0.1
to 6.4 mmHg) when UME increased from 4.7 μg (1st quartile value) to 11.5 μg
(3rd quartile value; Figure).

Figure 1. Estimated effect of UME on nocturnal SBP

Conclusion: An inverse dose–response association exists observed between
UME and nocturnal SBP among elderly individuals.

P5025 Characterization of isolated nocturnal hypertension in adolescents
E. Silva, G. Bermudez, J.J. Villamil, A. Gonzalez, M. Bracho,
C. Eiss. Instituto Regional de Investigacion y Estudios de
Enfermedades Cardiovasculares, Universidad del ZuL, Maracaibo,
Venezuela

Objective: To determine the prevalence and characteristics of isolated nocturnal
hypertension (INH) in adolescents from Maracaibo, Venezuela.

Methods: It was conducted a prospective and transversal study that included
621 subjects, 264 males and 357 females, mean-age: 14.6 ± 1.7 years, who were
unlimited 24-h ambulatory blood pressure (BP) monitoring (ABPM) to obtain
BP during awake and sleep periods. The presence of INH was defined as sleep
BP higher or equal than 95th percentile and awake BP less than 95th for age
and gender. Demographic (age, gender), anthropometric data [weight, height,
waist circumference (WC) and hip circumference (HC) ] and office blood pres-
sure were registered. Also, serum glucose, lipids, fibrinogen and insulin, as well
as C-reactive protein (CRP) were determined. The prevalence of INH and its 95%
confidence intervals (95% CI) was calculated in all adolescents and by gender.
The ANOVA test was used to study the effects of all factors included in the study
on the INH.

Results: The INH prevalence was 15.8% [n=98; 95%CI: 12.9-18.7] in all sub-
jects, 15.5% [n=41; 95%CI: 11.1-19.9] in males and 16.0% [n=57; 95%CI: 12.2-
19.8] in females (p: NS). Adolescents with INH showed significant higher val-
ues than normotensives in the following factors: weight (60.7 ± 16.5 vs. 54.8 ±
10 kg, p=0.001), height (161.7 ± 9.7 vs. 159.7 ±10 cm, p= 0.001), WC (75.1 ±12
vs. 71.0 ±10 cm, p=0.001), HC (93.2 ±10 vs. 89.3 ±9 cm, p=0.001), office
BP (129.4±12/82.2±8 vs. 102.9±11/58.6±6 mmHg, p=0.001) and triglycerides
(89.5±44 vs. 77.7±36 mg/dl, p=0.001). Age and gender did not show statisti-
cally significant effects on INH.

Conclusions: There is a very high INH prevalence in adolescents. In this age
group, the anthropometric measures are important factors to be evaluated in order
to establish the presence of INH. This condition is extremely important because
from the early age the subjects could be in cardiovascular risk.

AMBULATORY BLOOD PRESSURE MONITORING AND
TARGET ORGAN DAMAGE

P5026 Abnormal blood pressure rise post mild exercise
protocol in newly diagnosed hypertensive subjects is
associated with significant cardiovascular
functional/structural abnormalities
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Center at Cardiovascular Center of Sarasota, Sarasota, United States of America

Purpose of the study: In previous publications we reported positive correlation
between cardiovascular disease risk and abnormal (Abn.) blood pressure (BP)
rise post exercise (PME).

The purpose of this study was to assess whether abnormal BP rise PME in
subjects with newly diagnosed Hypertension (HTN) is associated with func-
tional/structural cardiovascular (CV) abnormalities, which might require more ag-
gressive therapeutic approach.

Methods: We evaluated 2174 consecutive asymptomatic subjects, who pre-
lected to our Center for Cardiovascular Disease (CVD) risk assessment, using the
Early Cardiovascular Disease Risk Score (ECVDRS), age range from 20 to
38 years. The majority of these subjects were self-referred. The ECVDRS con-
sists of 10 non-invasive tests: large (C1) and small (C2) artery stiffness, BP at rest
and PME according to a pre-specified protocol, carotid and abdominal aorta ultra-
sound, retinal photography, Microalbuminuria, ECG, LV ultrasound, and pre-BNP.
We defined HTN according to JNC VII.

Results: Among the subjects screened1277 were not receiving any CV medica-
tions, 198 of them met criteria for HTN: 90 female (45.5%) and 108 male (54.5%).
Among the 198 subjects 36 females (40%) and 40 males (37%) had no other
comorbidities. Detailed results are outlined on table 1.

Conclusion: 1. Asymptomatic newly diagnosed hypertensive subjects with Abn.
BP rise PME have significantly higher CV functional/structural abnormalities re-
gardless of sex, than those with normal BP rise PME; 2. Hence we propose that
asymptomatic subjects with newly diagnosed HTN should be screened for evi-
dence of any functional/structural CV abnormalities; which will mandate more
aggressive therapeutic interventions
Combined effects of blood pressure and aldosterone on cardiac left ventricular mass - ethnic differences between Han, Kazakh and Uygur subjects


Abstract

Purpose: Hemodynamic factors such as blood pressure have been established to be major determinants of cardiac left ventricular structure. However, factors other than blood pressure have also been shown to influence cardiac mass. We performed a medical survey and found that cardiac left ventricular mass index (LVMI) in an ethnic group of China with higher blood pressure was smaller than in another ethnic group with lower blood pressure. Here, such contradictions were analyzed with regard to blood pressure, LVMI and chemical parameters of blood and urine.

Methods: In a medical survey conducted in Xinjiang, China, 303 subjects (age, 65-70 years) from 3 ethnic groups (Han, Kazakh and Uygur) from two separate regions provided blood and urine samples, and underwent 24-hour ambulatory blood pressure monitoring (ABPM). The Ethics Committee of Xinjiang Medical University approved all study protocols. All subjects provided informed consent. A control group in which there were 27 males and 33 females, the mean age was 54.5±1.2 years, the mean body mass index (BMI) was 24.0±1.7 kg/m², and urinary sodium excretion value was 93.6±10.1 mmol/24 h. The other group was observed between PA and urinary sodium excretion value. The other group was observed between PA and urinary sodium excretion value. The other group was observed between PA and urinary sodium excretion value.

Results: Systolic and diastolic blood pressure obtained by ABPM were significantly higher in the Kazakh than Han and Uygur groups. However, LVMI in Kazakh was lower than in both other groups. Univariate sodium excretion value was significantly lower in Uygur than in the other 2 groups. Plasma aldosterone (PA) and plasma renin activity (PRA) were significantly lower in Kazakh. Values for LVMI in all ethnic groups were positively correlated with both blood pressure and PA. An inverse correlation was observed between PA and urinary sodium excretion value.

Conclusions: These results suggest that blood pressure is not always a determinant of LVMI value. It is possible that relatively low PA resulting from higher sodium intake suppressed the increase in LVMI caused by higher blood pressure in Kazakh subjects.
Antihypertensive treatment less efficacious when evaluated by Ambulatory Blood Pressure Monitoring

V. Gjini, G. Gjini. Internal Medicine Clinic, Hospital of Fier, Albania

Ambulatory blood pressure monitoring (ABPM) is now widely used not only for a better diagnosis of hypertension, but also for considering of antihypertensive treatment.

Purpose: We aimed to study the efficacy of antihypertensive drug treatment by analyzing office and ABPM recorded values.

Methods: From a database of more than 1000 ABPM recordings we have selected 146 pts whose BP was monitored twice, first without and then 2 weeks after starting a 2-week treatment.

Office measured peak and mean systolic and diastolic values were selected for comparison. Treatment was considered efficacious when BP values (either systolic or diastolic) were reduced ≥10 mm Hg, or when were returned to normal (<130/80 mm Hg).

Results: After a 2-week treatment the Office BP values were significantly reduced to 138±16 (<p=0.001) and 91±11 mm Hg (p<0.001), Peak BP values to 167±19 (<p=0.001) and 107±15 (<p=0.001) mm Hg and Mean BP values to 133±14 (<p=0.001), 79±5 mm Hg, respectively.

Office-measured BP values (sys or dia) were reduced ≥10 mm Hg in 121/146 pts (83%) and were found normal in 82/146 pts (56%).

Peak BP values were reduced ≥10 mm Hg in 101/146 pts (69%) and were within normal limits in only 40/146 pts (27%).

Mean BP values were returned to normal in 110/146 (75%) pts.

Conclusion: These data indicate that when evaluated by ABPM antihypertensive treatment results less efficacious than when traditionally evaluated.

AMBULATORY BLOOD PRESSURE MONITORING

Masked hypertension and atherogenesis: the impact of nocturnal continuous positive airway pressure treatment

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Purpose: Recent evidence demonstrates that masked hypertension (MH) is a significant predictor of cardiovascular disease, while hypoaipelinemia and hyporenalaxinemia may contribute to vascular damage facilitating atherogenesis.

Aim of our study was to examine the apelin and relaxin plasma levels in patients with and without MH and compare the findings to those of healthy normotensives matched for age, sex, body mass index and the rest of risk factors.

Methods: One hundred-thirty (60 M, 70 F) healthy subjects mean age 45±12 years and 132 pts with masked hypertension were included in our study. The whole study population underwent 24 hour ambulatory blood pressure monitoring (ABPM). The ABPM recordings, 18 individuals (7M, 11 F) had MH (daytime systolic diastolic blood pressure ≥135 mm Hg and 85 mm Hg - group A) and the remainder 112 subjects (53 M, 59 F) had normal ABPM recordings. Group B. Apelin and relaxin plasma levels were determined in both groups (ELISA method).

Results: Our findings and the comparisons between the two groups are shown in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Group A (n=132)</th>
<th>Group B (n=132)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apelin (pg/ml)</td>
<td>220±121</td>
<td>318±147</td>
</tr>
<tr>
<td>Relaxin (pg/ml)</td>
<td>153±8.7</td>
<td>53.8±28</td>
</tr>
</tbody>
</table>

Conclusions: Our findings suggest that subjects with masked hypertension have increased apelin and relaxin plasma levels compared to healthy individuals. This observation may have prognostic significance for future cardiovascular events in subjects with masked hypertension and needs further investigation.

The prevalence of masked hypertension and blood pressure variability in patients with renal transplantation

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Purpose: Arterial hypertension is a risk factor affecting graft function in renal transplants (Rx). In pediatric Rx, high prevalence of masked and nocturnal hypertension was reported. Most of the Rtx had a history of hypertension and some of them are normotensive in outpatient control, however home blood pressure levels are higher. Masked hypertension (MHT) is defined as a normal office blood pressure but an elevated ambulatory blood pressure. Use of ambulatory blood pressure monitoring (ABPM) enables the identification of MHT. Previous reports have demonstrated the role of MHT in the outcome of hypertensive patients. However, the true prevalence of MHT in Rx is still unknown.

Methods: The study enrolled Rtx with normal office blood pressure level (SBP<DBP<140/90mmHg) admitted to the outpatient clinic of Nephrology and Transplantation over a year. ABPM was performed in all patients during 24-h period. MHT was defined as normal office BP associated with daytime ambulatory hypertension (SBP<DBP>135/85).

Results: The prevalence of MHT and nocturnal hypertension in our group were 49% and 61%, respectively. Fifty-four (54%) patients had a history of HT. Fifty-eight patients (58%) were being treated with antihypertensive medications. Non-dipping was present in 81.5% of patients. There were no significant differences regarding demographic and clinical features between patients with and without MHT (Table).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>With MHT (n=58)</th>
<th>Without MHT (n=50)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40±11</td>
<td>42±11</td>
<td>0.53</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>123±12</td>
<td>122±11</td>
<td>0.79</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>78±5</td>
<td>77±5</td>
<td>0.32</td>
</tr>
<tr>
<td>BMI, mg/ml</td>
<td>26±5</td>
<td>26±4</td>
<td>0.71</td>
</tr>
<tr>
<td>Sympathetic tone</td>
<td>76±24</td>
<td>78±20</td>
<td>0.18</td>
</tr>
<tr>
<td>Hypertension, n</td>
<td>30</td>
<td>24</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes, n</td>
<td>8</td>
<td>4</td>
<td>0.18</td>
</tr>
<tr>
<td>CCB, n</td>
<td>30</td>
<td>28</td>
<td>0.41</td>
</tr>
<tr>
<td>BMI, body-mass index, CCB, calcium channel blocker, BB, beta blocker.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: We demonstrated an increased prevalence of MHT and BP variability in Rtx population. These results may explain high cardiovascular events in Rtx patients. Therefore routine recommendation of ABPM in Rtx patients may be reasonable.

Impact of nocturnal continuous positive airway pressure therapy on ambulatory blood pressure in patients with obstructive sleep apnea and prehypertension

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Background: We aimed to investigate the short term effects of CPAP treatment on blood pressure (BP) and nondipper or dipper status in OHAS patients without a prior diagnosis of hypertension (HT).

Methods: We included a total of 24 patients (19 male, mean age: 48.7±10.4 years). The study group was divided into 2 groups: group 1 with mild-moderate OHAS (AHI<30) and group 2 with severe OHAS (AHI>30). Patients with OHAS were passively treated with CPAP therapy (8 hours/day) and were monitored with ABPM (daytime systolic and diastolic BP were 135 mm Hg and 85 mm Hg - group A) and for the remainder 112 subjects (53 M, 59 F) had normal ABPM recordings. Group B. Apelin and relaxin plasma levels were determined in both groups (ELISA method).

Results: Mean ambulatory 24 hour systolic and diastolic BP were 126±6.9 mm Hg and 79.5±10.2 mm Hg respectively.CPAP treatment significantly decreased 24 hour mean BP after 12 weeks irrespective of AHI. OHAS group 2 had a significant reduction in BP after 6 weeks. After 6 weeks CPAP treatment, non-dippers reduced to 16.6% and at the end of 12 week CPAP treatment 12.5% of the patients were non-dipper (<p=0.008). Multiple linear regression analysis revealed that male gender, Ewspr work sleepiness scale, apnea-hypopnea index, smoking and mean 24 hour BP were the predictors of BP reduction in patients between baseline and after 12 week CPAP (<p=0.05).

Multiple linear regression analysis for the predictors of BP reduction after CPAP therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>β coefficient</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>-5.76</td>
<td>-8.2 to -3.34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ewspr score</td>
<td>-0.35</td>
<td>-0.577 to -0.197</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AHI</td>
<td>-0.14</td>
<td>-0.191 to -0.097</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline BMI (kg/m²)</td>
<td>-0.29</td>
<td>-0.504 to -0.052</td>
<td>0.002</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.26</td>
<td>0.75 to 4.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>5.59</td>
<td>2.96 to 8.23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.7</td>
<td>7.6 to 1.8</td>
<td>0.003</td>
</tr>
<tr>
<td>Baseline 24 MBP (mmHg)</td>
<td>-0.70</td>
<td>-0.32 to 0.84</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Effective CPAP therapy reduces BP levels in OSAS patients with out hypertension and improves dipper-nondipper status.
**P5036** Metabolic syndrome increases morning blood pressure surge

E. Chatzistamatiou, G. Moustakas, E. Androulakis, D. Toussoulis, A. Avgeropoulou, N. Kalivosdouris, M. Divanis, C. Liakos, C. Stefanadis, I. Kallikazaros. 1Hippokration General Hospital, Cardiology Department, Athens, Greece; 2Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

**Purpose:** Large scale studies suggest that systolic blood pressure morning surge is an independent predictor of target organ damage. Aim of our study was to investigate associations between 24hr ambulatory blood pressure (ABPM) levels and morning surge in never-treated essential hypertensive (EH) patients with and without metabolic syndrome (MS).

**Methods:** We studied 366 consecutively newly diagnosed EH patients stage I-III (age 51±12 years, 60% males) without prevalent cardiovascular disease. In all participants anthropometric data were recorded. Also, all subjects underwent a 24-hr ambulatory blood pressure monitoring (ABPM) and morning surge index was calculated as: the mean systolic blood pressure (SBP) during the 2 hours after waking minus mean SBP during the 1 hour that included the lowest sleep BP. Heart rate variability was calculated as the ratio of day-night mean heart rate difference normalized to mean day heart rate. According to ATP III criteria, the study cohort was divided in two groups: A (n=210, MS-) and group B (n=156, MS+).

**Results:** The two groups did not differ regarding age, sex, smoking and snoring status, alcohol and coffee consumption, serum cholesterol, office systolic and diastolic blood pressure and 24-hr ABPM blood pressure levels. Group B compared to A exhibited increased BMI (31.9±4 vs. 26.3±3, p<.001), 24hr average (74.9±9 vs. 72.8±8, p=.019) and night (66.8±6 vs. 63.8±6, p=.002) heart rate, heart rate variability (12.3±7 vs. 15.7±7, p<.007) and morning surge index (23.1±13 vs. 19.5±12, p<.009).

**Conclusion:** In never-treated EH patients, the presence of metabolic syndrome unfavourably affects autonomic function as expressed not only by decreased HR variability, but also by increased blood pressure morning surge. These autonomic disturbances may be the link between MS, subclinical target organ damages and prevalent CVD.

**P5037** A novel non-invasive continuous system for estimating arterial blood pressure: first-in-man clinical results

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**Purpose:** There was growing interest on noninvasive technologies for arterial blood pressure (BP) measurement on beat-to-beat basis. Our aim was to clinically evaluate the accuracy of a novel device for estimating real-time BP using an algorithm based on pulse-wave transit time (PTT).

**Methodology:** This device measures PTT between ECG R wave and the onset of photoplethysmography (PPG) and is estimated using an improved technique first reported by Heath. BP estimation involves the delay between R-wave and the inflection point of positive slope of PPG and the instantaneous heart rate. PPG sensor was attached to the right index finger. R-wave was registered using lead I. Values were obtained with this method were compared with a validated oscilometric device (Omron M6 Comfort) measured in the left arm. Duration of study was 49.3±0.38±0.30±0.45min (healthy volunteers/hypertensive patients). Results are presented as median (interquartile interval).

**Results:** 10 subjects (3Healthy/7Patients) were evaluated, 5 female. Base-line systolic BP (SBP) was 121.0±1.0mmHg, diastolic BP (DBP) was 77.0±1.0mmHg and heart rate was 60.0±3.0mmHg normal values were 112.6±3.8±8.0/128.0±7.0mmHg.

**Conclusions:** The present study is the first to establish reference and normal values for central BP estimated by the Omron device. This noninvasive estimation shows close correlation with that by SphygmoCor device, but the Omron device requires its own reference values because of technological differences between SphygmoCor and Omron. Thus, the present study was designed to establish normal and reference values for central BP estimated by the Omron device.

**P5038** Establishment of reference values for central blood pressure estimated by Omron HEM-9000AI

S. Tanaka, H. Takase, T. Sugiana, S. Yamashita, Y. Dohi, G. Kimura. 1Nagoya City University, Graduate School of Medical Sciences, Dept of Cardio-Renal Medicine & Hypert., Nagoya, Japan; 2Enshu Hospital, Hamamatsu, Japan

**Purpose:** Although central blood pressure (BP) is more closely associated with cardiovascular events than conventional brachial BP, a wider implementation of central BP into clinical practice is hampered by the lack of established reference values. Recently, an automated device for the estimation of central BP has been introduced (Omron HEM-9000AI). This noninvasive estimation shows close correlation with that by SphygmoCor device, but the Omron device requires its own reference values because of technological differences between SphygmoCor and Omron. Thus, the present study was designed to establish normal and reference values for central BP estimated by the Omron device.

**Methods:** Consecutive 10756 subjects (55.3±12.5 years) who visited our hospital for a health checkup were enrolled in this study. Of these, 7348 subjects received no anti-hypertensive, anti-diabetic, or lipid-lowering drug treatment, constituting the reference value population. Subjects with no cardiovascular risk factors and that were in the optimal or normal brachial BP categories (n=5672) were selected to establish normal values.

**Results:** Estimated central BP was higher than brachial BP and was significantly correlated with age and brachial BP. Reference and normal values of central BP were established according to age decade (table) and brachial BP categories. Reference values (mmHg, mean±SD) were 113.5±16.6 in normal, 128.6±16.8 in high normal, and 155.3±27.9 in hypertension categories and normal values were 112.5±19.2 in optimal and 129.2±14.9 in normal BP categories.

**Conclusions:** The median absolute error was 2.94±1.29.77±3.38 (SBP), 1.67±0.51/ 5.59±1.79 (DBP), in healthy/patients. Relative low error was 2.75±0.01%/ 9.13±0.04% (SBP) and 2.53±0.01%/7.17±0.02% (DBP) in healthy/patients. Figure 1 shows estimated BP in a healthy volunteer.

**P5039** Enhanced external counterpulsation has no lasting effect on blood pressure

O. May, W.A.M. Khair. Region Hospital Herning, Herning, Denmark

**Purpose:** To assess the effect of a course of EECP on BP using ambulatory BP (ABP) measurements.

**Method:** Patients referred for EECP due to refractory angina pectoris were consecutively included in the study and treated with EECP for 1 hour 5 days a week in 7 weeks. The ABP were measured for 24 hours using a Spacelab Ultralite 90217 device 2 months before an EECP course, just before the EECP course, just after, 3 and 12 months after EECP. The anti-hypertensive medication was held constant during the study period. Changes in BP were tested by repeated measure analysis and changes in anti-hypertensive medication by Friedman's test for related samples.

**Results:** The median absolute error was 2.94±1.29.77±3.38 (SBP), 1.67±0.51/ 5.59±1.79 (DBP), in healthy/patients. Relative low error was 2.75±0.01%/ 9.13±0.04% (SBP) and 2.53±0.01%/7.17±0.02% (DBP) in healthy/patients. Figure 1 shows estimated BP in a healthy volunteer.
Results: Fifty patients were included, 72% were males, mean age was 63 years, mean BMI was 29.7 kg/m² and 64% had hypertension. The mean baseline clinic BP was 118/75 mm Hg. Fifty two percent were treated with ACE/ARB, 90% beta-blocker, 66% calcium antagonist, 92% long acting NTG and 42% with diuretics. The CCS class improved from mean 2.6 to 1.5. No significant change was found in medication. The mean daytime and night time ABP did not change significantly during the study period (p>0.05), see table. Further, when controlling for baseline level of ABP, the interaction was found between ABP and baseline level.

Conclusion: EEEP treatment has no lasting effect on blood pressure.

The strongest correlation was observed in pts with excessive nocturnal decline in bp and non-dipper and the morning BP peak in three ABPM obtained in patients with heart failure living near the site, and the weather data recorded by a local weather station from Jan 2009 to Aug 2010. The readings from the weather station were performed with a frequency of 1 measurement per minute.

In the first stage of statistical analysis authors determined the Pearson correlation (r) between systolic BP and AP.

In order to explain the observed correlations was examined the impact of the season of a year, distribution of age groups and distribution of dippers and non-dippers.

Result: In large proportion of pts 24% (110 pts), systolic BP shows a strong dependence on AP (r = 0.4). 34.8% of pts (145 pts) systolic BP shows a weak correlation with AP (0.2 < r < 0.4). In group of 193 pts BP remain without correlation to AP.

In analysis of subgroups it was noticed that strong correlations with AP occurred only in groups of dippers and extreme dippers.

Conclusion: Systolic BP in ABPM is related to AP in 58.8% of study population.

| Group          | Number of investigation | Age | |r| (p-value) |
|----------------|-------------------------|-----|-----------|
| Inverse Dipper| 102/26                  | 69±14.10,34±0.24(0.027±0.00) |
| Non-Dipper    | 199/89                  | 61±33.13±14.13(0.030±0.03) |
| Dipper        | 163/77                  | 59±15.07±18.00(0.10±0.20) |
| Extreme Dipper| 16/77                   | 56±18.33±13.34(0.01±0.026) |
| All           | 448/201                 | 60±46±14.43(0.21±0.02±0.29) |

1. correlation coefficient; p-value < 0.05 = statistical significance.

Conclusion: Systolic BP in ABPM is related to AP in 58.8% of study population. The strongest correlation was observed in pts with excessive nocturnal decline in BP and AP.

Spts with labile HA and evidence of sensitivity to changes in AP should monitor their Ambulatory Blood Pressure Monitoring (ABPM) in pts with labile HA living near the site, and the weather data recorded by a local weather station from Jan 2009 to Aug 2010. The readings from the weather station were performed with a frequency of 1 measurement per minute.

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Conclusion: Systolic BP in ABPM is related to AP in 58.8% of study population. The strongest correlation was observed in pts with excessive nocturnal decline in BP and AP.

Conclusions: The CRUSADE and ACUITY-HORIZONS risk scores showed an excellent predictive value for in-hospital bleeding in our cohort of STEMI patients. The CRUSADE risk score seemed to perform better than the ACUITY-HORIZONS risk model for bleeding prediction.
Real-world primary PCI with bivalirudin: a report from the prospective, multi-centric EUROVISION registry

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Purpose: In primary PCI, bivalirudin (BIVA) is superior to heparin+GPIAs inhibitors (GPI) as shown in the HORIZONS-AMI trial (HOR) due to significant reduction in bleeding and improved survival. However, a higher incidence of acute stent thrombosis was observed in BIVA-treated patients. The purpose of this analysis was to evaluate 30-day outcomes from a real-world STEMI population from the EUROVISION (EUR) registry treated with a BIVA alone strategy.

Methods: Among the 2018 EUR BIVA-treated patients, 663 underwent primary PCI for STEMI. Outcomes measures were 30-day death, re-infarction (MI), stroke, stent thrombosis, urgent revascularization (URV), bleedings, and thrombocytopenia. The net adverse cardiovascular events (NACE) rate combining death, MI, URV and major bleeding was also calculated.

Results: Early from HOR, in EUR patients BIVA infusion was frequently continued post-PCI (62%, median 122 min, 60-290 IQR). Pre-PCI thienopyridine loading was performed in 95%, GPI used in 5%, and radial approach performed in 30% of cases. BIVA patients in EUR were older (p<0.001), but with similar 30-day mortality to HOR BIVA-treated patients. Thirty-day outcomes (MI, URV or bleedings) were lower in EUR resulting in lower NACE rates compared with HOR (Table 1). In EUR patients there were no acute (<24 hrs) stent thrombosis cases and no cases of thrombocytopenia.

Conclusions: Real world data from EUR confirm the HOR trial results with a favorable impact of a BIVA alone strategy on STEMI patients’ outcome. Prolongation of BIVA infusion after the end of PCI seems a safe strategy that may further contribute to improve patient’s outcome.

Impact of one versus multiple heparins administration on clinical outcome after primary PCI for STEMI: a prespecified analysis of the ATOLL trial

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Background: The ATOLL trial evaluated the efficacy and safety of IV enoxaparin versus UFH in primary PCI. Patients who had received any anticoagulation before randomization were not enrolled. Cross over to a different anticoagulant after randomization was not allowed.

Objective: To evaluate the impact of anticoagulant cross over on clinical outcome. Baseline clinical characteristics, duration of administration, clinical outcome as defined in the original ATOLL trial were first compared between patients who received more than one (n=100) versus only one anticoagulant (n=800). Patients who did not receive any anticoagulation were excluded (n=10).

Results: Patients who administered more than one heparin were more frequently older, female, treated with long-term insulin therapy than patients who started on one heparin as allocated by randomization. They also presented more frequently with acute stent thrombosis and/or occlusive shock. They were treated for a longer duration (7.9±9.1 vs. 3.9±3.2 days, p<0.001). A significant interaction was measured between “one” versus “multiple” heparins for the primary EP (p for interaction=0.001) and main secondary EP (p for interaction=0.001). The primary endpoint was reduced by 11% after anticoagulation with one versus more than one anticoagulant. The composite endpoint of death, recurrent myocardial infarction, or urgent revascularization was halved in one versus more than one anticoagulant administration as well all its individual components. Conversely, major and minor bleed was significantly reduced.

Conclusions: In primary PCI for STEMI, crossover to the other anticoagulant (technical indication) resulted in significant higher rates of both ischemic and bleeding events and should be discouraged.

Thrombus aspiration reduces plaque volume in non-ST elevation acute coronary syndromes: the reduction of myocardial necrosis achieved with n°-dose-manual thrombus aspiration study

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Purpose: Thrombus and plaque microembolization is the main cause of myocardial damage during percutaneous coronary intervention with stenting (S-PCI). Thrombus aspiration (TA) has proved useful in limiting myocardial damage in ST-elevation myocardial infarction (STEMI), but its role in non-ST elevation acute coronary syndromes (NSTE-ACS) is not yet defined. We hypothesized that TA reduces the atherothrombotic burden in such patients before S-PCI, thus having the potential of limiting periprocedural myocardial damage.

Methods: Patients with ≥1 “high-grade” (>90%) lesions at coronary angiography subjected to PCI for a NSTE-ACS were submitted to TA before S-PCI. Exclusion criteria were the presence of visible thrombus, total occlusion, degenerated vein graft, restenotic lesions. TA successfully crossed the lesion in 38/45 patients. We evaluated the effect of TA on thrombus burden and lesion characteristics by angiography and intravascular ultrasound (IVUS) before and after TA and after S-PCI. The aspirated material was also processed for histology.

Results: Mean patients’ age was 65±10 years; 82% were male; 34% underwent PCI for a recent STEMI; 66% for a NSTE-ACS. Mean lesion and stent lengths were 25±11 and 28.9±9 mm, respectively. Drug-eluting stents were used in 77% of cases. Peak CK-MB and cardiac troponins-I were 23±11 and 28.9±9 mm, respectively. Main findings are related to the effects of TA are summarized in the Table. The aspirated material was composed of fibrin in 45% of cases, red thrombus in 19%, plaque fragments in 25%, with a lymphocyte infiltration in 16%, and signs of intraplaque hemorrhage in 16%.

Effects of TA on angiographic and IVUS

<table>
<thead>
<tr>
<th>Baseline</th>
<th>After TA</th>
<th>After S-PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVUS volumes (n=38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIVUS volumes (n=38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4±0.7</td>
<td>5.82±0.39</td>
<td>2.16±0.55</td>
</tr>
<tr>
<td>11.0±3.2</td>
<td>25.3±13.1</td>
<td>26.0±13.6</td>
</tr>
<tr>
<td>73.2±12.5</td>
<td>206.6±105</td>
<td>371.152</td>
</tr>
<tr>
<td>*P&lt;0.001 vs previous assessment; MLD = minimum lumen diameter; DI = diameter stenosis; P+M = Plaque+Media; EEM = external elastic membrane.</td>
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</tbody>
</table>

Conclusion: TA reduces the “mobilizable” atherothrombotic plaque burden and may be safely performed before S-PCI in high-risk NSTE-ACS pts as an alternative to balloon predilation. These data are encouraging for a beneficial role of TA in reducing peri-procedural myocardial damage also in S-PCI in the setting of NSTE-ACS.

Evidence of ischemic post-conditioning in newly treated patients with myocardial infarction

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Purpose: Ischemic post-conditioning (PC) has been shown to reduce myocardial
infarction (MI) size. The objective of our study was to determine whether PC has a long-term benefit on left ventricular (LV) remodelling and function in optimally treated patients with MI.

**Methods:** Patients presenting, within 12h of the onset of chest pain, with a first STEMI, and for whom the clinical decision was made to perform revascularization by percutaneous coronary intervention, were eligible for enrolment. After reperfusion by direct stenting, 47 patients were randomly assigned to either a control (no intervention; n=23) or a post-conditioning group (repeated inflation and deflation of the angioplasty balloon; n=24). MI size was assessed by cardiac enzyme release during 72h after reperfusion. At 3 days and 6 months after MI, LV size and function was evaluated by echocardiography.

**Results:** The 2 groups had similar ischemic duration, area at risk and medical treatment during and after reperfusion. PC significantly reduced MI size (~34% compared to controls). At Day+7 after MI, no difference was observed on LV size and function (LV ejection fraction: EF: 55±8% in Controls, 54±10% in PC, p=0.7). At 6 months, controls displayed LV end-diastolic volume enlargement compared to initial echocardiography (91±29 vs. 100±30 ml, respectively; p=0.02) and no significant improvement on LVEF and wall motion score index (Figure 1). In contrast, PC patients displayed no LV enlargement (90±28 vs. 95±35 ml, respectively, p=0.27) and improved both their LVEF and wall motion score index compared to the initial echocardiography (Figure 1, *p<0.05 vs baseline*).

**Conclusions:** Ischemic PC on top of optimal therapy reduces MI size in patients with acute MI and improves remodelling at 6 months compared to controls.

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**P0504**

**Enoxaparin is superior to unfractionated heparin in primary PCI for STEMI: results of the prespecified per-protocol analysis of the ATOLL trial**

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**Background:** The ATOLL trial evaluated the efficacy and safety of intravenous enoxaparin versus unfractionated heparin (UFH) in the contemporary interventional management of STEMI. Patients who had received any antiagouulant before randomisation could not be enrolled. Cross over to a different antiagouulant after randomisation was not allowed. Enoxaparin was shown to be significantly better than UFH for all ischemic endpoints without safety issue but the 17% risk reduction of the primary endpoint of death, complication of MI, procedure failure or major bleeding was not significant (p=0.06).

**Objectives and methods:** To present the results of the pre-specified per-protocol analysis excluding patients that received more than one heparin (protocol violation). A total of 850 patients (87.8%) were treated according to the protocol with consistent antiagouulant using enoxaparin (n=403) or UFH (n=447). Primary endpoint analyses as for the intent-to-treat analysis were performed in this cohort of patients.

**Results:** Enoxaparin resulted in significantly reduced rates of the primary endpoint and main secondary endpoint (table). The net clinical benefit of death was also reduced with enoxaparin (table). There were favorable trends for enoxaparin on bleeding complications and blood transfusion as well.

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**P0505**

**Effect of mechanical ischemic post-conditioning and thrombus aspiration on microvascular obstruction in patients with acute ST-segment elevation myocardial infarction**

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**Aims:** Mechanical postconditioning during primary percutaneous coronary intervention (PCI) may cause thrombus dislodgement with distal embolization and its combination with thrombus aspiration on microvascular obstruction (MVO) and infarct size (IS) have not been assessed. We assessed the short-term effects of mechanical ischemic postconditioning with or without thrombus aspiration on early and late MVO size, IS and left ventricular ejection fraction (LVEF) in acute ST-elevation myocardial infarction (STEMI) patients.

**Methods and results:** Fifty-one patients undergoing PCI for a first STEMI with TIMI grade 0-1 and no collaterals were randomized to ischemic postconditioning (n=26) or controls (n=25). Ischemic postconditioning consisted in the application of four consecutive cycles of 1 minute balloon occlusion, each followed by 1 minute deflation at the onset of reperfusion. Thrombus aspiration was applied at the discretion of the treating physician. MVO size, IS, LVEF and volumes were assessed by contrast enhanced cardiac-MRI 72 hours after reperfusion. Postconditioning was associated with smaller early (3 minutes post-contrast) and late (10 minutes post-contrast) MVO size (5.1±6.7 vs. 11.3±11.0 g in controls for early MVO; P<0.02; and 2.5±4.6 vs 5.9±6.1 g in controls for late MVO; P<0.03) even after adjustment for thrombus aspiration. Overall, there was a non-significant
IS reduction in the postconditioning group (29±15 vs. 37±19 g; P=0.16), but there was a significant IS reduction in infarcts of the anterior territory (35±14 vs. 48±18 g; P<0.05). No significant difference in LVEF was found between groups but there was a significant dilation of the LV end-diastolic volume in the control group (P=0.02). Thrombus aspiration did not have any significant effect on IS or MVO (P=0.34 and P=0.42).

Conclusion: Mechanical postconditioning reduces MVO in patients with acute STEMI treated with PCI. The impact of postconditioning seems to be independent of thrombus aspiration and our data suggest that it does not increase distal embolization.

**P5050**
Addition of ivabradine during beta-blockers titration improves systolic and diastolic LV function in patients with recent Q-wave myocardial infarction

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Heart rate (HR) is a powerful predictor of mortality and heart failure (HF) in pts with acute myocardial infarction (AMI), β-blockers are the first line treatment for these pts but time is needed for their titration and side effects can limit their use in appropriate dose. Ivabradine may be a good alternative for HR reduction during β-blockers titration.

80 pts with recent (36-72 h after symptoms onset) Q-wave AMI and HR >70 bpm were studied. β-blockers were initiated in all the pts. 40 pts were randomized for ivabradine 5mg bid in addition to standard treatment and 40 pts were controls. Dosage of ivabradine was increased to 7.5 mg if HR remained > 70 bpm after 24 h of treatment. 69 (86.3%) pts had anterior AMI and 55 (68.8%) pts had symptoms of acute heart failure (Killip II). Study and control groups did not differ in regards of baseline, clinical characteristics, reperfusion and initial treatment. Standard two-dimensional, M-mode, spectral, color and tissue Doppler were performed at baseline and day 7.

Ivabradine significantly decreased HR after the first 24 h of treatment and helped to keep HR 7-10 bpm lower than in control group throughout the period of investigation. Addition of ivabradine to standard recommended treatment increased EF (without any changes of EDV) and improved LV diastolic function. At day 7, early diastolic velocity of lateral LV wall (E) was significantly higher in ivabradine group than in controls. Ivabradine also prevented left atrium dilatation.

**Table 1**

<table>
<thead>
<tr>
<th>ivabradine (40 pts)</th>
<th>Control (40 pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Day 7 p</td>
<td>Baseline Day 7 p</td>
</tr>
<tr>
<td>EDI, mm²</td>
<td></td>
</tr>
<tr>
<td>58.8±1.6</td>
<td>59.3±1.4</td>
</tr>
<tr>
<td>LA, mm</td>
<td></td>
</tr>
<tr>
<td>36.2±0.5</td>
<td>37.5±0.6</td>
</tr>
<tr>
<td>EF</td>
<td></td>
</tr>
<tr>
<td>39.3±0.8</td>
<td>44.4±0.7</td>
</tr>
<tr>
<td>E/A</td>
<td></td>
</tr>
<tr>
<td>1.09±0.1</td>
<td>1.06±0.1</td>
</tr>
<tr>
<td>DT, ms</td>
<td></td>
</tr>
<tr>
<td>153±9.7</td>
<td>169±3.7</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td></td>
</tr>
<tr>
<td>89±7.3</td>
<td>94±3.5</td>
</tr>
<tr>
<td>E'/cm/s</td>
<td></td>
</tr>
<tr>
<td>6.8±0.4</td>
<td>8.1±0.5</td>
</tr>
<tr>
<td>E'/E</td>
<td></td>
</tr>
<tr>
<td>0.10±0.6</td>
<td>0.90±0.4</td>
</tr>
</tbody>
</table>

In patients with recent Q wave AMI and HR >80 bpm ivabradine can be used during β-blockers uptitration for LV systolic and diastolic function improvement.

**Conclusions:** In the present study cohort, poor pre TIMI grade seemed to result to the later exacerbated microcirculation. In patients with STEMI showing poor pre-PCI TIMI grade, thrombectomy and distal protection may be promising remedies for the myocardial salvage with lower risk of bleeding complication.

**P5051**
The utility of thrombectomy and distal protection in patients with ST-segment elevation myocardial infarction showing poor coronary artery flow prior to primary percutaneous coronary intervention

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Introduction: Previous studies had shown that poor coronary artery flow prior to primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) is associated with exacerbated clinical outcomes, although the positive clinical results of the facilitated percutaneous coronary intervention have not been shown. The aim of this study was to evaluate the efficacy of thrombectomy and/or distal protection device in PCI for STEMI patients showing poor pre TIMI grade.

Methods: Out of 696 STEMI patients enrolled either in the two multicenter randomized trials (VAMPIRE trial: tested the efficacy of thrombectomy or thrombus aspiration; ASYMPA- GUS trial: tested the efficacy of distal protection device), 185 lesions in 185 patients who underwent the primary PCI for proximal or mid left anterior descending coronary artery lesion and have complete sets of angiographic data (Ejection fraction [EF] evaluated by left ventriculography, myocardial blush grade [MBG] and TIMI grade) at baseline and 6-months follow-up were evaluated. Delta EF was calculated by [follow up - baseline].

Results: Table shows the results. MBG 3 was achieved more frequently at pre TIMI 2-3 group. However, in patients who underwent aspiration and/or distal protection, the difference in MBG:3 rate was insignificant between pre TIMI 0-1 and 2-3 group.

**Table 1**

<table>
<thead>
<tr>
<th>Infarct mass (g)</th>
<th>Infarct thickness (mm)</th>
<th>Infarct length (L) (mm)</th>
<th>Infarct circumference (% segmental)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Day 7</td>
<td>Baseline Day 7</td>
<td>Baseline Day 7</td>
<td>Baseline Day 7</td>
</tr>
<tr>
<td>Post MI</td>
<td>Control (N=128)</td>
<td>Control (N=57)</td>
<td>Control (N=57)</td>
</tr>
<tr>
<td></td>
<td>IVT (N=6)</td>
<td>IVT (N=3)</td>
<td>IVT (N=3)</td>
</tr>
<tr>
<td></td>
<td>Control (N=126)</td>
<td>Control (N=66)</td>
<td>Control (N=66)</td>
</tr>
<tr>
<td></td>
<td>IVT (N=6)</td>
<td>IVT (N=6)</td>
<td>IVT (N=6)</td>
</tr>
<tr>
<td></td>
<td>Post MI</td>
<td>Post MI</td>
<td>Post MI</td>
</tr>
<tr>
<td></td>
<td>Control (N=37)</td>
<td>Control (N=17)</td>
<td>Control (N=17)</td>
</tr>
<tr>
<td></td>
<td>IVT (N=12)</td>
<td>IVT (N=6)</td>
<td>IVT (N=6)</td>
</tr>
</tbody>
</table>

Conclusions: Despite early revascularization strategies, poor ventricular (LV) remodeling and dysfunction after myocardial infarction (MI) remain of clinical significance. Intracoronary therapy (IPT) has been shown to limit infarct size and subsequent LV remodeling when applied during early reperfusion. Here we investigated the effects of chronic IPT on global and regional LV function and infarct composition in a preclinical porcine model of reperfused infarction.

Methods: Fourteen pigs underwent proximal LCx ligation for 2h followed by reperfusion to induce a transmural infarction, and were instrumented with a pacemaker connected to an epicardial LV lead positioned in the anterior peri-infarct zone. Three days later, LV function and infarct-size were assessed with 3.0 Tesla cardiac MRI and animals were stratified into Control therapy and IPT groups (after which all pigs survived). IPT consisted of LV pacing twice daily for 3 x 5 min separated by 5 min of normal sinus rhythm until 5 wk post-implantation, after which follow-up cardiac MRI was obtained and myofibroblasts were quantified in the infarct zone, using a smooth muscle actin staining.

Results: Although IPT had no significant effect on global LV remodeling or function (data not shown), or infarct mass, it markedly influenced infarct geometry (Table). Thus, in control pigs the reduction in infarct mass over time was principally due to infarct thinning. In contrast, in the IPT pigs it was principally due to decreases in circumference and longitudinal length (both p <0.05) with no significant change in infarct thickness. Subsequently, histological scoring of myofibroblast in the infarct zone revealed an increase in myofibroblasts in IPT animals (10.9±2.1%) compared to controls (5.4±1.6%, p<0.05).

Conclusions: IPT favorably modified infarct remodeling, likely by enhancing myofibroblast numbers in the infarct zone.
Gender differences in major bleeding with bivalirudin versus heparin during primary PCI in Acute Myocardial Infarction: results from the HORIZONS-AMI trial

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Purpose: Previous studies have shown that women are at increased bleeding risk post AMI and primary PCI. Bivalirudin (BIV) has been shown to reduce bleeding complications compared with heparin plus glycoprotein IIb/IIIa inhibitor (HEP + GPI). The purpose of this study was to examine the differential impact of BIV on short- and long-term outcomes (>1 year) in women vs. men.

Methods: We examined 3-year outcomes from the HORIZONS-AMI trial according to sex and assignment to BIV vs. HEP + GPI. We used Cox proportional-hazards methods with stepwise selection using entry and exit criteria of p < 0.1 to determine the independent predictors of major bleeding among women. Candidate variables tested were assignment to BIV vs. HEP + GPI, age, prior history of hypertension, history of smoking, prior MI, prior PCI, CABG, Killip class >1, baseline creatinine, creatinin, radial vs. femoral access, and symptom onset to balloon time.

Results: Women (n=842), as compared with men (n=2760), were significantly older and had higher prevalence of hypertension and hyperlipidemia but were less likely to have a prior history of MI, PCI, CABG or smoking (all p < 0.05). BIV was associated with reduced in-hospital and 30-day major bleeding in both men and women (all p < 0.05). At 3 years, men receiving BIV compared with HEP + GPI had reduced major bleeding (5.3% vs. 9.1%, p=0.0002), however the difference among women did not reach statistical significance (12.3% vs. 15.1%, p=0.16). After multivariable analysis, randomization to BIV vs. HEP + GPI showed a trend towards reduced major bleeding among women (Figure 1).

Conclusions: In the HORIZONS-AMI trial, BIV significantly reduced short-term bleeding in men and women, and 3-year bleeding in men. Among women, BIV was associated with a trend toward reduced 3-year bleeding.

ADVANCES IN NON-ST ELEVATION MYOCARDIAL INFARCTION ACUTE CORONARY SYNDROMES – DIAGNOSTICS AND TREATMENT

P5053

Prospective evaluation of the diagnostic accuracy of the novel ESC 2011 guidelines for rapid rule-out of NSTEMI using high sensitive cardiac troponin T

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Purpose: High-sensitive cardiac troponin (hs-cTn) assays have been shown to significantly improve the early diagnosis of acute myocardial infarction. The novel 2011 ESC guidelines for the management of acute coronary syndromes in patients with persistent ST-segment elevation contain for the first time a new fast track rule-out protocol including hs-cTn. We intended to verify the safety of this fast track protocol in our prospective study setting.

Methods: Out of our ongoing prospective international multicenter study 1871 consecutive patients who presented with symptoms suggestive of acute myocardial infarction and absence of significant ST-elevations in the ECG were included. The final diagnosis was adjudicated by two independent cardiologists using all available informations including high sensitive cardiac Troponin T (Roche). We examined the diagnostic accuracy of the novel ESC rapid rule-out protocol using the Roche high sensitive cardiac troponin T (hs-cTn) 99th percentile defined as 0.014 ng/l performed on blood samples obtained in the emergency department at presentation and after 3 hours according to the novel guidelines. All patients were divided in line with the ESC algorithm into the subgroups of late presenters with chest pain onset/maximum (CPM) ≥ 6 hours and early presenters with CPM < 6 hours. In the former group rapid rule-out was based on a single measurement using hs-cTnT, and in the latter group on two hs-cTnT values, at presentation and at 3 hours.

Results: Of all late presenters (n=619), 19% (n=117) received the final diagnosis of NSTEMI, compared to 17% (n=214) of early presenters (n=1256). Six late presenters and two early presenters with the final diagnosis of NSTEMI had hs-cTnT levels below the cutoff of 0.014 ng/l. The overall negative predictive value (NPV) applying only the hs-cTnT criteria was for CPM ≤ 6 h: 98.4% (95% CI 96.6 to 99.4%) and for CPM > 6 h: 99.4% (95% CI 97.9 to 99.9%). As such, none of the late presenters had a GRACE Score > 140 and two were not free of symptoms when the troponin became available after one hour, the NPV increased to 99.2%.

In this subgroup:

Conclusions: Using a high sensitive assay for troponin T, the novel ESC guidelines provide an effective way of rapid rule-out of NSTEMI with a very high how-ever not perfect negative predictive value. These results indicate some room for future improvement of the algorithm.
recommendations on secondary prevention (9 studies) and pharmacological interventions (29 studies) were based on the largest amount of non-gov't/industry-sponsored trials. This finding suggests that industry-sponsored trials. This finding suggests that industry-sponsored trials provide an important and positive impact on clinical guidelines in identifying many new strategies and treatments for ACS.

P5057
Role of active coronary vasoconstriction in patients with NSTEMI

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Objective: We designed a study to evaluate the role of coronary vasoconstriction in precipitating non-ST-elevation myocardial infarction in patients presenting at angiography with a significant coronary obstructive lesion. Methods: We enrolled consecutive patients admitted for non-ST-E, and presenting with a significant atherosclerotic obstruction of the culprit vessel at coronary angiography. A pressure/luminal wire (ComboWire, Volcano Therapeutics, Rancho Cordova, California) was advanced across the culprit lesion to measure FFR and intracoronary nitrates were administered to assess the dynamic component of the disease. Results: We included 25 consecutive pts (63±11 year old, 20 males). At quantitatively coronary angiography the diameter reduction of the culprit stenosis was 77±8% and the translesion pressure gradient of the culprit lesion was 30.4±5.4 mmHg. The Fractional Flow Reserve (FFR) was 0.63±0.13 and the Coronary Flow Reserve (CFR) was 2.26±1.3. Following intracoronary nitrates, the pressure gradient across the stenosis decreased to 14.0±5.8 mmHg (p=0.001), FFR improved to 0.82±0.11 (p=0.0001), and CFR was 2.52±1.2 (p=0.02). In 18 patients of the 25 (72%), FFR crossed the 0.75 threshold level and normalized after intracoronary administration of nitrates.

Figure 1. FFR in acute phase of NSTEMI

Conclusions: These data are consistent with the hypothesis that active vasoconstriction contributes to the coronary obstruction at the level of the culprit lesion in ACS (non-STEMI) patients.

P5059
Performance of high-sensitivity troponin T in the early diagnosis of non-ST-elevation myocardial infarction in elderly patients presenting to an emergency department

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Purpose: Age >65 years has been reported to be the dominant factor associated with elevated high-sensitivity troponin T (hs-cTnT) levels in emergency room (ER) patients. We hypothesized that a protocol implementing a serial hs-cTnT measurement on admission and after 3 hours - as proposed by the latest ESC guidelines - could be beneficial in the rule-out of non-ST-elevation myocardial infarction (NSTEMI) in the elderly. Therefore, we examined the accuracy of hs-cTnT for an early diagnosis of NSTEMI in elderly patients presenting to our ER.

Methods: During a 6-month period, we included all consecutive patients presenting to our hospital emergency department with an age ≥70 years. Patients with STElevation acute coronary syndrome (STEMI), hospital admission for acute coronary syndrome (ACS), heart surgery or percutaneous coronary intervention within 3 months prior to the index hospital stay were excluded. Measurement of hs-cTnT (Elecsys Troponin T high-sensitive, Mannheim, Germany) was performed in a blinded fashion on admission and after 3 hours. Echocardiography was used to rule in or rule out differential diagnosis in all patients. The final diagnosis was adjudicated by two independent cardiologists after reviewing all available medical records.

Results: Among 307 recruited patients (mean age 81±6 years), 206 (67%) patients had elevated hs-cTnT levels ≥0.014 μg/L. 45 (15%) of all patients had a NSTEMI and 161 (52%) were diagnosed as having a non-ACS-condition. The median time from symptom onset to admission was not significantly different in both groups (4.1 vs. 4.7 h, p=0.06). 36% of non-ACS-patients had heart failure, 20% rhythm disorders, 19% severe renal insufficiency, 11% hypertensive heart disease, 6% valve disease, 4% endo-myocardialis and 4% sepsis. Using hs-cTnT levels obtained at 3 hours after admission, the sensitivity was 93.6% and the negative predictive value was 97.1% to rule-out NSTEMI. The diagnostic performance for the absolute hs-cTnT concentration - as quantified by the area under the receiver operating characteristic curve (AUC) - significantly improved for serial measurements from 3 hours after admission (AUC 0.80 vs. 0.84, p=0.018). The diagnostic performance of absolute delta-changes tended to be better than relatives changes in the entire study population (AUC 0.58 vs. 0.53, p=0.054).

Conclusions: Many elderly patients presenting to the emergency department revealed elevated hs-cTnT mainly due to non-ACS conditions. In elderly patients, a serial measurement in hs-cTnT from admission to 3 hours after admission was beneficial for an early diagnosis of NSTEMI.

P5060
Direct comparison of absolute and relative changes in high-sensitive cardiac troponin I in the early diagnosis of AMI

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Background: The current guidelines for the diagnosis of acute myocardial infarction (AMI) require, especially in non-ST-elevation infarction, a rise and/or fall in the levels of cardiac troponin (cTn). We evaluated whether absolute or relative changes in high-sensitive cTn have a higher diagnostic accuracy. Methods: In a prospective, observational, multicenter study, we analysed the diagnostic performance of absolute and relative changes in high-sensitive cTn as measured with a novel pre-commercial prototype assay (Siemens: LioT 0.5ng/l, 99th percentile 9ng/l and <10% CV at 3ng/l) in 1127 patients presenting to the emergency department with symptoms suggestive of AMI. Blood samples were collected at presentation and after 1, 2, 3 and 6 hours in a blinded fashion. The final diagnosis was adjudicated by 2 independent cardiologists using all available information including hs-cTnT (Roche) levels.

Results: Baseline high-sensitive cTn levels were higher in patients with AMI (16.4% of the cohort) than in patients with other diagnosis of chest pain (p < 0.01).
Cardiac magnetic resonance tissue characterization in the acute and chronic phase of reperfused Non-ST elevation myocardial infarction

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Background: In ST elevation myocardial infarction cardiac magnetic resonance (CMR) tissue characterization has been described in details. However, little is known about the infarct area, microvascular obstruction (MVO), area at risk and papillary muscle involvement in the acute and chronic phase in non-ST elevation myocardial infarction (NSTEMI). Aim of our prospective study was to evaluate and compare tissue characteristics in the acute and chronic NSTEMI.

Methods: Forty NSTEMI patients who were revascularized within 48 hours after symptom onset were enrolled into the study. CMR at 1.5T (Philips Medical Systems) was performed within 3-5 days and 3 months after symptom start. Left ventricular volumes were calculated using a short axis cine stack. Area at risk was evaluated using a 3D T2-weighted sequence in the same contiguous short axis orientation. Ten minutes after application of 0.2 mmol/kg gadolinium-based contrast agent (Guerbet), a 3D late gadolinium enhancement (LGE) sequence in the same orientation for evaluation of infarct size, MVO and papillary muscle involvement.

Results: Median age of the patients was 62.5±12.9 years, N=9 (22.5%) were female. The area at risk as determined using a 2-standard deviation threshold was 29.1±20.4 g. LGE revealed a significantly larger infarct size in the acute in comparison to the chronic phase (22.5±17.7 vs. 15.9±13.9 g, p=0.0003). In 6 (15%) patients presence of papillary muscle involvement was detected which was associated with larger infarct size in comparison to patients without papillary muscle involvement (43.5±21.8 g vs. 18.6±13.7 g, p=0.0003). MVO could be visualized in 16 (40%) patients in the acute phase and 7 (17.5%) after 3 months. MVO was significantly reduced at follow-up in comparison to baseline (0.2±0.6 g vs. 1.3±2.3 g, p=0.05) and was associated with larger infarct size (30.1±22.1 g vs. 17.5±12.1 g, p=0.025). Infarct size negative correlated with increase of ejection fraction at follow-up (r=-0.56, p=0.0002).

Conclusion: CMR provides a lot of information about myocardial tissue characteristics in NSTEMI patients. MVO and papillary muscle involvement correlate with infarct size. Further studies are warranted to prove clinical significance of described characteristics.


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Purpose: The management of acute coronary syndromes (ACS) has changed over the last decade as new treatments have been introduced. We sought to find out how treatments have changed in the UK over the last decade and whether these reflect contemporary guidelines.

Methods: Patterns of treatment were identified for patients enrolled in three consecutive multicentre UK registries (mid-year of recruitment, number of patients; PRAXIS-UK (1998, n=939), PROMIS-UK (2004, n=911) and EQUIP-ACS (2008, n=935)). Our main outcomes of interest were patterns of treatment at discharge, rates of angiography and revascularisation.

Results: (N=5466, 64% years, diabetes ≤ 16%), and entry systolic blood pressure (≤ 144mmHg) were similar in all three registries. However the proportion of men and those with hypertension rose over time, while prior MI decreased. PRAXIS-UK had 16% normal ECGs and 19.4% ST depression while EQUIP had 23% and 24% respectively. Mean creatinine and troponin I levels were higher in PRAXIS-UK (0.29 g/l and 95 ng/l) compared with EQUIP-ACS (0.20 g/l and 68 ng/l) respectively (p<0.001).

Conclusion: A major increase in the use of evidence based treatments, measures to achieve glycaemic control and enter ST-segment elevation ACS have occurred in the UK mainly from 1998 to 2004 with modest changes from 2004 to 2008. The lack of change from 2004 to 2008 suggests that more needs to be done to ensure that ACS patients receive the best care in the UK.

Complementary intravenous Enoxaparin during percutaneous coronary interventions and NSTE-ACS. Is it necessary?


Objectives: To assess the incidence of thrombotic complications during percutaneous coronary intervention (PCI) in patients (p) with non ST elevation acute coronary syndrome (NSTEACS) pretreated with subcutaneous (sc) enoxaparin (ENX) with two different anticoagulation strategies.

Methods and Results: We analyzed two retrospective cohorts of patients with NSTEACS pretreated with sc ENX 1mg/kg and PCI performed within 8 hours after the last dose of ENX. Cohort 1 (C1) includes 48p with additional doses of ENX during PCI from 05/2009 to 12/2010. Cohort 2 (C2) includes 41p with additional doses of ENX at the beginning of PCI from 01/2011 to 01/2012. We evaluated baseline, (10 minutes and 2 hours after iv ENX) activated clotting time (ACT) and antiXa activity (antiXa). Thrombosis was defined as the detection of angiographically visible thrombus not present previously or macroscopic thrombus observed in the material in contact with the blood (guiding catheter or angioplasty guidewires) during the procedure that required specific treatment. The primary endpoint was the incidence of thrombosis (including cathethers). Secondary endpoints were: incidence of bleeding complications, in-hospital and 30 days death and non fatal acute myocardial infarction (AMI). Both groups had comparable baseline characteristics. There were no differences in baseline of ACT or antiXa. The incidence of thrombosis was 37.5% (18/48p) in C1 versus 2.4% (1/41p) in C2 (p=0.007; OR 0.058). There were no bleeding complications in either group nor any differences in mortality (2.2% C1 versus 2.4% C2) or AMI (2.2% C1 vs 0% C2) at 30 days. There was a greater need for additional doses of unfractionated heparin and/or ENX during PCI in C1 (31% C1 versus 2.4%,C1). In C2 antiXa level 10 minutes after bolus administration was 145±0.55 and 2 hours after was 1.13±0.40. In C2 ACT level 10 minutes after bolus administration was 189±49 sec. In the multivariate analysis, the administration of bolus of ENX (p=0.011; OR 0.019) showed a protective effect while the total duration of the procedure (p=0.014; OR 1.034) was related to thrombotic complications.

Conclusion: A high incidence of thrombotic complications occurs during PCI performed within 8 hours after the last dose of sc ENX in patients with NSTEACS. The intravenous administration of an additional ENX bolus of 0.75mg/kg at the beginning of the PCI significantly reduces the incidence of such complications while AntiXa levels observed after this extra bolus are within the safety range reported in previous studies.

Early diagnosis of acute myocardial infarction in patients with kidney disease using more sensitive cardiac troponin assays

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Purpose: The rapid and reliable diagnosis of acute myocardial infarction (AMI) is a major unmet clinical need, particularly in patients with kidney disease (KD), who are known to have elevated levels of cardiac troponins (cTn) already in the absence of AMI, which may lead to a lower diagnostic value of cTn in this high-risk subgroup.

Methods: We conducted an international multicenter study to examine the diagnostic accuracy of new, more sensitive cTn assays in 1291 consecutive patients presenting to the ED with symptoms suggestive of AMI, of whom 186 (14%) were determined to have KD (MDRD GFR <60ml/min/1.73m2). cTn levels were determined in a blinded fashion using three sensitive assays (Roche high-sensitive Troponin T (hs-TnT), Siemens Troponin I Ultra (Tnl Ultra), Abbott-Architect Troponin I (Tnl Abbott)) and a standard assay (Roche Troponin T (TnT)).

Results: The final diagnosis was adjudicated by two independent cardiologists based on hs-TnT.

Results: AMI was the final diagnosis in 33% (n=61) of all KD-patients as compared to 17% in patients with normal kidney function (p<0.001). Among KD-patients, hs-TnT levels were in all patients who had the 99th percentile with hs-TnT in 67%, with Tnl-Ultra in 16% and Tnl Abbott in 12%. In patients with KD the diagnostic accuracy at presentation, quantified by the area under the receiver-operator-characteristic curve (AUC), was significantly
greater for the sensitive cTn-assays compared to the standard assay (AUC for hs-TnT, 0.88; TnI Ultra, 0.89; and TnI Abbott, 0.89 vs. AUC for the standard assay, 0.83, p=0.05 for all comparisons). In patients presenting within three hours after the onset of chest pain, TnI Ultra (AUC 0.90) and TnI Abbott (AUC 0.93) were superior to hs-TnT (AUC 0.82, p=0.05 and p=0.015 for comparisons, respectively) and TnT4 (AUC 0.73, p=0.01 for both comparisons), whereas hs-TnT no longer performed superior to TnT4 (p=0.07). Using the predefined 99th-percentile cutoff of the sensitive cTn-assays, specificity and diagnostic accuracy was significantly reduced in KD-patients compared to the subgroup with normal kidney function, whereas sensitivity remained similar.

Conclusions: Sensitive cTn-assays have high diagnostic accuracy also in KD and are superior to conventional cTn-assays. In addition, there seems to be a difference among the sensitive assays in the early presenters with a higher diagnostic accuracy of TnI Ultra and TnI Abbott as compared to hs-TnT. Mid elevations are common in non-AMI patients and test-specific optimal cut-off-levels tend to be higher in KD-patients than in patients with normal kidney function.

Use of troponin testing in internal emergency medicine

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Purpose: Troponin is recommended as the preferred biomarker for the diagnosis and risk stratification of non-ST myocardial infarction (NSTEMI). Per definition, the diagnosis AMI requires not only a positive test result but also corresponding signs and symptoms. We analyzed the association of chief complaint, cardiac main hospital diagnoses and troponin testing in two large EDs over one-year period to evaluate its use in Emergency Medicine.

Methods: Data of all 34,333 patients who presented to either one of the two EDs were retrieved from the hospital information system. The patient’s chief complaint was documented in the electronic ED form by the treating physician.

Results: Troponin testing was performed in 38.1% (n=13071) of all patients. Of these, 23.3% presented with chest pain, 10.4% with dyspnoea, 5.8% with abdominal pain, 3.3% with headache. The vast majority (57.1%) presented without one of these pre-specified chief complaints.

Of all patient tested, 10.4% had a positive test result at admission, of these 24.6% with chest pain, 22.1% with dyspnoea, 2.5% with abdominal pain, 0.6% with headache and 50.2% with none of these symptoms. Even though 52.3% had a cardiac main hospital diagnosis, only 4.6% were diagnosed with a NSTEMI and -22% with STEMI presented without known coronary artery disease, inconclusive ECG and Troponin T < 0.03 μg/L. GLS was -1.5±3% in those with high-grade stenosis (n=22) and -2.2±2% in those without high-grade stenosis (n=19). In a receiver-operator characteristic curve analysis, GLS (AUC=0.90) was significantly better than both WMSI (AUC=0.72) and EF (AUC=0.65) at discriminating between no high-grade and high-grade coronary artery stenosis (p=0.01). A GLS of < -20% excluded high-grade coronary artery arteriopathy with 90% sensitivity and 96% specificity.

Conclusions: Myocardial strain by echocardiography is an accurate and easily available tool to exclude high-grade coronary artery stenosis among patients with suspected NSTEMI-ACS with inconclusive ECG and normal cardiac biomarkers.

The diagnostic accuracy of novel biomarkers of myocardial injury in the unselected emergency room population

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Objective: To examine the diagnostic accuracy of novel biomarkers of myocardial injury compared to highly sensitive troponin assays for the diagnosis of myocardial infarction using the universal definition of myocardial infarction.

Methods: The study was a sub study of the point of care arm of the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers), set in the emergency departments of six hospitals. Prospective admissions with chest pain and a non-diagnostic echocardiogram were randomised to point of care assessment or conventional management. Blood samples were taken on admission and 90 minutes from admission for measurement of a panel of cardiac markers. An additional blood sample was taken at admission and 90 minutes from admission, separated and the serum stored frozen until subsequent analysis. Samples were analysed for high sensitivity cardiac troponin I (cTnI) by the Stratus CS (CS) for cardiac troponin T (cTnT) by the Roche high sensitivity cardiac troponin T assay, for heart fatty acid binding protein (HFABP) and copeptin. Diagnostic accuracy was compared by construction of receiver operator characteristic curves against the universal definition of myocardial infarction utilising laboratory measurements of cardiac troponin performed at the participating sites together with measurements performed in a core laboratory.

Results: Admission samples were available from 838/1132 patients enrolled in the study. There were 66 patients with a final diagnosis of myocardial infarction. Areas under the curve were as follows (confidence intervals in parentheses) cTnI CS 0.94 (0.90 - 0.98), cTnI T 0.92 (0.88 - 0.96), FABP 1.04 (0.77 - 0.90) copeptin 0.62 (0.57 - 0.68).

Both HFABP and copeptin were diagnostically inferior to troponin. The combination of HFABP(at the 95th percentile) and either troponin (at the 99th percentile) increased diagnostic sensitivity, cTnI CS 0.794 (0.673-0.885) to cTnI CS + HFABP 0.921 (0.824-0.974), cTnI T 0.778 (0.655-0.873) to cTnI T + HFABP 0.857 (0.746-0.933) with a small loss in specificity, cTnI CS from 0.980 (0.967-0.989) to 0.923 (0.901-0.941) cTnI T from 0.962 (0.946-0.975) to 0.916 (0.894-0.935). Addition of Copeptin (from an optimised decision level) increased sensitivity for cTnI CS to 0.905 (0.804-0.964) but reduced specificity to 0.591 (0.555-0.626) and for cTnT to 0.841 (0.727-0.921) but reduced specificity to 0.596 (0.561-0.631). 

Conclusions: Additional measurement of copeptin is not useful in the chest pain population. Simultaneous measurement of HFABP improves sensitivity.
Reduction of medical consumption in low risk chest pain patients

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Background: Patients with chest pain are often admitted for clinical observation, and treated as ACS awaiting final diagnosis. Consequently, unnecessary diagnostics and treatment are common. The HEART score serves the making of a quick diagnosis and consists of five elements: History, ECG, Age, Risk factors and Troponin.

Methods: This study was performed in 260 patients in three hospitals in the Netherlands. These patients were participants of a prospective validation study of the HEART score in 2388 chest pain patients in the ED of ten hospitals. Numbers of hospitalization days, exercise tests, echocardiography and various other cardiac examinations were counted.

Results: Chest pain patients visiting the ED were classified as low-risk, based on the HEART score, in 102/260 (39.2%) of the cases. MACE did not occur in these 102 patients; the risk of MACE was 15/870 (1.7%) in the low HEART score group of the entire prospective study. Eighteen patients (17.6%) were hospitalized for a total of 28 days and additional cardiology work-up was done in 52 patients (51%). Numbers of examinations were: 27 (26.5%) exercise tests, 16 (15.7%) echocardiograms, 5 (5%) CT scans and 6 (5.9%) SPECT.

Conclusions: When a policy would be made to withhold redundant medicine in low-risk chest pain patients, with a HEART score ≤3, hospitalizations would be saved in one fifth and various examinations in half of the patients. Improved risk stratification in chest pain patients may result in a reduction of medical consumption.

Mitrail annular excursion in patients with suspected non-ST-elevation acute coronary syndrome can identify coronary occlusion and predict mortality

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Background: Many non-ST-elevation acute coronary syndrome (NSTE-ACS) patients have coronary occlusions but do not receive acute reperfusion therapy as the occlusion is not readily identified. Identification and closer follow-up of high risk patients may reduce mortality. Mitrail annular excursion (MAE) reflects the global longitudinal shortening deformation of the left ventricle (LV). We therefore hypothesized that MAE may differentiate between coronary occlusion and non-occlusion in NSTE-ACS patients, and predict mortality.

Methods: 167 patients were examined in relation to NSTE-ACS at two Scandinavian centers. 47 healthy individuals were used as controls. Tissue Doppler by echocardiography was performed before or at admission. MAE was defined as the change in mitral annular excursion (MMAX-MMIN) from at least 20 pulse beats. A median, MAE was measured in a newly developed software (Gripping Heart AB, Stockholm, Sweden). Mortality data was collected over a mean period of 1477 days.

Results: MAE was significantly reduced in NSTE-ACS patients as compared to healthy individuals (9.5±2.1mm vs. 13.1±2.0mm, p<0.001). In 10.9 mm identified the NSTE-ACS diagnosis with a sensitivity and specificity of 89% and 71%, respectively, area under curve (AUC) 0.89. In the NSTE-ACS population, 56 of 167 (34%) patients had coronary occlusions. MAE could differentiate between coronary artery occlusion (9.9±2.2mm) and non-occlusion (10.0±2.0mm, p<0.001), and MAE of 9.2 mm yielded sensitivity and specificity levels of 68% and 61% respectively, AUC 0.65. During follow up, 22 patients died. Cox regression model gave a hazard ratio for MAE of 1.52 (95% CI 1.24-1.92), p<0.001.

Risk stratification in non-ST-elevation Acute Coronary Syndromes: utility of both GRACE and CRUSADE models

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Background: According to ESC guidelines, patients (pts) presenting with non-ST-elevation acute coronary syndromes (NSTE-ACS) should have their prognosis and bleeding risk determined using established risk scores (RS), namely GRACE RS for in-hospital mortality and ischemic events and CRUSADE RS for bleeding. However, the clinical implications and utility of combining both risk scores is less well established.

Aim: Evaluate how risk stratification combining GRACE and CRUSADE performs in pts with NSTE-ACS

Methods: Analysed 1425 pts (66±13 years, 72% male) with NSTE-ACS and exclusively included in a nationwide registry. CRUSADE RS and CRUSADE RS at hospital admission were calculated for each patient and tested, respectively, for
predicting in-hospital death and major bleeding (defined using CRUSADE criteria). Pts were divided according to low, intermediate or high risk of fatal events, using GRACE RS (≤108, 109-140 or >140, respectively) and then stratified into low, intermediate or high risk of major bleeding, according to CRUSADE RS (≤31, 31-40 or >40, respectively). In-hospital pharmacological treatment, procedures and events were compared between groups.

Results: GRACE and CRUSADE had a good performance in predicting in-hospital death (AUC 0.880, p<0.001) and major bleeding (AUC 0.755, p<0.001), respectively. Only 53% of pts had a concordant risk by both RS (table). Stratification using CRUSADE was useful for identifying major bleeding risk across all categories of GRACE RS. Use of ib/ll inhibitors, fondaparinux and radial access for catheterization diminished with increasing bleeding risk (p<0.001).

Conclusion: Both GRACE and CRUSADE RS have good performance for predicting in-hospital death and major bleeding, respectively. Half of NSTE-ACS pts have a discordant fatal and bleeding risk. CRUSADE RS can be used for identifying pts at risk of bleeding events, independently of risk estimated with GRACE RS.

P5072 Rapid rule-out of NSTEMI by using a high sensitive prototype assay for troponin I: a prospective evaluation of the safety of the novel ESC 2011 guidelines

Purpose: High-sensitive cardiac troponin (hs-cTn) assays have been shown to significantly improve the early diagnosis of acute myocardial infarction. The novel 2011 ESC guidelines for the management of acute coronary syndromes in patients without persistent ST-segment elevation contain for the first time a new fast track rule-out protocol including hs-cTn. We intended to verify the safety of this fast track protocol in our prospective study setting.

Methods: Out of our ongoing prospective international multicenter study 1102 consecutive patients who presented with symptoms suggestive of acute myocardial infarction and absence of significant ST-elevation in the ECG were included. The final diagnosis was adjudicated by two independent cardiologists using all available informations including high sensitive cardiac Troponin T (Roche). We examined the diagnostic accuracy of the novel ESC rapid rule-out protocol using the pre-commercial Beckman Coulter high sensitive cardiac troponin I assay (hs-cTnI, 99th percentile defined as 9.2 ng/l) performed on blood samples obtained in the emergency department at presentation and after 3 hours according to the novel guidelines. All patients were divided in line with the ESC algorithm into the subgroups of late presenters with chest pain onset/maximum (CPM) ≥ 6 hours and early presenters with CPM < 6 hours. In the former group, rapid rule-out was based on a single measurement using hs-cTnI and in the latter group, on two hs-cTnI values, at presentation and at 3 hours.

Results: Of all late presenters (n=393), 17% (n=67) received the final diagnosis of NSTEMI, compared to 15% (n=104) of early presenters (n=709). Three late presenters and three early presenters with the final diagnosis of NSTEMI had hs-cTnI levels below the cutoff of 9.2 ng/l. The overall negative predictive value (NPV) applied only to the hs-cTnI criteria was for CPM ≥ 6 hours (97.5% (95% CI 96.3 to 99.7%)) and for CPM < 6 hours (98.7% (95% CI 96.3 to 99.7%)). All missed patients had a GRACE Score below 140. As two late and two early presenters were not free of symptoms at the point of time when the decisive troponin became available, the NPV increased to 99.6% in both subgroups.

Conclusions: Using a novel high sensitive prototype assay for troponin I, the 2011 ESC guidelines provide an effective way of rapid rule-out of NSTEMI with a very high however not perfect negative predictive value. (ClinicalTrials.gov number, NCT00470587)

P5073 The nature and clinical outcomes of total occlusion in non-ST elevation myocardial infarction; is it bad or good?
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Background and Objectives: Non-ST-elevation MI is a different disease entity from ST-elevation MI. While undergoing coronary angiography, there are lesions in NSTEMI with TIMI grade 0, showing near total occlusion. Our objectives are to get a knowledge in these situations.

Subjects and Methods: In 2011, 5694 patients were registered in COREA-AMI (Convergent Registry of athalic and chronic AMI university for AMI registry). 2324 patients were NSTEMI, and we divided these patients into two groups, based on TIMI flow. Occluded lesion was defined as a lesion with 100% stenosis, or TIMI flow 0.1, 1009 patients had occluded lesion, and 1315 patients had non-occluded lesion. We compared baseline characteristics, EC findings, in-hospital treatment, and long-term outcomes between patients with and without occluded culprit arteries.

Results: In baseline characteristics, initial creatine level, peak troponin before PCI, initial ejection fraction in echocardiography, total stent length, follow-up hsCRP showed significant difference between two groups. Also former as-pirin, statin, metformin use was different between two groups. Total occlusion in NSTEMI was frequent in left circumflex artery. Using multivariate cox-regression analysis, the hazard ratio for occluded infarct artery was 1.67 (95% confidence interval 1.30-2.10, p<0.001). Kaplan-Meier curve for median follow-up of 36months showed a significant difference between occluded and non-occluded lesion group.
all age groups. We investigate whether the impact of temporal advances in cardiac care for the elderly with AMI extend beyond the hospital stay.

Methods: A mixed-effects regression analysis of the Myocardial Ischaemia National Audit Project (MINAP) was performed stratified by STEMI/NSTEMI, sex, and age group on 30-day mortality and opportunity-based composite scores (OBCS) for aspirin, ACE-inhibitor, statin, β-blocker, and referral for cardiac rehabilitation for 475542 patients with AMI between 2004 and 2009 from 215 hospitals in England and Wales.

Results: From 2004 to 2009 30-day mortality rates (95% CI) decreased: STEMI: 2004/5: 12.0% (11.7 to 12.3%); 2006/7: 10.8 (10.6 to 11.1); 2008/9: 9.6 (9.4 to 9.9); NSTEMI: 2004/5:10.1 (9.9 to 10.3); 2006/7: 8.8% (8.6 to 9.0%); 2008/9: 7.8% (7.7 to 8.0%). The proportion of patients with AMI achieving an OBCS >80% increased over time. 2004/5: 84.0%, 2006/7: 90.0%, 2008/9: 93.2%, P<0.001. The proportion of patients achieving an OBCS >80% was lower in females than males (P<0.001), and decreased with increasing age group for STEMI (P<0.001) and NSTEMI (P<0.001). Of patients ≥80 years, only females with STEMI did not show a significant reduction in 30-day mortality risk. Male STEMI and NSTEMI demonstrated significant reductions in 30-day mortality risk, except STEMI aged <65 years. For females, the only group to demonstrate a significant reduction in 30-day mortality risk were those aged ≥80 years with NSTEMI.

Conclusions: In England and Wales, for patients hospitalized with AMI there are sex- and age-dependent differences in temporal improvements in 30-day mortality risk, as proportion of patients with an OBCS >80%. Compared with in-hospital mortality, equivalent temporal improvements in mortality do not appear to extend beyond the hospital stay for all groups of patients.

P5076 The rs12526453 polymorphism in intron of the PHACTR1 gene is associated with 5-year mortality of patients with ST-elevation myocardial infarction

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Purpose: The rs12526453 (C/G) is a single nucleotide polymorphism in intron of the PHACTR1 gene (phosphatase and actin regulator 1). It was shown to be associated with early-onset myocardial infarction in a genome-wide association study with cysteine as a risk allele (1). The mechanism, however, remains unknown. The aim of our study was to investigate the association of the polymorphism with 5-year overall mortality in patients with ST-elevation myocardial infarction (STEMI) treated invasively.

Methods: We included in our registry consecutive patients with STEMI treated with primary PCI who survived 48 hours from hospital admission. Genotyping was performed with a TaqMan SNP Genotyping Assay using the ABI 7500 Real Time PCR System (Applied Biosystems). The analyzed end-point was total 5-year mortality.

Results: The study group comprised 629 patients (mean age 62±12 years; 25% of females; n=157; TIMI 3 obtained in 93.1% of patients; n=586). The percentages of CC, CG and GG genotypes were 10% (n=63), 44.7% (n=261) and 45.3% (n=285), consecutively. No significant differences in clinical characteristics were found between the genotypes. The 5-year total mortality was 16.2% (n=103). There died 28.5% (n=18) of CC high-risk homozygotes, 16.4% (n=46) of heterozygotes and 13.3% (n=38) of GG homozygotes (Figure 1). The difference was statistically significant (p=0.009, log-rank test).

Figure 1. 5-year survival for specific genotypes

Conclusions: The CC genotype of the rs12526453 polymorphism in intron of the PHACTR1 gene is associated with increased 5-year mortality in patients with STEMI treated invasively.


P5077 High 3-year-mortality rates in females with newly diagnosed diabetes after acute STEMI and NSTEMI in clinical practice in Germany: results of the Sweetheart-registry

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Background: Many patients with coronary artery disease suffer from diabetes and/or its pre-states. Joint guidelines of the ESC and the EASO recommend testing for diabetes using OGTT in patients with established CAD and without previously known diabetes.

Methods: Since 2007, 2,767 consecutive patients with STEMI or NSTEMI were enrolled into the MI-registry SWEETHEART to identify abnormal glucose metabolism and to document acute treatment and outcome. In patients with previously unknown diabetes, oral glucose tolerance test (OGTT) was performed at day 4 after acute MI. We examined gender differences in the prevalence of abnormal glucose metabolism and the impact of newly diagnosed diabetes on 3-year-mortality of MI.

Results: Female patients with MI were older, less often had prior MI and prior PCI as compared to males. Female patients had a higher rate of known diabetes as well as a longer duration of diabetes at the time of MI. The prevalence of newly diagnosed impaired glucose metabolism was much higher in females than in males. In females, OGTT identified another 19.8% with manifest diabetes and 18.1% with impaired glucose tolerance (IGT)/impaired fasting glucose (IFG) as compared to 15.3% and 23.3% in males respectively. After 3 years of follow up, female patients with newly diagnosed diabetes had a 30.5% mortality similar to that of females with already known diabetes (30%).

Conclusion: Although the prevalence of known diabetes was already much higher in females, the rate of newly diagnosed diabetes was significantly increased in females as compared to males. Females with newly diagnosed diabetes had the same 3-year mortality as those high risk patients with MI and already known diabetes.

P5078 The clinical significance of right ventricular dysfunction with or without pulmonary hypertension after acute myocardial infarction

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Background: Right ventricular (RV) dysfunction may accompany inferior wall infarction and is not uncommon in patients with acute anterior infarction. Pulmonary hypertension (PH) may exacerbate RV dysfunction (RVD). However, with severe RVD, pulmonary arterial pressure may decrease as a consequence of low RV output. We sought to determine the prognostic implications of RVD in relation to PH in acute myocardial infarction (AMI).

Methods: Echocardiography was performed in 1054 patients with AMI. RV function was assessed both visually and by measuring the RV fractional area change (RV-FAC) and RVD (RV-FAC<35%). The primary end-point was all-cause mortality with a mean follow-up of 3 years.

Results: RV was present in 141 patients, with 91 (6.6%) and 50 (4.7%) patients with and without PH, respectively. Compared with patients with RVD without PH, patients with RVD and PH presented with higher Killip class (Killip class II or higher: 48% vs. 14%, P<0.01) and were more likely to have reduced left ventricular (LV) systolic function (LV ejection fraction<45%: 71% vs. 44%, P<0.01).
The results of a multivariable Cox regression model are shown in the Figure. Patients with RVD and normal pulmonary pressures had the highest adjusted risk for mortality.

Conclusion: Patients with RVD without PH are at a particularly high risk for mortality despite better LV systolic function. These results emphasize the importance of interpreting RV function in combination with pulmonary pressures data.

**P5079 One year outcome in HIV-infected patients with myocardial infarction**

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**Background:** Risk of myocardial infarction (MI) in HIV infected patients is increased and short term prognosis is good. One year outcome remain to be determined in large scale study.

**Methods:** From the French nationwide hospital medical information database, all the consecutive patients hospitalized in the 1546 French hospital/clinics for myocardial infarction from 1st January 2005 to 31st December 2009 were included. We compared one year outcome between patients infected or not by HIV.

**Results:** Among the 628454 patients included, 1286 (0.2%) was infected by HIV. At one year of follow-up, we observed an increased rate of recurrent MI in HIV-infected patients than non-infected patients (14.9% vs 12.9%; p=0.02) and respectively 14.9% vs 11.3% (p<0.01) in a sub-group of patients matched for age, sex and type of MI (ratio 1:2).

**Conclusion:** From our large scale nationwide study, HIV patients have an increased risk of recurrent MI during follow-up, thus emphasizing the benefit of secondary prevention in such patients.

**P5080 Accuracy of high-sensitive cardiac troponins for long-term mortality**

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**Background:** Several high-sensitive cardiac troponins (hs-cTn) have recently been introduced. It is unknown which hs-cTn is most accurate for long-term prognosis and whether early changes improve prognostic accuracy.

**Methods:** In a prospective, international multicenter study, hs-cTn was measured with three assays (hs-cTnT: Roche Diagnostics; hs-cTnI: Beckman-Coulter; hs-cTnI: Siemens) in a blinded fashion at presentation and 1 hour later in 849 unselected patients with acute chest pain. Patients were followed-up 2 years regarding mortality.

**Results:** Acute myocardial infarction was the adjudicated final diagnosis in 150 (17.7%) patients. 62 (7.3%) patients died during the first 2 years. The prognostic accuracy of hs-cTnT (Roche Diagnostics) at presentation for mortality in the first 2 years as quantified by the ROC curve (AUC) was 0.756 (95% CI 0.726-0.785) and outperformed both hs-cTnI (Beckman-Coulter) 0.704 (95% CI 0.672-0.734; p=0.029 for comparison) and hs-cTnI (Siemens) 0.687 (95% CI 0.653-0.718; p=0.010 for comparison) (Figure 1). Absolute changes in the first hour of hs-cTnT were more accurate than relative changes (AUC 0.660; 95% CI 0.627-0.692 vs. 0.512; 95% CI 0.477-0.546; p=0.035 for comparison) (Figure 2). Combining presentation values of hs-cTnT with the absolute changes in the first hour did not further improve their prognostic accuracy (AUC 0.747; 95% CI 0.717 to 0.776; p=0.064 for comparison). Similar results were obtained for both hs-cTnI assays regarding the incremental value of changes.

**Conclusion:** Hs-cTnT seems to be more accurate than hs-cTnI in the prediction of long-term mortality. Absolute changes outperformed relative changes in the first hour as to long-term mortality in all three hs-cTn assays but were inferior to respective presentation values.

**P5081 Large differences between patients with acute myocardial infarction included in two Swedish health registers**

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**Background:** Acute myocardial infarction (MI) is a leading cause for morbidity and mortality in Sweden. We aimed to compare patients with an acute MI included in the Register of information and knowledge about Swedish heart intensive care admissions (RIKS-HIA, now included in the register Swedeheart), and the Swedish statistics of acute myocardial infarctions (S-AMI).

**Methods:** Population based register study including RIKS-HIA, S-AMI, the National patient register and the Cause of death register. Odds ratios were determined by logistic regression analysis.

**Results:** From 2001 to 2007, 114 311 cases in RIKS-HIA and 198 693 cases in S-AMI were included with a discharge diagnosis of an acute MI. Linkage was possible for 110 958 cases. These cases were younger, more often males, had less concomitant diseases and were more often treated with invasive coronary artery procedures than patients included in S-AMI only. There were substantial regional differences in proportions of patients reported to RIKS-HIA.

**Conclusion:** Approximately half of all patients with an acute MI are included in RIKS-HIA. They represent a relatively more healthy population than patients included in S-AMI only. These limitations are important to know about since the register has become increasingly important in international research. S-AMI covers almost all patients with an acute MI but has limited information about the patients. Used in combination these two registers can give better prerequisites for improved quality of care of all patients with acute coronary syndromes.
Non-ST-segment elevation acute coronary syndrome caused by the left main stem stenosis - impact of multivessel diseases on treatment strategy and 12-month. Analysis from the PL-ACS Registry


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The aim was to improve the impact of multivessel disease on 12-month mortality in patients with NSTE-ACS caused by LM stenosis.

Methods: All patients with NSTE-ACS caused by LM stenosis registered in the PL-ACS between 10.2003 and 11.2009 were included. Patients were divided into 4 groups according to the number of significantly stenosed vessels:

1. LM + 2 Vessels
2. LM + 3 Vessels
3. LM + 4 Vessels
4. LM + 5 Vessels

Results (table): In PL-ACS Registry 1654 (2.5%) pts from 65767 had NSTE-ACS caused by LM stenosis. As the number of stenosed vessels increased the percentage of pts treated by PCI decreased and by CABG raised. In-hospital and 12-month mortalities increased together with the number of stenosed vessels. For diagnosis adjust the number of significantly stenosed vessels remains significantly associated with higher 12-month mortality (relative risk = 1.14, 95%CI = 1.01-1.29, p=0.038).

Conclusion: The implementation of this universal health plan in Chile was associated with an increase in 1-year survival in AMI patients. This has been achieved through a better use of evidence based medicine and reperfusion strategies. This effort has contributed to improving inequity in the health care attention of AMI patients.

P5084 Prognostic factors in chest pain patients: a quantitative analysis of the HEART score

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Purpose: Risk stratification for chest pain patients at the emergency department is recommended in several guidelines. The HEART score is based on medical literature and expert opinion and calculates the risk of a major adverse cardiac event (MACE). We aimed to assess the predictive effects of the five HEART components and to compare performance of the original HEART score with a model based on regression analysis.

Methods and results: We analyzed prospectively collected data from 2388 patients, of whom 407 (17%) had a MACE within 6 weeks (AMI, PCI, CABG, significant stenosis with conservative treatment and death due to any cause). Univariate regression analysis showed the same pattern of predictive values as used in the HEART score. An adjusted score was based on multivariable logistic regression analysis (HEART-adj), which showed slightly better calibration and discrimination than the HEART score (c-statistic HEART 0.83, HEART-adj 0.85). HEART-adj proved in a decision curve analysis to be clinically more useful than HEART for decision thresholds over 25% (figure 1). Nevertheless, the original HEART classified patients better than HEART-adj, when the previously defined thresholds of 25% and 40% were applied (NRI=14.1%).

P5085 Occurrence of major bleeding during long-term follow up of unselected patients with STE vs NSTE Acute Coronary Syndrome


Background: The occurrence of bleeding following ACS has been well described in clinical trials but little is known in the real world, especially in the long-term.

Purpose: To evaluate bleeding rates during long-term follow-up of a large, unselected ACS population with particular reference to comparison between STE and NSTE.

Methods: A retrospective cohort study was conducted of all AMI patients included in the Chilean Registry of Myocardial Infarction (REGMI Registry) in 6 public tertiary hospitals before (2001-2005) and after GES (2008-2009). We compared demographic and clinical characteristics, hospital treatments and revascularization procedures between the two periods. Multivariate Webull regression was used to evaluate the impact of GES in 1-year survival, adjusted for clinical and demographic characteristics.

Results: 1867 AMI patients (77.8%) were discharge alive before and 534 patients after the implementation of GES, respectively. 25% were women in both periods. There was a higher prevalence of hypertension and dyslipidemia after GES. After GES was observed an increase in the use of beta-blocker (56% vs 44%; p<0.001) and an increase in the indication of primary angioplasty (2% vs 3%; p<0.001), as well as in the use of elective angioplasty. The use of pharmacological treatment at discharge increase also significantly (beta-blocker 62% to 71%; Statins 40% to 90%; p<0.001 for both). 1-year survival rate increase from 90% to 94% (hazard ratio = 0.66; IC 95% 0.46-0.96). After multivariate adjust ment for differences in baseline clinical characteristics, GES was associated with a lower 1-year mortality (hazard ratio = 0.63; IC 0.43-0.95).

Conclusion: The implementation of this universal health plan in Chile was associated with an increase in 1-year survival in AMI patients. This has been achieved through a better use of evidence based medicine and reperfusion strategies. This effort has contributed to improving inequity in the health care attention of AMI patients.

Figure 1
Early mortality of acute coronary syndromes (ACS) has vastly declined thanks to interventional and pharmacological therapy. However there is growing evidence of high events in the long run, but data are mainly derived from large clinical trials. Studies addressing long term follow up of unselected patients with ACS are few and led to conflicting results.

Purpose: To compare 5-year outcome of unselected patients with STE versus NSTE ACS in a real world context of contemporary acute treatment and secondary prevention.

Methods: All consecutive patients with ACS admitted in 2004-2005 were enrolled. The main study endpoint was 5-year mortality. The Kaplan Meyer method was used to analyze the occurrence of death. A landmark analysis was performed: 0-30 days, 30 days-1 year and from 1 year to 5 years.

Results: 2046 patients were enrolled (896 STE,1150 NSTE). Patients in the former group were younger, had fewer comorbidities and more often received anti-thrombotic drugs/PCI. Of note, almost 70% of NSTE patients were managed conservatively: 0-30 days, 30 days-1 year and from 1 year to 5 years.

Conclusion: Despite the extensive use of antithrombotic therapies and PCI, the rates of in-hospital MB are acceptably low in the real world and similar to those reported for trials of ACS. On the contrary occurrence of MB is still high in the long run and greater than shown in trials.

P5087 High rate of bleeding complications in a real-life Swedish population with ACS

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Purpose: Early revascularization and aggressive antplatelet therapy in patients with acute coronary syndromes (ACS) has significantly reduced death and ischemic complications. However, bleeding complications has recently been shown to increase both mortality and ischemic complications during long-term follow up. Incidence of bleeding complications in a Swedish cohort of patients with ACS is not known. The aim of this study was to determine the incidence, severity and type of bleeding after ACS. Secondary endpoints were death, myocardial infarction or stroke associated with bleeding complications.

Methods: A review of medical records for 402 consecutive patients treated for ACS in the county of Östergötland, Sweden during 2010 was performed. Incidences of in-hospital bleedings and bleedings within 1 year after discharge were determined. Differences in bleeding complications between men and women were assessed.

Results: In total 107 individuals developed non-surgery or surgery related bleeding (26.6%; n=402). Forty two (10.4%) developed in-hospital non-surgery related bleeding and forty two (10.4%) developed non-surgery related bleeding within 1 year after discharge. There were 7 (2.2%) TIMI major bleedings (9.5%) TIMI minor and 61 (15.2%) TIMI minimal non-surgery related bleedings. Most bleedings were due to gastrointestinal (GI) bleeding, 45.2% of the in-hospital bleedings and 54.8% of the follow up bleedings. Significantly more women developed GI bleedings (9.8% vs. 3.7%; P=0.013) during follow up. Otherwise no gender differences in bleeding incidence were found. No increased risk of mortality or ischemic events during follow up was found in patients who developed bleeding complications.

Conclusion: In a Swedish real life ACS population we found a substantial amount of bleeding complications during one year follow up. The majority of the non-surgery related bleedings were gastrointestinal and potentially preventable. In this relatively small cohort we could not verify earlier reported mortality risk associated with bleeding complications.

P5088 Impact of contrast-induced nephropathy on long-term cardiovascular events in acute coronary syndrome patients with Chronic Kidney Disease: results from icas registry

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Background: Chronic kidney disease (CKD) is associated with the increase of the risk of the cardiovascular event. However, the association of contrast-induced nephropathy (CIN) and chronic kidney disease (CKD) in patients with acute coronary syndrome (ACS) treated with percutaneous coronary intervention (PCI) has not been fully reported. We evaluated the impact of CIN on cardiovascular events in ACS patients with CKD.

Methods: A total of 1059 ACS patients who underwent emergent PCI in Ibaraki Cardiovascular Assessment Study (ICAS) multi-center registry who were enrolled (69±12 yrs, 804 men, STEMI 604 patients). CIN was defined as an increase of ≥0.5mg/dl or ≥25% in pre-PCI serum creatinine in the week after the procedure. CKD was defined as estimated glomerular filtration rate <60ml/min/1.73m². Primary endpoints were defined as cardiovascular death, myocardial infarction, and cerebrovascular disorders.

Result: In our study, 368 (34.7%) patients had CKD. During follow-up periods (435±330 days), CIN was occurred in 164 patients (15.5%) and primary endpoints were occurred in 106 patients (10.0%). Multivariate Cox proportional-hazards model revealed that CIN and CKD were independent predictor of primary endpoints (hazard ratio 2.759; 95% confidence interval, 1.823 to 4.175; p=0.0001), (hazard ratio 1.689; 95% confidence interval, 1.101 to 2.591; p=0.0164). Kaplan-Meier analysis showed that primary endpoints were significantly increased with an increasing CKD stages and presence of CIN (p=0.0001) (figure).

Conclusion: Our long-term follow up study revealed that CIN was incremental significant predictor of cardiovascular events in ACS patients with CKD.
Pathological Q-wave development in myocardial infarction in patients treated by primary percutaneous coronary intervention

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Background: The criteria for pathological Q-waves after acute myocardial infarction (MI) have changed in recent years. Also, there is limited data regarding correlation of Q-wave regression and preservation of left ventricular fraction (LVEF) in patients with an initial Q-wave MI.

Methods: Standard 12 lead electrocardiogram (ECG) was recorded in 200 ST-elevated myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention. ECGs were recorded before and following PCI, as well as at 1, 4, 12 and 24 months of follow-up. Cardiac magnetic resonance imaging (CMR) examination was performed at 4±2 days after reperfusion and repeated after 4 and 24 months.

Results: The incidence of Q-wave MI according to the 2007 criteria was 58%, 1 hour after PCI. At 24 months of follow-up, 22% of patients with initial Q-wave MI displayed Q-wave regression. The “classic” ECG criteria showed strongest correlation with infarct size as measured by CMR. Patients with Q-wave MI had larger infarct size and lower LVEF on baseline CMR respectively (24±10% LV mass and 37±8% vs 24±9% LV mass and 45±6%, p<0.001). Patients with Q-wave regression displayed significantly larger LVEF improvement in 24 months (9±11%) as compared to both Q-wave MI (2±8%) as well as non-Q-wave MI (3±8%, p=0.04 for both comparisons).

Conclusion: Association of Q-waves with infarct size and LVEF is strongest when using the “classic” Q-wave criteria. Q-wave regression is associated with the largest improvement of LVEF over a 2 year follow-up.

Long-term prognosis estimation after acute coronary syndrome: is there a role for angiographic scores?

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Background: Angiographic scores are useful tools to assess the severity of coronary lesions and can provide prognostic information. We aimed to explore the association of Leaman Score (LS) and Duke Jeopardy Score (DJS) with 10-year mortality in patients (Pts) with acute coronary syndrome (ACS).

Methods: Retrospective analysis of consecutive Pts with ACS submitted to coronary angiography. Extension of coronary disease was calculated using LS and DJS. ROC curves were performed to test sensitivity and specificity of the scores for the prediction of 10-year mortality. The area under the curve (AUC) and the AUC for LS was 0.61 (IC) and for DJS 0.58 (IC) with cut-off points of 2.0 and 4.0, respectively. Pts with LS and DJS over the cut-off displayed significant increase in mortality. A multivariable Cox regression analysis was performed to test the independent association of scores with mortality. Rates of severe bleedings were low, but higher in women (Table 1).

Results: Of the 662 Pts included (mean age 62±11 years, 80% male), 151 (22.8%) died. The mean values were 3.9±3.0 for LS and 2.6±2.0 for DJS. The AUC for LS was 0.61 (IC) and for DJS 0.58 (IC) with cut-off points of 2.0 and 4.0, respectively. Pts with LS and DJS over the cut-off presented significant increase in 10-year mortality, compared with Pts under the cut-off (Figure). Multivariable analysis revealed an independent association of LS with 10-year mortality (HR 1.06, 95% CI 1.01-1.12; p=0.018), not shown by the DJS (HR 1.03, 95%CI 0.92-1.14; p=0.65).

Conclusions: In this population of patients with ACS submitted to coronary angiography, both scores were associated with 10-year mortality in univariate analysis but only the Leaman score was an independent predictor of long-term mortality.

Bleeding complications in patients with acute myocardial infarction. A gender perspective

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Purpose: During last years bleeding complications associated with acute myocardial infarction (AMI) has gained increased attention. Many, but not all, studies have shown a higher incidence in women. Furthermore bleedings has been shown to have a large impact on outcome. Whether there are gender differences in consequence of a bleeding complication is not well known.

Methods: From the Swedish national quality register, SWEDHEART, we included 97862 cases diagnosed with AMI (35747 women and 62115 men). Between the year 2003 and 2009 with one year follow up. Major bleeding was defined as fatal, intracranial or Hemoglobin decrease with ≥50 g/L. Non-major bleeding was defined as a bleeding requiring transfusion or surgical intervention. We used chi square test and students t-test for statistical analyses with a significance level of p<0.05.

Results: Women were older (75 vs 69) and had more diabetes and hypertension, while men were more likely to be smokers or to have previous kidney disease. Men had more AMI in the history and also significantly more revascularization with either PCI or CABG.

Rates of severe bleedings were low, but higher in women (Table 1).

Table 1. Incidence of severe bleeding during hospital stay

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<th>Men</th>
<th>Women</th>
<th>P-value</th>
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<tr>
<td>No bleeding</td>
<td>98.3%</td>
<td>97.2%</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.3%</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Non-major bleeding</td>
<td>1.4%</td>
<td>2.3%</td>
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Non-bleeding women had significantly higher mortality than non-bleeding men, both short- and long-term mortality, 7.7 vs 5.2% (p<0.001) in 14 d and 19.9 vs 13.9% (p<0.001) in one y. Major bleeding had a high impact on outcome in both women and men regarding mortality at 14d (36.6 vs 42.9%, p=0.211) and 1y (46.2 vs 53.9%, p=0.921) but without difference between the genders. In patients with a bleeding complication requiring transfusion or surgery there was an indication of higher mortality in men at 14 d (11.4 vs 8.2, p=0.03) and at 1y (28.5 vs 24.6 p<0.01).
Conclusion: The major finding of this study is that women with AMI have a higher rate of bleeding complications than men. Even though women have an overall higher short- and long-term mortality, among bleeding patients there is no difference between the genders or even higher mortality in men. Consequently, the prognostic impact of a bleeding complication appears higher in men.

Copeptin predicts long-term mortality in patients with non-st-elevation myocardial infarction

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Purpose: Copeptin has been shown to improve diagnostic sensitivity when used in combination with conventional measured cardiac troponin T (cTnT) in patients with suspected acute coronary syndrome (ACS). However, less is known about the predictive value of differences in patients with and without acute myocardial infarction. Therefore, in the present study we aimed to analyse the possible predictive value of copeptin in patients with Non-ST-Elevation myocardial infarction (NSTEMI) and unstable angina (UA).

Methods: 321 patients with suspected Non-ST-Elevation ACS (NSTEMI)-ACS were included in the study. Final diagnosis of NSTEMI was made in 201 patients (62.6%), 67 patients (21.2%) had unstable angina pectoris (UA). The remaining 53 patients (16.2%) were without coronary artery disease (CAD) documented by coronary angiography. Copeptin was measured on admission. Blood was taken immediately after admission and was sent to the laboratory for centrifugation and frozen stored at −80°C until assayed.

Results: Copeptin plasma levels were higher in patients with NSTEMI compared to patients with UA (14.0 pmol/ml). There was no difference in copeptin plasma concentrations in patients with UA compared to patients without documented CAD (17.2 pmol/ml IDR [10.7;34.4] vs. 17.3 pmol/ml IDR [8.3;31.7]; p=0.08). During 5-year follow-up 29 (14.4%) patients with NSTEMI and 6 (5.9%) patients with UA and 3 (9.0%) patients without CAD died. The mortality rate among patients with NSTEMI and copeptin plasma concentration ≥14.0 pmol/ml was higher during 5-year follow-up (LogRank 12.1; P=0.001; multivariate Cox-Rossregression 95% CI 1.003-1.023; P=0.01). Excluding patients with NSTEMI from the analyses mortality did not differ in patients with copeptin plasma concentration ≥14.0 pmol/ml compared to patients with copeptin levels <14.0 pmol/ml.

Conclusion: Copeptin has a predictive value for long-term mortality in patients with NSTEMI. However, this difference is restricted to patients with NSTEMI.
were significantly predictive of future MACE. Only Mon2 counts were an independent predictor of MACE after adjusting for age and sex (Table 1).

Table 1. Predictive value of monocytes in MACE

| Monocyte Type | Odd Ratio (95% confidence interval) | p-
<table>
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<tbody>
<tr>
<td>Total Monocytes (μl/μl)</td>
<td>1.002 (1.000–1.004)</td>
<td>0.032</td>
</tr>
<tr>
<td>Mon1</td>
<td>1.001 (0.998–1.003)</td>
<td>0.111</td>
</tr>
<tr>
<td>Mon2</td>
<td>1.008 (1.003–1.013)</td>
<td>0.047</td>
</tr>
<tr>
<td>Mon3</td>
<td>1.01 (0.999–1.022)</td>
<td>0.368</td>
</tr>
</tbody>
</table>

Conclusion: Increased total monocyte and Mon 2 counts in the first 24 hours post infarction are predictive of MACE in STEMI patients. Mon 3, despite an assumed role in reparation and fibroblast deposition, was not predictive of MACE in post-STEMI patients. This suggests a specific role for Mon2 monocyte subset in post-infarct recovery in STEMI, and a potential role of this subset as a future therapeutic target. Remodelling data from cardiac magnetic resonance is awaited.

**P5096**

Prediction of late mortality after myocardial infarction by means of the GRACE Score in contemporarily treated patients

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Background: The GRACE Score (GS) was proposed for prediction of early and late mortality risk in acute coronary syndrome (ACS) patients. The GS includes age, history of congestive heart failure and previous myocardial infarction, heart rate, systolic blood pressure and presence of ST-segment depression at admission, and serum creatinine, cardiac enzymes and percutaneous coronary inter- vention (PCI) during hospitalization. GS was developed and validated in patient with ACS collected in a multinational registry between 1999 and 2003. Less than one third of the registry patients were treated with PCI. Aim of this study was to investigate the predictive power of the GS in contemporarily treated post-infarction patients.

Methods: 941 consecutive AMI patients aged <81 yrs were included. 93% underwent a PCI, 95% received beta-blockers, 94% ACE inhibitors and 93% statins. The GS was calculated according to the published protocol. Uni- and multivariable analyses were performed with traditional risk stratiﬁers like LVEF <35%, and dia- betes mellitus Follow-up was up to 5 years. Primary endpoint was total mortality. Follow-up was 5 years. Primary endpoint was total mortality.

Results: During follow-up, 72 patients (7.7%) died. The GS shows the strongest association with mortality in the uni- and multivariable analysis followed by reduced LVEF and Diabetes mellitus (see table). By analyzing the different components of the GS in a multivariable analysis, only age, serum creatinine and history of previous myocardial infarction were independent and significantly associated with mortality (HR CI) 1.59 (1.06 – 1.12); 1.82 (1.42 – 2.34); 2.01 (1.12 – 3.63)).

Conclusion: The GS is a strong risk predictor of 5-year mortality after acute myocardial infarction in a contemporary treated patient population and independent of reduced LVEF and diabetes mellitus. Age, serum creatinine and history of prior myocardial infarction carried the most predictive information of the GRACE score.

**P5097**

Clinical outcomes after percutaneous or surgical revascularization of unprotected left main coronary artery related myocardial infarction: a single-center experience

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Purpose: Unprotected left main coronary artery (ULMCA) related acute myocardial infarctions (AMI) are clinically catastrophic events. Due to the rarity of these events, only limited clinical data is available. Therefore, we evaluated 30-day and 1-year clinical outcomes after percutaneous or surgical coronary revascularization in these patients.

Methods: Between January 1998 and December 2008, 87 patients with ULMCA related AMI have undergone revascularization treatment in our institution (57 with PCI, 30 with CABG). Clinical follow-up was obtained retrospectively by means of the GRACE Score in contemporarily treated post-infarction patients. This is the first study to report ULMCA related AMI data including both PCI and CABG treated patients.

Results: 30-day mortality rate was 51%: 64% in the PCI group and 24% in the CABG group. One-year mortality rate was 54% (69% PCI; 24% CABG, figure 1). Major adverse cardiac and cerebrovascular event (MACE) rates were 58% (30-day) and 84% (1-year). Diabetes mellitus (HR 2.9, 95% CI 1.3–6.3, p=0.009) and TIMI 0 flow (HR 3.1, 95% CI 1.2–8.3, p=0.017) were independent predictors for 30-day mortality. Angiographic characteristics were independent predictors for revascularization treatment: TIMI 0 flow strongly predicted performing PCI, and distal (bila) vein LM lesion predicted performing CABG.

Conclusions: This is the first study to report ULMA related AMI data including both PCI and CABG treated patients. Clinical outcomes of these rare patients, most likely due to selection bias. This is demonstrated by TIMI 0 flow and distal LM disease to be independent predictors for treatment choice.
Probable effects of obstructive sleep apnea on plaque vulnerability and progression of atherosclerosis in patients with acute myocardial infarction

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Aims: Impact of OSA on the clinical and angiographic follow-up outcomes in patients undergoing primary percutaneous coronary intervention (PPCI) has not been fully elucidated. We hypothesized that OSA may contribute to plaque vulnerability and cause adverse cardiovascular outcomes in patients who experienced acute myocardial infarction (AMI).

Methods: This study included a total of 272 patients with AMI who underwent PPCI. Polysomnography at first admission determined 124 patients with OSA defined as apnea-hypopnea index ≥ 15 events/h. Clinical outcomes measured were cardiac death, recurrence of acute coronary syndrome (ACS), and re-admission for heart failure. Major adverse cardiac events (MACE) were defined as composite end points of individual clinical outcomes. Follow-up angiography was performed in 222 patients. Intervention measures were target lesion recanalization (TLR) and newly necessitated PCI (new PCI) owing to disease progression.

Results: A mean follow-up duration was 4.0±1.7 years. Patients with OSA had more experienced the recurrence of ACS and MACE than control patients (17.6% vs. 6.6%, p=0.010; 21.8% vs. 10.8%, p=0.014). TLR was not different between the groups. In contrast, new PCI was significantly higher in OSA patients than in controls (28.4% vs. 14.8%, p=0.012). Cox regression hazard model showed that the OSA was an independent predictor for recurrence of ACS and MACE (hazard ratio=1.98, p=0.027). Logistic regression analysis adjusting for OSA and other known risk factors identified that only OSA was positively correlated with new PCI (odds ratio=2.23, p=0.021). Treatment with continuous positive airway pressure could not improve the outcomes.

Conclusions: OSA may be related to plaque vulnerability and a risk factor for progression of coronary atherosclerosis.

Prognostic impact of plasma aldosterone levels on long term outcome after myocardial infarction

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Background: It was reported higher aldosterone (ALD) levels were predictors of mortality risk in patients with heart failure or myocardial infarction (MI). The prognostic significance of ALD in the Japanese patients with acute myocardial infarction remains unknown.

Methods: Baseline plasma ALD levels were quantified in a prospective cohort study of 214 consecutive Japanese patients with acute MI (170 men, 44 women, age 67.8±12.6) to determine if there was an association of ALD levels and long term cardiac events. The subjects were divided into two groups of elevated ALD group (group H) and non-elevated ALD group (group L) according to the median value of baseline plasma ALD for data analysis. The primary end point of the study was cardiac death. The secondary end point was left ventricular ejection fraction (LVEF) at 6-month follow-up. Heart failure required hospitalization and all cause death.

Results: The median value of baseline ALD was 104.5 pg/ml in all patients. During a median follow-up of 1194 days, cardiac death occurred in 15 patients (7.0%). Twenty two patients (11.7%) experienced the failure. All cause mortality was 9.8%. Patients of group H (N=107) with higher ALD had a significantly higher incidence of cardiac death, as compared to those of group L (N=107) with lower ALD (12.2% vs. 1.9%, P=0.0489). The LVEF at 6-month follow-up of group H was significantly lower than those of group L (55.2% vs. 64.3%, P=0.0001). The incidence of hospitalization due to heart failure tended to be higher in the group H than in the group L (18.7% vs. 4.7%, P=0.0357). Higher ALD were independent predictors of increased cardiac mortality in Cox regression analysis adjusted for age, sex, body mass index, LVEF, brain natriuretic peptide and medication at acute phase (adjusted hazard ratio=1.13 (95% CI 1.07-1.19), P=0.0009).

Conclusion: Among Japanese patients with MI, higher ALD were associated with long term left ventricular remodeling. Elevated ALD levels at acute phase were independent predictor of cardiac mortality.
Baseline hypercalcaemia in acute coronary syndrome patients: a five-year outcome study


Background: Serum calcium level has been associated with ischaemic myocardial disease but its role as a predictor of outcome in patients with acute coronary syndromes (ACS) was not determined. The aim of this study was to assess the role of admission calciumaemia in predicting also to, among ACS patients.

Methods: Serum calcium was measured at admission in 365 patients with ACS. Data on sociodemographic and clinical characteristics were evaluated. The occurrence of a composite outcome (all-cause mortality and hospitalization for congoestablish heart failure [CHF] or ACS) was assessed at 60 month follow-up.

Results: Among all, 71% patients were male and the mean age was 64±13 years. Mean serum calcium was 2.38±0.33 mmol/L and 20% of patients had hypercalcaemia (≥2.60 mmol/L). Patients with hypercalcaemia were more frequently women (45% vs 25%; p=0.001), diabetic (43% vs 24%; p=0.001), hyper-tensive (74% vs 60%; p=0.017) and presented more kidney disease (KD) (49% vs 21%; p=0.001) as well as left ventricular (LV) systolic dysfunction (45% vs 28%; p=0.010).

At 5-year follow-up, composite outcome occurred in 92 (25%) patients and occurred more frequently in patients with hypercalcaemia (41% vs 22%; p=0.001). Furthermore, this patient group presented a significant preponderance of adver-ses events: ACS (25% vs 12%; p=0.005), CHF requiring hospitalization (16% vs 5%; p=0.003) and death (25% vs 10%; p=0.001). LV dysfunction (44% vs 27%; p=0.003), diabetes (37% vs 25%; p=0.020), hypertension (72% vs 60%; p=0.021) and KD (40% vs 22%; p=0.001) were also associated with the occurrence of compo-site outcome.

Kaplan-Meier analyses indicated that hypercalcaemia was a predictor of the com-posite adverse outcome (HR 2.2; CI 1.4-3.4). Multivariable survival analysis using Cox's regression model, including hypercalcaemia, LV systolic function and KD confirmed the independent association of hypercalcaemia with adverse outcome (HR 1.7; CI 1.1-2.7).

Conclusions: Hypercalcaemia is an independent predictor of long-term adverse outcomes.

Table 1. Outcomes by age

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>≤65 yrs</th>
<th>65–74 yrs</th>
<th>75–84 yrs</th>
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<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>% Adjusted OR (95% CI)</td>
<td>% Adjusted OR (95% CI)</td>
<td>% Adjusted OR (95% CI)</td>
<td>% Adjusted OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>IH death</td>
<td>15.0</td>
<td>15.8</td>
<td>15.8</td>
<td>15.8</td>
</tr>
<tr>
<td>IH MACE</td>
<td>10.3</td>
<td>17.7</td>
<td>17.7</td>
<td>17.7</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.4</td>
<td>1.8</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>IH in-hospital</td>
<td>OR: odds ratio; CI: confidence interval; MACE: major adverse cardiac event. All P values &lt; 0.001.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Predictive value of advanced glycation end products for the development of post-infarction heart failure

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Introduction and objectives: Taking into account that the post-infarction heart failure (HF) determines a great morbidmortality, together with the physiopathologi-cal implications of advanced glycation end products (AGE) in the genesis of my-cardial dysfunction, it was aimed to show the prognostic value of these molecules to predict the development of HF after a coronary event.

Methods: AGE were measured by fluorescence in 194 patients consecutively admitted to the coronary unit due to a myocardial infarction. It was analyzed the

to the high risk GRACE score group.
Mitral regurgitation in postmyocardial infarction

Independent contribution of additional risk factors to variables (HR 8.282, 95% CI 5.821 to 11.784, p<0.001), together with NT-proBNP and the infarction extension (measured by the troponin I peak), were predictors of the development of post-infarction HF. AGE levels over the median multiplied by 5.6 the risk of developing HF during the follow-up.

Conclusions: High levels of advanced glycation end products (AGE) are an independent predictor for the development of post-infarction HF.

### P5107

Mitrail regurgitation in postmyocardial infarction patients

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**Background:** The association between mitral regurgitation (MR) and localization of previous myocardial infarction (MI) remains debatable. Results of studies with patients with no MR or 403 patients with moderate or severe MR.

**Results:** The patients with MR were significantly older (55±8 vs 50±7.6 years) with more severe New York Heart Association (NYHA) functional class (III-IV) (35±11.2%). Echocardiographic indices of aortic annulus 23±5.9 vs 20±3.5 cm² and extent of left ventricular (LV) wall motion abnormalities (32.8±14.9 vs 23.6±12.7%) were higher in patients with MR as well as reduced LV systolic function (LV ejection fraction <50% 63±25% and LV dilation (64±16 cm³/m²). The levels of total cholesterol and triglycerides were higher in patients without MR (5.5±1.2 vs 5.2±1.3 mmol/l, 20.1±12 vs 1.7±1.0 mmol/l, respectively, all p<0.001). The levels of total cholesterol and triglycerides were higher in patients without MR (5.5±1.2 vs 5.2±1.3 mmol/l, 20.1±12 vs 1.7±1.0 mmol/l, respectively, all p<0.001). The rates of three or more affected coronary arteries (27.5 vs 18.3%, p=0.001), lesions of left main coronary artery (7.2 vs 1.1%, circumflex artery (3.6±2.6) and right coronary artery (57.3 vs 44.9%, all p<0.001) were higher in patients with MR. According to results of multivariate analysis, MR was independently associated with LV dilation, NYHA class of congestive heart failure, index of the left atrial size, and extent of LV wall motion abnormalities. The groups did not differ in localization of previous MI.

**Conclusions:** LV dilation, NYHA class of congestive heart failure, index of the left atrial size, and extent of LV wall motion abnormalities were associated with moderate or severe MR in postmyocardial infarction patients.

### P5108

Risk stratification by killep class and left ventricular systolic function in patients with acute myocardial infarction in modern era from Korean acute myocardial infarction registry

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**Purpose:** The aims of this study were to determine the interactive effect of Killip class and left ventricular function on 12-month mortality in patients with acute myocardial infarction (AMI) in modern era.

**Methods:** Between November 2005 and January 2008, 8,418 eligible patients (5,842 men, mean age 62.7±12.5 years-old) were analyzed from the Korean AMI Registry. Patients were stratified into 4 groups based on Killip class (1 vs 2 or 3 vs 4) and left ventricular ejection fraction (LVEF; <50% vs ≥50%); group 1 (Killip class 1 and LVEF ≥50%, n=4,003), group 2 (Killip class 1 and LVEF <50%, n=851), and group 4 (Killip class ≥2 and LVEF <50%, n=1,344). The LVEF were measured by two-D echocardiography.

**Results:** The 12-month mortality was 2.0% in group 1, 7.2% in group 2, 10.6% in group 3, and 22.5% in group 4, respectively. Kaplan-Meier survival showed there was significant difference in 12-month mortality among 4 groups (log-rank p<0.02). Patients in group 2 had significantly higher 12-month mortality compared with patients in group 1 (hazard ratio [HR] 3.912, 95% confidence interval [CI] 2.728 to 5.610, p<0.001), as did patients in group 3 (HR 3.991, 95% CI 2.592 to 6.145, p<0.001) after adjustment for clinical variables and angiographic variables in Cox proportional hazards model. In fully adjusted model including also medications during hospitalization and discharge, patients in group 2 had significantly higher 12-month mortality compared with patients in group 1 (HR 4.041, 95% CI 2.708 to 6.006, p<0.001), as did patients in group 3 (HR 3.935, 95% CI 2.125 to 7.310, p<0.001). The patients in group 4 had the highest 12-month mortality compared to patients in group 1 after adjustment for clinical and angiographic variables (HR 8.292, 95% CI 5.821 to 11.784, p<0.001), and after adjustment for clinical, angiographic, and discharge medications (HR 7.748, 95% CI 5.372 to 11.176, p<0.001).

**Conclusions:** Despite technical improvement and new treatment modality in modern era, conventional risk stratification by Killip class and LVEF still provide prognostic implication on 12-month mortality in post-MI patients.

### P5109

Early effects of ivabradine in combination with beta-blockers compared to beta-blockers uptration on systolic and diastolic function, NYHA class and exercise capacity in pts after Q-MI with EF<45%

K. Amosova, I.U. Rudenko, I. Prudyk, Yu. A. Bezrodnyi. National O.O. Bohomolets Medical University, Kyiv, Ukraine

**Purpose:** To compare the early impact of heart rate (HR) control with ivabradine plus metropolon and metropolon uptration on left ventricular (LV) systolic and diastolic function, serum NT-proANP and exercise capacity in anterior Q-MI pts with EF<45%.

**Methods:** In single-blind parallel-group study 62 pts with a first Q-MI, EF 30-45%, sinus rhythm >60 bpm, Killip class II were randomised 1:1 in ivabradine plus beta-blockers (BB) and BB uptration groups. Pts with anterior MI (24 and 18 respectively) were included in this analysis. Pts in Group 1 from day (D) 1 ivabradine metabolite latrinate uptrated to D 4 to 50mg bid (66±1.9 mg pd) on top of which from D 4-6 ivabradine 2.5 mg bid was uptrated to 7.5 mg bid. Pts in Group 2 were uptrated to 75 mg metropolon bid (117±4 mgpd). Besides, EF, survival infow DT at D 1 and 25 early intrakinolus velocity (E') was filling velocity (E') by TDI at D 5 and 25, serum NT-proANP at D 2 and 25 were estimated. Symptom-limited treadmill test (Bruce protocol) was performed at D 1 and 25.

**Results:** Resting HR was similar in both groups at D 1 (86±7.1 vs 87.5±1.6 bpm), D 5 (68±4.1 vs 68.1±1.4 bpm) and D 25 (60±7.1 vs 61.8±6.1 bpm, p=0.05). Echo-Doppler and NT-proANP data (M±s) see in the Table. Group 1 compared to Group 2 higher exercise capacity (49.5±37 vs 4.0±25 MET) and duration (206±11.2 vs 168±12.3 s, p<0.05) were attained in spite of higher HR at peak load (105±2.1 vs 99±2.3 bpm, p<0.01).

**Echo-Doppler and NT-proANP data**

<table>
<thead>
<tr>
<th>Group</th>
<th>EDP, mm Hg</th>
<th>EF, %</th>
<th>E/E'</th>
<th>DT, ms</th>
<th>NT-proANP g/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10±2</td>
<td>38±5</td>
<td>8±6</td>
<td>26±12</td>
<td>56±13±268</td>
</tr>
<tr>
<td>2</td>
<td>11±2</td>
<td>36±10</td>
<td>9±1</td>
<td>24±10</td>
<td>2315±2398</td>
</tr>
</tbody>
</table>

**Conclusions:** In pts after anterior MI with LV systolic dysfunction, addition of ivabradine to metropolon, in comparison with uptration of metropolon was associated with decrease of serum NT-proANP level, improvement of systolic and diastolic function and exercise capacity in spite of larger increase of HR at peak workload by 0.25.
end of observation; cut-off of 105 points displayed 58.5% sensitivity and 70.7% specificity). Multivariate analysis identified additional independent risk factors for long-term mortality (table).

**Conclusions:** There are some risk factors obtained both from the medical history and during the hospitalization that could increase the power of the risk stratification model. This suggests need for particular risk stratification performed to discharge in context of long-term period.

**P5111**

**Prognosis importance of absence of angina in non-ST elevation myocardial infarction**

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**Purpose:** Cardiac troponins increased myocardial infarction diagnosis in patients without specific electrocardiographic changes. Absence of angina has become common and prognostic significance remains unclear.

**Methods:** We followed 204 consecutive patients after myocardial infarction non-ST elevation (NSTEMI) at emergency department. Outcomes were in-hospital death and follow-up death or cardiac readmission.

**Results:** No-angina (NAG) group (n = 27, 13.2%) had more women (p = 0.001), higher blood glucose (p = 0.011) and B-type natriuretic factor (p = 0.001). In-hospital (14.8% vs 4.5%; p = 0.035) and 20-months follow-up mortality (43.5% vs 12.9%, p < 0.001) were higher in NAG. Combination of death and cardiac readmissions was similar (70.4% vs 53.1%, p = 0.093). Age (HR = 1.038, 95% CI 1.006 to 1.071), absence of angina at admission (HR 2.554, 95% CI 1.037 to 6.289), female gender (HR 2.706, 95% CI 1.099 to 6.667) and dyspnea (HR 3.113, 95% CI 1.417 to 6.842) were independent predictors of long-term mortality.

Conclusion: The absence of chest pain in NSTEMI implies in higher in-hospital and long-term mortality.

**P5112**

**Is female gender a real independent predictor of mortality after acute coronary syndrome?**

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**Background:** Female gender has been described as an important predictor of outcome after elective coronary interventions. Is this ominous impact of female gender also present in the context of acute coronary syndromes (ACS)?

**Methods:** Study of consecutive patients admitted for an ACS at a single-centre coronary care unit. Kaplan-Meier analysis and Cox regression analysis regarding the primary end-point of all-cause mortality at 30 day and one-year follow-up were performed to investigate the influence of gender on outcome.

**Results:** The study included 1423 patients, with a mean age of 64±13 years, 31% females. Thirty-day and one-year mortality were 6.7% and 8.5% respectively. ST-segment elevation acute myocardial infarction (STEMI) was present in 60.2% of the patients. Females were more elderly (70±12 vs 61±12 years, p<0.001), had more hypertension and diabetes and were less smokers. Heart rate and GRACE risk score were higher in females and estimated glomerular filtration rate lower. Females presented more often in Killip class ≥ 2, but had similar left ventricular ejection fraction. STEMI was more frequent in males (64.6% vs 50.6%, p<0.001). Kaplan-Meier analysis in the entire population, showed a significant increase in the incidence of the primary endpoint in females in comparison to males (Logrank, p=0.030, HR 1.49, 95% CI 1.01 – 2.15). However, analysing different age strata, females had identical mortality compared to males of the same age group (Table 1). On the other hand, 69% of women had an age ≥ 65 years, suggesting an important effect of age. After adjustment for age, female gender was no longer a predictor of mortality (HR 0.85, 95% CI 0.58 – 1.24, p=0.404).

**Conclusions:** Female gender is not a predictor of all-cause mortality after ACS. In fact, age is a major confounder in the influence of gender on outcome and must be taken into account, since women admitted with an ACS are significantly older than men.

**P5113**

**Peak Systolic Velocity (PSV) using colour-coded Tissue Doppler Imaging (TDI) is a strong and independent predictor of outcome in acute coronary syndrome patients**

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**Background:** Traditional echocardiographic methods like left ventricular ejection fraction (EF) and wall motion scoring (WMS) and new methods like speckle tracking (ST) based 2D strain and strain rate carry important prognostic information in acute coronary syndrome (ACS) patients. Parameters from tissue Doppler imaging (TDI), with its high time resolution, may further increase the prognostic value. Peak systolic velocity (PSV) of the basal segments of the left ventricle from TDI is a robust and user independent parameter. The aim was to investigate the prognostic value of PSV compared to EF, WMS, 2D strain and strain rate.

**Methods:** Echocardiographic images were collected and post processed in 227 ACS patients. Additional clinical data was prospectively gathered and patients were followed for 3-5 years regarding the combined endpoint of death or re-admission due to ACS or heart failure.

**Results:** The combined endpoint occurred in 84 (37%) patients. Those with an event had lower median PSV than those without (4.4cm/s vs. 5.3cm/s), (p = 0.001). In a ROC analysis, the AUC was larger for PSV (0.74) than for EF (0.68), WMS (0.65), 2D strain (0.71) and strain rate (0.69). The combined endpoint increased with decreasing PSV (figure). When adjusting for differences in baseline characteristics in a COX-regression model, PSV remained independent associated with outcome where the others did not. PSV was also less sensitive to image quality with fewer values missing or unacceptable for analysis.

**Conclusions:** Peak systolic velocity (PSV) using colour-coded TDI is a robust measurement that seems to have a stronger association with outcome than traditional measurements such as EF and WMS, and more recently measured measurements such as 2D strain and strain rate, in ACS patients.

**PATHOPHYSIOLOGY – BASIC MECHANISMS AND ATRIAL FUNCTION**

**P5114**

**Left atrial volume and dynamics in chronic kidney disease**

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**Background:** Left ventricular changes in end stage renal failure are well recognised; however, little is known about the same in early stages of chronic kidney disease (CKD) and associated changes in atrial function.

**Methods:** 50 CKD patients (eGFR 30-60 ml/min/1.73m2) underwent a transthoracic echocardiogram and were compared with 49 normal subjects as well as 30 hypertensive subjects. LV ejection fraction and LV mass indexed to body surface area (LVM) were measured. Biplane LA volume indexed to body surface area (LAVI). LA global and segmental function was measured using 2-dimensional strain imaging in the apical four and two chamber views from the septal and lateral walls using 2D speckle tracking. Systolic (S-SR), early (E-SR) and late (A-
SR) diastolic strain rate were also measured. One-way ANOVA with Bonferroni correction used to examine the differences between the groups.

**Results:** LVMH was increased significantly in the hypertensive group (P<0.03). LAVI was increased in the CKD group compared with both the normal and hypertensive group (Table 1). There was an associated reduction in global strain compared to normal and hypertensives (Table 1). LA reservoir function (S-SR), and conduit function (E-SR) were significantly reduced in the CKD group compared with normals and hypertensive group. However, there was no significant difference in atrial contractile function as A-SR was similar in all 3 groups.

**Conclusion:** LV diastolic dysfunction starts in early stages of CKD with consequent atrial changes as demonstrated by LA enlargement and reduced global as well as phasic functions. The severity of LA changes in CKD appears to exceed that due to the presence of LV hypertrophy as LAVI was significantly greater and LA function parameters significantly lower even compared to a cohort with hypertension with preserved kidney function.

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**Table 1. Differences in LA volume, strain and strain rate in CKD group vs HT group vs controls**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal (N=49)</th>
<th>CHD (N=50)</th>
<th>HT (N=30)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>LAVI (ml/m²)</td>
<td>24.7±6.5</td>
<td>39.9±10.6</td>
<td>27.1±7.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Global strain (%)</td>
<td>32.5±6.2</td>
<td>19.96±6.2</td>
<td>24.4±6.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-SR (1/s)</td>
<td>1.7±0.4</td>
<td>1.1±0.3</td>
<td>1.5±0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>E-SR (1/s)</td>
<td>1.6±0.5</td>
<td>1.0±0.3</td>
<td>1.4±0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>A-SR (1/s)</td>
<td>1.7±0.6</td>
<td>1.5±0.4</td>
<td>1.7±0.5</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Nicorandil improved electrical and structural remodeling and prevented ventricular tachyarrhythmias in a mouse model of desmin-related cardiomyopathy

P.118

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Introduction: It is well known that cardiac arrhythmias were observed in patients with desmin-related cardiomyopathy. Transgenic (HSBPS R120G-TG) mice with overexpression of an arg120gly (R120G) missense mutation in HSBPS display desmin-related cardiomyopathy. Recently, cardioprotective effect of nicorandil, a K+ATP-sensitive potassium channel opener and NO donor, prolongs survival in HSBPS R120G-TG mice. However, whether the TG mice induce ventricular arrhythmias and nicorandil can inhibit the arrhythmias remains unknown. Therefore, we examined the effects of chronic administration of nicorandil on ventricular electrical and structural remodeling and arrhythmias in HSBPS R120G-TG mice.

Method and Results: Nicorandil (15mg/kg/day) was orally was orally administered in HSBPS R120G-TG mice from 5 weeks to 30 weeks of age. Ventricular function was investigated at the age of 30 weeks using two-dimensionally-directed M-mode echocardiography. Electrocardiogram (ECG) lead II and optical action potentials were recorded from HSBPS R120G-TG mice and the epicardial surface of the Langendorff-perfused TG mouse hearts, respectively at the age of 30 weeks. We also examined the expression of ventricular gap junction proteins (connexin43) in the TG mice using western blots. Nicorandil improved ventricular dysfunction, determined by reduction of LV fractional shortening in HSBPS R120G-TG mice. Nicorandil also improved the prolonged P, PQ, and QT intervals at 60 min monitoring (7,6 < 1,1 ml/60 min).

Conclusion: In summary, our data indicate that CyPA is critically involved in the pathophysiology of virus-induced myocarditis. CyPA may represent a target to modulate myocardial remodeling in myocarditis.

Left ventricular diastolic and systolic and atrial dysfunction in patients with hypertension might be related to increased oxidative stress and inflammation-final results

P121

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Purpose: To study the presence of oxidative stress, inflammation, hypercoagulability and neuroendocrine activation in patients with hypertension (HT).

Methods: Results from >60-year-old 112 patients (18 controls and 94 patients with HT) were presented. All subjects had echocardiography with assessment of atrial and left ventricular (LV) systolic and diastolic function. Determination of (1) oxidative stress [measurement of total scavenger capacity (TSC), protein carbonylation (PK), tetrahydrobiopterin (BHV)] levels, (2) inflammatory [measurement of C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)] levels. (3) coagulation [measurement of fibrinogen levels, plasminogen activator inhibitor-I (PAI-I), and von Willebrand factor (VWF)] levels and (4) neuroendocrine parameters [dehydroepiandrosterone, DHEA] were included in the study.

Results: CRP, IL-6, TNF-α, and PAI-I levels were significantly increased in HT patients compared with controls. No between groups difference was found in other laboratory parameters. The absolute values of the mean of maximal longitudinal systolic LV strain (S) (p < 0.05 for both groups) and systolic (p < 0.05 for both groups) and early diastolic (p < 0.05 for HG- and p < 0.01 for HG+ groups) strain rates (SR) and those of atrial contraction period (p < 0.05 for both groups) and atrial reservoir period (p < 0.01 for both groups) SRs in both patient groups were reduced compared with controls. Numerous significant correlations between echocardiographic and laboratory parameters were found. Typically the degree of oxidative stress and inflammation, BNP and PAI-I levels correlated inversely with LV systolic and diastolic and atrial function.

Conclusion: In patients with HT and normal EF, the most common precursor of heart failure with preserved EF, oxidative stress [partly might be due to myocardial nitrogen oxide synthesis (NOS)] uncoupling, as indicated by the increased plasma nitric oxide synthase (NOS) cofactor BH4 level, which is usually associated with decreased tissue BH4 levels and inflammation might have a role in LV systolic and diastolic and atrial dysfunction.

Decreased left ventricular compliance but preserved left ventricular relaxation in a risk factor-based porcine model of heart failure with preserved ejection fraction (HFPEF)

P.122

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Background: The pathophysiology of left ventricular (LV) heart failure with preserved ejection fraction (HFPEF) is poorly understood, in part due to the lack of appropriate animal models. We aimed to model HFPEF in pigs by induced hypertension and western diet.

Methods/Results: Eight landrace pigs were implanted with subcutaneous 90 day release DOCA pellets (an aldosterone analog) and subsequently fed a high fat high lipid high sugar diet for 90 days (DOCA). Eight weight-matched pigs (no DOCA, regular diet) served as controls. After 90 days, tail-cuff systolic blood pressure during light sedation was 139±11 mmHg in DOCA vs 95±6 mmHg in control (p < 0.05). Echocardiography demonstrated pronounced concentric hypertrophy in DOCA group and deep areas of wall motion abnormalities (WMA) were assessed by pressure-volume (PV) analysis at baseline and during right atrial pacing. In DOCA vs control, baseline cardiac output (6.0±0.2 vs 6.6±0.5 l/min), peak LV pressure (107±4 vs 101±3 mmHg), as well as baseline (95±5 vs 84±6 bpm) and maximum (175±5

Right atrial stretching does not inhibit fluid intake with myocardial infarction

P.119

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Purpose: Low-pressure cardiopulmonary receptors are important in maintaining body fluid balance. One set of these receptors is located in the superior vena cava-right atrium junction (SVC-RAJ). Heart failure following myocardium infarction (MI) presents increased body fluid and may have an impairment of the mechanoreceptors receptors at SVC-RAJ function. The aim of this study was to investigate the effect of SVC-RAJ stretching on water and sodium intake in rats after MI.

Methods: Male Wistar rats (BW: 280-300g) underwent surgical left coronary artery ligation (n=9) or sham operation (n=5). Four weeks later an echocardiogram of an arg120gly (R120G) missense mutation in HSPB5 mice. Interestingly,nicorandil improved ventricular impulse conduction slowing and the increased protein expression levels ofconnexin43 in HSBPS R120G-TG mouse hearts. The electrical signal was rapid pacing at the ventricle induced ventricular tachyarrhythmias (VT) in 6 of 8 vehicle-treated HSBPS R120G –TG mouse hearts but in none of 8 nicorandil-treated HSBPS R120G–TG mouse hearts (p < 0.05).

Conclusion: These findings suggest that nicorandil can inhibit ventricular electrical and structural remodeling and prevent VT induction in a mouse model of desmin-related cardiomyopathy.

Characterization of cyclophilin A in coxsackievirus B3-induced myocarditis

P.120

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Background: The Extracellular Matrix Metalloproteinase Inducer (EMMPRN, CD147) and its ligand Cyclophilin A (CyPA) modulate MMP activity and appear to modulate inflammatory processes. To our knowledge the functional role of this receptor/ligand pair has not been characterized in inflammatory cardiomyopathy. Therefore we investigated the role of CD147 and CyPA in mouse models of acute and chronic coxsackievirus CBV3 myocarditis.

Methods and Results: CyPA+/− (SV129) and CyPA−/− mice were infected with CBV3. EMMPRIN and CyPA were upregulated at 8 days (western blot, immunohistochemistry). Myocardial tissue of CyPA−/− mice showed a significantly reduced number of infiltrated T-cells and macrophages at day 8 (macrophages: 7.6±0.1±3% vs. 100±7.0±1%, p < 0.05; T cells: 58.3±14.5% vs. 100±9.9%, p < 0.01). Consistently, in ABY/SvJ mice, which are susceptible to chronic CVB3 myocarditis, treatment with the CyPA inhibitor NIM811 starting at the day of infection significantly reduced macrophage and T-cell recruitment at day 8 (p < 0.05), which was associated by increased virus elimination. Interestingly, NIM811 treatment of CVB3-infected A.BY/SvJ mice starting at day 12 p.i. significantly reduced the myocardial amount of collagen in myocardial lesions.

Conclusion: In summary, our data indicate that CyPA is critically involved in the pathophysiology of virus-induced myocarditis. CyPA may represent a target to modulate myocardial remodeling in myocarditis.

Decreased left ventricular compliance but preserved left ventricular relaxation in a risk factor-based porcine model of heart failure with preserved ejection fraction (HFPEF)

M. Schwarz1, S. Seiler1, P. Steenki2, B. Pieske3, H. Post1. 1Medical University of Graz, Department of Cardiology, Graz, Austria; 2Leiden University Medical Center, Leiden, The Netherlands.

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Olmesartan inhibits ventricular remodeling and arrhythmias in a mouse model of chronic heart failure

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Introduction: While beneficial effects of olmesartan, an angiotensin II type 1 receptor blocker, on chronic heart failure (CHF) have been demonstrated, whether it has inhibitory effects on ventricular arrhythmias induced by CHF is still unclear. Recently, we demonstrated that a transgenic mouse with transient cardiac expression of activated G protein (Ga q)-TG develops CHF and frequent ventricular arrhythmias. We examined the effects of chronic administration of olmesartan on ventricular function, the number of premature ventricular contractions (PVCs), and ventricular remodeling in Ga q-TG mice.

Method and Results: A lower dose of olmesartan (1DL, 1mg/kg/day) or vehicle was orallyadministered to 30 Ga q-TG mice from 6 weeks to 32 weeks of age. At the age of 32 weeks, systolic blood pressure (SBP) and electrocardiogram (ECG) were measured and ventricular function was investigated using echocardiography. The degree of fibrosis was elucidated from left ventricular sections stained with Masson's trichrome. Mean SBP was significantly decreased in HDO-treated Ga q-TG mice compared with those in LDO and vehicle-treated Ga q-TG mice (45±3.3 vs. 77±1.4 and 72±4.8 mmHg; p<0.001). Both LDO and HDO-treated mice showed improved ventricular dysfunction, determined by reduction of LV fractional shortening (p=0.01) in Ga q-TG mice. During 10 min of ECG recording, PVCs were frequently (more than 20 beats/min) observed in 9 of 10 vehicle-treated Ga q-TG mice but in none of 10 LDO-treated Ga q-TG mice (p=0.01 by Fisher's exact test). Interestingly, the number of PVCs was not decreased in HDO-treated Ga q-TG mice. Collected QT interval was significantly shorter in LDO-treated Ga q-TG mice than in HDO and vehicle-treated Ga q-TG mice (p=0.05). The degree of interstitial fibrosis in the left ventricle was significantly less in both LDO and HDO-treated Ga q-TG mice than in vehicle-treated Ga q-TG mice (p=0.05).

Conclusions: These findings demonstrated that lower but not higher doses of olmesartan inhibited ventricular electrical remodeling and decreased the number of PVCs in a mouse model of CHF, suggesting that relatively low dose of olmesartan is enough to treat CHF-induced ventricular arrhythmias.

Enhancement of cardiac histone deacetylase 6 (HDAC6) activity protects against cardiac disease in alpha-B-crystallin arg210gly transgenic mouse

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Background: An Arg120Gly (R120G) missense mutation in crystallin, alpha B (CRYAB), a member of the small heat shock protein family, causes myofibrillar myopathy (MFM), which is characterized by the formation of argosomes containing CRYAB and desmin. It is known that these argosomes are formed around nuclei by the retrograde transportation of small heat shock proteins (sHSP), alpha-B-crystallin (CRYAB) causes a myofibrillar myopathy (MFM) characterized by the formation of aggregates containing CRYAB in the cardiomyocytes. It is known that apoptotic cell death occurs in the hearts of CryAB R120G transgenic mice, a mouse model of alpha-crystallinopathy. The role of apoptotic cell death induced by CryAB R120G in disease progression, however, remains uncertain.

Methods and Results: Apoptotic cell death induced by overexpression of CryAB R120G was analyzed in neonatal rat cardiomyocytes using an adherent vector. Overexpression of the mutant CryAB led to up-regulation of BCL2 and down-regulation of BAX in the cardiomyocytes. Cell viability was dose-dependently recovered in myocytes overexpressing CryAB R120G by treatment with nicardipine, a mitochondrial ATP-sensitive potassium channel opener. Nicardipine treatment also inhibited the increase in BAX, the decrease in BCL2, the activation of caspase-3, and apoptotic cell death as a consequence of mutant CryAB. The protective effects of nicardipine were completely blocked by treatment with 5-HD, a specific mitochondrial channel blocker, and by treatment with small interfering RNA (siRNA) targeting BCL2 that clearly reduced BCL2 protein level. These results suggest that the opening of the mito(ATP) channel by nicardipine and the maintenance of BCL2 protein in the mitochondrial fraction play important roles in cellular protection in cardiomyocytes expressing R120G.

Conclusions: Nicardipine treatment appeared to reduce apoptotic cell death by opening the mito(ATP) channel and maintaining the BCL2 protein level.
The mitochondrial translocator protein ligands, 4'-chlorodiazepam and TRO40303 protect cardiomyocytes against doxorubicin toxicity

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Introduction: Mitochondrial dysfunction is a leading cause of heart failure, as recent studies performed on mice indicate. Our results suggest that VAV3 could be involved in predisposition to chronic heart failure.

Etiology and genotype

<table>
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<th>P5127</th>
<th>The mitochondrial translocator protein ligands, 4'-chlorodiazepam and TRO40303 protect cardiomyocytes against doxorubicin toxicity</th>
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<td>Purpose: Doxorubicin is widely used as a chemotherapeutic agent for the treat- ment of a large spectrum of human neoplastic diseases but its administration in humans is limited by severe cardiotoxicity. Reactive oxygen species (ROS) production and mitochondrial permeability transition pore opening (mPTP) have been identified as major events in doxorubicin-induced damage. As the mitochondrial Translocator Protein (TSPPO) ligands 4'-chlorodiazepam (CDZ) and TRO40303 have been shown to protect mitochondria and to reduce left ventricular dysfunction during myocardial ischemia-reperfusion through the inhibition of the opening of the mPTP, we examined their potential protective effect on doxorubicin-induced loss of contractility and ultimately on cell death in isolated rat cardiomyocytes.</td>
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<td>Methods: The effects of doxorubicin (0.25–20 μM) on contractile function were evaluated in isolated adult rat cardiomyocytes paced at 1Hz by electric field stim- ulation. Cell viability and ROS were determined with the fluorescent probes prodimidol and dichlorofluorescein, respectively. Direct mPTP opening was assessed by the estimations of the calcium loading CoCl2 quenching technique. Mitochondrial exposure to doxorubicin the cardiomyocytes were pretreated by the TSPPO ligands at concentrations previously shown as cardioprotective against ischemia- reperfusion injury.</td>
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<td>Results: At higher concentrations than 5 μM doxorubicin significantly reduced the velocities of contraction and relaxation of the cardiomyocytes and caused cell death. The deleterious effects of doxorubicin were associated with an increase in ROS production and involved mPTP opening as demonstrated using the calcein CoCl2 staining method and confirmed by the preventive effect of cyclosporin A. CDZ and TRO40303 improved cell viability, prevented the alterations of contractility of the cells and attenuated the collapse of maximal velocities of contraction and relaxation induced by doxorubicin. The cytoprotective effect of TSPPO ligands involved a high reduction of doxorubicin-induced ROS production associ- ated with inhibition of mPTP opening as attested by the maintenance of the mitochondrial calcium fluorescence observed in the presence of CDZ or TRO40303.</td>
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<td>Conclusion: These data demonstrate that the TSPPO ligands CDZ and TRO40303 protect cardiac cells against doxorubicin toxicity and that this protection is at least in part mediated by prevention of ROS production and mPTP opening. Thus TSPPO may represent a relevant pharmacological target for protection of the heart against doxorubicin-induced toxicity.</td>
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Adrenomedullin, ghrelin and leptin as potential biomarkers of chronic heart failure: an experimental study

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Introduction: Pathophysiology and biomarkers of heart failure are under extensive research. Recently, several regulatory peptides - primarily of non-cardiac origin - including adrenomedullin (ADM), ghrelin (GHR) and leptin (LPT) under extensive research. Recently, several regulatory peptides - primarily of non- cardiac origin - including adrenomedullin (ADM), ghrelin (GHR) and leptin (LPT) were suggested to be potential biomarkers of heart failure.

Study of vav3 ser298thr polymorphism in patients with heart failure

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Background: Vascular endothelial growth factor (VEGF) plays a key role in angiogenesis and is required for preventing the transition from compensatory left ventricular hypertrophy (LVH) to left ventricular systolic dysfunction (LVSD). Soluble VEGF receptor-2 (sVEGFR-2), which retains an affinity for VEGF but is unable to activate its signal transduction, acts as an endogenous inhibitor of VEGF. Recently, we demonstr- ated that serum sVEGFR-2 levels are increased in subjects with metabolic syndrome. However, the possible role of sVEGFR-2 in LVH or HF in human is unknown.

Methods and Results: We recruited 434 consecutive outpatients with or without HF, whose NIHYA classes were stable for at least 3 months. Among them, 19 had LVH (LV mass index [LVM]: male-<116 g/m2 and female-<104 g/m2) and systolic dysfunction (LV ejection fraction [LVEF] -<50%) (LVM-HF). From leaving 415 patients we selected 383 aged >60 years, and the LV mass index in the 81 with LVH was significantly higher in LVH+HF than LVH+HF+ and LVH only. We assessed the sVEGFR-2 levels in these patients. Their mean sVEGFR-2 levels were significantly lower in LVH+HF+ than LVH+HF+ and LVH only. In contrast, sVEGFR-2 was significantly correlated with LVMI and NT-proBNP. Stepwise regression analysis revealed that independent determinants of the sVEGFR-2 level were age, NT- proBNP, and triglycerides. Multiple logistic regression analyses including data on age, a male gender, the body mass index, systolic and diastolic blood pressures, VEGF, sVEGFR-1, and sVEGFR-2 revealed that a decrease in sVEGFR-2, but not VEGF or sVEGFR-1, was independently associated with both LVH and sys- tolic dysfunction.

Conclusion: Our results suggest that VAV3 could be involved in predisposition to chronic heart failure, as recent studies performed on mice indicate.
Conclusions: Serum levels of sVEGF-R2, but not those of VEGF or sVEGF-R1, are decreased in HF patients with LHV. sVEGF-R2 might play a role in modulation of angiogenesis in hypertrophied LV with systolic dysfunction in human.

Matrix metalloproteinase level can predict left ventricular remodeling and systolic dysfunction after myocardial infarction

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Purpose: Assessment of serum biomarker evidence of the early course of the cardiac type I collagen degradation (matrix metalloproteinase, MMP type -2) after myocardial infarction (MI) and relationship to left ventricular (LV) remodelling. Methods: Our study included 28 patients (14 males & 14 females with a mean age of 57.8 yrs) with acute anterior STEMI (group) and 12 healthy volunteers (7 males & 5 females with a mean age of 59 yrs) as a control group (groupII). All patients were subjected to clinical evaluation, 12-lead ECG, echo-doppler study and laboratory work-up which included estimation of plasma activity level of MMP-2 within 24 h and 2 months post infarction. Echocardiography was performed within 48 h and 2 months after MI for assessment of LV volumes and ejection fraction (EF) by Simpson's method.

Results: The mean level of MMP was higher in group I than group II (20.74 vs 1.27 mg/mL, p < 0.001). The mean EF in group I was 47.8 and 37.0 within 48 hr and 2 months post MI respectively (p < 0.017). ANOVA test was conducted to evaluate the relationship between LV systolic function and MMP level both at baseline and 2 months after MI. The mean baseline MMP was 3.19, 18.6, 24.4 mg/mL in patients with normal (EF=54%), mild (EF=45-54%), moderate (EF=30-44%) LV systolic dysfunction. The mean MMP 2 months post MI was 2.74, 6.21, 23.7 and 35.3 mg/mL in patients with normal, mild, moderate and severe LV systolic dysfunction. ROC analysis revealed a cut off level of MMP >3 mg/ml can predict the development of LV systolic dysfunction with a sensitivity and specificity of 89% and 84% respectively.

MMP increase after MI. The increase of MMP is associated with deterioration of LV systolic function both at baseline and 2 months later. A level ≥3 mg/ml can predict the development of LV systolic dysfunction with a sensitivity and specificity of 89% and 84% respectively.

Activation of agonistic proteins for toll-like receptor 4 in patients with dilated cardiomyopathy

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Background: Although there is a growing body of evidence for a potential role of the innate immune receptor Toll-like receptor 4 (TLR4) in heart failure and pharmacological antagonists are currently under investigation in clinical trials regarding inflammatory diseases, the activation cascade of this receptor in cardiovascular diseases is still unknown. Therefore we investigated agonistic proteins of TLR4 in blood from patients with dilated cardiomyopathy (DCM).

Methods: Classical agonistic proteins of TLR4, namely lipopolysaccharide binding protein (LBP), soluble CD14 (sCD14), lipopolysaccharide (LPS) and MD-2, were quantified in serum from 158 patients with early stage of DCM (disease duration <1 year, LV EF <50%, LV end-diastolic diameter >60 mm) by ELISA. Other reasons for heart failure were excluded by coronary angiography, myocardial biopsy and echocardiography. Healthy blood donors served as controls (n=33). Protein contents of LPS were significantly reduced in patients with DCM (50%; P<0.05) when compared to healthy controls. In contrast, protein level of LBP (+78%; P<0.05) and sCD14(+19%; P<0.001) were significantly decreased in DCM patients when compared to healthy controls. MD-2 serum protein level were increased in direction in DCM patients when compared to healthy controls, but it did not reach a statistically significant value (P=0.06).

Conclusion: In a carefully characterised cohort of DCM patients, we showed for the first time the level of LBP as agonist of TLR4 agonists on protein level suggesting a potential role of TLR4 in DCM. Our findings might give a basis of further therapeutic approaches.

Oxidative stress, inflammation and low levels of apelin as risk factors of left ventricular hypertrophy in type 2 diabetics with renal disease


Introduction: The pathophysiology of left ventricular hypertrophy is multifactorial and not completely understood. Recent studies have demonstrated the role of oxidative stress, inflammation and apelin in cardiovascular morbidity and mortality.

Purpose: The aim of this study was to evaluate the factors associated with the left ventricular hypertrophy (LHV) in a population of type 2 diabetics with mild and moderate kidney disease.

Methods: In this cross-sectional study we included 78 type 2 diabetic patients (f = 39, m = 48), with a mean age of 61 years and a mean estimated glomerular filtration rate (MDRD) of 43.5 ml/min, followed in our outpatient nephrology clinic. We analyzed several laboratory parameters, such as: interleukin 6 (IL6), adiponectins (visfatin, resistin, apelin)-36, oxidative stress (oxLDL), as well as the left ventricular mass index (LVMI) in our patients.

Results: In a simple regression model, the LVMI was positively correlated with age (r=0.322 p<0.004), IL6 (r=0.722 p<0.001), oxidative stress (visfatin= r=0.769 p<0.001), oxLDL (r=0.752 p<0.001) and inversely with apelin-36 (r=-0.901 p<0.001) and the glomerular filtration rate (r= -0.381 p<0.001), where these parameters were significantly different than the controls. In a multiple regression model, only IL6 (r=0.148 p=0.049), oxLDL (r=-0.267 p=0.0294) and apelin-36 (r=-0.736 p=0.001), independently influenced the LVMI. ROC curve analysis showed that oxLDL (AUC= 0.852 p<0.001) and IL6 (AUC= 0.931 p<0.001) are predictors of left ventricular hypertrophy.

Conclusion: Our study showed that in type 2 diabetic patients with nephropathy, the oxidative stress, the inflammation and the adipokines are determinants of left ventricular hypertrophy. Surely they also contribute to the complexity of CKD associated cardiovascular risk.

Cardiomyocyte structural deterioration and metabolic response in human DCM hearts

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Dilated cardiomyopathy (DCM) is associated with cardiac dysfunction and various histopathological characteristics and poorly known metabolic deterioration during structural and functional remodeling. The aim of this study was the expression pattern of structural deterioration and metabolic responses in human DCM hearts. The archive tissue samples of left ventricle originated from DCM hearts divided in respect to ≤EF on three groups: (1) 45-55% (n=13), (2) 30-40% (n=8) and (3) ≤30% (n=10) were investigated histopathologically, ultrastructurally, histochemically by PAS staining and immunohistochemically with antibodies anti-desmin, PPAPalpha, SMAalpha and caspase-3, then quantified by morphometric methods. Controls (ctr) were tissue samples from hearts with myocarditis (n=8) and recovered from myocardics (n=8), all with EF=50%. Correlation coefficients between each set of data were determined by Spearman rang regression analysis. Analysis of histopathological data in relation to decreased EF have shown predominance of desmin appearance with increased expression and normal pattern in group 1 and declined with abnormal pattern and/or lack expression in some cardiomyocytes in group 2 and 3, and cumulating ultrastructural pathology as loss of contractile filaments, increased number and size of mitochondria or mitochondria matrix and crista deterioration. Increased cardiomyocytes diameter and fibrosis were significant only in 3 vs 1 and 2 group and both ctr. The decrease of PAS(+) material, and expression of fetal phenotype in about 1-2% cardiomyocytes and PPAPalpha in predominant number of nuclei was observed in group 1. Contrary, in group 2 further advanced cellular pathology followed by minor number of nuclei PAS(+) and PPAPalpha cytoplasmic positivity. PAS and PPAPalpha pattern of structural deterioration. Either glycogen nor SMAalpha and apoptosis were not detected in tissue sections in group 3. In this group PPAPalpha expression was present in various number of nuclei (from 0 to 50%), PPARalpha in scarce nuclei, and presence of PAS(+) material and re-expression of fetal phenotype in many cardiomyocytes were characteristic features of ctr. There was a significant correlation between PPAPalpha and %EF (R=0.684, p<0.001) and %SMAalpha and cardiac remodeling (R=0.545, p<0.001). The collective findings reveal a close relationship between functional, structural and metabolic remodeling of cardiomyocytes and PPAPalpha expression. Disturbance in glycogen presence and PPAPalpha expression in biopsies of DCM hearts seem to be markers of cardiomyocytes metabolic shift.

Abrogation of S100B expression in S100A1 deficient mice improves survival post myocardial infarction

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Post-myocardial infarction (MI) ventricular remodeling involves ventricular dilatation, hypertrophy of non-infarcted myocardium, myocyte apoptosis, the induction of S100B and the downregulation of S100A1. Whereas S100A1 deficient mice result in cardiac functional impairment and high early mortality post-MI, abrogation of S100B preserves cardiac function in the setting of augmented hypertrophy post-MI. To assess the consequences of S100B expression in S100A1 knock out (KO) mice, wild-type (WT), S100B KO, S100A1 KO and S100B-A1 double KO mice were subjected to 35 days after left anterior descending coronary artery ligation with age-matched sham-operated controls. S100A1-B KO mice demonstrated better survival as compared to S100A1 KO and WT mice.
Impact of the PPARGC1A Gly482Ser polymorphism on left ventricular structural and functional abnormalities in patients with cardiovascular risk factors

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The Gly482Ser polymorphism in peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PPARGC1A) has been demonstrated to be involved in some pathophysiological aspects of metabolic and hemodynamic regulation; however, the exact data linking these genomic variations with cardiac derangements are incomplete. We sought to investigate the association between the PPARGC1A Gly482Ser polymorphism and left ventricular (LV) structural and functional abnormalities in patients with cardiovascular risk factors: hypertension, diabetes, and obesity.

Methods: Each of 150 enrollees (age 59 ± 8 years) underwent echo study with assessment of LV systolic (strain and strain rate, SR) and diastolic function (mitral inflow E/A ratio) as compared with subjects with the Gly/Gly genotype. No differences between these groups in metabolic control parameters (fasting glucose, HOMA IR and HbA1c), as well as in blood pressure were noted. Multivariate analysis showed independent correlates of LV mass index were hypertension (β = 0.31 ± 0.04), Ser allele (β = 0.32 ± 0.01), HbA1c (β = 0.25 ± 0.01), BMI (β = 0.25 ± 0.01), and patient age (β = 0.22 ± 0.02). Em velocity was independently associated with age (β = 0.22 ± 0.04), HbA1c (β = 0.25 ± 0.02), BMI (β = 0.25 ± 0.02) and hypertension (β = 0.21 ± 0.08), and Ser allele (β = 0.19 ± 0.02).

Results: Patients with the Ser allele (Ser/Ser or Ser/Gly) showed a greater extent of LV hypertrophy and LV diastolic function impairment compared to the wild type and mitral E/A ratio as compared with subjects with the Gly/Gly genotype. No differences between these groups in metabolic control parameters (fasting glucose, HOMA IR and HbA1c), as well as in blood pressure were noted. Multivariate analysis showed independent correlates of LV mass index were hypertension (β = 0.31 ± 0.04), Ser allele (β = 0.32 ± 0.01), HbA1c (β = 0.25 ± 0.01), BMI (β = 0.25 ± 0.01), and patient age (β = 0.22 ± 0.02). Em velocity was independently associated with age (β = 0.22 ± 0.04), HbA1c (β = 0.25 ± 0.02), and hypertension (β = 0.21 ± 0.08), and Ser allele (β = 0.19 ± 0.02).

Conclusions: In patients with cardiovascular risk factors, the PPARGC1A Gly482Ser polymorphism contributes to LV hypertrophy and diastolic dysfunction with the Ser allele promoting these abnormalities.
PREDICTORS FOR OUTCOME

P5140 Lung ultrasound for the evaluation of pulmonary congestion in a pre-transplantation heart failure outpatient clinic: comparison with natriuretic peptides
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Purpose: Evaluation of pulmonary congestion is a frequent diagnostic challenge even by highly skilled clinicians. Recently, lung ultrasound (LUS) has been proposed for a reliable, easy evaluation of pulmonary congestion, by assessment of B-lines (also called ultrasound lung comets). Our aim was to define the relationship between B-lines and natriuretic peptides (NT-proBNP) as part of the evaluation of pre-transplant heart failure (HF) patient in an outpatient clinic.

Methods: Fifty-eight patients admitted to a pre-transplantation clinic due to advanced systolic HF (65.5% men, mean age 49±11 yrs, 47.2% with idiopathic and 29.3% with post-ischemic cardiomyopathy) were enrolled. Clinical assessment, NT-proBNP analysis and LUS evaluation were independently performed.

Results: Feasibility was 100%. Mean time to perform LUS was 9.91±2.45 minutes. Significant pulmonary congestion was present in 57.9% by LUS (total B-lines number ≥ 15). B-lines number was significantly correlated to NT-proBNP values (r=0.74, p<0.0001). Assuming NT-proBNP > 1000ng/ml as a reference for decompensated HF, ROC analysis showed a C statistic of 0.88 (95% CI: 0.72-0.92, p<0.0001) for LUS, providing the best accuracy with a cut-off of 14 B-lines (sensitivity 96.2, specificity 71.9%).

Conclusion: In a pre-transplantation heart failure outpatient clinic, B-lines evaluated by LUS are significantly correlated to NT-proBNP values. Given its accuracy, low cost and portability, LUS may be considered as a reliable tool for a quick and easy evaluation of pulmonary congestion in decompensated HF patients.

P5141 Depressed midwall fractional shortening is a powerful prognostic determinant in cardiac AL amyloidosis
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Background: Systemic amyloidosis are characterized by extracellular deposition of insoluble fibrils in various tissues. Clinical presentation is variable, depending on the extension of deposits and on the extent of organ dysfunction. In AL amyloidosis, the amyloidogenic protein is an immunoglobulin light chain or a fragment of an Ig light chain that is synthesized by clonal plasma cells in bone marrow. Cardiac involvement is not only frequent, but it is also the most common predictor of clinical outcome.

Purpose: To evaluate the relationship between midwall fractional shortening (i.e. a marker of myocardial contractile dysfunction) and clinical outcome in cardiac AL amyloidosis patients.

Methods: We evaluated 221 consecutive untreated subjects in whom a first diagnosis of cardiac AL amyloidosis was concluded between 2006 and 2009. Patients in whom cardiac involvement was excluded served as controls (n=121). All patients underwent complete echocardiographic evaluation as well as NT-proBNP determination at diagnosis. Patients with ejection fraction below 50% (n=28) were excluded. Prognosis was assessed after a median follow-up of 561 days.

Results: When compared with AL patients without myocardial involvement, cardiac AL was characterized by increased wall thickness (p<0.001) and reduced end-diastolic LV volumes (p<0.001). As expected, diastolic dysfunction was evident in all cardiac AL patients, as evident by increased E/E’ ratio (p<0.001). Midwall fractional shortening was markedly depressed (11.2±4.3 vs 22.1±4.4%, p<0.001), despite preserved ejection fraction. At multivariable analysis, midwall fractional shortening (p=0.003) and NT-proBNP (p<0.0002) were the only significant prognostic determinants, whereas other indices of diastolic (E/E’ ratio, transmural and pulmonary vein flow velocities) and systolic function (tissue-Doppler systolic indices, ejection fraction) did not enter the model.

Conclusions: In cardiac AL amyloidosis with normal ejection fraction, depressed midwall fractional shortening, a marker of myocardial contractile dysfunction, is a powerful predictor of survival.

P5142 The electrocardiographic/echocardiographic mass ratio in the diagnosis of cardiac amyloidosis
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Background and Aim: In cardiac AL amyloidosis the increase in wall thickness caused by extracellular amyloid deposition leads to marked increases in left ventricular (LV) mass. At variance with other forms of cardiac hypertrophy, this is often associated with abnormally low electrocardiographic (ECG) voltages, due to amyloid negative effects on intracardiac electrical conduction. Although such a discrepancy (low ECG “electrical” LV mass/high echo-derived LV mass) might be a powerful diagnostic clue, this is often missed since almost 40% of cardiac AL patients do not strictly fulfil the definition of “ECG low voltages” (<5 mV in all peripheral leads).

Methods: To evaluate its possible clinical relevance, an index of the ECG/echo mass estimate was developed in 1000 consecutive patients with cardiac AL (n=315), hypertrophic cardiomyopathy (n=207), hypertension with different degrees of LV hypertrophy (n=478). Echo-derived LV mass was indexed for body-surface area (g/m²), whereas peripheral QRS score (sum of QRS width in the peripheral leads, mV) was used as an index of “electrical” LV mass. ECG/Echo ratio was expressed as [mV/(g/m²)]. Also total QRS score and Sokolow-Lyon index were computed and divided by echo-derived LV mass to evaluate potential causes of low QRS voltages (large pericardial effusions, obesity, chronic obstructive lung disease, and severe peripheral edema) were excluded.

Results: In a preliminary evaluation, the peripheral QRS score/echo LV mass ratio showed a 91.43% sensitivity and a 74.53% specificity in identifying the presence of cardiac involvement in 145 out of 200 consecutive AL patients. When compared to both hypertrophic cardiomyopathy [0.37 (0.30-0.53) mV/(g/m²)] and hypertensive [0.33 (0.27-0.40) mV/(g/m²)] subjects, the ECG/Echo mass ratio was markedly depressed in patients with cardiac AL [0.14 (0.10-0.20) mV/(g/m²), p<0.001 vs. all the other groups]. The area under the ROC curve for the detection of cardiac AL involvement was high: 0.970 (95% CI, 0.956 to 0.980; p<0.0001).

Figure 1. ROC Curve - B-lines number

Conclusion: In a pre-transplantation heart failure outpatient clinic, B-lines evaluated by LUS are significantly correlated to NT-proBNP values. Given its accuracy, low cost and portability, LUS may be considered as a reliable tool for a quick and easy evaluation of pulmonary congestion in decompensated HF patients.
Evidence of subclinical perimyocardial involvement in patients with systemic lupus erythematosus: late gadolinium enhancement study

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Purpose: Increased inflammation has been linked to myocardial dysfunction and heart failure. We investigated whether patients with systemic inflammatory diseases, such as systemic lupus erythematosus (SLE), free of cardiac symptoms, have evidence of subclinical inflammatory myocardial involvement.

Methods and results: A total of 27 SLE patients (male=0, mean age 41 ± 11 years) with no previous cardiac history underwent cardiovascular magnetic resonance imaging for assessment of function and late gadolinium enhancement on a 3 T esla scanner. In these patients, the presence of significant coronary artery disease was excluded by virtue of negative adenosine myocardial perfusion or normal high-resolution magnetic resonance coronary angiography. Fifteen age-matched subjects with a low pretest probability acted as a control group. In SLE group, there was deceased global systolic function (SLE vs. controls: 47.7 ± 60.5% vs. 60.5%, p<0.05) and increased LV mass index (62.8 ± 43.4 g/m2 vs. 43.4 g/m2, p<0.05). Late gadolinium enhancement was seen in 20 SLE subjects: 14 patchy areas of intramyocardial enhancement and 6 subjects showed intramyocardial stria. Myocardial enhancement was invariably affecting the basal segments of inferior septum, inferior and inferotral walls and right ventricle insertion points. None of the subjects showed regional myocardial fibrosis. Pericardial effusion was present in 4 patients. Pericardial enhancement was present in 17 patients (5 of these had no myocardial enhancement), enveloping globally right and left ventricle, with mean thickness of the pericardial space along the free LV wall of 3.1 ± 0.7 mm.

Conclusions: We demonstrate that in SLE patients free of significant coronary artery disease there is evidence of subclinical perimyocardial involvement.

Cardiac myosin binding protein C gene polymorphisms and diastolic heart failure

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Objective: Myosin binding protein C (MYBPC) plays a role in ventricular relax-

ation. The aim of the study was to investigate the association between cardiac myosin binding protein C (MYBPC3) gene polymorphisms and diastolic heart fail-

ure (DHF) in a human case-control study.

Methods: A total of 352 participants of 1752 consecutive patients from the National University Hospital and its affiliated hospital were enrolled. 176 patients diag-

nosed with DHF confirmed by echocardiography were recruited. Controls were matched 1:1 by age, sex, hypertension, diabetes, renal function and medica-

tion use. We genotyped 12 single nucleotide polymorphisms (SNPs) according to HapMap Han Chinese Databank across a 40 kb genetic region containing the MYBPC3 gene and the neighboring DNA sequences to capture 100% of hap-

lotype variance in all SNPs with minor allele frequencies ≥5%. We also analyzed associations of SNPs and haplotypes with DHF and linkage disequilibrium (LD) structure of the MYBPC3 gene.

Results: In a single locus analysis, SNP rs2290149 was associated with DHF (allele-specific p = 0.004; permuted p = 0.031). The SNP with a minor allele fre-

quency of 9.4%, had an odds ratio 2.14 (95% CI 1.25-3.66; p = 0.004) for the additive model and 2.06 for the autosomal dominant model (GG+GA, 95% CI 1.17-3.63; p = 0.013), corresponding to a population attributable risk fraction of 12.02%. The haplotypes in a LD block of rs2290149 (C-C-G-G) was also significantly associated with DHF (odds ratio 2.10 (1.53 - 2.89); permuted p = 0.029).

Conclusions: We identified risk-conferring genetic variants of MYBPC3 gene for DHF in a Chinese population.

Subclinical abnormalities of the arterial tree and left ventricular myocardial deformation, relaxation and twist in chronic kidney disease

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Purpose: Chronic kidney disease (CKD) associates with adverse cardiovascular outcomes. However, the disadvantageous effects of renal dysfunction on left ventri-

cular systolic and diastolic function remain unclear. The objective of this study was to look at the effect of CKD on (i) left ventricular (LV) systolic and diastolic strain patterns and LV twist with the use of conventional and 2D speckle tracking echocardiography, and (ii) arterial stiffness as measured by pulse wave velocity (PWV).

Methods: Seventy-four consecutive CKD patients were assessed using conventional, 2D speckle tracking echocardiography (EchoPAC-GE) and applana-
tomometry (Sphygmocor). Patients with (i) LV systolic dysfunction or regional wall motion abnormalities, (ii) moderate to severe valvular disease or (iii) heart rhythm other than sinus were excluded (N=5). Global systolic strain (GS) and strain rate (GSRe), early (GSRe) and late (GSRd) diastolic longitudinal strain rate, LV twist and twist rate, mitral inflow, tissue PW Doppler velocities and PWV were recorded.

Results: The mean age of CKD patients was 54 ± 15 years and 34 (49.3%) was female. Mean baseline LV ejection fraction (EF) was 62.2±5.4%. Six (8.7%) patients were stage 1 CKD, 17 (24.6%) stage 2, 29 (43.7%) stage 3, 12 (17.4%) stage 4 and 5 (7.3%) stage 5. Estimated Glomerular Filtration Rate (eGFR) corre-
lated significantly with PWV (r=0.27, p=0.05) and GSRe (r=0.26, p=0.028), LV twist rate (r=0.275, p=0.026) and E/E’ (r=0.370, p=0.002). There was a trend of a correlation between eGFR and LV twist (r=0.216, p=0.083), isovolumic relax-
tion time (IVRT) (r=-0.232, p=0.058) and E/E’ ratio (r=0.217, p=0.073). There was no correlation between eGFR and GS, GSRd or biplane ejection fraction recorded. When including the echocardiographic parameters in a linear regression model with dependent variable eGFR, E/E’ (beta -1.75, p=0.007) and LV twist rate (beta -0.17, p=0.021) were independent significant predictors. Amongst CKD stages 1,2 patients there were 6 (33.3%) with diastolic dysfunction, in stage 3 the figure increased to 17 (75%) and in stages 4,5 further to 14 (62.4%) (Chi-Square 13.7, p=0.033).

Conclusions: Arterial stiffness and LV relaxation demonstrate progressive deter-
roration with worsening eGFR whereas LV filling pressure and twist rate appear to increase, compensating for the impaired diastolic filling. Outcome studies may be required to identify the association of these early markers of cardiovascular disease in CKD patients.
predicting mortality in SHF. CPO has the potential to be a key diagnostic marker in HFrEF and may enhance the ability to accurately identify patients at greatest risk for heart failure related complications.

**P5147**  
**Relationship of pro-collagen biomarkers of myocardial fibrosis with myocardial dysfunction and metabolic derangement in type 2 diabetes**  
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**Purpose:** Myocardial fibrosis is a potential contributor to non-ischemic diabetic dysfunction (DD) in type 2 diabetes (T2DM). We sought the relationship between fibrosis markers, myocardial dysfunction and metabolic derangement.

**Methods:** Clinical, imaging and biochemical data were measured in 390 asymptomatic subjects (216 men, 58±10 yrs) with T2DM. Myocardial function was examined with standard 2D echo, early diastolic (eM) and systolic velocity, strain, strain rate, and backscatter (cIB). Amino-terminal propeptides of pro-collagen type I (PINP) and type III (PIIINP) were measured by radio-immunoassay, and the carboxy-terminal propeptide of pro-collagen type I (PICP) was measured by enzyme linked immunosorbent assay.

**Results:** Patients were stratified by metabolic derangement; 53 (14%) had isolated T2DM, 67 (17%) had T2DM with isolated hypertension, 178 (45%) had T2DM with chronic kidney disease, and 92 (24%) had T2DM with chronic kidney disease and end-organ involvement (microalbuminuria). Progressive metabolic derangement was mirrored by worse DD (em p=0.001), increased cIB (p=0.016), greater insulin resistance (log HOMA-IR p<0.001) and worse exercise capacity (VO2 max p=0.001) but only a trend towards proportionally higher PIIINP levels. PIIINP (3.9±1.9 μg/L) was associated with insulin resistance (log HOMA-IR r=0.206, p=0.008) and independent of age (β=0.086, p=0.017) and renal function (creatinine r=0.227, p=0.004). PINP (42.2±28.4 μg/L) and PICP (27.2±90.4 ng/ml) were not associated with metabolic parameters or myocardial properties.

**Conclusions:** Metabolic derangement in T2DM is proportionally associated with worsening DD and increased myocardial signal intensity (cIB). The association with PIIINP levels is weak, suggesting a limited role of type III collagen turnover in subclinical, non-ischemic diabetic heart disease.

**P5148**  
**Acute improvement of left atrial mechanics and left ventricular diastolic function after Transcatheter Aortic Valve Implantation**  
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**Purpose:** Aortic stenosis leads to remodelling of the left ventricle and atrium that causes systolic and diastolic dysfunction. Transcatheter aortic valve implantation (TAVI) is a rapidly evolving therapy for severe aortic stenosis in high-risk patients. Two-dimensional speckle tracking echocardiography (STE)-derived strain measurements enable the regional assessment of left atrial (LA) mechanics. The goal of this study was to describe the acute effects on myocardial deformation of the LA and left ventricle (LV) function after TAVI.

**Methods:** 32 consecutive patients (17 female, mean age 76 years, mean Euroscore 18.7%, mean LVEF 52.5±15.7%) with severe aortic stenosis (0.73±0.19 cm²) were enrolled into our study. We performed transthoracic echocardiography including STE of the basal septal segment of the left atrium to determine peak positive strain (LApS), strain during early diastole (eLApS) and, if feasible, strain during atrial contraction (LAaS) representing LA reservoir, conduit, and contractile function, respectively. In addition, the corresponding strain rate values such as systolic atrial strain rate (SSr), early diastolic atrial strain rate (ESr), and late diastolic atrial strain rate (ASr) were analyzed. Diastolic assessment of the left ventricle included standard indices and the atrial fraction. LA volumes throughout the cardiac cycle were also assessed.

**Results:** At baseline, 24 (75%) of our patients were in sinus rhythm. Heart rate and NYHA class (II - IV) were unchanged. This was accompanied by improvement of the early LV diastolic function indicating acute recovery of LV relaxation and LA function.

**Conclusion:** One week after TAVI only the reservoir and conduit function of the left atrium improved, whereas the late diastolic LA contraction and the LA volume were unchanged. This was accompanied by improvement of the early LV diastolic function indicating acute recovery of LV relaxation and LA function.

**P5149**  
**Diagnostic value of pulsatile hemodynamics for heart failure with normal ejection fraction**  
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**Purpose:** Increased arterial stiffness and wave reflections are present in most patients with heart failure with normal ejection fraction (HFNEF). We tested whether measures of pulsatile arterial function are useful for diagnosing HFNEF, in comparison with and in addition to Tissue Doppler Echocardiography (TDE).

**Methods:** Patients with dyspnea as leading symptom were categorized as having HFNEF or no HFNEF, based on invasively derived filling pressures and natriuretic peptide levels. Pulse wave velocity was measured invasively (aPWV), aortic pulse pressure (aPP) and its components (incident pressure wave height – P1, forward wave amplitude – P2, augmented pressure – AP, backward wave amplitude – P3) were quantified non-invasively from radial tonometry, using pulse waveform analysis and wave separation analysis.

**Results:** 71 patients were classified as having HFNEF, and 65 as no HFNEF (in 223 patients, intermediate results were present). Patients with HFNEF were older, more often had hypertension and diabetes, and had more advanced coronary artery disease, larger left atria and higher left ventricular mass; blood pressures and all measures of arterial stiffness and wave reflections were higher in HFNEF group. Receiver operating curve analysis derived area under the curve values were 0.823 for E/E’ (medial aorta), the best TDE parameter, and 0.867, 0.851, 0.812, 0.813, 0.804, and 0.825 for aPWv, aPP, P1, P2, AP, and P3, respectively (Figure). Multivariable logistic regression models proved that measures of pulsatile arterial function provided independent and additive diagnostic information.

**Conclusion:** Measures of arterial stiffness, central pressures and wave reflections complement TDE for the diagnosis of DHF.

**P5150**  
**Perhexiline corrects energy deficiency and improves symptoms in chronic heart failure**  
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**Background:** We hypothesized that the metabolic modulator perhexiline would ameliorate myocardial energy deficiency and improve symptoms in dilated cardiomyopathy.

**Methods and Results:** 50 patients with heart failure (NYHA II - IV, LVEF -40%) were randomised to 100mg bd (n=25) or placebo (n=25) for 1 month in a double blind fashion. Myocardial ratio of phosphocreatine to adenosine triphosphate, an established marker of cardiac energetic status, as measured by 31P magnetic resonance spectroscopy, echocardiography, symptoms and quality of life scores were assessed at baseline and at study end. Perhexiline improved the primary

**Effect of perhexiline and placebo**

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<th>Placebo Group</th>
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end point of PCr/ATP ratio (from 1.16 ± 0.08 to 1.51 ± 0.11 versus 1.38 ± 0.07 to 1.34 ± 0.07, P = 0.0005) and New York Heart Association class (P = 0.0002). Conclusions: Perhexiline ameliorates cardiac energetic impairment and improves symptom status with short term administration. This study supports the hypothesis of energy-related symptom in heart failure and further consideration of metabolic therapies in heart failure.

**P5151**

**Index of lectin-like oxidized low-density-lipoprotein receptor is independently associated with left ventricular systolic dysfunction**

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**Background:** Lectin-like oxidized low-density-lipoprotein receptor-1 (LOX-1) is a multiple ligand receptor induced by oxidative stress. The LOX-index represents levels of soluble LOX-1 (sLOX-1) multiplied by levels of LOX-1 ligands containing apolipoprotein B (LAB), and serves as a marker of cardiovascular risk in a general population. Recently, we reported that left ventricular (LV) expression of LOX-1 is markedly increased in a rat model of heart failure (HF). However, the significance of LOX-index in patients with HF in the clinical situation is unknown.

**Methods and Results:** We carried out a cross-sectional study involving 335 out-patients whose NYHA classes were stable for at least 3 months. They were divided into 3 groups: 22 patients with systolic dysfunction (HF+); LV ejection fraction (LVEF) < 50%, 35 patients with LV hypertrophy (LHV: LV mass index (LMI) ≥ 116 in male, >104g/m² in female) but without systolic dysfunction (LHV+HF-), and 278 patients without LHV or systolic dysfunction (LHV-HF-). We examined serum levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hsCRP), leptin, and adiponectin and the LOX-index. The body mass index, blood pressures, low-density-lipoprotein cholesterol (LDL-C), hsCRP, leptin, and adiponectin were similar among the 3 groups. However, both NT-proBNP and LOX-index were significantly increased in HF+ compared to LHV+HF- and LHV-HF-.

**Conclusions:** In contrast to NT-proBNP, LHV, and LOX-index we did not find any correlation with LVEF, but did not affect NT-proBNP levels or clinical symptom score. The treatment was well tolerated without any increase in atrial fibrillation or ventricular arrhythmias.

We hypothesised that levosimendan will improve myocardial regional contractility without harmful side effects in acute PCI treated STEMI patients complicated by decompensated heart failure.

**Method:** Patients developing clinical signs of heart failure (including cardiogenic shock) within 48 hours after a primary PCI treated STEMI, with decreased wall-motion in ≥ 3 of 16 segments evaluated by echocardiography, were randomised to a 216 hours levosimendan infusion or matching placebo in a double blind design. Primary endpoint was change in wall-motion score index (WMSI) from baseline to day 5. Infarct size was measured by single photon emission computed tomography (gated SPECT) at 6 weeks.

**Results:** (mean ±SD): A total of 61 patients were included. Age (64±13 years), peak cardiac troponin T (1308±6996 ng/l), BP (104/66 mmHg) and left ventricular EF (42±9%) at inclusion, were not significantly different between groups. Infarct size at 6 weeks (42±16%) was similar in both groups. There was significantly larger improvement in WMSI from baseline to day 5 in the levosimendan group compared to placebo from (1.94±0.21 to 1.66±0.31 vs. 2.02±0.26 to 1.83±0.26 respectively, p=0.03). There were no significant between-group-differences from baseline to day 5 in changes in NT-proBNP levels, a clinical composite score, frequency of atrial fibrillation or ventricular arrhythmia, new ischaemic episodes or use of inotropy as rescue therapy. There were significantly more episodes of hypotension during study drug infusion in the levosimendan group (63% vs 36%, p=0.03), but no difference in blood pressure at the end of infusion or in use of vasopressors. One patient died in the levosimendan group and 4 patients in the placebo group during 6 months follow-up. No significant between-group-differences at 6 months in MACE (death, nonfatal myocardial infarction or revascularisation of the infarct related artery) or in rehospitalisation for heart failure, were present.

**Conclusion:** Levosimendan treatment improved regional contractility measured by WMSI in patients with acute PCI treated STEMI complicated by heart failure, but did not affect NT-proBNP levels or clinical symptom score. The treatment was well tolerated without any increase in atrial fibrillation or ventricular arrhythmias.

**P5152**

**Levosimendan improves contractility in post ischemic myocardium in patients with acutely revascularised infarction complicated by decompensated heart failure**

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**Background:** Reduced calcium sensitivity of the myofilaments is believed to be part of the injury seen after reperfusion of ischemic myocardium. The role of the calcium sensitizer levosimendan in patients with acute STElevation myocardial infarction (STEMI) is unresolved.

**Methods and Results:** We randomized (1:1) 102 patients with idiopatic dilated cardiomyopathy to levosimendan or placebo. Levosimendan was infused over 90 minutes followed by 6 hours, or matching placebo, in addition to recommended therapy. The end points were primary: change in LV ejection fraction (LVEF) of ≥ 5% or ≥ 10% absolute value, or secondary: change in left ventricular end-systolic volume (LVESV) of ≥ 10% or ≥ 20% absolute value, or change in wall-motion score index (WMSI) of ≥ 1 or ≥ 2 segments.

**Results:** The therapy with Spironolactone has not significantly modified systolic arterial pressure, diastolic arterial pressure and differential pressure in the two groups.

**Conclusion:** The therapy with aldosterone – antagonist Spironolactone reduced atrial fibrillation and ventricular arrhythmias in patients with idiopathic dilated cardiomyopathy.

**Aims of study:** To evaluate the effect of a therapy with aldosterone – antagonist Spironolactone on aortic stiffness in patients with idiopathic dilated cardiomyopathy.

**Methods:** We randomized (1:1) 102 patients with idiopathic dilated cardiomyopathy and New York Heart Association class I – II to receive Spironolactone 25 mg/day or placebo, in addition to recommended therapy. The end points were aortic stiffness index and aortic strain, assessed before and after 6 months treatment. All measures were obtained with echocardiography M – mode at 3 cm above the aortic valve on parasternal long axis view and simultaneous brachial arterial pressure with sphygmomanometer.

**Results:** Ascending aorta measures, aortic stiffness index, aortic distensibility and aortic strain were similar at randomization in the two groups. After 6 month of therapy in the treated group we found a statistically significant reduction of aortic strain index (7.4±3.4% vs 9.6±4.3% ± 10^-6; P<0.05) with a significant increase of aortic distensibility (3.1±10^-6 vs 3.9±10^-6 cm² dyn⁻¹, P<0.05) and systolic aortic strain (10.0±5.5% vs 8.0±2.8% ± 2.1%, P<0.01). The therapy with Spironolactone has not significantly modified systolic arterial pressure, diastolic arterial pressure and differential pressure in the two groups.

**Conclusion:** The therapy with aldosterone – antagonist Spironolactone reduced aortic stiffness in patients with idiopathic dilated cardiomyopathy. This effect could improve haemodynamics suggesting the use of aldosterone – antagonist in patients with low NYHA class (III).

**P5154**

**The treatment in patients with chronic heart failure with erythropoietin failure**

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**Purpose:** Anaemia although common in chronic heart failure (CHF) patients reduces functional status quality of life and is an independent risk factor for hospital admission and mortality. Erythropoietin stimulating agents (ESA) are frequently used for its treatment. The effects of ESA treatment in patients CHF with anaemia remain largely unknown. Therefore, our aim was to perform the study to determine the effect of continuous erythropoietin reseptor activator C.E.R.A.-
P5155

Acute heart failure patients with high initial blood pressure show paradoxical hemococoncentration on admission

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Introduction: As volume overload is a major profile of acute heart failure syndrome (AHFS), diuretics as well as oxygen, nitrates, and morphine, are a mainstay of therapeutic strategy for those patients. Though decongestion/diuretic therapy is started immediately after admission in most patients, changes in concentration of blood components in this period remain to be investigated.

Method: We studied 135 patients admitted to our hospital with symptoms of AHFS between January and December 2010. Changes in hematocrit levels between on admission and 24±12 hours postadmission were evaluated. Patients with cardiogenic shock, hemodialysis, blood transfusion, and/or urgent coronary angiography were excluded.

Results: In spite of decongestion/diuretic therapy started immediately after admission, hematocrit level on admission was paradoxically higher than the level of 24±12 hours postadmission in 95 patients (70%). Patients in the top tertile of admission hematocrit were defined to have an evidence of admission hemococoncentration. The ΔHb in patients with admission hemococoncentration was 1.8±0.7 g/dL (12±2.5 g/dL on admission and 11.6±2.4 g/dL at 24 h, p<0.001) whereas 0.1±0.7 g/dL (11.6±2.1 g/dL on admission and 11.5±2.1 g/dL at 24 h, p=0.71) in those without admission hemococoncentration. Moreover, ΔHb was positively and significantly correlated (r=0.37, p=0.02) with the waist-to-hip ratio (r=0.37, p=0.02). Furthermore, ΔHb was positively and significantly correlated not only with initial SBP (r=0.43, p=0.001) but also initial heart rate (r=0.29, p=0.001). Suggesting a presyncpeptic effect on the pathophysiology of admission hemococoncentration. Patients with admission hemococoncentration had significantly higher ejection fraction (31±12 vs. 39±14%, p=0.003), higher presence of New York Heart Association class 4 (45% vs. 17%, p=0.02), and night time admission (52% vs. 30%, p=0.09) than those without admission hemococoncentration. Age, sex, renal function, history of hypertension, diabetes, and dyslipidemia, presence of ischemic heart disease are comparable between two groups.

Conclusion: AHFSs with high initial SBP shows paradoxical hemococoncentration on admission. Sympathetically mediated fluid shifts between extracellular and circulating volume may underlie the development of AHFS.

P5156

Myocardial and vascular dysfunction in young subjects, are related to dyslipidemia and abdominal obesity but not to glycaemia

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Purpose: To investigate the relationships between cardiovascular risk factors and subclinical myocardial and vascular dysfunction in young adults.

Methods: We recruited 53 young subjects under 30 years of age including 34 healthy volunteers (mean age 24.6±2.9 years) and 19 subjects with type 1 diabetes mellitus (mean age of 21.1±3.6 years, mean duration of diabetes 9.0±7.5 years; mean HbA1c 8.8±1.6%).

All subjects had detailed echocardiography; all type 1 diabetics and 21 controls had myocardial velocity measurements of LV long-axis function (at the mitral annulus). Applanation tonometry was used to measure augmentation index and carotid-femoral pulse wave velocity. Local arterial stiffness parameters (beta and epsilon) and carotid intima media thickness (cIMT) were assessed using high-resolution B-mode ultrasound of the common carotid artery. Fasting blood samples were taken at baseline and posttreatment.

Results: Conduit arterial stiffness was related to body weight (beta, r=0.32, p=0.023; and epsilon r=0.41, p=0.003). Pearson correlations The stiffness parameter epsilon correlated with the waist-hip ratio (r=0.37, p=0.008). Early diastolic myocardial function was inversely related to waist-hip ratio (r=0.15, p=0.004). There was no correlation with body weight. Fasting albumin was negatively correlated with cIMT (r=0.39, p=0.001). balloon and cIMT (r=0.39, p=0.001). HDL cholesterol (r=0.39, p=0.001). All measurements of vascular and myocardial function were unrelated to blood glucose, glycaemic control, and hCGP.

Conclusions: In young adults, abdominal obesity and dyslipidaemia may be more important risk factors for early myocardial and vascular dysfunction than is glycaemia.

P5157

Which adjunctive test to clinical evaluation is better to diagnose pulmonary congestion in a pre-transplantation heart failure outpatient clinic?


Purpose: Patients with heart failure (HF) are often evaluated with some degree of uncertainty, even by highly skilled clinicians. Optimal evaluation includes balance of symptoms, physical examination and adjunctive testing. Our aim was to define more clearly the relationship between B-lines assessed by lung ultrasound (LUS), chest x-ray (CXR), clinical congestion score (CCS) and the natriuretic peptides

Conclusions: A high initial SBP shows paradoxical hemococoncentration on admission. Sympathetically mediated fluid shifts between extracellular and circulating volume may underlie the development of AHFS.
(NTproBNP) as part of the evaluation of pre-transplant HF patient in an outpatient clinic.

**Methods:** Fifty-eight patients admitted to a pre-transplantation clinic due to advanced systolic HF (65.4±11.9 yrs, mean age 49±11 yrs, 47.2% with diabetic and 29.3% with post-ischaemic cardiomyopathy) were enrolled. All evaluation were independently performed.

**Results:** CXR and LUS feasibility was 100%. Mean radiation dose to perform CXR was 0.38±0.29mGy. Mean time to perform LUS was 9.9±4.25 minutes. Significant congestion was present in 52.6% estimated by a clinical conges-
tion score, 57.9% by LUS (total B-lines number≥15), in 45.6% by NTproBNP ≥100pg/mL and in 43.9% by CXR evaluation. Assuming CXR as a refer-
ence for decompensated HF, ROC analysis showed a C statistic of: CCS=0.69 (95%IC: 0.55-0.83, p<0.0001), LUS B-lines number ≥15 = 0.82 (95%CI: 0.71-
0.93, p<0.001) and NTproBNP ≥0.81 (95%IC: 0.69-0.93, p<0.0001). When NT-proBNP was assumed as a reference for decompensated HF the C statistic was: CCS=0.71 (95%CI: 0.57-0.84, p<0.0001), LUS B-lines number ≥15 = 0.88 (95%CI: 0.79-0.97, p<0.0001) and CXR=0.79 (95%CI: 0.66-0.91, p<0.001).

**Conclusion:** Our data shows that clinical evaluation understimates the presence of pulmonary congestion. Given its accuracy, low cost, radiation free and portabi-
ility, LUS may be considered as a reliable tool for quick and easy evaluation of pulmonary congestion.

**P5180**

Sonographic pulmonary comet sign in diagnosis and monitoring of pulmonary congestion in HF

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**Background and Aim:** Pulmonary congestion is useful marker of decompensated HF. The aim was to study the importance of Lung “Comet Tail” artefactual in diagnosis and monitoring of Pulmonary Congestion in patients with different types Heart Failure.

**Methods:** We studied 430 patients with II-IV NYHA class HF. 338 Patients have Systolic HF (SHF), 92 patient – HF with preserved systolic function (DFH), 70 patients with chronic obstructive pulmonary disease (COPD) and 155 patients with heart diseases but without HF (control). Sonographic evaluation of a lung was done in horizontal or vertical positions of patient, from 10 points of thoracic wall which corresponded to the projection lung lobes.

**Results:** In patients with HF we significantly often found the “Comet Tail” arte-
fact (CTa) There was good correlation between the count of CTa registration points from the thoracic wall and the heart failure NYHA class (r=0.57), left ventricular systolic (r=0.43) and diastolic (r=0.34) diameters and negative correlation with EF% (r= -0.44). In the HF gr. CTa was registered from 3 or more points of thoracic wall in 89.6%, in SHF -91.4%, in DFH -86.2%, in COPD -9.1% and in control -7.1% of patients. If we take 4 points and more as a reference value the sensitivity of sign in diagnosis of pulmonary congestion was 83.5% an specify – 97.6%. In CHF group CTpH was prominent, protracted and multiple while in the II group it was single and short lasting. After use of diuretics CTa disappear or was less prominent than before treatment.

**Conclusion:** Thoracic US is accurate method for evaluation and monitoring of pulmonary congestion in patients with systolic and diastolic HF. The US sign of pulmonary congestion is a CTa, which is multiple and registered from larger area of thoracic wall (3 points or more). The intensity of CTi is reduced if the dehy-
dration is successful.

**P5190**

Circladian variation of the occurrence of acute heart failure syndromes contributes to long-term prognosis in patients with non-ischemic cardiomyopathy

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**Background:** Although previous studies reported that the occurrence of acute myocardial infarction peaked in the morning, little is known for the clinical signif-
ificance of circadian variation in the occurrence of acute heart failure syndromes (AHFS) in patients with non-ischemic cardiomyopathy (NICM). We aimed to in-
vestigate the clinical significance of the occurrence of AHFS during the morning in NICM patients.

**Methods:** We have retrospectively studied consecutive 201 NICM patients admis-
ted for AHFS. We defined the patients of AHFS, who developed their symptoms from the midnight until 8 a.m. as the morning-HF group, and the others as the control-HF group.

**Results:** Twenty seven patients with the occurrence of AHFS during the mor-
ing were recognized in the present study, whose characteristics were signifi-
cantly higher age, increased systolic blood pressure (BP) than in the control-HF group (72±13 vs 66±16 y.o., 156±156 vs 124±24 mmHg, p<0.05). Although in-
and out-of hospital mortality did not differ between the morning-HF and control-
HF groups, but the rate of re-hospitalization for heart failure in the morning-HF group was significantly higher than the control-HF group. Sub-analysis using polysomnography revealed that the prevalence of sleep apnea was significantly higher in the morning-HF group compared with in the control-HF group (100% vs. 74%, p=0.001).

**Conclusion:** The occurrence of acute heart failure syndromes in the morning itself predicts poor clinical prognosis in association with higher age and sleep apnea, suggesting that increased sympathetic nerve activity (SNA) in the morning may play a significant role in deteriorating HF. Management to control SNA by treating sleep apnea or BP control in chronic phase would be the key to reduce the re-hospitalization for the worsening heart failure.

**P5160**

Correlations between hemodynamic parameters and serum high sensitive troponin-T

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Serum troponin-T is widely accepted as a prognostic biomarker of heart failure. However the correlation and cause of elevation of serum troponin-T has not been studied well.

**Method:** Heart stable heart failure patients who were performed right and left heart invasive catheterization were analyzed (male 110, median age 72). Serum high sensitive troponin-T (Roche diagnostics) were detected in all the patients (median 0.012 inter quartile range 0.007-0.021ng/ml). Stepwise regression analysis revealed age (coefficient 0.0012, 95% confidence interval 0.0002[0.0002], p<0.001), serum hemoglobin concentration(0.000, [0.016;0.022]), p(0.045), estimated glomerular filtration rate(0.005, [0.019;0.001], p=0.031), ejection fraction(0.013, [0.019;0.007], p<0.0001), left ventricular end diastolic pressure (0.015, [0.004;0.026], p<0.002) were associated with serum high sensitive troponin-T.

**Adjusted associations with troponin-T**

| Coefficient SE 95% CI p-value |
|-----------------|---------------|-----------------|---------------|
| Intercept       | -3.575        | 0.559           | -4.817; -2.479 | <0.0001       |
| Age, years      | 0.022         | 0.004           | 0.000; 0.020   | 0.010         |
| Hemoglobin, g/dL| -0.069        | 0.024           | -0.116; -0.022 | 0.005         |
| eGFR, min/ml    | 0.005         | 0.002           | -0.010; -0.001 | 0.002         |
| Ejection fraction, % | -0.013  | 0.003           | -0.019; -0.007 | <0.0001       |
| Left ventricular end diastolic pressure, mmHg | 0.016 | 0.006 | 0.004; 0.026 | 0.009 |

**Conclusion:** In heart failure patients, serum troponin-T concentration was in-
creased by older age, anemia, impaired renal function, reduced left ventricular ejection fraction, and elevated left ventricular end diastolic pressure.

**P5161**

A New Radiologic 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 infar-
ction (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 edemas signs. LI reflects LFC and was measured by new 50 times more sensitive surfaces impedance (LI) that decreases with increasing LFC may be indicator of LFC, but

**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.
Predictors of augmented peripheral chemosensitivity in patients with systolic heart failure

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Background: Augmented peripheral chemosensitivity is typical feature of chronic heart failure (CHF), associated with poor prognosis, however its clinical predictors remain poorly understood.

Purpose: We investigated clinical predictors of peripheral chemosensitivity in contemporary CHF patients receiving optimal medical treatment.

Methods: Thirty CHF patients were studied (NYHA class III, mean LVEF 27.1±7.1%, who were treated with beta-blocker (100%), angiotensin converting enzyme inhibitor and/or angiotensin receptor blocker (98%) and aldosterone antagonist (87%). Peripheral chemosensitivity was assessed with the transient hyperaemia response (THR) using nitrogen gas administration and expressed by area under the curve of SaO2 (%) and minute ventilation (l/min). On previous experience, high peripheral chemosensitivity was defined as a response ≥ 0.7 l/min%. Statistical significance was defined at p<0.05.

Results: Thirteen (43%) CHF patients showed high chemosensitivity. The following clinical parameters differentiated those with high vs normal chemosensitivity: elevated NT-proBNP (4534±2719 vs 2051±2232 pg/ml), lower peakVO2 (14.1±1.8 vs 18.6±6.3 ml/kg/min), shorter pulmonary acceleration time (84.2±18.8 vs 103.0±16.7 ms), greater right ventricle end-diastolic diameter (31.7±10.8 vs 27.0±5.4 mm) and more frequent incidence of atrial fibrillation (69% vs 24%)(high vs normal chemosensitivity, respectively, p<0.05 in all comparisons).

Contrasting for all these factors, NT-proBNP alone significantly predicts chemosensitivity.

Conclusions: High peripheral chemosensitivity is common in contemporary CHF patients despite optimal haemorrhoidal blockade. Correlation of NT-proBNP, peakVO2, pulmonary acceleration time and AF with chemosensitivity suggests 1) an association between peripheral chemosensitivity and 2) that common clinical measurements might be used to screen patients for peripheral chemosensitivity. Assessment of these parameters may therefore be useful for selection of patients for novel therapies targeting peripheral chemoreceptors.

Artificial neural network in early identification of heart failure progression in OptiVol telemonitoring management of chronic heart failure

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Daily acquisition and analysis of vital sign data and clinical symptoms in chronic heart failure patients allow for early recognition of an emerging decomposition. Artificial Neural Networks (ANN) are a statistical model, which is able to learn probability distributions of a dataset by inductive example training. Here, the capability of a personalized ANN was tested to predict the progression of chronic heart failure in the individual patient.

Methods: In 169 patients hospitalized due to chronic heart failure decompensation, a multiparameter telemonitoring was performed after discharge for up to 3.5 years with 150,000 patient days in total. Daily recording of vital signs (ECG, body temperature, blood pressure, BP; CO2 saturation, heart rate, fever, tachycardia, fluid accumulation) was recorded by a high energy data monitoring system. We defined that primary endpoint was the difference of log BNP between OptiVol alert and baseline, and secondary endpoint was the difference of other parameters between OptiVol alert and baseline.

Results: From April 2010 to December 2011, 200 patients in 12 institutes were enrolled in the present study. Mean age was 65.3±12.2 years, mean ejection fraction BNP was 5.6±5.9. During a mean follow-up period of 15.3±4.2 months, we had 255 OptiVol alert events in the OptiVol threshold of 60. In primary endpoint, log BNP was higher in OptiVol alert than at baseline, but not significantly (5.2±1.1 vs 5.1±1.1, p = 0.06). However, the rate of change in ITI was negatively correlated with the rate of change in log BNP (r = -0.35, p = 0.01). In OptiVol alert events with ITI equal to or less than 96% of mean ITI, there was no significant difference in log BNP between OptiVol alert and baseline. In secondary endpoint, red blood cell, hemoglobin, hematocrit, total protein and albumin were significantly lower in OptiVol alert than at baseline.

Conclusion: OptiVol alert with decreased ITI, rather than OptiVol alert only, seems to reflect fluid retention.

Predictors for outcome

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Background: Heart failure (HF) is one of the most common causes for hospitalizations. A major cause of HF related hospitalizations is fluid accumulation. Recent studies have suggested that intrathoracic impedance (ITI) may be a useful parameter to track daily changes in pulmonary fluid status. OptiVol alert, which is based on a predictor algorithm calculated from ITI, is reported to predict fluid accumulation at an early stage. However, the sensitivity and specificity of OptiVol alert for deteriorated HF have not been sufficient for it to be a clinically useful parameter. Therefore, we examined the relationships of OptiVol alert and ITI with various parameters.

Methods: This study was a prospective multicenter study. Patients who suffered from structural heart disease and who had been implanted with a high energy device with an OptiVol feature were included in this study. The patients underwent various examinations, including body weight, chest X-ray, electrocardiogram, a blood sample such as BNP concentration and echocardiography, at enrollment and following an OptiVol alert. We examined difference in various values between OptiVol alert and baseline. All patients were followed by a wireless remote monitoring system. We defined that primary endpoint was the difference of log BNP between OptiVol alert and baseline, and secondary endpoint was the difference of other parameters between OptiVol alert and baseline.

Results: From April 2010 to December 2011, 200 patients in 12 institutes were enrolled in the present study. Mean age was 65.3±12.2 years, mean ejection fraction BNP was 5.6±5.9. During a mean follow-up period of 15.3±4.2 months, we had 255 OptiVol alert events in the OptiVol threshold of 60. In primary endpoint, log BNP was higher in OptiVol alert than at baseline, but not significantly (5.2±1.1 vs 5.1±1.1, p = 0.06). However, the rate of change in ITI was negatively correlated with the rate of change in log BNP (r = -0.35, p = 0.01). In OptiVol alert events with ITI equal to or less than 96% of mean ITI, there was no significant difference in log BNP between OptiVol alert and baseline. In secondary endpoint, red blood cell, hemoglobin, hematocrit, total protein and albumin were significantly lower in OptiVol alert than at baseline.

Conclusion: OptiVol alert with decreased ITI, rather than OptiVol alert only, seems to reflect fluid retention.
ments of weight, systolic and diastolic BP and heart rate as well as time intervals were used as input parameters. Target output values were based on the study endpoint, e.g. 0 for a "stable health state" and 1 for the primary endpoint "new heart failure hospitalization". An ANN with 225 hidden neurons within 3 hidden layers, backpropagation training and squared error function was used. The network topology has been determined experimentally. Network training lasted 4000 iterations and has been stopped as training root mean squared error (RMSE) converged towards 1.6%, indicating a good adaption to the training set.

**Results:** RMSE on the group 2 data was 9.5%, indicating a reasonable generalization of the training data onto this group. Mean value measurement data by the ANN classified for the primary endpoint "new heart failure hospitalization" were 0.80(±0.17), classified as "stable health state" were 0.20(±0.25). Measurement data hinting towards "unstable health state" have been assessed with mean of 0.44(±0.24) allowing for good group separation.

**Summary:** Out of the data of daily multiparameter telemonitoring recordings in patients with chronic heart failure an ANN was trained to predict the most probable healthstate of the monitored patient. This model analyzing telemonitoring data for heart failure deterioration may be used for decision support and alerting.

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**P5166 Abnormal acetylcholine - induced vasoreactivity in Takotsubo cardiomyopathy, novel pathophysiology insights on Takotsubo cardiomyopathy**

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More than 10 years has passed since the first report of Takotsubo Cardiomyopathy (TTC), but a clear definition of the pathophysiology is still lacking. Several hypotheses have been described, but clinical data are still very poor. We sought to test coronary vasoreactivity with administration of intracoronary Acetylcholine (ACh) in the patients with TTC. Consecutive patients were prospectively collected in a clinical Registry that involves 3 Hospitals. Since 2011 in one of the 3 Institutions, stable TTC pts were tested with intracoronary administration of acetylcholine (boluses of 4 – 20 – 100 micrograms). Positive test was defined as coronary spasm, with a >75% reduction of the epicardial artery diameter or diffuse vasoconstriction in ≥ 1 vessel with transient slow – no flow. 174 consecutive TTC patients were enrolled in the Registry. A Subgroup of 11 patients underwent ACh test. The incidence of abnormal response after ACh administration was 54% (N=6 pts). In 4/5 patients intracoronary ACh induced a focal or multilocal spasm in the left anteri- rior descending artery (LAD). 1 patient developed a diffuse spasm involving also the circumflex artery. 1 patient developed a ~50% spasm with transient no flow in the LAD. Intracoronary NTG administration promptly reversed the abnormal vasoreactivity in all of the patients.

These data are quite similar to those reported in the CASPAR study that tested intracoronary ACh in patients with acute coronary syndromes and nonsignificant CAD. In our population prevalence of abnormal coronary vasomotor response to Acetylcholine is high and comparable with that reported in acute coronary syndromes with no CAD. Our findings suggest that abnormal coronary artery vasomotion related to endothelial dysfunction could play a significant pathogenetic role in TTC.

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**P5167 Heart failure symptoms and sleep-disordered breathing in patients with chronic heart failure - results from the SchlaHF registery**

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**Objective:** In patients with stable chronic heart failure (CHF) we investigated the clinical value of different heart failure symptoms and its relationship to the presence of sleep-disordered breathing (sDB).

**Patients and Methods:** The ongoing multi-center SchlaHF registry documents demographic and clinical data on stable CHF patients. We analyzed the data of 3504 CHF prospectively enrolled patients from cardiology outpatient clinics and practices. Induction criteria are New York Heart Association (NYHA) class II and left-ventricular ejection fraction (LVEF) <45%. SDB was determined by a two-channel screening (nasal airflow, pulse oximetry) using ApneaLink (ResMed, Sydney, Australia).

**Results:** The symptoms analyzed were naptime, nocturnal dyspnea and nocturia. The median naptime was 30 min. In an univariate analysis AHI ≥ 15 (OR 1.217; CI 1.067-1.400) and ODI ≥ 5 (OR 1.365; CI 1.155-1.613) were statistically significant (p < 0.05) predictors for a naptime > 30 min while in a logistic regression it wasn’t. There was an increase in nocturia (> 3 times a night) in patients with sdb being in NYHA functional class III and IV depending on severity of sdb, while this could not be seen in patients in NYHA functional class II. A logistical regression analysis for nocturia (> 3 times a night) were AHI≥15/h as a significant predictor (OR = 1.583; 95% CI 1.338-1.872). Other significant variables were NYHA III/IV (OR = 1.548; 95% CI 1.291-1.855), age (per 10 years increment: OR = 1.128; 95% CI 1.042-1.216), BMI – 30 kg/m² (OR = 1.442; 95% CI 1.208-1.721) and LVEF – 25% (OR = 1.624; 95% CI 1.289-2.045).

**Conclusions:** The multi-center SchlaHF registry shows that HF symptoms are linked to the presence and the severity of SDB. Age and the severity of CHF were other important clinical predictors.

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**P5168 Heart rate control is important even in heart failure patients - an interim analysis of the CHART-2 study**

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**Purpose:** Elevated heart rate (HR) is an independent risk factor for mortality in heart failure (HF) patients. However, the medications for the management of HR often lower systolic blood pressure (SBP) that may worsen the prognosis of HF patients. We examined the importance of HR control in terms of SBP in patients of our Chronic Heart Failure Analysis and Registry in the Tohoku district 2 (CHART-2) Study.

**Methods:** The CHART-2 Study (N=10,219) is a multicenter prospective cohort study enrolling Stage B/C/D patients. The study subjects were 2,761 overt HF patients with sinus rhythm and divided them into 6 groups based on the ter- tiles of SBP and the median HR as follows; G1 (SBP < 135 and HR <70, N=430), G2 (SBP < 135 and HR >70, N=469), G3 (SBP <120, ≤ 135 and HR >70, N=444), G4 (SBP <120, ≤ 135 and HR >70, N=410), G5 (SBP <120, > 120, HR >70, N=490), G6 (SBP <120, HR >70, N=518).

**Results:** G3 had the lowest NYHA class and brain natriuretic peptide (BNP) level. On the other hand, G6 were characterized by lower beta-blocker use, lower left ventricular ejection fraction, and the highest BNP level. During a mean follow-up of ~3.1 years, non-adjusted Kaplan-Meier curves for all-cause death and cardio-vascular death showed that G3 had better prognosis and G6 had poorer prognosis (Figure). In multivariable Cox model including covariates that might influence HR and SBP, Groups with elevated HR showed ~169% increased hazard ratios for all-cause death as compared to G3 (reference). Furthermore, G4 and G6 had significant higher cardiovascular mortality.

**Conclusions:** Regardless of SBP, elevated HR was associated with higher mor- tality. In view these results and well-known importance of increased HR for mor- tality, HR control (<70/min) should be given higher priority even in the HF patients with relatively low SBP.

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![Figure 1](https://example.com/image1.png)
Incident heart failure with preserved ejection fraction in the general population

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Purpose: The incidence of heart failure (HF) with preserved ejection fraction (HF-PEF) is increasing, compared to HF with reduced ejection fraction (HF-REF). Data on distinctive epidemiology and prediction of incident HF-PEF and HF-REF in a general population have not been described.

Methods: In 8569 HF-free subjects of a general population based cohort study (PREVEND), we studied the performance of established cardiovascular risk factors on incident HF, their hazard ratios given per 1-SD increment and 95% confidence interval (CI), and the additive value of N-terminal pro-B-type natriuretic peptide (NT-proBNP), C-reactive protein (CRP) and high-sensitive troponin T (hs-TnT) by c-statistics and net reclassification improvement (NRI). Incident HF was diagnosed by record linkage with databases of regional hospitals. All cases were reviewed and scored as HF-PEF or HF-REF by an independent adjudication committee.

Results: During median follow-up for 10 years, 135 individuals were diagnosed with HF-PEF and 239 with HF-REF. When adjusted for age, sex and body mass index, development of HF-PEF showed strongest associations with hypertension (HR: 2.08, 95% CI: 1.02-4.27, p=0.045), cystatin-C (HR: 1.49, 95% CI: 1.05-2.11, p=0.024) and urinary albumin excretion (HR: 1.37, 95% CI: 1.14-1.65, p=0.001). In similar analyses, development of HF-REF showed strongest associations with history of myocardial infarction (HR: 2.45, 95% CI: 1.53-3.93, p=0.001), smoking (HR: 1.69, 95% CI: 1.07-2.68, p=0.025) and hypercholesterolemia (HR: 1.55, 95% CI: 1.03-2.34, p=0.037). NT-proBNP was independently associated with both incident HF-REF and incident HF-PEF (HR: 1.55, 95% CI: 1.21-1.97, p<0.001 and HR: 1.36, 95% CI: 1.03-1.80, p=0.030, respectively). Hs-TnT was independently associated with incident HF-REF (HR: 1.39, 95% CI: 1.22-1.60, p<0.001), but not with HF-PEF. CRP was not associated with either type of incident HF. For HF-PEF, NT-proBNP, hs-TnT and CRP significantly improved the model c-statistic from 0.85 to 0.86 (p=0.015) and enhanced risk reclassification (NRI=0.06, p=0.048). For HF-REF, the model c-statistic improved from 0.84 to 0.88 (p<0.001) and also enhanced risk reclassification (NRI=0.26, p<0.001).

Conclusions: HF-PEF shows a clear distinctive baseline profile compared to HF-REF, with a blood pressure and renal function pressure-load driven profile for the former and an ischemic driven profile for the latter. The incremental value of biomarkers seems to be less strong for predicting HF-PEF than for HF-REF.